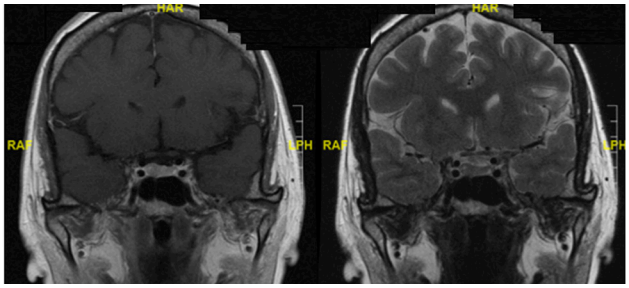
VOLUME 36 NUMBER 4 OCTOBER - DECEMBER 2021

Academic Journal of Health Sciences

MEDICINA BALEAR



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ACADEMIC JOURNAL OF HEALTH SCIENCES

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Academic Journal of Health Sciences Medicina Balear is the organ of the ***Royal Academy of Medicine of the Balearic Island***,It was created in 1986 with the aim of following up the scientific concerns and promoting the research spirit of health professionals in the Balearic Islands and with the additional objective of projecting health issues of interest to society.

Currently ***Academic Journal of Health Sciences Medicina Balear*** publishes in English, Spanish or Catalan original papers, review articles, letters to the editor and other writings of interest related to health sciences. The journal submits the originals to the anonymous review of at least two external experts (peer review).

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With the collaboration

Fundació
Patronat Científic
Col·legi de Metges
Illes Balears

CONCESIÓN DE BECAS Y PREMIOS 2021

Becas de Innovación, Becas *Fundació Banc Sabadell* de rotación externa para MIR, Premios de investigación, Premio *Fundació Mutual Mèdica* al mejor proyecto de tesis doctoral, Premio Camilo José Cela de Humanidades Médicas y Certamen de casos clínicos para MIR.

El jurado calificador de los premios y becas convocados por la *Fundació Patronat Científic* del COMIB, reunido el día 16 de septiembre del presente, acordó la concesión de las siguientes becas y premios:

BECAS DE INNOVACIÓN

Desierta la adjudicación.

BECAS FUNDACIÓ BANC SABADELL DE ROTACIÓN EXTERNA PARA MIR

Dos becas para estancias en hospitales extranjeros, dotadas cada una con 3.000€:

- María Elena Monleón Rivera, residente de la especialidad de Psiquiatría en el Hospital Universitario Son Espases, para una estancia de dos meses en el Centro Experto de Depresiones Resistentes y Trastornos Obsesivos Compulsivos del *CHU-Grenoble Alpes* en Grenoble, Francia, y para una segunda estancia de otros dos meses más en la Unidad de Psiquiatría transcultural *Maison de Solenn* en el *Hôpital Cochin* en París, Francia.
- Unai Díaz-Moreno Elorz, residente de la especialidad de Pediatría en el Hospital Universitario Son Llàtzer, para una estancia de dos meses en el Servicio de Neurología pediátrica del *Children's National Medical Center* en Washington, Estados Unidos.

Dos becas para estancias en hospitales nacionales, dotadas cada una con 1.500€:

- Albert Massó Van Roessel, residente de la especialidad de Cardiología en el Hospital Universitario Son Espases, para una estancia de tres meses en la Unidad de Cuidados Intensivos Cardiológicos del *Hospital Universitari de Bellvitge* en *Hospitalet de Llobregat*, Barcelona.
- Marta López García, residente de la especialidad de Pediatría en el Hospital Universitario Son Espases, para una estancia de tres meses en el Servicio de la Unidad de Cuidados Intensivos Pediátricos del *Hospital Sant Joan de Déu* en Barcelona.

PREMIOS DE INVESTIGACIÓN

Tres premios de 1.500 €:

"Premio Mateu Orfila", Al trabajo científico titulado "*Near-infrared fluorescence cholangiography at a very low dose of indocyanine green: a prospective experimental study*", cuyos autores son Natalia Pujol-Cano y Francesc Xavier Molina-Romero.

"Premio Metge Matas", Al artículo "*Diagnosis and management of aspiration using fiberoptic endoscopic evaluation of swallowing in a Pediatric Pulmonology Unit*", cuyos autores son Fernando Rafael Aguirregomezcorta García, Borja Osona Rodríguez de Torres, José Antonio Peña Zarza, José Antonio Gil Sánchez, Joan Figuerola Mulet y Catalina Bover Bauzà..

"Premio Damià Carbó", Desierta la adjudicación.

PREMIO CAMILO JOSÉ CELA DE HUMANIDADES MÉDICAS

Desierta la adjudicación.

CERTAMEN DE CASOS CLÍNICOS PARA MIR

Se otorga un primer premio de 1.000 € y un segundo premio de 500 €.

El jurado propuso los cinco mejores casos que se presentarán el próximo miércoles día 13 de octubre en el COMIB y, posteriormente, se notificará el veredicto de los dos premiados. Los cinco casos finalistas son:

1. "*Desmopressin as treatment of anemizing hematuria secondary to platelet dysfunction in the setting of uremia*".
   Autora: Laura Aizpiri Antoñana.
2. "Dificultad en el aprendizaje; la punta del iceberg".
   Autor: Unai Díaz-Moreno Elorz.
3. " El manejo multidisciplinar en una úlcera tórpida, la clave del éxito".
   Autores: Ana Llull Ramos, Inés Gracia Darder, Daniel Finch Domínguez-Gil y Juan Gabriel Garcías Ladaria.
4. "No todo es lo que parece".
   Autores: Alexandre Pascual Olmos Torres y Elena Prados Pérez.
5. "Niña con síndrome coronario agudo de causa alérgica (Síndrome de Kounis), a propósito de un caso ".
   Autores: Lluís Galmés Rosselló, Paula Greciano Calero, Silvia Escribá Bori y José Antonio Gil Sánchez.

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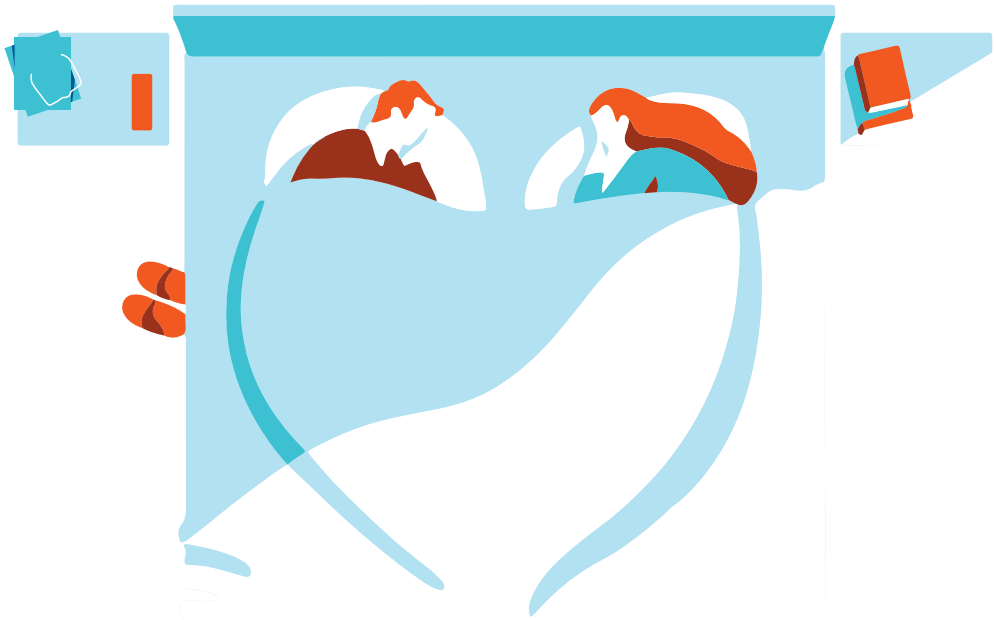
Haz algo grande por tu salud



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EDITORIAL

Balance of the first year of Academic Journal of Health Sciences

Balance del primer año de "Academic Journal of Health Sciences"

Ángel Arturo López González

Editor in Chief of AJHS

In 2021 the Royal Academy of Medicine of the Balearic Islands decided that our journal Medicina Balear, created in 1986, would be renamed Academic Journal of Health Sciences (AJHS). This change was not just a change of name but rather a change of direction in the trajectory of our publication. Local journals are currently finding it very difficult to survive due to the high competition for quality articles. This fact motivated our institution to decide to internationalise the journal.

There are many bibliographic repositories where our publication is included: DIALNET, Latindex, IME, DOAJ, REDIB, Imbiomed, Google Scholar and Emerging Sources Citation Index (ESCI) among others. Although our aspiration is to be part of other prestigious collections such as SCIELO, SCOPUS and Web of Science. To achieve this goal we have developed a series of actions among which we could highlight the increase in the periodicity (we have gone from three to four volumes per year), the increase in the number of articles published, the increase in the number of articles written in English and the diversification of the origin of the articles (in this year 2021 we have received original articles with authors from 15 countries).

As we can see in the attached graphs comparing the last five years of the journal, there has been a very important change that has exceeded all our expectations.

In the years 2017, 2018 and 2019 no articles were published in English, in the year 2020 two articles were published in English which accounted for 8.3% of those published that year. In 2021, the number of articles in English has multiplied to 54, which represents 83.1% of the total (**Figure 1**).

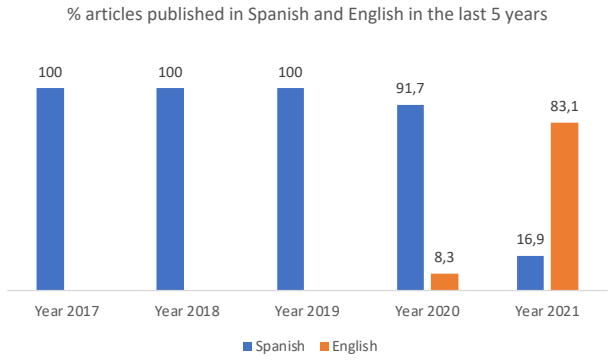
Between 2017 and 2019 all the articles that appeared in AJHS came from Spain, in 2020 one article was published from Turkey and in 2021 there were 39 articles from abroad (60% of the total number of articles published), with very diverse origins: Germany, Saudi Arabia, Armenia, Bolivia, Canada, Scotland, the United States, the Philippines, India, Iran, Mexico, the Czech Republic, South Africa and Sweden (**Figure 2**).

In the first three years (2017 to 2019) between 10 and 12 articles were published each year (it should be remembered that in these years three volumes were published each year). In 2020, coinciding with the increase in periodicity (from four-monthly to quarterly), 24 articles were published, and in 2021 the figure rose to 65 articles (**Figure 3**).

The number of articles published in each volume also shows significant changes over the last five years. Between 2017 and 2019, between 3 and 4 original articles were published per volume. This number increased in 2020 to 6 articles and to 16.3 in 2021 (**Figure 4**).

We hope that the new orientation that is being given to the journal and taking into account the changes that have taken place will allow us to achieve the indexing objectives that the editorial team has set for itself in a short period of time.

Figure 1: .



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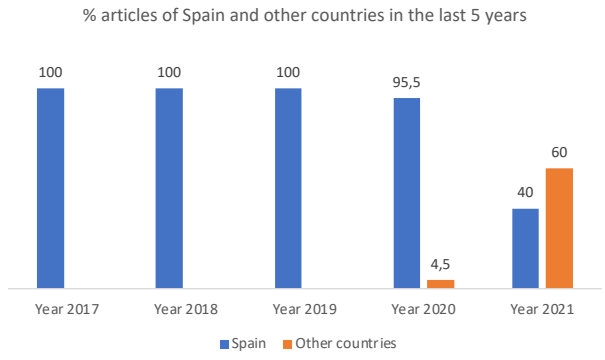

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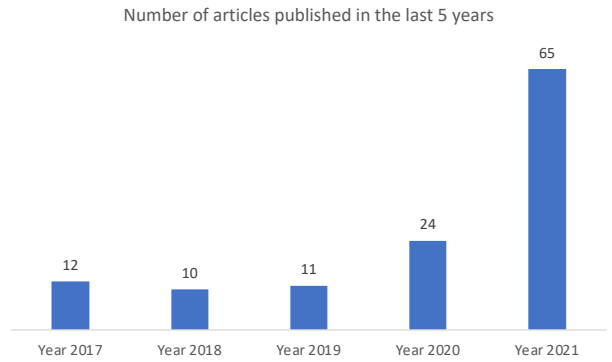

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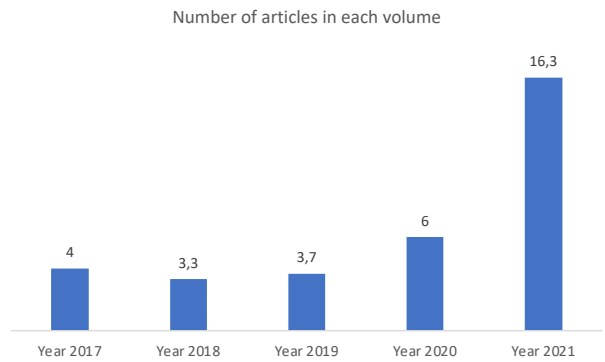

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ORIGINAL

Effectiveness of clobetasol and nitroglycerin ointment therapy: a systematic review

Efectividad de la terapia con pomadas de clobetasol y nitroglicerina: revisión sistemática

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Abstract

Introduction: The aim of this study was to determine the effect of clobetasol ointment with nitroglycerin ointment on the prevention of superficial phlebitis caused by Angio catheter.
Materials and methods: This study was performed as a clinical trial on 110 patients admitted to the surgical ward. Patients were randomly divided into three groups: clobetasol, nitroglycerin group and control group. The data collection tools of the questionnaire included demographic information, information about intravenous treatment and phlebitis measurement scale. In the intervention groups, after venipuncture, 1.5 cm (about 2 g) of ointment was applied in the distal part of the Angio catheter and the site was dressed with sterile gauze. In three time periods of 24, 48 and 72 hours from the time of venipuncture, the site was examined for phlebitis.
Results: The results showed that the age group of 18 to 30 years was the most common age group. The most common site of cannulation was 62.5% in the clobetasol group, 59.5% in the nitroglycerin group and 46.9% in the control group. The incidence of phlebitis in the study groups by the time elapsed since the placement of the Angio catheter showed that, in the first 72 hours after the placement of the Angio catheter, there was no significant difference between the three groups. But at 96 and 118 hours after catheter placement between intervention and control groups was significant (P <0.0001).
Conclusion: The results of this study showed that the use of nitroglycerin ointment was more effective than clobetasol ointment in preventing superficial phlebitis caused by Angio catheter. Therefore, based on the results of this study, it is recommended to use clobetasol ointment and nitroglycerin ointment to prevent the occurrence of phlebitis in patients who need long-term use of Angio catheter (more than 96 hours).

Keywords: Surgery, patient, clobetasol ointment, nitroglycerin ointment, phlebitis, angio catheter.

Resumen

Introducción: El objetivo de este estudio fue determinar el efecto de la pomada de clobetasol con la pomada de nitroglicerina en la prevención de la flebitis superficial causada por el angiocatéter.
Materiales y métodos: Este estudio se realizó como un ensayo clínico en 110 pacientes ingresados en la sala de cirugía. Los pacientes se dividieron aleatoriamente en tres grupos: clobetasol, grupo de nitroglicerina y grupo de control. Los instrumentos de recogida de datos del cuestionario incluían información demográfica, información sobre el tratamiento intravenoso y la escala de medición de la flebitis. En los grupos de intervención, tras la venopunción, se aplicó 1,5 cm (unos 2 g) de pomada en la parte distal del angiocatéter y se vendó el lugar con una gasa estéril. En tres periodos de tiempo de 24, 48 y 72 horas desde el momento de la venopunción, se examinó el lugar en busca de flebitis.
Resultados: Los resultados mostraron que el grupo de edad de 18 a 30 años fue el más frecuente. El lugar de canulación más frecuente fue el 62,5% en el grupo del clobetasol, el 59,5% en el grupo de la nitroglicerina y el 46,9% en el grupo de control. La incidencia de flebitis en los grupos del estudio según el tiempo transcurrido desde la colocación del angiocatéter mostró que, en las primeras 72 horas tras la colocación del angiocatéter, no había diferencias significativas entre los tres grupos. Pero a las 96 y 118 horas después de la colocación del catéter, la diferencia entre los grupos de intervención y de control fue significativa (p <0,0001).
Conclusión: Los resultados de este estudio mostraron que el uso de la pomada de nitroglicerina fue más eficaz que la pomada de clobetasol en la prevención de la flebitis superficial causada por el angiocatéter. Por lo tanto, basándose en los resultados de este estudio, se recomienda utilizar la pomada de clobetasol y la pomada de nitroglicerina para prevenir la aparición de flebitis en los pacientes que necesitan un uso prolongado del angiocatéter (más de 96 horas).

Palabras clave: Cirugía, paciente, pomada de clobetasol, pomada de nitroglicerina, flebitis, angiocateter.

Introduction

Intravenous therapy is 70 years old, but the injection of drugs into the arteries has undoubtedly been a human dream for centuries. Today, more than 80 to 90% of hospitalized patients receive intravenous treatment during their treatment, and more than 500 million peripheral venous catheters are placed annually. In a study conducted in Yazd and 50% of similar studies in Tehran, 55% of hospitalized patients were treated intravenously, which indicates the extent of the use of this treatment in the country. More than 25 million intravenous catheters are placed in American hospitals each year[1-3].

Catheters are used to deliver nutrients to the body, to correct or prevent water and electrolyte disturbances, to transfuse blood or blood products, to prescribe drugs, and to draw blood[4]. Harrison writes that the intravascular method is appropriate when oral medications are ineffective, the level of drug concentration in the blood is unknown, or higher doses of the drug are required for treatment. Intravascular is associated with many risks, but the intravenous route is often the best or only option[5-6]. The purpose of venipuncture is to access the venous bloodstream to obtain blood for laboratory or diagnostic tests, fluid injections, electrolytes, medications, blood products, nutritional supplements, and hemodynamic monitoring. One of the most common invasive methods of medical care today is the use of intravenous injections. Phlebitis, in addition to being dangerous on its own, leads to clot formation, thrombophlebitis 1, embolism 2, and shortened lifespan of 3 venous cannulas. Research has shown that the main reason for removing peripheral catheters is phlebitis[7-9].

The high prevalence of phlebitis increases economic costs, wastes nurses 'time, increases patients' problems such as infection, patient discomfort, and ultimately leads to catheter removal and placement in a new location, which in turn makes access more difficult. The arteries become narrower and may lead to more invasive procedures, such as catheter insertion into central veins, which have far more complications. Intravenous medications may also be delayed and even the length of hospital stay may be increased.[10-11]

In the presence of bacterial phlebitis, the risk of septicemia increases up to 18-fold. Phlebitis is a potentially dangerous source of systemic infections, so the chances of developing systemic infections in the presence of phlebitis increase eightfold. The American Nursing Association puts the acceptable prevalence of phlebitis at 5 percent or less, while studies from 1966 to 1801 reported an overall prevalence of phlebitis of 25 to 35 percent. Another study reported a prevalence of phlebitis in patients with intravenous injections of between 25 and 70%. The results of research show that the prevalence of complications due to intravenous injections in our country is higher than other parts of the world (18 to 80%). In the 1950s, the average survival of peripheral catheters was less than 118 hours, in the 1970s from 96 to 118 hours, and today it is 96 to 96 hours. What is certain is that many of the complications of intravenous injections are preventable.

The important point for nurses is that the best treatment for chemical, mechanical and bacterial phlebitis is to prevent its occurrence. Frequent control of the Angio catheter placement area and, if the first signs of redness, tenderness, and inflammation are observed, change the location of the Angio catheter[12- 13].

Studies to prevent superficial phlebitis due to fluid infusion into peripheral veins have been performed for many years, the use of each of which is controversial for a number of reasons. A study by Schussler in 2016 stated that although in several studies the use of chlorhexidine solution was significantly different from that of betadine in reducing phlebitis and catheter infection, in other studies there was a significant relationship between the use of chlorhexidine solution. Alcohol and betadine have not been reported for phlebitis and catheter infection[14-15].

In other studies, such as the study of Iwachow et al. And Rashid et al, there was no significant difference in the use of chlorhexidine solution compared to alcohol and betadine, and its use is controversial. Also, the discussion about the effects of different types of dressings on the catheter entry site is still ongoing. On the other hand, studies have not yet been able to show the significant effect of using antiseptic ointment at the catheter entrance site on reducing the prevalence of phlebitis. For many years, the prevention of infection and phlebitis caused by infusion and its relationship with the choice of dressing has been controversial[16-18].

There is a great difference between the two methods of fixing the venous catheter using ordinary adhesive and wound adhesive with sterile gas. Given what has been said about the variety of dressing procedures at the catheter insertion site, it is clear that there is still insufficient research infrastructure to determine and support preferred dressings to reduce the prevalence of phlebitis. Heparin 1, corticosteroids 2, venous fluid filtration (intracellular filters) and topical nitroglycerin 3 ointment have been suggested[19].

However, the use of heparin is associated with the possibility of bleeding in the surgical area following the reduction of platelets and the use of intracellular filters is also expensive. Other methods to prevent phlebitis include the use of nonsteroidal anti-inflammatory drugs (NSAIDs). NSAIDs, such as diclofenac, have been used both systemically and topically as a gel, which only reduces some of the symptoms of phlebitis, but it should be noted that nonsteroidal anti-inflammatory drugs

(NSAIDs) have gastrointestinal side effects.

Avaze et al. Conducted a clinical trial to investigate the effect of topical nitroglycerin on the incidence and severity of venous catheter phlebitis.[39] The study was performed as a double-blind trial on 82 patients admitted to the teaching hospitals. Patients were randomly divided into case and control groups. After intravenous catheter placement, nitroglycerin ointment was used in the case group and 1.5 cm in the control group with a width of2×4cm in the distal part of the catheter and it was covered with 5× 5 cm sterile gas. After 12 hours, the catheter site was examined for the presence or absence of phlebitis symptoms and its severity using a checklist and the dressing was replaced by reusing the ointments. This operation was repeated at 118, 36, 96, 60 and 118 hours later. Data were analyzed using the results using t-test, chi-square and relative risk. The results showed that there was a significant difference between the frequency (p = 0.001) and severity of phlebitis (p = 0.005) in the case and control groups. The results also showed an increase in catheter lifespan in the case group compared to the control group (p = 0.01). Therefore, he suggested the use of nitroglycerin ointment in cases where a catheter is needed for more than 96 hours.

This clinical trial was performed on 64 patients admitted. Patients were randomly divided into two groups, 32 patients in the experimental group using sterile gauze and 32 patients in the control group routinely glued. The results of research on phlebitis with P<0.05 showed that gauze dressing Sterile is effective in preventing its occurrence. While Fisher's exact statistical test with P> 0.05 showed that sterile gauze dressing was ineffective in preventing local infection of venous catheters. In the end, the researchers concluded that the use of sterile gauze dressing can be effective in preventing phlebitis and colonization[20].

Mosca et al. conducted a study to investigate the effect of sesame oil on the prevention of chemotherapy-induced phlebitis. This study was performed as a randomized clinical trial on 60 patients with colorectal cancer undergoing chemotherapy and hospitalization in the oncology ward, based on the characteristics of the study units. According to the results of the study, the external use of sesame oil has an effective role in the prevention of phlebitis caused by chemotherapy and has been suggested by the researcher as a suitable prevention method to reduce the rate of this complication[21-23].

Taghinejad et al in a study to compare the effect of skin disinfection with chlorhexidine solution and alcohol on the incidence of peripheral venous catheter phlebitis in cardiac patients admitted to the emergency, CCU and post-CCU wards of Shahid Mostafa Khomeini Hospital affiliated to the University Medical sciences and health services in Ilam[24].
The results showed that the incidence of phlebitis in the chlorhexidine group was 15% and, in the alcohol, group was 37.5%. The researcher suggested the use of chlorhexidine solution before peripheral venous catheter placement to reduce phlebitis. Conti et al conducted a study on the prophylactic and therapeutic effect of clobetasol ointment on superficial phlebitis caused by the drug. In this study, the drug DP-b99, which is used as a neuroprotective agent after stroke, causes post-injection phlebitis[25]. Finally, the researcher states that although an animal study cannot be a basis for human studies, but this study guarantees the positive effect of clobetasol on phlebitis in human samples and if the use of topical corticosteroids in humans is proven, it can replace the drug Heparin and other non-steroidal anti-inflammatory drugs[26]. Singhal et al. conducted a study on the effect of corticosteroids on phlebitis caused by injecting chemotherapy drugs into rabbits. Histopathological results showed that dexamethasone injection significantly reduced phlebitis compared to the control group. The researcher suggested the use of dexamethasone as a way to treat phlebitis caused by vinorelbine[27].

Therefore, due to disagreements over various studies in the field of prevention of phlebitis and studies on the effectiveness of different methods in this the field is not sufficient and they do not have a solid scientific foundation and are not routinely performed in hospital wards. Also, due to the high cost of nitroglycerin ointment, it is often not possible for the patient to supply it[27-29]. Due to the importance and disagreement of people in the use of various devices and drugs, in this study to prevent superficial phlebitis venous catheter placement of clobetasol ointment, which is a strong, available and inexpensive anti-inflammatory ointment for the first time to prevent Angio catheter-induced superficial phlebitis was compared with nitroglycerin ointment[30]. Due to differences in the use of other methods to prevent the occurrence of Angio catheter-induced phlebitis, we decided to conduct a study comparing the effect of clobetasol ointment and nitroglycerin ointment on the prevention of Angio catheter-induced superficial thrombophlebitis[31-35].

Methodology

Study population, sampling method and sample size: This study is a single-blind clinical trial that was performed on all patients admitted to the surgical ward who met the inclusion criteria.

Sampling method: All patients admitted to the surgical ward were selected provided they met the inclusion criteria. Necessary explanations were given to the patients in the study and written informed consent was received from all patients. Then, all patients were removed from the bag by the patient himself using a simple random allocation using three named balls, and according to the removed ball, the patient was placed

in the same group. "Clobetasol ointment (intervention)", group B "nitroglycerin ointment (intervention)", group C "routine (usual method)" was divided.

Sample size: Taking into account alpha 0.05, Power = 80% and maximum effect size equal to EF = 0.45, and using Altman nomogram, the number of sample size in each group was calculated 96 people, which the total number of patients in the three groups was 144.

Execution Method
(research and data collection method)

The data collection tools consisted of three sections: demographic information, information on intravenous therapy, and checklist on the presence and severity of phlebitis. Demographic information included: age and type of disease. Information on intravenous therapy included: site of cannulation, type of serum received, amount of serum 118 hours, and medications received. Patients were divided into three groups in terms of disease type, serum intake, 118-hour serum intake and medications.

The Phlebitis Symptoms Checklist included the Phlebitis Visual Measurement Scale. This scale was introduced by Jackson in 1998 and was introduced to the Intravenous Injection Nursing Association in 1806 as a measure of phlebitis. Its reliability has been confirmed. The visual scale of phlebitis is as follows:

Zero-degree phlebitis: no clinical symptoms.
Grade 1 phlebitis: One of the symptoms of pain or redness.
Grade 2 phlebitis: pain, redness or edema at the site, unclear vein boundaries, no rope vein on touch.
Grade 3 phlebitis: pain, redness or edema at the site, clear blood vessels, no rope vein on touch.
Grade 4 phlebitis: the presence of pain and erythema or edema at the site, the clearness of the arteries and the rope of the vein on touch.

Venipuncture and dressing in all patients with the help of the first researcher in accordance with the principles mentioned in the reference books (washing hands before starting work and wearing disposable gloves, choosing the right place, choosing the right vein, cutting the hair at the injection site with scissors, Disinfect the area for at least 30 seconds with alcohol (70%) evenly with pink Angio catheter No. 18 manufactured by Haryana factory in India. If the vein is removed more than twice, a new location was chosen for the vein.

Patients were instructed in the maintenance of venipuncture. According to the group in which the patients were located, after venipuncture, 1.5 cm (about 2 g) of the ointment was rubbed in the distal part of the Angio catheter in a width of 2×4 cm and sterile gauze with anti-adhesive adhesive. Sensitivity was covered.

Due to the fact that in some studies, serum set replacement was considered effective in the occurrence of phlebitis, in this study, serum sets were changed equally every 96 hours in both groups. The maximum storage time of Angio catheter was 118 hours in three groups.

To measure the incidence and severity of phlebitis according to the Jackson scale, patients were evaluated at 72, 96 and 118 hours after venipuncture. First the dressing was done. To determine the severity of phlebitis, observation, examination and interview were used and the information was recorded in a checklist related to data collection. In this method, 3 dressings were required in the first hour of placement, 118 and 96 hours after placement of the Angio catheter. Also, topical drugs based on the type of patient group were used for 3 times, in the first hour of placement, 118 and 96, one hour after Angio catheter placement. In order to blind the research, a similar coating was applied on the ointments so that patients and colleagues could not identify the ointments. At the same time, two assistants of the researcher, the first person undertook the cannulation and dressing, and the second person performed the examination for the severity of phlebitis in order to observe a research blindness.

Comparison of subjects in terms of contextual and confounding variables by study groups

Due to the fact that in this study, most of the confounding variables were removed by uniformity method, in this section, patients are examined in terms of two variables, age and location of cannulation.

Discussion and comparison

Comparison of Patients Based on Age Group and Type of Study Group

The mean age of clobetasol group was 1/17±1/45 years, nitroglycerin group was 5/18±6/45years and control group was 3/18±6/50years. Based on the results of one-way analysis of variance, the mean age of the studied age groups was statistically different. Not seen (P = 0/28).

Table I details the frequency distribution of different age groups. As the results of this table show, in the clobetasol group, the majority of patients were 41.7%, in the nitroglycerin group, 51.1%, and in the control group, 34.7%, in the age group of 18-30 years.

The age group of 18-30 years was the most common age group. There was no significant difference between the groups in the distribution of other age groups and finally the three groups did not have a statistically significant difference in terms of frequency distribution of different age groups (P = 0.31) (**Table I**).

Table I: Frequency distribution of different age groups in the studied patients by type of groups.

Age group	18-30 Number (Percent)	40-59 Number (Percent)	60-79 Number (Percent)	80≤ Number (Percent)	Total Number (Percent)	P Value (Percent)
Group Clobetasol	18 (7/41)	16 (3/33)	12 (25)	0 (0)	96 (100)	31/0
Group Nitroglycerin	118 (1/51)	8 (17)	13 (7/27)	2 (3/4)	47 (100)	
Group Control	17 (7/34)	14 (6/28)	15 (6/30)	3 (1/6)	49 (100)	

Table II: Frequency distribution of cannulation site in the studied patients by type of groups.

Location of cannulation group	Back of the hand	Forearm	Wrist	elbow	Total	P Value
Group Clobetasol	30 (5/62)	13 (1/27)	4 (3/8)	1 (1/2)	96 (100)	15 /0
Group Nitroglycerin	28 (5/59)	8 (17)	9 (1/19)	2 (3/4)	47 (100)	
Group Control	123 (9/46)	19 (8/38)	7 (3/14)	0 (0)	49 (100)	

Table III: Frequency distribution of phlebitis in the study groups by duration after cannulation.

Group and Phlebitis Time	Clobetasol		Nitroglycerin		Control		P Value
	has it	does not have	has it	does not have	has it	does not have	
	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	
118 hours after Convolution	3 (3/6)	45 (8/93)	1 (1/2)	46 (9/97)	3 (1/6)	46 (9/93)	56/0 Accurate Fisher
96 hours after Convolution	8 (7/16)	40 (3/83)	8 (17)	30 (83)	23 (9/46)	26 (1/53)	001/0> Squared
118 hours after Convolution	27 (3/56)	21 (8/43)	18 (6/42)	27 (4/57)	41 (7/83)	8 (3/16)	01/0001> Squared
Total	38 43/26)	106 63/73)	29 56/18)	122 44/79)	67 6/45)	79 4/54)	

Comparison of Patients Based on Location of Cannulation and Type of Study Group

Table II compares the frequency distribution of catheter cannulation sites in the three groups studied. As the results in the table show. In the clobetasol group, the highest cannulation site was 62.5% and the lowest elbow area was 2.1%, in the nitroglycerin group was 59.5% and, in the control, group was 46.9%. According to Fisher's exact test, there was no difference in the canola location between the three groups (P = 0.15).

Comparison of Subjects in Terms of Response Variables (phlebitis) by Study Groups

Table III compares the frequency of phlebitis (with any degree) at different times after cannulation in the three groups studied. On the first day (118 hours after placement) in the clobetasol ointment group 3 cases 6.3%, in the nitroglycerin ointment group 1 case 2.1% and in the control group 3 cases 6.3% phlebitis with different degrees was seen, which is based on a detailed test. Fisher The difference in the incidence of phlebitis in the first 118 hours by groups was not statistically significant (P = 0.56).

In the first 96 hours after cannulation, in the clobetasol ointment group 8 cases 16.7% and in the nitroglycerin group 8 cases 17% and in the control group 23 cases 46.9% phlebitis with different intensities was seen. It was statistically significant (P = 0.001).

In the first 118 hours after cannulation, in the clobetasol ointment group 27 cases were 56.3% and in the nitroglycerin ointment group 18 cases were 42.6% and in the control group 41 cases 83.7% phlebitis was seen with different degrees. The difference was statistically significant (P <0.0001).

Table IV: Frequency distribution of phlebitis severity in the study groups by duration after cannulation.

Time	group	Severity of phlebitis				P Value
		Classy	grade two	third degree	Total	
		Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	
118 hours after Convolution	Clobetasol	1 (3/33)	2 (7/66)	0 (0)	3 (100)	15/0
	Nitroglycerin	1 (100)	0 (0)	0 (0)	1 (100)	
	Control	3 (100)	0 (0)	0 (0)	3 (100)	
96 hours after Convolution	Clobetasol	7 (5/87)	0 (0)	1 (5/12)	8 (100)	079/0
	Nitroglycerin	5 (5/62)	2 (25)	1 (5/12)	8 (100)	
	Control	12 (3/52)	11 (8/47)	0 (0)	23 (100)	
118 hours after Convolution	Clobetasol	19 (4/70)	6 (3/22)	2 (4/7)	27 (100)	026/0
	Nitroglycerin	17 (85)	2 (10)	1 (5)	18 (100)	
	Control	18 (9/43)	18 (9/43)	5 (2/12)	41 (100)	

In **table IV**, the frequency distribution of phlebitis severity in the study groups is examined separately by the time elapsed since cannulation. In the first 118 hours after cannulation, 33.3% of first-degree phlebitis occurred in clobetasol 1 group and 66.7% of second-degree phlebitis in 2 cases, and 100% of first-degree phlebitis in nitroglycerin group and 100% in 3 control groups. All cases of phlebitis were first-degree, but according to Fisher's exact test, this difference was not significant (P = 0.15).

In the first 96 hours after cannulation, the majority of phlebitis in the clobetasol group was 87.5% first degree and 12.5% third degree and in the nitroglycerin group 62.5% was first degree phlebitis and 25% was second degree and 12.5% was third degree. In the control group, 52.2% were first degree and 47.8% second degree, but according to Fisher's exact test, this difference was not significant (P = 0.079).

In the evaluation performed at 118 hours after cannulation, in the clobetasol group 70.4% of cases were first-degree phlebitis and 22.2% were second-degree phlebitis and 7.4% were third-degree phlebitis, and in the nitroglycerin group 85% were first-degree phlebitis and 10% Phlebitis was second degree and 5% was third degree, but in the control group 43.9% were first degree phlebitis, 43.9% were second degree and 12.2% were third degree, which was significant based on Fisher's exact test (phlebitis degree Two and three were more in the control group than the other two groups (P = 0.026).

Comparison of subjects in terms of the relationship between contextual and confounding variables and response variables by study groups

Table V shows the frequency distribution of phlebitis in patients receiving clobetasol at different times after cannulation by age. As the results of the table show, in none of the 118, 96 and 118 hours after cannulation was there any difference in the incidence of phlebitis in the clobetasol group by age and different age groups (P> 0.05). Although in all three times the incidence of phlebitis in the age groups of 40-59 and 60-79 was higher than the age group of 18-30 years, but this difference was not statistically significant.

Table VI shows the frequency distribution of phlebitis in patients receiving nitroglycerin at different times after cannulation by age. As the results of the table show, in none of the 118, 96 and 118 hours after cannulation was there any difference in the incidence of phlebitis in the nitroglycerin group by age and different age groups which were not statistically significant based on the results of Fisher's exact test.

Table VII shows the frequency distribution of phlebitis in patients receiving clobetasol at different times after cannulation by site of cannulation. As shown in the table, in the first 118 hours, the most cases of phlebitis according to the location of cannulation in the wrist was 7.7% and the lowest was 0% in the elbow area, which according to Fisher's exact test, this difference was not significant (P = 0 / 94). In the first 96 hours after cannulation, the most cases of phlebitis in the wrist area were 23.1% and the lowest in the back area was 0%, but despite this difference, the difference in the frequency distribution of phlebitis according to the site of cannulation was not statistically significant. (P = 0/079). Also, in the first 118 hours after cannulation, the highest number of cases of phlebitis was 100% in the back of the hand, followed by 84.6% in the wrist, and the lowest was in the forearm, which according to Fisher's exact test, this difference was not significant (P = 0.068).

Table V: Frequency distribution of phlebitis in patients receiving clobetasol at different times after cannulation by age.

Age and Phlebitis Time	18-30		40-59		60-79		P Value
	has it	does not have	has it	does not have	has it	does not have	
	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	
118 hours after Convolution	0 (0)	18 (100)	2 (5/12)	14 (5/87)	1 (3/8)	11 (7/91)	28/0 Fisher exact test
96 hours after Convolution	2 (10)	18 (90)	3 (8/18)	13 (3/81)	3 (25)	9 (79)	79/0 Fisher exact test
118 hours after Convolution	8 (40)	12 (60)	10 (5/62)	6 (5/37)	9 (75)	3 (25)	12/0 Test Squared

Table VI: Frequency distribution of phlebitis in patients receiving nitroglycerin at different times after cannulation by age.

Age and Phlebitis Time	18-30		40-59		60-79		80≤		P Value
	has it	does not have	has it	does not have	has it	does not have	has it	does not have	
	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	
118 hours after Convolution	0 (0)	118 (100)	0 (0)	8 (100)	1 (7/7)	12 (3/92)	0 (0)	2 (100)	44/0
96 hours after Convolution	3 (5/12)	21 (5/87)	1 (5/12)	7 (5/87)	3 (1/23)	10 (9/76)	1 (50)	1 (50)	5/0
118 hours after Convolution	9 (5/37)	15 (5/62)	3 (5/37)	5 (5/62)	8 (5/61)	5 (5/38)	0 (0)	2 (100)	29/0

Table VII: Frequency distribution of phlebitis in patients receiving clobetasol in different times after cannulation, depending on the location of the cannula.

Place of cannulation and phlebitis time	Forearm		wrist		elbow		behind hand		P Value
	has it	does not have	has it	does not have	has it	does not have	has it	does not have	
	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	
118 hours after Convolution	2 (7/6)	28 (3/93)	1 (7/7)	12 (3/92)	0 (0)	4 (100)	0 (0)	1 (100)	94/0
96 hours after Convolution	4 (3/13)	26 (7/86)	3 (1/23)	10 (9/76)	1 (25)	3 (75)	0 (0)	1 (100)	079/0
118 hours after Convolution	13 (3/43)	17 (7/56)	11 (6/84)	2 (4/15)	2 (50)	2 (50)	1 1(100)	0 (0)	068/0

Table VIII: Frequency distribution of phlebitis in patients receiving nitroglycerin at different times after cannulation by site of cannulation.

Place of cannulation and phlebitis time	Forearm		wrist		elbow		behind hand		P Value
	has it	does not have	has it	does not have	has it	does not have	has it	does not have	
	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	Number (Percent)	
118 hours after Convolution	0 (0)	18 (100)	1 (5/12)	7 (5/87)	0 (0)	9 (100)	0 (0)	2 (100)	17/0
96 hours after Convolution	4 (3/14)	118 (7/85)	2 (25)	6 (75)	1 (1/11)	8 (9/88)	1 (50)	1 (50)	51/0
118 hours after Convolution	11 (3/30)	17 (7/60)	4 (50)	4 (50)	6 (7/66)	3 (3/33)	18 (6/42)	27 (4/57)	34/0

Table VIII shows the frequency distribution of phlebitis in patients receiving nitroglycerin at different times after cannulation by site of cannulation, which was not statistically significant based on the results of Fisher's exact test.

The effect of intervention on phlebitis

Due to the importance of intravenous injections and its complications, this issue has been discussed and studied for many years and has been researched from various aspects in different centers. Specific studies on the use of topical drugs in prevention Phlebitis due to venous catheters is limited and studies on phlebitis have further examined methods such as the use of different dressings or different skin disinfection methods. In the field of topical medicine, nitroglycerin ointment has been used in several studies in Iran and abroad, but clobetasol ointment has been used in only a few studies with animal samples abroad and in the country, Drug used, not found.

In this regard, this study was conducted to compare the effect of clobetasol ointment with nitroglycerin ointment on the prevention of superficial phlebitis caused by Angio catheter. Ascending progress and changes in the health system of the country, this rate in the control group compared to the results in Dastgerdi research decreased by 76.7% and is 36.1% higher than the results of the original study.[36]

But in both groups, the intervention decreased. However, this rate is far from the acceptable prevalence of phlebitis reported by the American Nursing Association, which is 5% or less. However, Callaghan writes that the reported prevalence of phlebitis in peripheral catheters varies widely because the definition of phlebitis, patient choice, duration of venous follow-up, and injection technique vary.[37]

Regarding the frequency of phlebitis in patients regardless of the degree of phlebitis at different times, the results showed that the frequency of phlebitis in the intervention groups in the first 118 hours after cannulation was not statistically significant compared to the control group.

The frequency of phlebitis in the first 118 hours in the clobetasol group was equal to the control group, which is probably due to the long-lasting effect of clobetasol ointment. The control group was observed to have a statistically significant difference between the two intervention groups and the control group.

In an 1803 study entitled Comparison of the effect of nitroglycerin ointment and anti-inflammatory gel on phlebitis, the incidence of nitroglycerin ointment was 30.8%. While in the present study, the amount of phlebitis in the clobetasol ointment group was 26.43% and in the nitroglycerin ointment group was 18.56%, which is probably due to the cannulation performed by a researcher and the use of sterile gas for dressing and it is good to fix the catheter.

Regarding the frequency distribution of phlebitis severity in the study groups by duration of cannulation, the results showed that statistically, the severity of phlebitis occurred in the intervention groups in the first 118 and 96 hours after cannulation compared to the control group. Was not however, comparing the severity of phlebitis in the intervention groups in the first 118 hours after cannulation compared to the control group, it was observed that there is a statistically significant difference between the two intervention groups and the control group, meaning that second-degree phlebitis and Three in the control group in the first 118 hours after cannulation were more than the two intervention groups.

In the intervention groups, the severity of phlebitis was lower in the nitroglycerin ointment group than in the clobetasol ointment group. Regarding the severity of first-degree phlebitis, the highest rate of phlebitis was observed between the experimental and control groups in the two groups of Clobetasol ointment and control. However, chi-square test did not show a significant difference between the three groups from the first 118 hours to the first 118 hours after catheter placement. In connection with the incidence of second-degree phlebitis between the experimental and control groups, the highest percentage of incidence of second-degree phlebitis was observed in the control group. Showed that this could be due to the effect of nitroglycerin ointment and clobetasol ointment in the two experimental groups. This result confirmed the findings of Saleh Moghadam et al in 2009 regarding the highest incidence of second-degree phlebitis from 118 hours to the first 118 hours.[38] Regarding third degree phlebitis, although the highest incidence was observed in the control group from 118 hours to the first 118 hours, but there was no statistically significant difference. In both experimental groups, the incidence of phlebitis with any degree in nitroglycerin ointment group was lower than clobetasol ointment group. Based on the results of the study and comparing it with the research hypotheses, the research hypothesis was confirmed. The research hypothesis states that the effect of clobetasol ointment and nitroglycerin ointment is different from the usual method on the incidence of phlebitis.

As the results showed, the use of clobetasol and nitroglycerin reduced the incidence and severity of phlebitis compared to the usual method used in the control group. Then, by comparing the effect of the two interventions with each other, it was found that the effect of nitroglycerin ointment was more than clobetasol ointment. In line with the present study, Avaze et al in 2003 conducted a study to investigate the effect of topical nitroglycerin on the incidence and severity of phlebitis caused by venous catheter.[39] In this study, phlebitis occurred at times 118, 36, 96, 60 and 118 after placement. Catheter was examined and the results showed that there was a

significant difference between the frequency (p = 0.001) and severity of phlebitis (p = 0.005) in the case and control groups. The results also showed an increase in catheter life in the case group compared to the control group (p = 0.01). At the end of this study, the use of nitroglycerin ointment was recommended in cases where a catheter was needed for more than 96 hours. In another study conducted by Foster et al. (2012), they concluded that the incidence of phlebitis in the experimental group (nitroglycerin ointment) was lower than the control group (P <0.001) and second-degree phlebitis in the control group.[40] It was significantly higher than the experimental group (P <0.05), so they suggested to use nitroglycerin ointment in cases where catheters are needed for more than 96 hours, which resulted in the present study which showed second-degree phlebitis in the control group. More intervention than the two groups is quite similar. Also, in a study conducted by Borzo et al in year 2003 with the aim of investigating the effect of topical nitroglycerin ointment in the prevention of phlebitis, the results showed that the use of topical nitroglycerin ointment is effective in cases where intravenous administration is required for more than 50 hours.[41] Was suggested as a method of choice. The results of these studies are consistent with the results of the present study. No research has been done on clobetasol ointment and its effect on the prevention of phlebitis due to catheter placement in human specimens and only in some cases in animal specimens. The treatment of clobetasol ointment in superficial phlebitis due to injection of DP-b99, which is used as a neuroprotective drug after acute stroke, was evaluated. As a result of injection of this drug, phlebitis occurs at the injection site. Phlebitis was measured at 1, 3, 5, 118, 32, 96, 56 and 118 hours after injection of the drug into the lateral vein of the ear. The highest rate of phlebitis was in the first 118 hours after catheterization.

Clobetasol reduced the symptoms of phlebitis throughout treatment and also shortened the duration of phlebitis. The highest effect of clobetasol was at 118 and 96 hours after clobetasol. Finally, the researcher states that although an animal study cannot be a basis for human studies, this study guarantees the positive effect of clobetasol on phlebitis in the human sample, and if the use of topical corticosteroids in humans is proven, it can replace heparin. And other non-steroidal anti-inflammatory drugs.

In the present study, clobetasol ointment reduced the incidence of phlebitis and the severity of phlebitis throughout the treatment compared to the control group, which was in line with the results of the study by Razavi et al. (2000), conducted a study entitled the effect of corticosteroids on phlebitis caused by injection of chemotherapy drugs in rabbits.[42] In this study, the prophylactic effect of intravenous dexamethasone on chemotherapy-induced phlebitis was investigated. Histopathological results showed that dexamethasone injection significantly reduced drug-induced phlebitis compared to the control group. Studies on clobetasol were consistent with the present study.

Finally, by examining the frequency distribution of phlebitis in patients in the intervention groups (clobetasol and nitroglycerin) at different times after cannulation by age and location of cannulation, the results showed that there was a statistically significant difference between the frequency of phlebitis and age and place of cannulation Does not exist.

Of course, it should be noted that in this study, most of the samples were between 18 and 30 years old, which may be one of the reasons for the insignificance of the study. Aslani (2017) in his research that aimed to determine the prevalence of phlebitis caused by environmental catheters did not find a significant relationship between the occurrence of phlebitis and age.[43] The results are similar to the present study.

But some researchers believe that age can play a role in the development of phlebitis. In the present study, the results between the incidence of phlebitis and the site of canola were the highest incidence of phlebitis in the back of the hand and then the wrist, but there was no statistically significant difference. These results are similar to the results of Sarani et al. (2000)[44].

According to the results of the present study, it was found that the most important factor in the incidence of phlebitis is time and the incidence of phlebitis increases over time. This result confirmed the findings of Ghadami in 2000 and Karadag et al. (2000) that the incidence of phlebitis increased with increasing catheter placement hours.[45-46]

While in the present study, in the two experimental groups that used nitroglycerin ointment and clobetasol ointment, the number of phlebitis cases in the two experimental groups was generally reduced compared to the control group over time, which could be due to the effect of clobetasol ointment and ointment Be nitroglycerin. In this study, it was found that the effect of drug use on phlebitis after 96 hours is significantly determined and due to the fact that Angio catheter replacement in patients has been done every 118 hours.

Therefore, the use of drugs to prevent phlebitis can delay the replacement of Angio catheter. In a study by Webster, (2011) which aimed to test two safe methods of catheterization, the group that used the dressing showed a 45% reduction in catheterization complications such as infection and phlebitis compared to the empty tape group.[47] In our study, in addition to using nitroglycerin ointment and clobetasol ointment, sterile gauze was used for dressing in the two intervention groups, which may have helped to reduce the incidence of phlebitis in the two intervention groups compared to the control group.

Conclusion

Early and frequent replacement of angiograms, in addition to the heavy costs imposed on the patient and the community, causes more physical and mental harm to the patient and makes him more susceptible to nosocomial infections. It also wastes nurses' time. As 81% of nurses spend more than 75% of their time on intravenous therapy, in addition, phlebitis itself is a potentially dangerous source of systemic infections, and the presence of phlebitis increases the chances of these infections 18-fold.

In a 1991 study on the durability of peripheral intravenous injections, Kawaja cited the impact of infusion at the infusion site as an important factor in the success of intravenous injections and stated that the skill of the catheter inserter is very important.[48] In this study, all stages of the venipuncture process were performed by a researcher, and on the other hand, the catheter with a large diameter was placed inside a small vein that causes inflammation of the inner layer of the vein, and the researcher, when choosing a vessel, the peripheral vessels that fit with pink Angio catheter, they were chosen. Injection-induced phlebitis causes the vessel to constrict at the injection site, which in turn can stimulate the endothelium with a catheter. The severity of this venous contraction is involved in the severity of phlebitis. Therefore, by keeping the vessel dilated and maintaining it with nitroglycerin ointment, the use of anti-inflammatory ointment, clobetasol, and its incidence can be reduced. Using nursing care to maintain the catheters for 118 hours, they reduced the rate of these symptoms from 12.6% to 2.6%. According to the research on the positive effect of using clobetasol ointment and nitroglycerin ointment on the prevention of phlebitis caused by Angio catheter, it is recommended that clobetasol and nitroglycerin drugs to prevent phlebitis in patients who need long-term use of Angio catheter, to be used. Considering that venous airway formation can be expressed as one of the first measures in the face of most patients and according to the results of this study, it is recommended in nursing and other treatment-related disciplines in connection with the complications. There should be more discussion about establishing a venous route, so that when students enter the field of treatment, they can prevent these complications as much as possible by taking small and low-cost measures.

Interests conflict

The researchers declare that they have no conflict of interest.

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ORIGINAL

Como influyen las creencias sobre la vacuna de la gripe de médicos y enfermeras de familia en la cobertura de vacunación propia y de sus pacientes

How beliefs about influenza vaccine influence primary care doctors and nurses vaccine coverage and that of their patients

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Resumen

Objetivo: Conocer la relación de las creencias y experiencias sobre a la vacuna de la gripe de profesionales de medicina y enfermería de atención primaria con su estado de vacunación (EV), y evaluar si existe relación entre estos factores y las tasas de vacunación (TV) de sus pacientes.
Material y métodos: Se realizó un estudio descriptivo transversal en 15 centros de salud de atención primaria de Mallorca. La población diana fueron los profesionales de medicina y enfermería de familia de los centros participantes. Se empleó un cuestionario auto-cumplimentado. Se obtuvieron variables sociodemográficas, EV del profesional, TV de sus pacientes, creencias y experiencias sobre la gripe y la vacuna.
Resultados: Respondieron 129/297 sujetos; 82 eran médicos (63,6%). Declaran estar vacunados 71 (55,0%). Los no vacunados declaran más experiencias con reacciones adversas en pacientes 21,8% vs 7,4% (P=0,020). Los no vacunados mostraron mayor nivel de desacuerdo respecto a la efectividad de la vacuna, la preocupación sobre contraer la gripe o sobre la probabilidad de contraer la gripe y de contagiar a los pacientes. No se encontró asociación entre las TV en <65 años y en ≥65 años y el estado de vacunación de los profesionales o sus creencias y experiencia sobre la gripe y la vacuna.
Conclusiones: La experiencia con efectos adversos de la vacuna en pacientes, las dudas respecto a la efectividad de la vacuna y poca preocupación por contagiarse se asocian a menor vacunación. El EV de los profesionales no tiene una repercusión significativa en las TV de los pacientes asignados como tampoco sus creencias respecto a la gripe y la vacuna.

Palabras clave: Influenza, vacuna de influenza, profesionales sanitarios, atención primaria.

Abstract

Objective: To assess the relationship of beliefs and experiences of family physicians and nurses about Influenza vaccination and their vaccination rate (VR), as well as to assess the relationship of these factors and vaccination rates of their patients (PVR).
Methods: A cross-sectional study was carried out in 15 health centers in Majorca (Spain). Family doctors and nurses from the health centers participated. The questionnaires were self-completed and included sociodemographic variables, RV and PVR of the professionals, as well as questions about beliefs and experiences with influenza disease and about influenza vaccination.
Results: 129 of 297 subjects answered the questionnaire; 82 were doctors (63.6%). Seventy one (55.0%) declared to be vaccinated. Those not vaccinated declared more experiences with adverse effects in patients 21.8% vs. 7.4% (P=0.020). Also, they showed higher level of disagreement about vaccine effectiveness, concern about getting the influenza disease or to transmit influenza to their patients. We did not find an association between the PVR in any group of patients and the VR of doctors and nurses. No association was identified between PVR and health professional's beliefs and experiences about influenza and its vaccine.
Conclusions: The experience with adverse effects of influenza vaccination in their patients, hesitancy about vaccine effectiveness and low worry about getting influenza were related with low rates of vaccination among doctors and nurses. Primary care professionals' VR do not have a significant impact on their patients' influenza PVR nor their experiences and beliefs about influenza and its vaccine.

Keywords: Influenza, influenza vaccine, health personnel, primary health care.

Introducción

La gripe es una enfermedad infecciosa de alta capacidad de transmisión, causante de muchas enfermedades que en ocasiones puede tener consecuencias graves especialmente en personas con enfermedades crónicas y de mayor edad. En el año 2016 afectó gravemente a entre 3 y 5 millones de personas y fue causa de muerte de entre 250.000 y 500.000 personas a nivel mundial[1]. La Organización Mundial de la Salud considera la vacuna como el mejor método para prevenir la gripe y sus consecuencias negativas, publicando anualmente las recomendaciones sobre el contenido de la vacuna para que ésta incluya las cepas que más probablemente circulen en el invierno siguiente.

En nuestro país hay instaurado un programa de vacunación antigripal anual, según las recomendaciones del Ministerio de Sanidad, dirigido a los grupos más vulnerables a sus complicaciones, entre ellos las personas ≥65 años; y menores de 65 años con patología crónica cardiovascular (no HTA) o pulmonar y otros problemas de salud de alto riesgo[2,3]. En España, por consenso, se recomienda la vacunación anual frente a la gripe para los trabajadores sanitarios, con argumentos de protección propia, éticos y de ejemplaridad[3].

Los profesionales sanitarios están expuestos a diario al virus influenza durante la epidemia estacional. Además, pueden actuar como fuente de infección para pacientes sanos[4]. A pesar de esto, la tasa de vacunación entre los profesionales sanitarios está entre 20-40%, lo que supone unas tasas de vacunación por debajo de los niveles requeridos para este grupo de riego[4-6]. Se han descrito algunas barreras que llevan a los profesionales sanitarios a no vacunarse frente a la gripe como son la falta de tiempo, la falta de confianza en la vacuna, el miedo a los efectos secundarios, la creencia de no necesitarla y la falta de efectividad de la vacuna[7-9]. También se han encontrado diferencias en los motivos de no vacunación entre las categorías de los profesionales sanitarios, siendo algunas barreras más comúnmente citadas por los profesionales de enfermería frente a los de medicina, como el miedo a las secuelas a largo plazo y violación del derecho a la autodeterminación[10,11].

También se ha observado en algunos estudios la importancia de los consejos sobre la vacunación antigripal de los profesionales de medicina de atención primaria para aumentar la adherencia a esta vacuna. Así mismo, se ha observado que aquellos profesionales que se vacunan tienen una mayor capacidad para realizar un consejo efectivo a sus pacientes[2,9].

El objetivo del estudio es conocer la relación de las creencias, experiencias y conocimientos sobre la vacuna de la gripe de los profesionales de medicina y enfermería de atención primaria con su estado de vacunación, y evaluar si existe relación entre estos factores y las tasas de vacunación de sus pacientes.

Material y métodos

Estudio descriptivo transversal realizado en los centros de salud de Mallorca durante 2017. Se incluyeron profesionales de medicina y enfermería de atención primaria de Mallorca que estaban activos durante la campaña de vacunación antigripal 2016. Se excluyeron médicos residentes, sustitutos y pediatras.

Los profesionales cumplimentaron un cuestionario durante una sesión de presentación del estudio en cada centro de salud. Los asistentes que aceptaron participar firmaron consentimiento informado. Para los profesionales sanitarios que no asistieron a las sesiones, se dejó el cuestionario y consentimiento en el centro para que se remitiera a los investigadores, una vez cumplimentados. El cuestionario fue pilotado en 10 médicos para valorar su comprensibilidad y se realizaron las modificaciones sugeridas. Por otro lado, las tasas de vacunación de la población adscrita a cada profesional se obtuvieron a través del sistema de información corporativa.

Mediciones: Código de identificación de asistencia sanitaria (durante los últimos 6 meses de 2016), sexo, edad, categoría profesional, centro de salud docente o no, tutorización de residentes, años de profesión, estado de vacunación en la campaña 2016 y "motivos de no vacunación" (respuesta múltiple). Variables de "Creencias, experiencias y conocimientos sobre la gripe y la vacuna antigripal'. Las creencias y los conocimientos se midieron mediante 6 ítems cada dimensión con respuestas tipo Likert que iban de muy de acuerdo a muy en desacuerdo; las experiencias profesionales con la vacuna mediante 2 preguntas y los motivos de no vacunación con 5 preguntas dicotómicas cerradas con respuesta sí, no, ns/nc. Se dedicó una pregunta a valorar su opinión sobre los mensajes a la población. También se recogieron las "Tasas de vacunación en pacientes menores de 65 años" y "Tasas de vacunación en pacientes de 65 años o mayores" del cupo de cada profesional expresadas en porcentajes.

Análisis estadístico

Las variables cuantitativas se han descrito mediante medidas de posición y dispersión y las cualitativas con frecuencias y porcentajes. Para explorar la relación entre las variables cualitativas y el 'estado de vacunación de los profesionales' y sus 'características sociodemográficas, clínicas' y variables de 'creencias, conocimientos y efectividad de la vacuna', se ha utilizado la prueba de Chi cuadrado, prueba exacta de Fisher (en el caso de valores esperados <5) o el test de t de Student en variables cuantitativas. Para determinar la relación entre las 'tasas de vacunación en los grupos < y ≥ de 65 años adscritos al cupo de cada profesional' y las 'características sociodemográficas y clínicas de los profesionales' y 'las creencias, experiencias y conocimientos de los profesionales' se ha utilizado la prueba U Mann Withney y la prueba de Correlación

Spearman para compararlas con la edad y años de experiencia profesional. La normalidad de las variables cuantitativas se ha explorado mediante el test de Kolmogorov-Smirnov. El nivel de significación pruebas estadísticas (bilaterales) $p < 0.05$. El análisis estadístico se realizó con el programa SPSS vs 23.

Resultados

De los 297 médicos y enfermeras de los 15 centros participantes, 129 respondieron, 82 eran profesionales de medicina y 47 de enfermería, tasa de respuesta del 43,9%. Un 73% eran mujeres, una media de edad de 50,6 (DE=9,4) años, 6 de cada 10 profesionales pertenecía a centros docentes y 4 de cada 10 eran tutores con una media de años experiencia profesional de 24,8 (DE=10,1) (**Tabla I)**. De los participantes, 71, (55,03%; IC95% 46,06%-64,01%) estaban vacunados de la gripe durante la campaña de 2016. Como se aprecia en la **tabla I** el estado vacunación de los profesionales no se relaciona de forma significativa con la mayoría de sus características sociodemográficas y clínicas. No obstante, se observa un porcentaje de vacunación significativamente menor en profesionales de centros docentes que en no docentes.

En cuanto a los motivos de no vacunación declarados entre los profesionales no vacunados, 21 (36,2%) pensaban que en su caso no era necesario, 16 (27,5%) por los efectos secundarios de la vacuna, 14 profesionales (24,1%) porque esta no les parecía efectiva, 10 profesionales (17,2%) por la posibilidad de contraer la gripe y 10 más porque se les pasó el plazo de vacunación.

Como se aprecia en la **tabla II**, un 13% declaran haber tenido algún paciente con una reacción adversa a la vacuna. La mayoría (95,3%) manifestaron que la gripe puede ser una enfermedad grave; un tercio, haber tenido algún paciente con una complicación grave de la gripe y algo más del 80% opinaban que la vacuna es efectiva tanto para prevenir la enfermedad como para evitar sus complicaciones. Por otro lado, la mitad de los participantes, indicaron que les preocupaba poder contraer la gripe al tener contacto con pacientes infectados, 8 de cada 10 opinan que vacunarse disminuye la probabilidad de contraer la gripe y 7 de cada 10 de contagiar a sus pacientes. Entre los no vacunados hay mayores porcentajes de profesionales que han tenido algún paciente con reacciones adversas a la vacuna, mayor número que no están de acuerdo con la frase 'la vacuna es efectiva para prevenir la enfermedad' ni con la de que 'la vacuna es efectiva para evitar complicaciones de la gripe'. Asimismo, los no vacunados declaran que les preocupa menos contraer la gripe por contacto con los pacientes que entre los vacunados así como que tengan más probabilidades de contagiar la gripe a sus pacientes. No se observaron diferencias significativas entre vacunados y no vacunados respecto a considerar la gripe como enfermedad grave o haber tenido pacientes que experimentaron efectos adversos de la vacuna.

Se observa que entre los vacunados hay mayor porcentaje que recomendarían la vacuna en todos los grupos propuestos, aunque estas diferencias son significativas sólo para el caso de la vacuna a pacientes hipertensos, en asmáticos controlados y en pacientes con síndrome de Down no institucionalizados.

El porcentaje medio de vacunación de pacientes < 65 años era de 18,6% (DE=12,5%) y ≥ 65 años de 44,9% (DE=12,5%). No se ha observado relación entre las características sociodemográficas y clínicas de los profesionales y las tasas de vacunación de su cupo, a excepción del tipo de centro. En centros no docentes los porcentajes de vacunación de ≥ 65 años eran significativamente más elevados (42,6% vs 45,7%) (**Tabla III**). Tampoco se observaron diferencias entre las tasas de vacunación del cupo de cada profesional y el estado de vacunación de los profesionales o las creencias sobre la gripe o la vacuna (**Tabla IV**).

Tabla I: Características sociodemográficas de los profesionales sanitarios y la relación con su estado de vacunación.

Características de los profesionales sanitarios	Total (%)	Vacunado (N=71) (55%)	No vacunado (N=58) (45%)	P-valor
Profesión				
Enfermería	47/129 (36,4%)	22/71 (31%)	25/58 (43,1%)	0.155
Medicina	82/129 (63,6%)	49/71(69%)	33/58 (56,9%)	
Sexo				
Hombres	34/129 (26,4%)	23/71 (32,4%)	11/58 (19,0%)	0.085
Mujeres	95/129 (73,6%)	48/ 71 (67,6%)	47/58 (81,0%)	
Edad				
(media años ± DE)	50 ,6±9,4	51,8 ± 8,8	49,2 ± 10	0.130
Tipo CS				
Docente	88/129 (68,2%)	43/71 (60,6%)	45/58 (77,6%)	0.039
No docente	41/129 (31,8%)	28/71 (39,4%)	13/58(22,4%)	
Tutor/a de residentes				
Sí	55/120 (45,8%)	28/62 (45,2%)	27/58 (46,6%)	0.879::
No	65/120 (54,2%)	34/62 (54,8%)	31/58 (53,4%)	
Años experiencia profesional (media años ± DE)	24,8±10,1	26,2±9,6	23,1±10,6	0.086

Tabla II: Experiencias, creencias y conocimientos de los profesionales sanitarios y la relación con su estado de vacunación.

Experiencias , creencias y conocimientos de los profesionales sanitarios	Total (%)	Vacunado (N=71) (55%)	No vacunado (N=58) (45%)	P-valor
Haber tenido algún paciente con una complicación grave de la gripe				
Sí	41/122(33,6%)	23/67 (34,3%)	18/55 (32,7%)	0.852
No	81/122 (66,4%)	44/67 (65,7%)	37/55 (67,3%)	
Haber tenido algún paciente con una reacción adversa a la vacuna				
Sí	17/123 (13,8%)	5/68 (7,4%)	12/55 (21,8%)	0.021
No	106/123(86,2%)	63/68 (92,6%)	43/55 (78,2%)	
La gripe puede ser una enfermedad grave				
Muy de acuerdo/de acuerdo	122/128 (95,3%)	68/70 (97,1%)	54/58 (93,1%)	0.177
Neutro	6/128 (4,7%)	2/70 (2,9%)	4/58 (6,9%)	
La vacuna de la gripe es efectiva para prevenir la enfermedad				
Muy de acuerdo/de acuerdo	105/128 (82,0%)	63/70 (90,0%)	42/58 (72,4%)	0.010
Neutro/desacuerdo/muy desacuerdo	23/128 (18,0%)	7/70 (10,0%)	16/58 (27,6%)	
La vacuna es efectiva para evitar complicaciones				
Muy de acuerdo/de acuerdo	114/128 (89,1%)	66/70 (94,3%)	48/58 (82,8%)	0.038
Neutro/desacuerdo/muy desacuerdo	14/128 (10,9%)	4/70 (5,7%)	10/58 (17,2%)	
Me preocupa poder contraer la gripe al tener contacto con pacientes infectados				
Muy de acuerdo/de acuerdo	63/126 (50,0%)	45/70 (64,3%)	18/56 (32,1%)	0.000
Neutro/desacuerdo/muy desacuerdo	63/126 (50,0%)	25/70 (35,7%)	38/56 (67,9%)	
Vacunarse disminuye la probabilidad de contraer la gripe en contacto con pacientes infectados				
Muy de acuerdo/de acuerdo	106/128 (82,8%)	64/70 (91,4%)	42/58 (72,4%)	0.005
Neutro/desacuerdo/muy desacuerdo	22/128 (17,2%)	6/70 (8,6%)	16/58 (27,6%)	
Vacunarse disminuye la probabilidad de contagiar la gripe a sus pacientes				
Muy de acuerdo/de acuerdo	94/124 (75,8%)	63/68 (92,6%)	31/56 (55,4%)	0.000
Neutro/desacuerdo/muy desacuerdo	30/124 (24,2%)	5/68 (7,4%)	25/56 (44,6%)	
Recomendarías la vacuna a mujeres embarazadas				
Sí	110/119 (92,4%)	62/65 (95,4%)	48/54 (88,9%)	0.297
No	9/119 (7,6%)	3/65 (4,6%)	6/54 (11,1%)	
Recomendarías la vacuna pacientes a Hipertensas/os				
Sí	68/113 (60,2%)	41/59 (69,5%)	27/54 (50%)	0.034
No	45/113 (39,8%)	18/59 (30,5%)	27/54 (50%)	
Recomendarías la vacuna a personas mayores de 65 años				
Sí	123/127 (96,9%)	68/69 (98,6%)	55/58 (94,8%)	0.331
No	4/127 (3,1%)	1/69 (1,4%)	3/58 (5,2%)	
Recomendarías la vacuna a pacientes asmáticas/os controlados				
Sí	117/127 (92,1%)	68/69 (98,6%)	49/58 (84,5%)	0.005
No	10/127 (7,9%)	1/69 (1,4%)	9/58 (15,5%)	
Recomendarías la vacuna a pacientes EPOC				
Sí	120/125 (96,0%)	67/68 (98,5%)	53/57 (93,0 %)	0.177
No	5/125 (4,0%)	1/68 (1,5%)	4/57 (7,0%)	
Recomendarías la vacuna a pacientes con Síndrome de Down no institucionalizados				
Sí	74/108 (68,5%)	49/58 (84,5%)	25/50 (50,0%)	0.000
No	34/108 (31,5%)	9/58 (15,5%)	25/50 (50,0%)	

Características de los profesionales sanitarios	Cupo < 65 años			Cupo ≥ 65 años		
	N	R	P-valor	N	R	P-valor
Edad	*108*	*-0.120*	*0.681*	*109*	*-0.040*	*0.212*
Años experiencia profesional	*107*	*-0.092*	*0.987*	*109*	*-0.002*	*0.345*

R: Coeficiente de Correlación

Tabla III: Características sociodemograficas de los profesionales sanitarios y la relación con las tasas de vacunación de personas < y ≥ 65 años adscritas a su cupo.

Características de los profesionales sanitarios	% vacunación cupo < 65 años		% vacunación cupo ≥ 65 años	
	Me% (P25%-P75%)	P-valor	Me (P25-P75)	P-valor
Sexo (n=129)	N=129		N=128	
Hombres	22,3 (5,0-25,5)	0.549	42,2 (38,1-46,6)	0.136
Mujeres	21,6 (5,4-29,1)		45,1 (38,5-52,4)	
Profesión (n=129)				
Enfermería	17,8 (5,1 - 27,2)	0.190	42,6 (37,5-50,0)	0.492
Medicina	23,8 (5,9 - 29,2)		44,8 (39,1-52,0)	
Tipo CS (n=129)				
Docente	21,7 (5,3-29,2)	0.959	42,6 (37,8-49,3)	0.022
No docente	21,2(5,2-28,1)		45,7(41,6-57,8)	
Tutor/a de residentes (n=120)				
Sí	21,7 (5,3-29,2)	0.902	42,5 (39,0-49,2)	0.534
No	23,0 (5,7-28,6)		45,5(37,5-51,8)	
Estado vacunación (N=129)				
Vacunados	21,7(5,4-28,1)	0.686	43,7(37,8-51,6)	0.765
No vacunados	21,5(5,3-29,2)		43,4(39,3-50,6)	

Tabla IV: Creencias sobre la gripe y la vacuna antigripal de los profesionales sanitarios y la relación con las tasas de vacunación de personas < y ≥ 65 años adscritas a su cupo.

Experiencias y creencias de los profesionales sanitarios	Tasa vacunación (%) cupo < 65 años		Tasa vacunación (%) cupo ≥ 65 años	
	Me (P25-P75)	P-valor	Me (P25-P75)	P-valor
Haber tenido algún paciente con una complicación grave de la gripe				
Sí	23,5 (5,8-30,4)	0.513	45,8 (38,5-51,1)	0.856
No	21,1 (5,2-29,0)		43,3 (38,2-52,5)	
Haber tenido algún paciente con una reacción adversa a la vacuna				
Sí	22,4 (6,4-35,3)	0.376	44,6 (38,6-50,5)	0.733
No	21,6 (5,3-28,0)		43,7 (38,0-51,5)	
La gripe puede ser una enfermedad grave				
En acuerdo	21,7 (5,3-28,3)	0.849	44,0 (38,3-51,6)	0.550
En desacuerdo	18,0 (2,7-33,1)		40,2 (39,2-46,6)	
La vacuna de la gripe es efectiva para prevenir la enfermedad				
En acuerdo	21,0 (5,2-28,2)	0.140	43,7 (39,0-52,2)	0.623
En desacuerdo	24,1 (20,8-31,0)		44,5 (38,1-49,7)	
La vacuna es efectiva para evitar complicaciones				
En acuerdo	21,5 (5,2-28,0)	0.114	43,6 (38,4-51,5)	0.495
En desacuerdo	25,6 (6,9-31,4)		45,6 (39,5-51,9)	
Les preocupaba poder contraer la gripe al tener contacto con pacientes infectados				
En acuerdo	22,4 (5,2-29,0)	0.845	45,6 (39,5-52,1)	0.148
En desacuerdo	21,6 (5,4-26,9)		42,2 (37,8-49,2)	
Vacunarse disminuye la probabilidad de contraer la gripe en contacto con pacientes infectados				
En acuerdo	22,3 (5,2-28,2)	0.924	43,7 (39,0-51,6)	0.934
En desacuerdo	19,4(5,3-30,0)		43,8 (38,5-49,9)	
Vacunarse disminuye la probabilidad de contagiar la gripe a sus pacientes				
En acuerdo	21,4 (5,4-25,7)	0.183	44,9 (39,1-51,6)	0.905
En desacuerdo	27,2 (5,3-31,4)		43,4 (38,3-50,0)	

Me= mediana; P25= percentil 25; P75 percentil 75

Resultados

De los 297 médicos y enfermeras de los 15 centros participantes, 129 respondieron, 82 eran profesionales de medicina y 47 de enfermería, tasa de respuesta del 43,9%. Un 73% eran mujeres, una media de edad de 50,6 (DE=9,4) años, 6 de cada 10 profesionales pertenecía a centros docentes y 4 de cada 10 eran tutores con una media de años experiencia profesional de 24,8 (DE=10,1) (**Tabla I**). De los participantes, 71, (55,03%; IC95% 46,06%-64,01%) estaban vacunados de la gripe durante la campaña de 2016. Como se aprecia en la **tabla I** el estado vacunación de los profesionales no se relaciona de forma significativa con la mayoría de sus características sociodemográficas y clínicas. No obstante, se observa un porcentaje de vacunación significativamente menor en profesionales de centros docentes que en no docentes.

En cuanto a los motivos de no vacunación declarados entre los profesionales no vacunados, 21 (36,2%) pensaban que en su caso no era necesario, 16 (27,5%) por los efectos secundarios de la vacuna, 14 profesionales (24,1%) porque esta no les parecía efectiva, 10 profesionales (17,2%) por la posibilidad de contraer la gripe y 10 más porque se les pasó el plazo de vacunación.

Como se aprecia en la **tabla II**, un 13% declaran haber tenido algún paciente con una reacción adversa a la vacuna. La mayoría (95,3%) manifestaron que la gripe puede ser una enfermedad grave; un tercio, haber tenido algún paciente con una complicación grave de de la gripe y algo más del 80% opinaban que la vacuna es efectiva tanto para prevenir la enfermedad como para evitar sus complicaciones. Por otro lado, la mitad de los participantes, indicaron que les preocupaba poder contraer la gripe al tener contacto con pacientes infectados, 8 de cada 10 opinan que vacunarse disminuye la probabilidad de contraer la gripe y 7 de cada 10 de contagiar a sus pacientes. Entre los no vacunados hay mayores porcentajes de profesionales que han tenido algún paciente con reacciones adversas a la vacuna, mayor número que no están de acuerdo con la frase 'la vacuna es efectiva para prevenir la enfermedad' ni con la de que 'la vacuna es efectiva para evitar complicaciones de la gripe'. Asimismo, los no vacunados declaran que les preocupa menos contraer la gripe por contacto con los pacientes que entre los vacunados así como que tengan más probabilidades de contagiar la gripe a sus pacientes. No se observaron diferencias significativas entre vacunados y no vacunados respecto a considerar

la gripe como enfermedad grave o haber tenido pacientes que experimentaron efectos adversos de la vacuna.

Se observa que entre los vacunados hay mayor porcentaje que recomendarían la vacuna en todos los grupos propuestos, aunque estas diferencias son significativas sólo para el caso de la vacuna a pacientes hipertensos, en asmáticos controlados y en pacientes con síndrome de Down no institucionalizados.

El porcentaje medio de vacunación de pacientes < 65 años era de 18,6% (DE=12,5%) y ≥ 65 años de 44,9% (DE=12,5%). No se ha observado relación entre las características sociodemográficas y clínicas de los profesionales y las tasas de vacunación de su cupo, a excepción del tipo de centro. En centros no docentes los porcentajes de vacunación de mayores de 65 años eran significativamente más elevados (42,6% vs 45,7%) (**Tabla III**). Tampoco se observaron diferencias entre las tasas de vacunación del cupo de cada profesional y el estado de vacunación de los profesionales o las creencias sobre la gripe o la vacuna (**Tabla IV**).

Discusión

De acuerdo con los resultados del estudio, de los 129 participantes un 55,0% se vacunaron durante la campaña del 2016. Entre los profesionales no vacunados, había un menor porcentaje que consideraban la vacuna como efectiva para prevenir la enfermedad y las consecuencias negativas derivadas de esta. También era menor el número de profesionales preocupados por contraer la gripe y que creen que vacunarse disminuye la probabilidad de contagiarse y contagiar a sus pacientes. En cambio, el porcentaje de profesionales que han presenciado una reacción adversa a la vacuna es mayor respecto al grupo de los vacunados. Así, el motivo principal de no vacunación de los profesionales fue que 'no se creía necesario', seguido de 'por los efectos secundarios' de la vacuna. Los profesionales no vacunados son también más propensos a no recomendar la vacuna a pacientes hipertensos, con asma o personas con síndrome de Down. En cambio, no se observaron diferencias de vacunación de los pacientes asignados a cada profesional y el estado de vacunación de estos.

La tasa de vacunación obtenida para los profesionales sanitarios (55,0%) se asemeja a la publicada por Domínguez *et al.*[7] mientras son superiores a las publicadas en trabajos realizados en décadas anteriores[12]. Así en 2003, R. Jiménez-García et al, determinaron valores alrededor del 20%[13] aunque existe gran variabilidad entre estudios[4]. Aun así en una revisión de 2012 se señala una ligera tendencia al alza de la tasa de vacunación entre el personal sanitario a lo largo de los últimos años, incluso con incrementos estadísticamente significativos durante algunos períodos[4]. Esto podría deberse a la realización de campañas de vacunación más activas y esfuerzos a la concienciación y 'educación' sobre la enfermedad y la vacunación realizados durante esta última década[14]. No obstante, también se han descrito cambios en el comportamiento de los profesionales sanitarios en España respecto a la vacuna de la gripe A (H1N1) tras la pandemia en el 2009[7,15,16]. En cualquier caso, el porcentaje de profesionales vacunados sigue estando por debajo del 80% estimado para obtener inmunidad de grupo y evitar la propagación del virus en centros sanitarios[4,6].

La experiencia con la enfermedad y las creencias respecto a la vacuna y a la gripe son aspectos clave en la predisposición a vacunarse de los profesionales sanitarios. En este sentido, en la revisión sobre estudios cualitativos realizada por Lorenc et al, los participantes expresaban preocupación por los efectos secundarios tanto de síntomas similares a la gripe como a síntomas más graves. Estas opiniones se basaban primordialmente en su experiencia personal o de compañeros o pacientes[17]. También en la revisión hecha por Herzog et al, se destaca la importancia de las creencias en la eficacia, seguridad y severidad de la enfermedad como importantes factores para no vacunarse[18]. Entre los motivos de no vacunación de los profesionales sanitarios más citados en la literatura encontramos la preocupación por la seguridad de la vacuna y los efectos adversos derivados de esta[6,19,20]. En este sentido, nuestros resultados confirman que entre los no vacunados hay más profesionales que han tenido experiencias con efectos adversos de la vacuna en pacientes y un tercio de los no vacunados mencionó los posibles efectos secundarios de la vacuna como motivo para no vacunarse.

La consideración de la gripe como enfermedad grave también puede influir en la vacunación. Así, Moretti et al observaron que, cuando los profesionales consideran que la gripe no es una enfermedad peligrosa aumenta la tasa de no vacunados[21]. También en muchos de los estudios revisados por Lorenc et al, los no vacunados mencionan que la gripe es una enfermedad poco seria y fácil de manejar en adultos sanos[17]. Este hecho no ocurre en nuestros profesionales pues la proporción de los que consideraban la gripe como una enfermedad grave es similar entre vacunados y no vacunados. En cambio, no hemos encontrado relación entre experiencia previa de complicaciones graves de la gripe en sus pacientes y el estado de vacunación del profesional, lo que se contradice con las afirmaciones de Maltezou HC que propugnan que la falta de experiencias previa con consecuencias graves o muerte por gripe en sus pacientes constituye un sustrato ideal para la reticencia a la vacunación[22].

De acuerdo con otros trabajos, el nivel de confianza en la efectividad de la vacuna se asociaba con mayores o menores tasas de vacunación entre los profesionales, siendo 'la falta de eficacia' uno de los motivos de no

vacunación que declaraba una cuarta parte de los no vacunados en nuestro estudio[7,15,20,21]. Esto podría deberse a que la evidencia disponible sobre el efecto de la vacunación en profesionales sanitarios todavía no es suficientemente rotunda y por ello mantienen reticencias respecto a su propia vacunación. En el estudio de Michiels[23], los resultados de efectividad de la vacuna en profesionales sanitarios eran inconsistentes. Por el contrario, otros trabajos muestran que la vacuna de la gripe en profesionales disminuye la incidencia de enfermedad y todas las causas de mortalidad entre los pacientes[24].

Asimismo, las creencias en la autoprotección y la protección de los pacientes se han visto como un importante motivador para vacunarse. Estos factores así como la protección de familiares y amigos también han sido considerados como importantes en la decisión de vacunarse[20,25]. Según el argumento de ejemplaridad, la vacunación del profesional implica que existe un mayor convencimiento científico de la utilidad y seguridad de la vacuna, por lo que este es más proclive a recomendarla y el paciente más receptivo a tomarla, ya que aumenta su nivel de confianza. En general, se ha descrito que la recomendación a sus pacientes de vacunarse puede ser tres veces mayores si el profesional en sí está vacunado[4]. En un estudio israelí se observó que el 84% de los médicos vacunados recomendaban la vacunación a sus pacientes, frente al 56% de los no vacunados[9]. También se ha descrito una mayor cobertura de vacunación de pacientes mayores de 65 en los cupos de los profesionales que están vacunados[5]. Aunque hemos observado que los profesionales vacunados suelen mostrar una mayor predisposición a recomendar la vacuna a determinados grupos de pacientes considerados de riesgo, no hemos encontrado asociación entre el estado de vacunación del profesional y la tasa de vacunación de su cupo de pacientes. Estos resultados pueden ser demostrativos del compromiso de los profesionales con las recomendaciones institucionales y con sus pacientes en concordancia con lo observado en algunos estudios, donde los participantes aducen a la vacunación como compromiso con el bienestar de los pacientes y como parte de la ética profesional[26,27].

Sigue siendo necesario desarrollar programas informativos basados en datos claros y objetivos sobre la gripe y la vacuna antigripal, para así eliminar percepciones o creencias erróneas preconcebidas/establecidas en la sociedad, y más concretamente entre los profesionales de la salud. La transmisión de información veraz y sólida a través de campañas educativas que promuevan la toma de decisión por propio convencimiento, y eliminando la sensación de obligatoriedad o coerción, lo que podría ayudar a incrementar la tasa de vacunación en este grupo.

Fortalezas y limitaciones

Este estudio incluye datos de profesionales tanto de enfermería como de medicina pertenecientes a 15 centros de salud de Mallorca lo que permite representar una realidad plural y otorgar mayor validez a los resultados obtenidos. A pesar de asegurar la anonimización de los datos, la tasa de respuesta fue solo de 43% lo que puede implicar que no estén representados todos los posibles posicionamientos de los profesionales sanitarios especialmente significativa es la infra-representación de los profesionales de enfermería. Todo ello puede conducir a un sesgo de selección donde estén sobrerrepresentados los profesionales vacunados.

Como la variable de vacunación es auto-contestada podría haber información no completamente veraz que iría a favor de la hipótesis nula. Esta variable en mayor medida, aunque también el resto del cuestionario, estarían influidas por la tendencia generalizada a dar respuestas teóricamente más deseables.

Conclusiones

Las tasas de vacunación de los profesionales sanitarios son superiores a las que se reportan en otros estudios, aunque no alcanzan valores óptimos para evitar la transmisión de la enfermedad en los centros de salud. Tanto el personal vacunado como el no vacunado consideran la gripe como una enfermedad grave. Las experiencias con reacciones graves a la vacuna y las dudas sobre su eficacia son factores asociados a la no vacunación entre el personal sanitario. Sin embargo, el estado de vacunación de los profesionales y sus creencias respecto a la gripe y a la seguridad y eficacia de la vacuna no son determinantes de la vacunación de los pacientes que tienen asignados.

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Cuestiones éticas

Los datos de identificación del profesional fueron anonimizados mediante la eliminación del código CIAS una vez obtenidas las tasas de vacunación de los pacientes. Se obtuvo consentimiento informado de los profesionales sanitarios. El estudio fue aprobado por la Comisión de Investigación de Atención Primaria de Mallorca. El estudio se ha llevado a cabo con respeto a los principios enunciados en la declaración de Helsinki y a las normas de buena práctica clínica.

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Conflicto de interés

Los investigadores declaran no tener conflicto de interés.

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ORIGINAL

Analyze the effective factors in the tendency to public and championship sports from the perspective of students, staff and professors of the Islamic Azad University of Qom Province in Iran

Analizar los factores efectivos en la tendencia a los deportes públicos y de campeonato desde la perspectiva de los estudiantes, el personal y los profesores de la Universidad Islámica Azad de la provincia de Qom en Irán

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Abstract

The purpose of this study is to analyze the effective factors in the tendency to public and championship sports from the perspective of students, staff and professors of the Islamic Azad University of Qom Province. The present study is part of descriptive comparative research and in terms of purpose is part of applied research. The statistical population of this study includes all students (12,000 people), staff (220 people) and professors (180 people) of the Islamic Azad University of Qom Province, whose total number is 12,400 people. The sampling method was stratified random according to Morgan table that 375 students, 136 employees and 118 professors were selected as the sample. The instrument used in this research was a questionnaire to determine the effective factors in the tendency to public and championship sports. The face validity of the questionnaire was confirmed by 15 experts and its reliability was calculated to be 0.980 through Cronbach's alpha. Descriptive and inferential statistics were used to analyze the data. In the descriptive statistics section, the frequency and frequency percentage and in the inferential statistics section to obtain the reliability of the questionnaire from Cronbach's alpha test, for normal distribution of data from Kolmogorov-Smirnov test and to test research hypotheses from the test one-way analysis of variance were used. Data analysis is performed with SPSS.23 software. According to the results of the study, from viewpoint of students, staff and professors of Islamic Azad University of Qom, there is a significant difference in the indicators of mass media, social demand, non-sports organizations, sports organizations, globalization and communications and social networks.

Keywords: Azad University, championship sports, public sports.

Resumen

El propósito de este estudio es analizar los factores efectivos en la tendencia al deporte público y de campeonato desde la perspectiva de estudiantes, personal y profesores de la Universidad Islámica Azad de la provincia de Qom. El presente estudio es parte de una investigación comparativa descriptiva y en términos de propósito es parte de la investigación aplicada. La población estadística de este estudio incluye a todos los estudiantes (12.000 personas), personal (220 personas) y profesores (180 personas) de la Universidad Islámica Azad de la provincia de Qom, cuyo número total es de 12.400 personas. El método de muestreo fue estratificado al azar de acuerdo con la tabla de Morgan que se seleccionaron como muestra 375 estudiantes, 136 empleados y 118 profesores. El instrumento utilizado en esta investigación fue un cuestionario para determinar los factores efectivos en la tendencia al deporte público y de campeonato. La validez aparente del cuestionario fue confirmada por 15 expertos y su fiabilidad se calculó en 0,980 mediante el alfa de Cronbach. Se utilizó estadística descriptiva e inferencial para analizar los datos. En la sección de estadística descriptiva, la frecuencia y el porcentaje de frecuencia y en la sección de estadística inferencial para obtener la confiabilidad del cuestionario de la prueba alfa de Cronbach, para la distribución normal de los datos de la prueba de Kolmogorov-Smirnov y para probar las hipótesis de investigación de la prueba unidireccional Se utilizaron análisis de varianza. El análisis de datos se realiza con el software SPSS.23. Según los resultados del estudio, desde el punto de vista de los estudiantes, personal y profesores de la Universidad Islámica Azad de Qom, existe una diferencia significativa en los indicadores de los medios de comunicación, la demanda social, las organizaciones no deportivas, las organizaciones deportivas, la globalización y las comunicaciones y redes sociales.

Palabras clave: Universidad Azad, campeonato de deportes, deportes públicos.

Introduction

In recent years, along with the emergence of fundamental and comprehensive changes in society and the development of technology and mechanization of life, obesity and diseases such as cardiovascular disease, which is often caused by inactivity, has spread [1]. With the mechanization and inactivity of community life, exercise is one of the ways that people can use it to overcome physical, psychological and social pressures[2]. Sport is a phenomenon to which all people have a strong tendency, whether they are involved in sports fields professionally or as amateurs, or spectators of beauty creators in local, national or international sports fields. Be[3]. Given the importance and benefits of grassroots sports and championships, different countries have put its development on their agenda. Increasing the population of championship sports, improving the quality and winning medals in international arenas, increasing the number of disciplines entering the Olympic Games, increasing the number of entrants to the Olympic Games, maintaining and improving the position of national teams in the rankings are the goals of championship sports[4].

The revenue-generating aspect of championship sports due to gaining medals, status, fame, popularity and receiving material rewards for athletes, championship sports attractions, advertising and marketing, attracting spectators has caused the government, the media and the main custodian of sports in the country, namely the Ministry. Sports and youth pay more attention to the dimension of championship sports and spend most of their budget and propaganda on the expenses of championship sports[5]. In contrast to championship sports, there is public sports (sports for all); Although championship sports are an important part of sports in any country, important aspect in this regard is the growth of championship sports depends on the inclusion of public sports and its establishment in society[6].

Therefore, public sports are the basis and platform for the development of championship sports and reaching an acceptable position in the world. Today, about 50 sports in the world are known as public sports, which include a range from jogging to elm games[7]. Public exercise is a form of physical activity or regular presence in physical activity that promotes physical and mental health, forms social relationships and leads to positive results. On the other hand, by strengthening the physical vigor and cultivating the psychological and social dimensions in this sport, it is linked to the sport in which competition is concerned, that is, the championship sport, and according to it, it can cause value in various fields. And national and international honors[8].

Various researches have been done in this regard, some of which are mentioned in this section. Seyed Ameri and Jamei in a study concluded that the effective factors in people's tendency to public sports and championship are globalization and communication, social demand, the structure of sports organizations, social networks, mass media, respectively. non-sporting organizations are in the first to sixth priority. The results also show the effectiveness of mass media in people's tendency to public sports and championships[9]. research showed that the indicators of proximity and access to sports complexes as well as the number of sports venues affect the level of sports participation.

In general, and according to the findings of this study, the more sports facilities and infrastructure, more appropriate and with better standards in terms of access and proximity to citizens, the amount of their sports participation will increase[10]. in a study investigated the effect of infrastructure and management factors on the development of sports participation in Iranian public universities. The results showed that for the development of student sports participation, the importance of development management factor is more than the development infrastructure factor and that university sports management, prior to hardware and software, with appropriate management intervention can lead to student sports participation[11]. in a study, prioritized the factors affecting the development of public sports and the country's championship. Based on the findings of this study, community health, media, natural spaces, low cost, development of homogeneity sports teams, Internet, physical education graduates, religious education and emphasis on free sports are the most important influential factors, respectively. They became known for the development of public sports in the country[12]. in a study found that there are 9 critical factors in the field of public sports in Iran, which are based on the priority of poor planning, poor community attitude, weak manpower, poor coordination, infrastructure problems, financial issues, structural and legal problems. Weak communication system and poor media performance. Al-Shami et al found in the study that mass media is a tool used to promote a physically active lifestyle[13]. Dund and Patil in a study introduced the media as the central nervous system of society and proved the positive role of mass media in the development of sports[14].

Prince et al. in a study concluded that sports participation is not highly dependent on the availability of sports facilities and parks, and the highest rate of adolescent participation in sports leisure time when both sports facilities and parks It was available and the social capital of the neighborhood was high[15]. Mol, in a study entitled Physical Education Specialists' Attitudes Towards Collective Roles in the Tendency to Championship and Public Sports, found a significant relationship between the media and the development of public and championship sports[16]. In a study in Australia, Greenwood found a

significant relationship between media advertising and changing attitudes toward physical activity[17].
The development of public sports is not specific to one place and for a specific group, and as the term implies, sports are for all sections of society of any color and race, any economic status, and so on. Universities are one of the environments that bring people together with all the characteristics and cultural differences. Universities are considered as the source of development of any society[18]. Despite the increase in public awareness about the effects and consequences of inactivity, according to the available evidence, only a small percentage of the country's academic community welcomes university sports programs. The university community can be defined as professors, staff, and students working in universities, institutions, and educational institutions. Paying attention to public sports and championships of this academic group can be very constructive and lead to positive results. Therefore, physical activity and participation in public and championship sports programs of the university can play a significant role in promoting the level of physical, mental and social health of the university community[19]. Islamic Azad University, as one of the prestigious universities in the country, like other universities, in order to improve public sports and championships, its students, staff and professors need to know the effective factors in the tendency of this group to public sports and championships.

Because this university has one of the largest cultural and sports clubs in the country in the Middle East and is active in various sports in the two sections of brothers and sisters and has so far won various championship titles at the level of the country's premier league competitions. The main problem is that the Islamic Azad University, due to its remarkable talents in most sports, has not been able to find a favorable position in the field of public sports and championships in the country, which is probably one of the important reasons for this lack of basic knowledge of the factors influencing the trend. Students, faculty and staff are involved in public and championship sports. According to the issues raised in this study, the researcher will analyze the factors affecting the tendency to public and championship sports from the perspective of students, staff and professors of the Islamic Azad University of Qom.

Methodology

The present study is a descriptive and comparative study. It is also part of applied research in terms of purpose and field research in terms of data collection. The statistical population of this study includes all students (12,000 people), staff (220 people) and professors (180 people) of the Islamic Azad University of Qom Province, whose total number is 12,400 people. In this study, stratified random sampling method was used according to Morgan table that 375 students, 136 employees and 118 professors were selected as a sample. The instruments used in this study include a demographic information questionnaire and a questionnaire to determine the effective factors in the tendency to public sports and championships Seyed Ameri and Jamei which includes 6 components (mass media, social demand, non-sports organizations, Sports organizations, globalization and communications and social networks) and 62 questions[6]. The questionnaire has five values that respondents answer questions from strongly disagree to strongly agree. The scoring of the questions is such that it is assigned to the answers I strongly disagree with grade 1, I strongly disagree with grade 2, I have no opinion grade 3, I agree with grade 4 and I totally agree with grade 5. The validity and reliability of the questionnaire for determining the effective factors in the tendency to public sports and championships of Seyed Ameri and Jamei were confirmed in that study[6]. Also in this study, the face validity of the questionnaire was approved by 15 sports science experts and the reliability of the questionnaire was calculated to be 0.980 through Cronbach's alpha. Library studies and Internet sites were used to formulate theoretical foundations and backgrounds. Due to the fact that the measurement tool in this research is a questionnaire, the questionnaires were distributed and collected in person and online among students, staff and professors of the Islamic Azad University of Qom.

A total of 629 questionnaires were analyzed. Descriptive and inferential statistics were used to analyze the data. In the descriptive statistics section, the frequency and percentage of frequency, and in the inferential statistics section, the Cronbach's alpha test will be used to obtain the reliability of the questionnaire, the Kolmogorov-Smirnov test will be used for normal data distribution, and the one-way analysis of variance test will be used to compare views. Data analysis is performed with SPSS.23 software.

Findings & Results

Demographic characteristics of students, staff and professors of Qom Islamic Azad University in terms of gender, education, sports background and marital status are listed in **tables I** to **III**.

According to the results of the Kolmogorov-Smirnov test in **table IV**, the indicators of mass media, social demand, non-sports organizations, sports organizations, globalization and communications, and social networks have a normal distribution in society. The results of one-way analysis of variance test for comparing the views of students, staff and professors are shown in **tables V** to **X**.

Table I: Demographic characteristics of statistical sample in students' section.

Variable	Components	Abundance	Frequency
Gender	Male Female Total	185 190 375	3/49% 7/50% 100%
Education	Associate of Arts BA, MA, PhD Total	7 358 1 9 375	9/1% 5/95% 3/ % 4/2% 100%
Sport experience	Public sports Championship sport Total	281 94 375	9/74% 1/25% 100%
Marital Status	Single Married Total	298 77 375	5/79% 5/20% 100%

Table III: Demographic characteristics of the statistical sample in the professor's section.

Variable	Components	Abundance	Frequency
Gender	Male Female Total	66 52 118	9/55% 1/44% 100%
Education	MA PhD Total	44 74 118	3/37% 7/62% 100%
Sport Experience	Public Sport Championship sport Total	73 45 118	9/61% 1/38% 100%
Marital Status	Single Married Total	45 73 118	1/38% 9/61% 100%

Table II: Demographic characteristics of the statistical sample in e employee section.

Variable	Components	Abundance	Frequency
Gender	male Female Total	91 45 136	9/66% 1/33% 100%
Education	Associate of Arts BA MA PhD Total	38 33 56 9 136	9/27% 3/24% 2/41% 6/6% 100%
Sport experience	Public Sport Championship sport Total	117 19 136	86% 14% 100%
Marital Status	Single Married Total	12 124 136	8/8% 2/91% 100%

Table IV: Results of Kolmogorov-Smirnov Test.

Indicator	N	Statistical value Z	Result
Mass media	629	117/0	normal
Social demand	629	151/0	normal
Non-sports organizations	629	107/0	normal
Sports organizations	629	084/0	normal
Globalization and communication	629	071/0	normal
Social networks	629	112/0	normal

Table V: Results of one-way analysis of variance test in comparing the views of students, staff and professors in the mass media index.

Indicator		Sum of squares	Degree of freedom	Average Squares	F	P
Mass media	Between group	500/67686	2	250/33843	773/944	001/0
	Total	305/22424	626	822/35		
	Intergroup	804/90110	628			

According to the results of one-way analysis of variance (**Table V**), from the perspective of students, staff and professors of the Islamic Azad University, Qom Branch, there is a significant difference in the mass media index, so the null hypothesis is rejected.

Table VI: Results of one-way analysis of variance test in comparing the views of students, staff and professors in the social demand index.

Indicator		Sum of squares	Degree of freedom	Average Squares	F	P
Social demand	Between group	316/116976	2	158/58488	729/1311	001/0
	Intergroup	453/27912	626	589/44		
	Total	769/144888	628			

According to the results of one-way analysis of variance (**Table VI**), from the perspective of students, staff and professors of the Islamic Azad University of Qom, there is a significant difference in the social demand index, so the null hypothesis is rejected.

Table VII: Results of one-way analysis of variance test in comparing the views of students, staff and professors in the index of non-sports organizations.

Indicator		Sum of squares	Degree of freedom	Average Squares	F	P
Non-sporting organizations	Between group	169/14896	2	085/7448	898/838	001/0
	Intergroup	888/5557	626	878/8		
	Total	057/20454	628			

According to the results of one-way analysis of variance test (**Table VII**), from the perspective of students, staff and professors of the Islamic Azad University, Qom Branch, there is a significant difference in the index of non-sports organizations, so the null hypothesis is rejected.

Table VIII: Results of one-way analysis of variance test in comparing the views of students, staff and professors in the index of sports organizations.

Indicator		Sum of squares	Degree of freedom	Average Squares	F	P
Sports organizations	Between group	031/22628	2	016/11314	679/691	001/0
	Intergroup	686/10239	626	357/16		
	Total	717/32867	628			

According to the results of one-way analysis of variance (**Table VIII**), from the perspective of students, staff and professors of the Islamic Azad University of Qom, there is a significant difference in the index of sports organizations, so the null hypothesis is rejected.

Table IX: Results of one-way analysis of variance test in comparing the views of students, staff and professors in the globalization and communication index.

Indicator		Sum of squares	Degree of freedom	Average Squares	F	P
Globalization and communication	Between group	864/21338	2	432/10694	555/452	001/0
	Intergroup	161/14793	626	631/23		
	Total	025/36182	628			

According to the results of one-way analysis of variance (**Table IX**), from the perspective of students, staff and professors of the Islamic Azad University, Qom Branch, there is a significant difference in the globalization and communication index, so the null hypothesis is rejected.

Table X: Results of one-way analysis of variance test in comparing the views of students, staff and professors in the social network index.

Indicator		Sum of squares	Degree of freedom	Average Squares	F	P
Social Media	Between group	926/23788	2	463/11894	136/788	001/0
	Intergroup	520/9447	626	092/15		
	Total	445/33236	628			

According to the results of one-way analysis of variance (**Table X**), from the perspective of students, staff and professors of the Islamic Azad University, Qom Branch, there is a significant difference in the social network index, so the null hypothesis is rejected.

Discussion

The purpose of this study is to analyze the effective factors in the tendency to public and championship sports from the perspective of students, staff and professors of the Islamic Azad University of Qom Province. According to the results of the research, from the perspective of students, staff and professors of the Islamic Azad University, Qom Branch, there is a significant difference in the mass media index. It seems that the tendency of students, staff and professors to public sports and championships according to the mass media index, varies according to their level of education and the tendency to public sports and championships of those with higher education is higher. This finding confirms Bourdieu's theory of action. Because this group has a higher cultural capital that allows them to choose a health-oriented standard of living for themselves and their family[19]. These results are consistent with the research of Al-Shami et al. and Mul[13-16]. In this regard, it is suggested that the amount of production programs on radio and television and the volume of publications with the content of public sports and championship training be increased. The advertising agent should also be given special attention. At present, advertising all over the world is one of the most important factors in changing people's attitudes and tendencies, and it is possible to encourage people to participate in public and championship sports by advertising, as well as by informing about public sports conferences encouraged. It is better to produce programs in the media, especially on television, that students, staff and professors, who are usually at work until the morning and do not have the opportunity to exercise, can exercise with these programs, and the limited time that prevents them from exercising. Resolve with the media, especially television. According to the results of the research, from the perspective of students, staff and professors of the Islamic Azad University, Qom Branch, there is a significant difference in the social demand index. Also, according to the results of one-way analysis of variance test from the perspective of students, staff and professors of the Islamic Azad University, Qom Branch, there is a significant difference in the index of non-sports organizations and the index of sports organizations. It seems that the sports facilities of sports organizations and non-sports organizations from the perspective of professors, staff and students of Qom Azad University have a great impact on the tendency to public and championship sports, but the amount is different from the perspective of professors, staff and students. The reason for this difference can be considered the level of education. Today, it is clear that a good sport that can be useful for people is a public sport that fortunately does not require expensive equipment and devices, and one of the best things that can be done in this regard is to try to set up a station. Morning sports are available in the existing spaces and in the university space, which is possible with the efforts of the officials.

According to the research results, from the perspective of students, staff and professors of the Islamic Azad University, Qom Branch, there is a significant difference in the globalization and communication index. The results also showed that from the perspective of students, staff and professors of the Islamic Azad University, Qom Branch, there is a significant difference in the social network index. In a study, most of the interviewees acknowledged that information in the field of sports and physical education in many ways can facilitate communication, sports advertising and improve public health. According to the results, social networks are another capacity of cyberspace, so that social networks strengthen communication by creating a communication network between Internet users. It is also emphasized that the creation of communication centers and networks in cyberspace. It leads to a sense of belonging, cohesion and proper information, information exchange, motivation and sports commonalities, so cyberspace can be used as an important tool in the development of academic sports and the creation of new sports structures. In other words, at the university level, there are specialized sports sites with topics and interests between different groups of students, staff, faculty members and even their families in order to encourage and encourage them to participate in sports and improve their health. Under the supervision of sports experts, he created social networks or dedicated pages of university websites and defined the advantages and positive points of using this space to encourage people in these forums[20].

Conclusion

Public sports are mentioned as the foundation of championship sports, so it is necessary to lead the people, especially the youth, to it in any way with proper programming in sports media, social networks and cyberspace, and the level of participation. He increased them in sports. In this case, it can be said that the media have acted correctly in the role of their social participation. Also, sports and non-sports organizations can play an important role in the development of public sports and championships by providing sports services.

Acknowledgments

It should be mentioned that this research is taken from a research project entitled Analyze the effective factors in the tendency to public and championship sports from the perspective of students, staff and professors of the Islamic Azad University of Qom Province in Iran. The authors would like to thank Qom Islamic Azad University for financial support in the study procedure.

Interests conflict

The researchers declare that they have no conflict of interest.

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ORIGINAL

Influence of tobacco consumption: anthropometric, social and demographic variables on the spirometric values among spanish workforce

Influencia del consumo de tabaco, variables antropométricas y sociodemográficas en los valores espirométricos de trabajadores españoles

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Abstract

Introduction: The association between tobacco consumption and a high number of chronical conditions -both respiratory and non-respiratory- has been established. Among the respiratory diseases, besides cancer: Chronic-Obstructive Pulmonary Disease (COPD), and conditions affecting the small airways, have been associated with smoking habit.
Aim: to determine the influence of tobacco consumption, physical activity, and different socio-demographic (age and sex) and anthropometric (BMI) variables, on spirometry values; and to assess the utility of spirometry as an early detection instrument of respiratory conditions in the occupational environment.
Material and Methods: A prospective, observational study, including 4,310 workers attending specific annual physical on a group of Spanish companies was run during 2019. Tests were performed by specially trained healthcare workers, to obtain high-quality, reliable data output. Smoker and non-smoker workers were separately studied.
Results: Results on the influence of cumulative tobacco consumption (packages-year) on pulmonary function show a gradual worsening of pulmonary function parameters as cumulative tobacco consumption increases. Multi-variate analysis, by separately taking smoker and non-smoker groups, shows that all analysed risk factors seem to influence on pulmonary function, although they do not all have same strength in it. Those having a stronger influence are age and physical exercise among non-smokers, and cumulative consumption (packages-year) among smokers.
Conclussions: Spirometry is a good screening and follow-up method for patients with a respiratory condition, particularly those with COPD, mostly among smokers. Our study shows a clear relation between tobacco consumption and pulmonary function deterioration, both on FVC, FEV1 and FEV1/FVC. This relation is mostly established with cumulative consumption (packages-year).

Keywords: Tobacco consumption, Spirometry, biometric characters, pulmonary function worsening.

Resumen

Introducción: Se ha establecido la asociación entre el consumo de tabaco y un elevado número de enfermedades crónicas -tanto respiratorias como no respiratorias-. Entre las enfermedades respiratorias, además del cáncer La Enfermedad Pulmonar Crónica-Obstructiva (EPOC), y las afecciones que afectan a las vías respiratorias pequeñas, se han asociado al hábito de fumar.
Objetivo: determinar la influencia del consumo de tabaco, la actividad física y diferentes variables sociodemográficas (edad y sexo) y antropométricas (IMC), sobre los valores de la espirometría; y valorar la utilidad de la espirometría como instrumento de detección precoz de afecciones respiratorias en el ámbito laboral.
Material y métodos: Durante el año 2019 se realizó un estudio prospectivo y observacional, que incluyó a 4.310 trabajadores que acudieron a un reconocimiento médico anual específico en un grupo de empresas españolas. Las pruebas fueron realizadas por personal sanitario especialmente entrenado, para obtener una salida de datos fiable y de alta calidad. Se estudiaron por separado los trabajadores fumadores y no fumadores.
Resultados: Los resultados sobre la influencia del consumo acumulado de tabaco (paquetes-año) en la función pulmonar muestran un empeoramiento gradual de los parámetros de función pulmonar a medida que aumenta el consumo acumulado de tabaco. El análisis multivariado, tomando por separado los grupos de fumadores y no fumadores, muestra que todos los factores de riesgo analizados parecen influir en la función pulmonar, aunque no todos tienen la misma fuerza en ella. Los que tienen una mayor influencia son la edad y el ejercicio físico entre los no fumadores, y el consumo acumulado (paquetes-año) entre los fumadores.
Conclusiones: La espirometría es un buen método de cribado y seguimiento de los pacientes con patología respiratoria, en particular de los que padecen EPOC, sobre todo entre los fumadores. Nuestro estudio muestra una clara relación entre el consumo de tabaco y el deterioro de la función pulmonar, tanto en la CVF, como en el VEF1 y en el VEF1/CVF. Esta relación se establece sobre todo con el consumo acumulado (paquetes-año).

Palabras clave: Consumo de tabaco, Espirometría, caracteres biométricos, empeoramiento de la función pulmonar.

Introduction

Smoking was a socially acceptable behaviour until recently. However, during the last fifty years, mostly thanks to the work by Sir Richard Doll[1], the association between tobacco consumption and a high number of chronical conditions –both respiratory and non-respiratory– has been established. Among the respiratory diseases, besides cancer, the following have been associated with smoking habit: Chronic-Obstructive Pulmonary Disease (COPD), and conditions affecting the small airways[2-4]. COPD is particularly linked with tobacco addition in 90% of patients, and there is commonly coexisting structural damage of several conditions within one same patient[5]. Tobacco consumption is the most important single cause for COPD; although its influence in the disease development has been signaled on medical publications since the beginning of the past century, it will be on the second half -particularly as of the '60s when scientific community reaches consensus to consider inhaled tobacco smoke as the fundamental cause for this condition[6]. There are several known ethiopathogenic mechanisms described on the origins of COPD; the disbalance proteolysis/anti-proteolysis that causes tissue destruction and oxidative stress, another mechanism is structural cells apoptosis[7].

Only Spain, tobacco consumption produced about 52,000 deaths every year in the 2010-2014 period, mostly on male population (9 of every 10) and almost 50% due to cancer[8]. To this figures, we should add about 3,000 originated by passive smoking[9]. COPD affects daily occupational and personal activities of those who suffer from it, causing interference on physical and psycho-social performance, and[10] causing severe disabilities on patients during last stages[11].

Nowadays, there is no argument regarding pulmonary function measurements to be a cornerstone to study pulmonary conditions and their possible aftermath. Spirometry is currently considered the basic test to measure pulmonary capacity and determine mechanic ventilatory function. It is also the easiest ,most accesible and most reproducible test to perform[12-13].

This study objective is twofold: first, to determine the influence of tobacco consumption, physical activity, and different socio-demographic (age and sex) and anthropometric (BMI) variables, on spirometry values; secondly, to assess the utility of spirometry as an early detection instrument of respiratory conditions in the occupational environment.

Methodology

Prospective, observational study, including 4,310 workers attending specific annual physical on a group of Spanish companies, from different occupational sectors, who accepted to be included during 2019 (January to December). In accordance with current local legislation, written informed consent was produced for each of them, as well as approval by the Occupational Health and Safety[14].

The following inclusion criteria were considered: active workers with no respiratory pre-existing conditions, voluntary acceptance to participate the study and personal data transfer for epidemiological purposes.

The following workers' demographic data were collected: age or gender; clinical data: height, weight, body-mass index (BMI), physical activity (self-referenced) and tobacco consumption: number of cigarettes per day, years of consumption and number of packages per year.

In order to sort BMI, Spanish Society for the Study of Obesity (SEEDO) criteria were followed[15]: low weight if BMI < 18Kg/m^2, normal weight if between 18,5 and 24,99Kg/m^2, overweight if between 25 and 29,99Kg/m^2, and obesity if > 30 Kg/m^2.

In order to calculate physical activity, the American Heart Association (AHA), American College for Sports Medicine and World Health Organization recommendations were followed. They all consider regular physical activity as 30 minutes per day nonstop, or 150 minutes per week, for a moderate-intensity aerobic activity, or 75 minutes per week for an intense activity[16].

Pulmonary function was assessed through forced spirometry, and the following parameters: Forced Vital Capacity (FVC). Normal values are >80% over theoretical value. Forced Exhaled Volume in the first second (FEV1). Normal values are >80% over theoretical value. Ratio FEV1/FVC: normal values are >70-75%.

GOLD (Global Initiative for Chronic Obstructive Lung Disease)[17] consensus was followed in order to classify COPD. Stade 0, normal spirometry; Stade I-mild, FEV1/CVF <70%; stade II-moderate, FEV1/CVF <70% and FEV1 50-80%; stade III-severe, FEV1/CVF <70%, FEV1 30-50%; and stade IV-critical, if FEV1/CVF <70% and FEV1 <30%, or FEV1 <50%.

Tobacco consumption was assessed as per the number of cigarettes and time since consumption began. Tobacco exposure has a cumulative effect, hence –besides current or punctual consumption– it is of outmost interest global consumption along life. In this sense, it is very interesting the so-called "packages-year" indicator, which is calculated by multiplying number of daily cigarettes times the number of years being smoker, divided by twenty.

Working protocole

An anamnesis was performed, including personal background, age and gender; anthropometric data, such as height, weight and BMI, and data on tobacco consumption. Later, a forced spirometry was taken.

Method

Spirometries were performed with Datospir-120 (manufactured by SIBEL S.A.) spirometers. In order to obtain optimal outcomes, manufacturers' instructions for use and calibration were followed. Tests were performed by specially trained healthcare workers, to obtain high-quality, reliable data output. Generic recommendations were followed to harmonise results and reduce inter-observers' bias, both on patients' preparation and test execution, following SEPAR (Spanish Society of Pulmonology and Thoracic Surgery) and ERS (European Respiratory Society) criteria[18].

Smoker and non-smoker workers were separately studied. An univariate and multi-variate study was performed for each of them. First study values the influence of the different risk factors considered (age, gender, BMI, physical exercise, packages-year and consumption time) over the spirometry parameters (FVC, FEV1, FEV1/FVC and %FEV1/FVC<70). Multi-variate analysis estimates which among risk factors really influence pulmonary function end values.

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Statistical analysis

SPSS™ 16.0 ran uni-variate and multi-variate analysis. For uni-variate análisis, average, standard deviation and 95% confidence interval were taken. Prior to analysis, a sample normal distribution test was run through a Kolmogorov-Smirnov test. In order to compare two parametric variables, Student's-t test was used; and Chi-square to compare two ratios. Multi-variate analysis was performed through multiple regression via stepwise regression, since this allows us to elaborate a predictive model on which among the analysed risks factors really have an influence on the dependent variable –in our case, pulmonary function parameters–. We chose forward stepwise regression, since it allows us to clearly observe how the different risk factors progressively add up, and proportionally to the weighing they have on the pulmonary function parameters. We will assess –among non-smokers– real influence of gender, age, BMI and physical exercise, taken together over the pulmonary function parameters: FCV, FEV1 and FEV1/FVC. For smokers –besides the previously stated factors–, we Will add tobacco consumption. Tobacco consumption will be assessed on one side, only calculating cumulative consumption (represented by the number of packages-year), and on the other, by also measuring the number of daily cigarettes and time since consumption started. For best tables understanding, we should focus our attention on the third box, called R squared. The value on top is the total pulmonary function parameter percentage being studied, and that can be explained by taking into account the risk factor with a higher impact; the second value (which will be greater than the first) will indicate the attributable percentage to the sum of the two most important risk factors, and so on. Last value indicates the pulmonary function parameter total percentage that can be explained by considering all the analysed risk factors that have an influence. If a risk factor under study does not appear on the box, this will mean it does not influence the pulmonary function parameter values. Risk factors are called predictor variables, and are: age, gender, BMI, physical exercise and tobacco consumption (packages-year, number of cigarettes, years consumption started)

Analysis were run on statistical package SPSS™ 27.0.

Table I: Population general features.

	Non-smokers n=2462 average (sd)	Smokers n=1848 average (sd)
Age	40,5 (11,7)	44,4 (10,7)
BMI	25,4 (8,3)	24,3 (8,1)
Number of Cigarettes		18,1 (9)
Years consumption		21,2 (10,2)
Packages/year		20,6 (8,5)
FVC	97,5 (10,8)	92,9 (11,8)
FEV1	95,2 (10,3)	86,3 (9,6)
FEV1/FVC	83,9 (5,9)	77,2 (8,3)
	%	%
Female	54,4	39,3
Male	45,6	60,7
No exercise	52,9	62,4
Yes exercise	47,1	37,6
FEV1/FVC < 70 (%)	1,4	24,5

*Packages-year ratio is obtained by multiplying the number of cigarettes by consumption years, divided by 20. FVC: Forced Vital Capacity. FEV1: Forced Espiratory Value on the 1st second of a forced exhalation. FEV1/FVC: Is the FVC percentage exhaled during the first second of forced exhalation manoeuvres.

Results

4310 participants (workers) are occupationally active within the 18-67YO age range. 2462 were non-smokers and 1848 frequent smokers. Study population features are show non **table I**.

The influence of variables gender, age, BMI and physical exercise on Pulmonary function spirometry results are displayed on table 2. FVC and FEV/FVC obtained values, both on non-smoking male and female subjects do not show statistically significant differences (P=,84 and ,93), whereas FEV1 values does seem to have a gender influence, showing higher values on females. All three parameters (FVC, FEV1 and FEV1/FVC) progressively decrease as age increases. There are statistically significant differences (P<,05) on FEV1 values among all considered age groups, whereas FVC and FEV1/

Table II: Variables of study influence on pulmonary function values among smokers and non-smokers

	Non-smokers				Smokers				
		FVC*	FEV1*	FEV1/ FVC*		FVC*	FEV1*	FEV1/ FVC*	FEV1/FVC < 70*
	n	average (sd)	average (sd)	average (sd)	n	average (sd)	average (sd)	average (sd)	%
Female	1340	97,5 (11,2)	95,8 (10,7)	83,9 (6,6)	727	92,6 (12,3)	87,1 (9,3)	78,2 (8,2)	20,5
Male	1122	97,5 (10,9)	94,4 (9,8)	83,8 (5,9)	1121	93,1 (11,4)	85,8 (9,8)	76,7 (8,3)	25,3
< 30 YO	492	99,0 (11,8)	98,7 (10,3)	86,0 (5,9)	227	97,1 (5,9)	94,6 (5,8)	81,9 (7,0)	4,8
30-39 YO	758	98,9 (10,8)	97,1 (9,9)	85,2 (6,1)	369	95,2 (7,0)	92,6 (6,7)	81,4 (7,1)	7,0
40-49 YO	616	97,5 (10,4)	94,6 (10,2)	83,2 (4,9)	578	92,0 (8,4)	86,2 (8,3)	77,1 (7,5)	22,0
50-59 YO	362	95,0 (10,5)	91,5 (9,8)	81,5 (6,3)	561	88,2 (8,6)	80,9 (8,8)	74,1 (7,8)	37,4
≥ 60 YO	234	93,4 (7,1)	88,6 (7,3)	80,6 (4,4)	113	84,4 (7,3)	76,6 (6,8)	71,4 (9,8)	52,2
Low weight	182	96,2 (9,3)	93,7 (8,7)	84,0 (5,9)	151	90,9 (9,6)	87,3 (9,5)	78,1 (9,3)	19,9
Normal weight	1080	100,7 (11,1)	98,5 (10,7)	84,9 (6,0)	681	94,4 (12,5)	87,6 (9,8)	77,8 (8,6)	23,8
Overweight	841	93,3 (9,7)	93,3 (8,9)	83,3 (6,2)	710	92,3 (11,0)	86,3 (9,2)	77,5 (7,6)	21,3
Obesity	359	92,6 (11,1)	90,0 (9,5)	82,0 (5,2)	306	90,2 (12,2)	82,7 (9,6)	75,3 (8,4)	29,4
Exercise	1160	100,1 (10,6)	97,4 (10,0)	86,0 (5,5)	694	96,3 (11,2)	90,1 (7,9)	80,0 (7,1)	9,1
No exercise	1302	95,3 (10,5)	93,1 (10,2)	81,9 (5,7)	1154	90,7 (11,7)	84,0 (9,8)	75,6 (8,6)	32,1

FVC also show statistically significant differences among all groups except those under 30YO and the interval between 30-39YO (p=,896 and ,467, respectively).

Higher values in all three pulmonary function parameters are shown among normal weigh sample population, and lowest among those with obesity. All three pulmonary function parameters show statistically significant (p<,05) differences among all BMI groups, except between low weight and obesity for FVC (p=,498), and between low weight and overweight for FEV1 and FEV1/FVC (p=,616 and ,14). FVC, FEV1 and FEV1/FVC values statistically significatively increase (p<,05) among those non-smoking individuales that regularly practice exercise.

Spirometry results and the influence of variables gender, age, BMI and physical exercise for somkers are displayed on **table II**. There are statistically significant differences (p<,05) between genders for FEV1/FVC and FEV1 (higher among women for both), and for the percentage of people with FEV1/FVC<70 -that is to say: with COPD according to GOLD criteria (higher on male). On the contrary, no statistically significant differences were observed for FVC values (p=,378). Age seems to have some influence on pulmonary function values, since a gradual worsening on all of them may be observed as age progresses, so FVC, FEV1 and FEV1/FVC decrease, whereas the FEV1/FVC%<70 increases. Differences observed among each age group are statistically significant for al pulmonary function parameters (p<,05), except for younger individuals, concretely those under 30YO and those between 30-39YO, when comparing FEV1/FVC values. BMI influence over respiratory function parameters is not homogeneous; hence, it is observed tha FVC higher values are obtained for normal weight and overweight population; this means values are influenced by low weight and obesity; differences are statistically significant among all groups except precisely those with low weight or obese (p=,53). FEV1 displays similar values on all groups except the obese, where they are significantly lower. Then FEV1/FVC ratio behaves alike to FEV1, showing significantly lower values on the obese too. The percentage of COPD workers is similar on all BMI groups, except the obese, where they are clearly and significantly more (p<,05), whereas the percentage of COPD workers is clearly and significantly higher among those who do not exercise.

Whereas for the influence of gender, age, BMI and physical exercise on COPD severity among smokers, we observed that the highest percentage on both sexes corresponds to those measured as 'moderate' (those with FEV1 between 50-80% of the expected value), only 0'7% among male and no female presented severe COPD. Differences encountered were statistically significant in all cases (p<,05). COPD severity increases as age grows (mild cases are less and moderate are more), and sever cases only appear on higher aged subjects. Differences are statistically significant (p<,05) on mild and moderate conditions among all age groups. Smokers with COPD who regularly exercise gobally present a lower intensity on their condition, so that mild cases predominantly prevail; this differs among those who do not exercise, where mid conditions are predominant, and even some sever cases appear. Severity distribution differences are statistically significant for both groups (p<,05). Full data are displayed on **table III**.

Results on the influence of cumulative tobacco consumption (packages-year) on pulmonaty function show a gradual worsening of pulmonary function parameters as cumulative tobacco consumption increases. This occurs in all cases: FVC, FEV1, FEV1/FVC and FEV1/FVC<70% (see **table IV**).

Multi-variate analysis, by separately taking smoker and non-smoker groups, shows that all analysed risk factors seem to influence on pulmonary function, although they do not all have same strength in it. Those having a stronger influence are age and physical exercise among non-smokers, and cumulative consumption (packages-year) among smokers (see **table V**).

Table III: Influence of sex, age, BMI and physical exercise on COPD severity among smokers.

	n	FEV1 > 80% (mild)	FEV1 50-80% (moderate)	FEV1 < 50% (severe)	p
Female	727	26,2	73,8	0,0	<0.0001
Male	1121	31,6	67,7	0,7	
< 30 YO	227	100,0	0,0	0,0	<0.0001
30-39 YO	369	84,6	15,4	0,0	
40-49 YO	578	34,6	65,4	0,0	
50-59 YO	561	22,4	77,6	0,0	
≥ 60 YO	113	13,3	85,0	1,7	
Low weight	151	20,0	80,0	0,0	<0.0001
Normal weight	681	41,0	58,3	0,7	
Overweight	710	29,0	71,0	0,0	
Obesity	306	26,7	72,2	1,1	
Exercise	694	66,7	33,3	0,0	<0.0001
No exercise	1154	23,5	76,0	0,5	

Table IV: Pulmonary function values as per packages.year consumption.

		FVC	FEV1 FVC	FEV1/ FVC <70	FEV1/	
Packages -year	**n**	**Average (sd)**	**Average (sd)**	**Average (sd)**	**%**	**p**
< 5	243	98,1 (10,7)	96,7 (5,7)	84,6 (7,0)	1,2	<0.0001
5-9,9	303	96,6 (11,3)	93,9 (4,2)	81,5 (5,1)	2,3	
10-14,9	209	93,0 (11,3)	90,4 (5,9)	79,9 (5,6)	4,8	
15-19,9	214	90,3 (10,4)	87,4 (6,3)	79,2 (6,6)	8,4	
20-24,9	198	89,0 (11,2)	83,8 (7,1)	77,8 (8,0)	23,2	
25-29,9	192	87,2 (11,4)	81,0 (8,1)	74,3 (7,3)	35,4	
30-34,9	192	86,2 (11,5)	79,3 (7,8)	71,8 (7,1)	50,0	
35-39,9	135	85,1 (12,5)	77,8 (5,0)	70,0 (7,3)	54,8	
≥ 40	162	84,6 (9,3)	74,2 (7,1)	68,9 (6,0)	69,1	

Table V: Multi-variate analysis. Percentage of pulmonary function parameters and their relation with each risk factor.

Risk factors	Non smokers			Smokers (packages-year*)			Smokers (all**)		
	FVC	FEV1	FEV1/FVC	FVC	FEV1	FEV1/FVC	FVC	FEV1	FEV1/FVC
Gender				0,6	0,4		0,4	0,4	
Age	1,1	8,9	10,2	2,2	5,2	1		5,2	
BMI	2,6	2,1	0,2		0,1	0,2			0,1
Physical exercise	4,9	4,9	11,6	3,2	3,2	2,4	3,4	3,1	2,4
Packages-year				12,0	48,4	33,2	1,4	48,4	33,2
No. Cigarettes								1,3	0,1
Years consumption							13,0	0,8	1,8
Total***	8,6	15,9	22,0	18,0	57,3	36,8	19,0	59,2	39,4

*Analysis only includes pachages-year. **Analysis includes packages-year, number of cigarettes and years of consumption. ***Total percentege of the considered pulmonary function parameter that can be explaind by the different risk factors under study.

Discussion

It is widely known that there is a narrow correlation between the respiratory conditions onset and tobacco consumption, and there are many studies to-date –both in the occupational and non-occupational area–, that correlate them. This link has been particularly studied for COPD[18-21].

There is also a consensus to accept spirometry as a good screening and follow-up method for patients with a respiratory condition, particularly those with COPD, mostly among smokers.

The newfangled contribution on this study is the large sample size, as well as the possibility to ascertain with a greater precision the impact of the different risk factors, mostly tobacco, over the pulmonary function; since some confounding aspects such as personal previous health problems that may affect the spirometry outcome are already eliminated, so are the presence of substances or occupational hazards that could also affect these spirometry output values. Finally, it also provides separate information about the influence of each risk factor on each of the spirometry output values, providing a numeric measurement on the influence of each factor in the final value of the pulmonary function parameter under study.

We would like to highlight as key study outcome data that, when performing the uni-variate analysis, all analysed risk factors seem to have a relation with the respiratory function parameters, except gender among non-smokers. However, when we performed a multi-variate analysis we see this changes, and age and physical exercise gain the spotlight among non-smokers, whereas it is cumulative tobacco consumption (packages-year) for smokers, and physical exercise to a lesser degree.

The close relation between BMI and pulmonary function parameters worsening we observed in our study –particularly for overweight–, concurs with other reviewed studies[22-25]. Data we found about the negative relation with low weight also concur with some reviewed study[26].

We observed that age keeps a close relation with all analysed parameters (FVC, FEV1 y FEV1/FVC); so, as our workers are older, their respiratory parameters worsen. These data also concur with practically all reviewed studies[27-32]. Study also shows there is a direct relation between age and percentage of population meeting COPD criterio as per GOLD consensus (FEV1/FVC < 70), these data were also found in other studies.[33-35]

Regular physical activity seems to positively influence spirometry values, particularly among non-smokers, whereas –although to a lesser degree– among smokers too. These data show non our study concur with most reviewed authors[26,36-37], but show discrepancias with those data obtained by others[38], where physical exercise improved different respiratory patterns, but not spirometry output.

As already mentioned, there is unanimity to correlate tobacco and pulmonary conditions, mainly COPD and lung cancer; besides, there is a wide consensus on the effects tobacco causes on the pulmonary function parameters[39]. Our study shows a clear relation between tobacco consumption and pulmonary function deterioration, both on FVC, FEV1 and FEV1/FVC. This relation is mostly established with cumulative consumption (packages-year), and apparently has les correlation with the number of cigarettes or the years of consumption. These data also repeat when we consider population under COPD criterio, where packages-year is the most influential parameter too. Data collected on scientific literatura predominantly concur with data we collected on this study[40-42], although some authors do not find correlation between tobacco consumption and COPD onset[43].

Tobacco consumption influence –measured as number of packages per year–, is the most important element to define the final spirometry value output for our researched workers group. This is particularly relevant for FEV1 and FEV1/FVC.

According to current recommendations by the Spanish Ministry of Health, as shown on the specific occupational health surveillance protocols[44], there is no indication to perform spirometry on workers with no pulmonary risk. If we consider this collective under study are those who particularly had no pulmonary occupational hazard, we believe the obtained data reinforce many occupational health professionals' opinion –among who we count–, who believe necessary to systematically integrate spirometry studies among those workers with evident risk factors, being tobacco consumption would be paramount. We also believe it could be useful the systematic spirometry test performance among all workers, as a systematic pulmonary function and evolution assessment; by having the possibility to compare a basal study (on enrolment checkup) and regular revisions throughout years, as well as the interference of both personal and occupational pulmonary risk factors.

Spirometry test inclusion, thus becomes a quick simple and cost-effective tool for respiratory conditions prevention and early diagnosis, that would reinforce one of the most important activities Occupational Health professionals develop, as it is Health promotion in the workplace, and would allow us to collaborate with Public Healthcare Services by providing with an evolutive tool among workers, to complement the diagnostic and therapeutic activities other primary or specialised care workers do, thus optimising the available resources among all healthcare workers.

Interests conflict

The researchers declare that they have no conflict of interest.

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ORIGINAL

Special Study of Earlobe Pulse Oximeter Using MAX30100 for Detecting SpO2 and Heart Beat

Estudio especial del oxímetro de pulso del lóbulo de la oreja con MAX30100 para detectar SpO2 y latidos cardíacos

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Abstract

In this project, we will be using MAX30100 Sensor by applying a breakout-board, integrated with Arduino and an LCD keypad shield that can measure the available oxygen in the blood and measuring the heartbeat, and displays it on an LCD monitor. The concentration of oxygen in the blood which is termed as "SpO2" is measured in percentage and the heartbeat/pulse rate is measured in BPM. The MAX30100 is a Pulse Oximetry and Heart rate sensor device that is designed for the demanding requirements of the other systems. It provides a very small solution size without damaging or destroying any optical or electrical performance. Very few external hardware components are necessary for integration into a device that is comfortable and easily wearable. This hardware is fully configurable through software registers. Also, it eliminates ambient and surrounding light that can interfere with an accurate reading of the values off the monitor. The data are transferred and read through a serial I2C interface to a computer for further processing. One of the advantages of this device is being portable and can be fitted in a person's pocket and connected to the earlobe only via a single wire. The end of this wire connects to a small sensor that attaches to the earlobe. The sensor receives the pulses emitted from the earlobe and transmits it to the Arduino board on the portable part of the device in the person's pocket. Then this board processes the received data from the sensor and by using the previously written program in the board, will transfer the data into the heartbeat signal. Then finally, it shows the data on the attached small LCD monitor of the device and can easily be observed.

Keywords: Pulse Oximetry, MAX30100 Sensor, SpO2, Heart Beat.

Resumen

En este proyecto, vamos a utilizar el sensor MAX30100 mediante la aplicación de una placa base, integrada con Arduino y un escudo de teclado LCD que puede medir el oxígeno disponible en la sangre y la medición de los latidos del corazón, y lo muestra en un monitor LCD. La concentración de oxígeno en la sangre que se denomina "SpO2" se mide en porcentaje y la frecuencia de los latidos del corazón / pulso se mide en BPM. El MAX30100 es un dispositivo de sensor de oximetría de pulso y frecuencia cardíaca que está diseñado para los exigentes requisitos de los demás sistemas. Proporciona un tamaño de solución muy pequeño sin dañar o destruir ningún rendimiento óptico o eléctrico. Son necesarios muy pocos componentes de hardware externos para su integración en un dispositivo cómodo y fácil de llevar. Este hardware es totalmente configurable mediante registros de software. Además, elimina la luz ambiental y circundante que puede interferir en la lectura precisa de los valores del monitor. Los datos se transfieren y leen a través de una interfaz I2C en serie a un ordenador para su posterior procesamiento. Una de las ventajas de este dispositivo es que es portátil y puede colocarse en el bolsillo de una persona y conectarse al lóbulo de la oreja mediante un único cable. El extremo de este cable se conecta a un pequeño sensor que se adhiere al lóbulo de la oreja. El sensor recibe los impulsos emitidos por el lóbulo de la oreja y los transmite a la placa Arduino situada en la parte portátil del dispositivo en el bolsillo de la persona. A continuación, esta placa procesa los datos recibidos del sensor y, utilizando el programa previamente escrito en la placa, transfiere los datos a la señal de los latidos del corazón. Finalmente, muestra los datos en el pequeño monitor LCD del dispositivo y puede ser observado fácilmente.

Palabras clave: Oximetría de pulso, sensor MAX30100, SpO2, latido del corazón.

Introduction

One of the usual and regular care procedures for continuous analysis of the saturation of blood oxygen in patients is to measure the heart rate and oxygen saturation (SpO2). Since the invention of pulse oximetry by Takuo Aoyagi in the early 1970s, its use has expanded beyond perioperative care into neonatal, pediatric, and adult intensive care units (ICUs). Pulse oximetry is the most important advances in respiratory monitoring, since its readings are used clinically as an indirect estimation of arterial oxygen saturation (SaO2)[1]. Using pulse oximetry is highly effective in accelerating the weaning from mechanical ventilation and intubation. It also reduces the frequency of bleeding needed for analysis of arterial blood gases (ABG). Because pulse oximetry could be a proper alternative for the patients who just need checking for oxygen saturation[2]. Easy usage, speed, and high accuracy in the detection of hypoxia and also continuous monitoring of patients are other features of pulse oximetry[5]. This device detects the amount of oxyhemoglobin and deoxygenated hemoglobin in arterial blood and heartbeat and shows them as Oxyhemoglobin saturation (SpO2) and heartbeat (BPM)[6], which is an indirect estimation of arterial oxygen saturation (SaO2)[7]. The typical amount of SpO2 in healthy individuals is 97% to 99%. However, in more critically ill patients, the amount of pulse oximetry error is recorded as 7.2%[9]. Many factors can affect the accuracy of the device including: physiological, environmental, technology failures, and human errors[11]. In different experiments, sensors were placed frequently on the sole, palm, ear lobe, or toes in addition to the finger. Finger pulse oximetry sensors are often used to obtain functional oxygen saturation (SpO2) and heartbeats. But these sensors may perform inadequately if the digit is badly perfused or there is excessive hand movement[13]. However, earlobe pulse oximetry system does not encounter these difficulties. A pulse oximeter with a probe can be used on the ear lobe. Ear lobe sensors require a pulse oximeter. The handheld pulse oximeter with an ear sensor can measure oxygen saturation and heart rate from the ear lobe. This device can also use a tabletop oximeter instead of a handheld one. Ear clip sensors are most effectively used when a patient has weak blood circulation in the fingers.

In this paper, the MAX30100 sensor has been used. This sensor is a commercial and precise sensor for the determination of the availability of oxygen in the blood and measuring the rate of the heartbeat. This sensor, according to the I2C protocol, is connected to the microcontroller. Then it finds the heartbeat rate and the value for the percentage of oxygen in the blood.

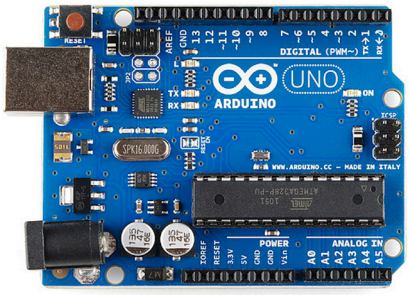
Materials and methods materials

1. Hardware:

1.1. Arduino Uno Board

This board is a microcontroller based on ATmega328. This board contains 14 incoming and outgoing digital pins, six incoming analog pins, one 16 megahertz Ceramic Resonator, one USB port, one power jack (for power inlet), one ICSP header, one reset button, and some other small chips. The required voltage for the Arduino Uno board can be supplied through either the USB connection or an external power supply; such as a battery or an AC/DC adaptor.(**Figure 1**)

Figure 1: Arduino Uno Board



1.2. MAX30100 Sensor

MAX30100 is integrated pulse oximetry and a sensor device for monitoring the heart-rate. This sensor integrates two LEDs (IR and Red lights), a photodetector (Red light), one optimized optics, and one low-noise analog signal processing. All these parts are used for detecting pulse oximetry and heart-rate signals. It can also be easily configured through software registers. Also, the digital output data is stored in a 16-deep FIFO which is within the device.

It has an I2C digital interface for communication with a host microcontroller. The pulse oximetry subsystem in MAX30100 consists of several parts including ambient light cancellation (ALC), 16-bit sigma-delta ADC, and a proprietary discrete-time filter. It has an ultra-low-power operation that consumes a little power and makes it ideal for battery-operated systems. MAX30100 operates by using a supply power in the range of 1.8 to 3.3V. It is practical to use in wearable devices, fitness assistant devices, medical monitoring devices, etc. (**Figure 2**)

Figure 2: MAX30100 Sensor

1.3. Module Pins

In design of the module circuit, there are 14 main pins for the sensor which seven of the pins are chosen to be connected to the microcontroller at the final connection as illustrated in **table I.**

Table I: Pin Description.

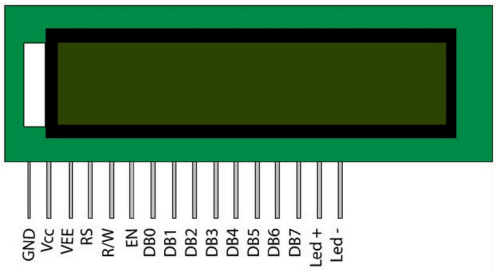
VIN	Modules' power source (3.3 volts)
SCL	I2C Clock Input
SDA	I2C Clock Data, Bidirectional
INT	Active-Low Interrupt
IR-DRV	IR LED Cathode and LED Driver Connection Point
R-DRV	Red LED Cathode and LED Driver Connection Point
GND	Analog Ground

1.4. LCD Monitor with 2*16 Characters

An LCD (Liquid Crystal Display) monitor is an electronic display module having a wide range of applications. A 16x2 LCD is a basic module and is widely used in various devices and circuits. A 16x2 LCD has two lines on it and sixteen characters can be displayed on each line.

Specifications of each one of the 16 Pins are described as **figure 3**.

Figure 3: LCD Monitor with 16*2 Pins



Pin no. 1 (GND): This pin is related to the power supply of the LCD and must be coupled to the negative supply or the GND pin on the Arduino Uno board.

Pin no. 2 (VCC): This pin is related to the power supply of the LCD and should be coupled to the positive supply or the 5-volt pin on the Arduino Uno board.

Pin no. 3 (VEE): This pin is related to the contrast adjustment of the LCD monitor. The adjustment is such that as the voltage of the power supply gets closer to the value of 5.0 volts, the color shown on the monitor is dimmer; on the contrary, as the voltage gets close to the value of zero volts, the color will appear brighter. In addition, a potentiometer with a capacity of 10 k Ω will be used for the interval of 0 to 5 volts for all circuits used in projects.

Pin no. 4 (RS): This pin is related to the registers and locators for reading or writing on the LCD driver chips.

Pin no. 5 (R/W): This pin will help the user to choose reading a value from LCD or to write on it. When the value on this pin is designated to zero, then the LCD is ready to receive the data, and whenever the value is set to one, then the user can read the values from the LCD monitor.

Pin no. 6 (EN): On some occasions, the LCD monitor may be set to be active or non-active.
Whenever the value of this pin is designated to zero, the LCD monitor turns off and when the value is set to one, the monitor will turn on and remains available for usage.

Pin no. 7 to 14 (D0-D7): At occasions when we want the monitor to display certain data, these eight pins will be used in the 4 bit or 8-bit format. In this project, a 4-bit format is used.

Pin no. 15 (backlight VCC): This pin is related to the positive polarity of the LED lamp which is the background light of the LCD monitor. It must be connected to the 5-volt pin on the Arduino Uno board.

Pin no. 16 (backlight GND): This pin is related to the negative polarity of the LED lamp which is the background light of the LCD monitor. This pin must be connected to the power supply or the GND pin on the Arduino Uno board.

1.5. Three resistors with 1 K ohm Capacity

Three resistors with 1k ohm capacity are connected and integrated with a parallel to divide voltage network. And it is designed to provide a specific amount of resistance in the circuit.

2. Software

The MAX30100 Launcher Program is written and run at the beginning stages and is specially written for Arduino Uno. Then, the special codes for displaying the heartbeat on the monitor is written and run.

Method of Work

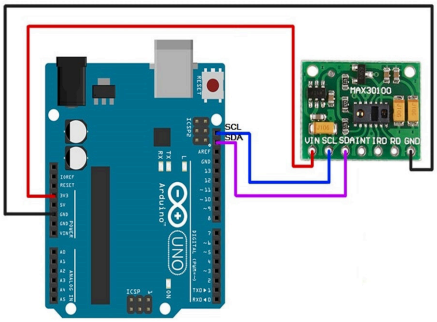
A small clamp-like device is placed on the earlobe and will be connected to the device only via a single wire. The wire is connected to a small sensor attached to the earlobe. The sensor receives the pulses emitted from the earlobe via the wire and transmits them to the Arduino board on the device. Then the board will process the received data from the sensor and transfers the data into the heartbeat signal by using the previously written program in the board. And finally, the board will show the result on a small LCD monitor which is also attached to the device that is fitted in the patient's pocket.

Connection to Arduino

The board is easily connected to the computer via the USB port and necessary programs can be written and

transferred to the board. This board may be powered by an AC/DC adaptor or a battery through the related jack. The power source pin of the sensor will be connected to the 3.3-volt source of the Arduino board, and similarly, I2C data and clock are connected to A4 and A5 analog, INT pin to D2, and GND is connected to the ground port on the Arduino board. When all the connections are made correctly, the LED light on the sensor module should turn on. (**Figure 4**)

Figure 4: Arduino connection to MAX30100



Conclusion

Pulse oximeters have been developed and widely used since the 1930s. The designs and products have evolved from large sizes to small ones. Devices that are large, heavy, expensive, and available only for military and sleep laboratories[20] have changed into ones that are cheap and small (ear-lobe usage, fingertip compatible[3].

The accuracy of pulse oximetry is reduced in patients with conditions like severe and rapid oxygen desaturation, low blood pressure, body temperature, and reduced blood perfusion conditions. While the earlobe pulse oximetry has more accurate and reliable performance regarding these changes[16]. Haynes (2007) claimed that the earlobe probe can be considered as the proper method of finger type pulse oximetry. He said "in finger probe, the body movement is limited and the risk of reduced tissue perfusion is increased"[18]. Thus, considering the results of our study, the earlobe probe can be used as the proper and reliable method for examining the oxygen saturation regarding the importance of continuous monitoring and maintaining hemodynamic stability in patients under heart surgery[17].

The MAX30100 is a complete pulse oximetry and heart rate sensor system solution that has been designed for the demanding requirements of wearable devices. The MAX30100 provides a very small total solution size without sacrificing optical or electrical performance. In order to integrate this device into a wearable oximeter, minimal external hardware components would be necessary to accomplish it.

The MAX30100 is fully configurable through software registers, and the digital output data stored in a 16-deep pins within the device. The pins allow the MAX30100 to be connected to a microcontroller or microprocessor on a shared bus, even though the data is not being read continuously from the device's registers.

The MAX30100 transmits data on SDA in sync with the master-generated SCL pulses. The master section acknowledges receipt of each byte of data. The SDA section operates as both an input and an open-drain output.

A pull-up resistor, typically with the size of 1kΩ, is required on SDA. SCL operates only as an input. A pull-up resistor, typically with the size greater than 1kΩ, however, is required on SCL. This is the case when there are multiple masters on the bus, or if the single master has an open-drain SCL output.

As was mentioned in this paper, the designer has chosen to use Arduino Uno for communication with the MAX30100 module. And besides, it uses the 2*16-character LCD monitor to show the data. In this way, a comfortable and portable device was fitted into the system. Since the sensor used in this project is a very delicate and sensible segment, the measurement of a patient's heartbeat will be done with more accuracy as compared to other methods of measurements. For the future improvement of this project, the second part of this sensor (the part which was not used in the project), which measures the percentage of oxygen in the blood, can be arranged to measure the amount of oxygen both before and after various exercises. One of the advantages of this device is its usage for people who have no hands and the measurement of heartbeat and rate of breathing through hands are not possible.

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Interests conflict

The researchers declare that they have no conflict of interest.

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ORIGINAL

The care of cancer patients in the Balearic Islands: Results of a collaborative agreement

La atención al paciente oncológico en las Islas Baleares: Resultados de un acuerdo de colaboración

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Abstract

The results of a collaboration agreement between the Balearic Islands Board of the Spanish Cancer Association and Atenzia are presented. The evaluation of the first signed agreement led to its renewal, which has led to proactively making 1,818 calls to cancer patients and / or their families and to responding and attending 592 calls, 19% of them due to social or health emergencies. Requests made from the four Balearic Islands were attended. The average age of the users of the offered resource has been between 70 and 80 years, 64% women and 36% men. New areas of joint action for the following years are presented.

Keywords: Atention, care, cancer patient.

Resumen

Se presentan los resultados de un convenio de colaboración entre la Junta de Baleares de la Asociación Española contra el Cáncer y Atenzia. La evaluación del primer convenio firmado llevó a su renovación, lo que ha permitido realizar proactivamente 1.818 llamadas a pacientes oncológicos y/o sus familiares y a responder y atender 592 llamadas, el 19% de ellas por emergencias sociales o sanitarias.
Se han atendido solicitudes realizadas desde las cuatro Islas Baleares. La edad media de los usuarios del recurso ofrecido ha sido entre 70 y 80 años, 64% mujeres y 36% hombres. Se presentan nuevas áreas de actuación conjunta para los próximos años.

Palabras clave: Atención, cuidados, paciente oncológico.

Introduction

In addition to promoting the culture of health and cancer prevention and supporting biomedical research in oncology[1], the Spanish Cancer Association (SCA) provides[2]:

- Medical and nursing guidance in order to clarify doubts related to the diagnosis and treatment of cancer and its possible side effects.
- Home and hospital accompaniment.
- Psychological and social care, to collaborate in facing the emotional discomfort caused by the disease and its treatments and, at the same time, improve communication with family and friends.

The psychological and social comfort of the cancer patient conditions their prognosis. We have known for a long time[3] that a positive environment around the patient causes their greater adherence to the treatment protocols in application and consequently improves their prognosis. In this line, the Balearic Islands Board of the SCA (BIB SCA) believed that reinforcing this action was a priority objective to be covered in the short term, a work proposal that was definitively settled with the publication by the European Union in February 2021 of its Policy Document on Cancer, in which, among others, it calls for unity of action to more effectively confront the fight against cancer in all its aspects[4].

To this end, the BIB SCA decided to establish a collaboration agreement with Atenzia, an organization with 25 years of experience in tele-assistance and permanent care, with a portfolio of services that includes emergency

care, psychosocial support, promotion of healthy habits, therapeutic adherence and monitoring of vital signs[5], a work that Atenzia carries out using three service modalities: home tele-assistance with a fixed line (TAD), home tele-assistance without a fixed line (TAD GSM) and tele- mobile assistance (TMA). In 2021, a fourth modality is incorporated to the service that is executed through an APP, integrating the service on the patient's and family's mobile, which makes it more comfortable and discreet. The service has also three strategic actions: 24-hour telephone service, proactive and personalized monitoring and group workshops.

This agreement, which gave rise to the *Servicio Contigo*, was signed on April 10, 2017 and in which it is literally stated that "The purpose of this Agreement is to establish a framework of action and joint relations between the BIB SCA and Atenzia, with in order to add value to the care offered by the BIB SCA to people suffering from the disease and their families, through Atenzia's fixed or mobile tele-assistance service that guarantees the patient security and 24-hour support, while at the same time allows and offers the BIB SCA, optimization of resources, active participation in its preventive and research work and recruitment of new partners / collaborators".

The main results obtained by the community application in the Balearic Islands of the *Servicio Contigo* are set out below.

Results

About the modality of the service

- Device modality: 13% TMA, 87% home TAD. The percentage of mobile TAM has decreased compared to other years, in 2019 it stood at 30%.
- Reasons for withdrawal: 50% due to death, 30% due to requiring other support such as residence admission, and 20% due to the end of the BIB SCA subsidy period: in 80% of these cases, 80% continued privately with the service, an obvious marker of satisfaction and usefulness of the service.

Performance data

- Average number of contacts: In 2020, a total of 1,818 calls were made from the Customer Service Center (CSC) (average of 151 calls / month). This figure increases, logically, with the increase in active patients. In 2021 (until 06/15/2021) the CSC has already made 1,100 calls, which represents an average of 183 calls / month.

Answered calls (alarms)

- Up to 06/15/2021, 592 calls made by patients and / or their families have been answered. According to 2020 figures, 19.60% of the alarms attended have been due to a health and / or social emergency that have required the immediate mobilization of emergency resources. 12.50% have been "unanswered alarms" corresponding to two types of situations: involuntary pressing or a serious emergency in which the person has been able to press to activate the service, but is not in a position to speak. The rest of the calls or alarms received (67.30%) correspond to various situations that do not imply an urgent action: call to speak, to communicate some information, to request information ...

Procedures and demands attended

Different types of situation / demand have been carried out and attended to:

- Positive COVID19
- Need for accompaniment to go to a medical appointment, for the purchase ...
- Situations of risk / need detected in the weekly follow-up calls: financial difficulties, emotional problems ...

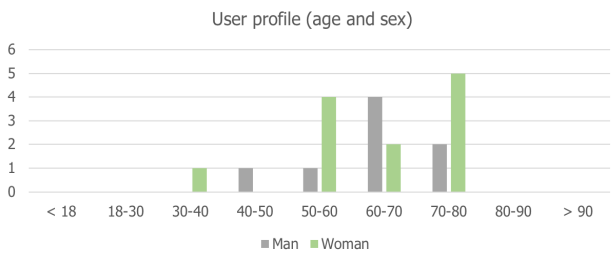
Participation and evaluation of activities (data until 2019)

Since the beginning of the service, a total of 13 activities have been carried out in the context of the BIB SCA - Atenzia collaboration. We have been increasing the number of activities each year (3 activities in 2017, 4 activities in 2018, 6 activities in 2019) with a reach of 168 people and an average of 12.92 participants per activity. Patients, relatives and the general population have attended these activities and in them we have been able to publicize the Servicio Contigo as well as put patients in contact with other people and strengthen their support network.

Data about the person attended

- **Age:** the band with the most users is 70-80 years, noting a progressive increase in the age of users.
- **Sex:** 64% women and 36% men. **Table I** shows how the percentage of women exceeds that of men in all ranges except those aged 60-70 years, in which men represent 66% of the total number of patients seen.
- Area of residence: 57% live in urban areas and 43% in rural areas. It is very important to objectify the territorial equity with which the service has been implemented: there are active patients on the four islands: Mallorca 61%, Menorca 4%, Ibiza 31% and Formentera 4%.
- Coexistence unit: 64% of the patients cared live accompanied and 36% live alone. Sometimes the partner is a family caregiver and on other occasions it is people who are in charge of the patient.

Table I



Time spent in the service

People active in the service accumulate an average of 11.04 months of service. There is a case that has been in service since the beginning and has already accumulated 4 years. There are 3 people who have been in the service for 2 years and 4 who have already been active in the service for 1 year. The rest of the active people (64%) have signed up for the service in 2021.

Discussion, conclusions and proposals

After analyzing this performance data of the *Servicio Contigo*, which we believe are very satisfactory, Atenzia and the BIB SCA considered renewing and expanding the terms and content of the *Servicio Contigo*, signature that was made on June 8, 2021. In the debate prior to this signature, it was proposed and agreed to collect more data from the beneficiaries, in an attempt to complete and consolidate the definition of their profile, as detailed below:

- Days and times of the calls received, in order to detect the time and day of the week in which the most calls are received and consequently arbitrate a consistent organization of resources.
- Identify and record which person in the coexistence unit usually answers the follow-up calls from the Attention Center.
- Precise characterization of the users and especially those who decide to continue with the Servicio Contigo after the end of the AECC subsidy, collecting and noting:
  - Cancer type.
  - Type of treatment.
  - Quality of life level.
  - Profession of the patient.
  - Profile of the people with whom he / she lives (family caregiver, minors in her charge, dependents in her charge ...)
  - Data about the caregiver:
    - State of health.
    - Dependency (yes / no)
    - Changes in their situation as a consequence of caring for the patient: work, economy, health, residence, family, personal projects….

In short, there is a firm commitment on the part of the two signatories and heads of the *Servicio Contigo* to reinforce and expand its application, thus contributing in a way that we believe can be decisive in the social and psychological well-being of cancer patients living in the Balearic Islands, commitment that we make public by publishing this article.

Interests conflict

The researchers declare that they have no conflict of interest.

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ORIGINAL

Antimicrobial resistance of *Helicobacter pylori* isolated from dental plaque specimens

Resistencia antimicrobiana de Helicobacter pylori aislado de muestras de placa dental

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Abstract

Background: *Helicobacter pylori* strains isolated from dental plaque samples may harbor severe antimicrobial resistance. The present research was performed to assess the antimicrobial resistance pattern of *H. pylori* strains isolated from dental plaque samples of individuals referred to dental clinics.
Methods: Forty-two *H. pylori* strains were isolated from dental plaque samples. Isolation was performed using routine instructions in a microaerophilic condition. Isolates were subjected to disk diffusion to assess their antimicrobial resistance.
Results: *H. pylori* strains harbored the uppermost resistance rate toward ampicillin (88.09%), clarithromycin (83.33%), amoxicillin (76.19%), metronidazole (71.42%), and tetracycline (69.04%) antimicrobials. *H. pylori* isolates harbored the lowermost resistance rate toward spiramycin (23.80%), furazolidone (26.19%), and rifampin (28.57%) antimicrobials. All isolates (100%) harbored simultaneous resistance toward at least 3 different antimicrobial agents, while simultaneous prevalence of resistance toward more than 7 antimicrobial agents was 35.71%.
Conclusion: Authorized spiramycin, furazolidone, and rifampin antimicrobial agents prescription can be a suitable choice for oral *H. pylori*.

Keywords: Helicobacter pylori, antimicrobial resistance, dental plaque.

Resumen

Antecedentes: Las cepas de *Helicobacter pylori* aisladas de muestras de placa dental pueden albergar una grave resistencia a los antimicrobianos. La presente investigación se realizó para evaluar el patrón de resistencia a los antimicrobianos de las cepas de *H. pylori* aisladas de muestras de placa dental de individuos remitidos a clínicas dentales.
Métodos: Se aislaron 42 cepas de *H. pylori* de muestras de placa dental. El aislamiento se realizó siguiendo las instrucciones de rutina en condiciones de microaerofilia. Los aislados se sometieron a difusión en disco para evaluar su resistencia antimicrobiana.
Resultados: Las cepas de *H. pylori* presentaron la mayor tasa de resistencia a los antimicrobianos ampicilina (88,09%), claritromicina (83,33%), amoxicilina (76,19%), metronidazol (71,42%) y tetraciclina (69,04%). Los aislados de *H. pylori* presentaron la menor tasa de resistencia a los antimicrobianos espiramicina (23,80%), furazolidona (26,19%) y rifampicina (28,57%). Todos los aislados (100%) presentaban resistencia simultánea a al menos 3 agentes antimicrobianos diferentes, mientras que la prevalencia simultánea de resistencia a más de 7 agentes antimicrobianos era del 35,71%.
Conclusiones: La prescripción autorizada de agentes antimicrobianos espiramicina, furazolidona y rifampicina puede ser una opción adecuada para *H. pylori* oral.

Palabras clave: Helicobacter pylori, resistencia antimicrobiana, placa dental.

Introduction

Dental plaque is a classic example of host-associated biofilm occurred mainlky due to the microbial accumulation with particular loa of bacteria. Subgingival and supragingival plaque provide an optimal microaerophilic and aerophilic conditions for the growth and survival of bacteria. About 6 billion microorganisms representing 400 resides in the oral cavity[1].

The microbial composition of the dental plaques varies at distinct sites on a tooth (approximal surfaces, fissures, and gingival crevice) and reflects the inherent differences in their anatomy and biology[2]. Previously, *Helicobacter pylorus* (*H. pylori*) has been isolated from the dental plaque samples of patinets with peptic ulcer diseases and also healthy one[3]. *H. pylori* is a microaerophilic and Gram-negative spiral coccoid bacterium known as a causative agent for gastric adenocarcinoma, peptic ulcer disease, duodenal ulcer, type B gastritis, and B-cell lymphoma[5,6]. The area around the dental plaque has a low oxidation potential promoting the growth of facultative anaerobes and even provide microaerophilic conditions[7]. Additionally, these area contained adequate nutritional components suitable for bacterial growth and survival[8].

Several antimicrobial choices are available for *H. pylori* infections, particularly in the oral cavity[8,10]. However, *H. pylori* isolates harbored severe resistance toward commonly used antimicrobial agents, particularly clarithromycin, amoxicillin, metronidazole and ampicillin[10,11]. Thus, studying the profile and pattern of antibiotic resistance amongst *H. pylori* isolates of dental plaques as novel reservoirs of bacteria seems essential.

According to the high importance of bacteria and the absence of epidemiological surveys in this field, the present research was performed to assess the antimicrobial resistance of *H. pylori* strains isolated from in dental plaque specimens collected from individuals referred to Armenian dental clinics.

Materials and methods

Ethics

All personal information of individuals included in the study were kept secret. Written informed consent was taken from all individuals. The study protocol was ethically approved by the University of Traditional Medicine of Armenia.

Bacteria

A total of 42 *H. pylori* strains were included in this survey. Strains were isolated from dental plaque specimens of patients referred to the Armenia dental clinics for routine check-ups. *H. pylori* isolation was performed using the protocol presented previously by Ghorbani et al. (2016)[5]. Breifly, microaerophic conditions (5% oxygen, 85% nitrogen, and 10% CO_2) were performed for bacterial growth. All culture media were supplemented with 5% of horse serum (Sigma, St. Louis, MO, USA), vancomycin (10 mg/L), nalidixic acid (30 mg/L), trimethoprim (30 mg/L), and cycloheximide (100 mg/L) (Sigma, St. Louis, MO, USA). Suspected colonies were then identified using Gram stain, motility, colony morphology, and biochemical tests such as urease, oxidase, and catalase tests[4].

Antimicrobial resistance profile of isolates

Mueller-Hinton agar (Merck, Germany) was applied to assess antibiotic resistance patterns using the simple disk diffusion technique. Antibiotic resistance profile of *H. pylori* bacteria was researched toward different antibiotic against (Oxoid, UK) using the guidelines of previous research[12] and also those of Performance Standards for Antimicrobial Susceptibility Testing-Clinical and Laboratory Standards Institute - NCCLS, 2007[13]. Bacterial suspensions were adjusted to the 0.5 McFarland standard (equivalent to 1–2 × 108 CFU/mL) and were used to inoculate Muller Hinton agar plates (Merck, Germany). The resistance of bacteria was experienced toward levofloxacin (5 µg), ampicillin (10 µg), clarithromycin (2 µg), metronidazole (5 µg), streptomycin (10 µg), amoxicillin (10 µg), cefsulodin (30 µg), tetracycline (30 µg), erythromycin (5 µg), furazolidone (1 µg), trimethoprim (25 µg), rifampin (30 µg), and spiramycin (100 µg) (Oxoid, UK). Positive controls (NCTC 13206 (CCUG 38770) and NCTC 13207 (CCUG 38772)) were accompanied in this experiment. Antibiotic disks were placed on media contained the bacteria, and the plates were incubated under microaerophilic conditions at 35°C for 16–18 h. The zones of growth inhibition produced by each antibiotic were measured and interpreted by standard procedure[14-18].

Data analysis

Data were subjected to Microsoft Office Excel (version 15; Microsoft Corp., Redmond, WA, USA). The statistical analysis was performed employing the SPSS 21.0 software (SPSS Inc., Chicago, IL, USA). Chi-square test and Fisher's exact two-tailed test were applied to measure any significant relationship. *P*-value <0.05 was considered as a significant numerical level[19-26].

Results

Disk diffusion pattern

Figure 1 shows the patterns of antimicrobial resistance of *H. pylori* isolates of dental plaque samples.

Antimicrobial resistance

Table I shows the disk diffusion antimicrobial pattern of *H. pylori* strains isolated from dental plaque samples. According to obtained data, *H. pylori* strains harbored the uppermost resistance rate toward ampicillin

(88.09%), clarithromycin (83.33%), amoxicillin (76.19%), metronidazole (71.42%), and tetracycline (69.04%) antimicrobials. Reversely, *H. pylori* isolates harbored the lowermost resistance rate toward spiramycin (23.80%), furazolidone (26.19%), and rifampin (28.57%) antimicrobials. Statistically significant differences were obtained for for the resistance rates between different antimicrobial agents (P <0.05).

Mulktidrug resistance pattern

Figure 2 shows the prevalence of multidrug resistance amongst examined *H. pylori* isolates. Data showed that all H. pylori isolates (100%) harbored simultaneous resistance toward at east 3 different antimicrobial agents. Results showed that only 35.71% of *H. pylori* isolates harbored simultaneous resistance toward more than 7 antimicrobial agents.

Figure 1: Disk diffusion pattern of isolated *H. pylori* strains of dental plaque samples.

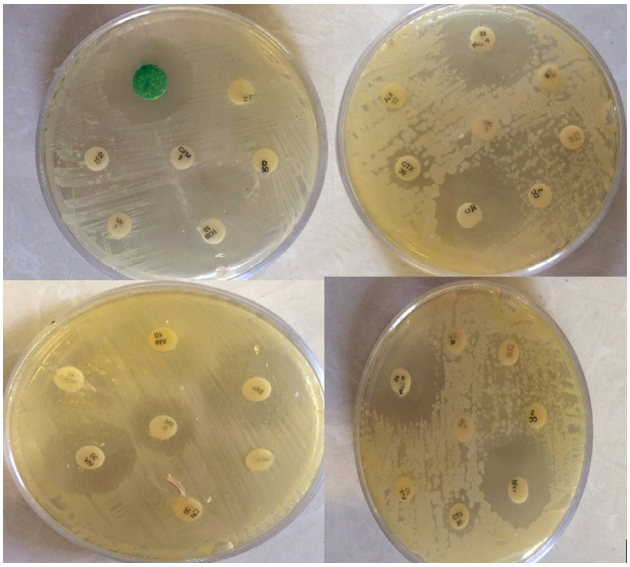
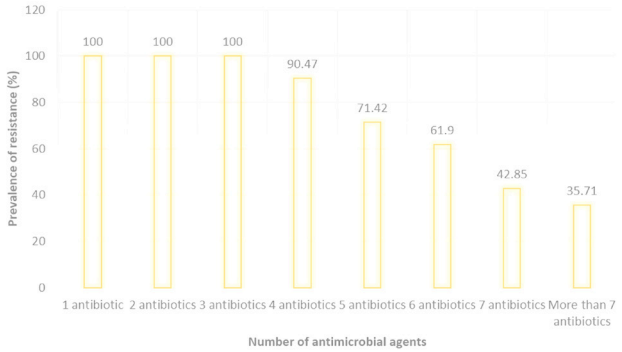


Figure 2: Prevalence of multidrug resistance amongst examined *H. pylori* isolates.



Discussion

Despite the huge developments occurred in medicine, diverse complicated infectious diseases faced with the human[27-32]. For example, *H. pylori* have become a developed public health issue in the last century[33].

To date, *H. pylori* has been detected in samples of dental plaque, saliva, and dental pulp[34,35]. Some researches have reported an association between *H. pylori* infection and its presence in the oral cavity. Okuda et al. (2000)[36] stated that 22% of *H. pylori*-infected subjects harbored *H. pylori* in their dental plaque. Likewise, Bagot et al. (2011)[37] showed that 21% of *H. pylori*-infected subjects possessed the bacterium in their saliva. Therefore, the *H. pylori* presence in the oral cavity appears to be indicative of *H. pylori* infection.

The present investigation revealed that *H. pylori* strains isolated from dental plaque samples harbored the highe prevalence of resistance toward commonly used antimicrobial agents, particularly amoxicillin, ampiucillin, metronidazole, and clarythromixin. High and illegal antibiotic prescription in veterinary and medicine caused a significant increase in antibiotic resistance. Additionally, excessive use of disinfectants and self-treatment by antibiotics are other reasons. High *H. pylori* resistance toward amoxicillin, ampiucillin, metronidazole, and clarythromixin antimicrobials was reported from Russia[38], Mexico[39], Iran[40], United States[41], Brazil[42], Malaysia[43], and Greece[44]. Thus, it seems that amoxicillin, ampiucillin, metronidazole, and clarythromixin prescriptions are not effective against human *H. pylori*. Reversely, High efficacy of spiramycin, furazolidone, and rifampin antimicrobials against *H. pylori* strains has been reported from Korea[45], Italy[46], and Iran[47].

Some tested strains harbored simultaneous resistance against diverse kinds of antimicrobials. Comprehensive surveys conducted on Taiwan, India, Saudi Arabia, Senegal, China, Thailand, Nigeria, Brazil, Egypt, Colombia, and Argentina presented the high resistance of *H. pylori* toward amoxicillin, ampicillin, tetracycline, trimethoprim, erythromycin, and clarithromycin antibiotic agents[48], which was similar to our report. Similar reports indicated that the mean prevalence of resistance of *H. pylori* strains toward spiramycin, furazolidone, trimethoprim, levofloxacin, tetracycline, amoxicillin, clarithromycin, erythromycin, and metronidazole antibiotic agents ranged

Table I: Disk diffusion antimicrobial pattern of *H. pylori* strains isolated from dental plaque samples.

Types	N. isolates harbored resistance toward each antibiotic disk (%)												
Specimens (N. positive)	Clr*	Amx	Met	Amp	S10	Frz	Lev	Tet	Rif	Ert	Trp	Spr	Cfs
Dental plaques (42)	35 (83.33)	32 (76.19)	30 (71.42)	37 (88.09)	25 (59.52)	11 (26.19)	20 (47.61)	29 (69.04)	12 (28.57)	24 (57.14)	23 (54.76)	10 (23.80)	20 (47.61)

*Clr: clarithromycin (2 µg), Amx: amoxicillin (10 µg), Met: metronidazole (5 µg), Amp: ampicillin (10 µg), S10: streptomycin (10 µg), Frz: furazolidone (1 µg), Lev: levofloxacin (5 µg), Tet: tetracycline (30 µg), Rif: rifampin (30 µg), Ert: erythromycin (5 µg), Trp: trimethoprim (25 µg), Spr: spiramycin (100 µg), Cfs: cefsulodin (30 µg),

between 9.00-16.00%, 9.00-29.00%, 34.00-63.00%, 36.00-58.00%, 63.00-90.00%, 72.00-94.00%, 53.00-80.00%, and 27.00-89.00%, respectively*9, 49-50.*

The present research was limited to the lack of the study of the nutritional resistance pattern of patiuents without dental plaques and absence of genotic distribution of antibiotic resistance amongst the *H. pylori* isolates. Lack of demographical characters of the targeted population is another important limitation.

Conclusion

Considering the low prevalence of resistance of *H. pylori* strains against spiramycin, furazolidone, and rifampin antimicrobial agents, their proper and authorized prescription can diminish the risk of *H. pylori* in dental plaque samples as a reservoir for extra oral infections.

Interests conflict

The researchers declare that they have no conflict of interest.

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ORIGINAL

Latest trends in medical education during COVID pandemic: a cross sectional study

Últimas tendencias en educación médica durante la pandemia de COVID: un estudio transversal

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Abstract

Introduction**:* Parallel to past technological revolutions, along with existing pandemic crises has made digitally assisted tools, and formats for e-learning an essential component of medical Curriculam. This current study objectives were to find out the opinion of the students about the use and efficacy of the distance learning tools during the Covid-19 crises and its impact on learning and academic achievements among medical students of Saudi Arabia. ***Methods: Cross-sectional study was conducted among 1021 medical college students of Saudi Arabia by developing a survey questionnaire composed of sociodemographic characteristics of participants, study habits assessment including teacher engagement and student-teacher interactions, assessment of distance teaching approaches such as availability of internet services at home, the usefulness of live sessions or recorded videos, number of hours one can attend the sessions and stay motivated, assessment of academic performance, evaluation of respondents experience and technical infrastructure, psychosocial assessment of respondents, and their coping with COVID-19 crises. ***Results:*** Among 1021 students, 503 (49%) were males and 518 (51%) females. 64% agree that distance teaching tools used by the teachers were easy to understand and use, and 55% responded that they are very much satisfied with E-learning provided by their institute. There was no significant difference observed between students on the usefulness of different approaches in facilitating learning experience except 'Self-study using text and/or video materials provided by the teacher approach' (P=0.043). ***Conclusion:*** The findings showed satisfactory results, showing that Saudi Arabia's respective medical universities offered good online support and orientation to overcome COVID 19 crises, and students found distance learning tools easy to use and understand as the support provided by the medical universities staff. Future steps would be taken based on the observed results, and further improvement would be implemented to make the learning process easier for medical students.

Keywords: Assessment, COVID-19, E-learning, education, medical students.

Resumen

Introducción: Paralelamente a las revoluciones tecnológicas pasadas, junto con las crisis pandémicas existentes, ha hecho que las herramientas y los formatos asistidos digitalmente para el aprendizaje electrónico sean un componente esencial del currículo médico. Los objetivos de este estudio eran averiguar la opinión de los estudiantes sobre el uso y la eficacia de las herramientas de aprendizaje a distancia durante las crisis de Covid-19 y su impacto en el aprendizaje y los logros académicos entre los estudiantes de medicina de Arabia Saudí. ***Métodos:*** Se llevó a cabo un estudio transversal entre 1021 estudiantes universitarios de medicina de Arabia Saudí mediante la elaboración de un cuestionario compuesto por las características sociodemográficas de los participantes, la evaluación de los hábitos de estudio, incluido el compromiso del profesor y las interacciones entre estudiantes y profesores, la evaluación de los enfoques de la enseñanza a distancia, como la disponibilidad de servicios de Internet en el hogar, la utilidad de las sesiones en directo o de los vídeos grabados, el número de horas que se puede asistir a las sesiones y mantenerse motivado, la evaluación del rendimiento académico, la evaluación de la experiencia de los encuestados y la infraestructura técnica, la evaluación psicosocial de los encuestados y su afrontamiento de las crisis de COVID-19. ***Resultados:*** De 1021 estudiantes, 503 (49%) eran hombres y 518 (51%) mujeres. El 64% estaba de acuerdo en que las herramientas de enseñanza a distancia utilizadas por los profesores eran fáciles de entender y utilizar, y el 55% respondió que estaba muy satisfecho con el E-learning proporcionado por su instituto. No se observaron diferencias significativas entre los estudiantes en cuanto a la utilidad de los distintos enfoques para facilitar la experiencia de aprendizaje, excepto el "enfoque de autoaprendizaje con materiales de texto y/o vídeo proporcionados por el profesor" (P=0,043). ***Conclusión:*** Los hallazgos mostraron resultados satisfactorios, demostrando que las respectivas universidades médicas de Arabia Saudí ofrecieron un buen apoyo y orientación en línea para superar las crisis de COVID 19, y los estudiantes encontraron las herramientas de aprendizaje a distancia fáciles de usar y entender como el apoyo proporcionado por el personal de las universidades médicas. A partir de los resultados observados, se tomarán medidas futuras y se introducirán nuevas mejoras para facilitar el proceso de aprendizaje a los estudiantes de medicina.

Palabras clave: *Helicobacter pylori*, resistencia antimicrobiana, placa dental.

Introduction

Worldwide the coronavirus disease (COVID-19) has impacted medical students. Medical students want to be prepared to provide the best healthcare services, but in the present world, this starts with finding the best way to educate them. This begins with understanding the opportunities that professors, teachers, and medical college authorities have at their fingertips and using all the resources, considering the barriers that COVID-19 has created. Social distancing is the most effective strategy of prevention since COVID-19 emerged pending the discovery of a vaccine, medication, or both. This makes it difficult for students to meet in learning classrooms, lecture halls, or nice community areas[1,2]. Most teachers have been flipping the classrooms past few year's by providing "anytime / anywhere" individualized training for interactive learning. Nonetheless, students still gathered for small-group activities, laboratory sessions, simulations, and technology sessions (e.g., bedside ultrasonography sessions), as well as clinical guidance for standardized patient procedures and practical patient care environments[3].

Many e-learning and online learning resources and methods have been addressed in the literature as valuable tools and methods to expand the teaching and learning possibilities in the medical health profession. It was evident that e-learning in terms of the gain of information and performance of students is equivalent to traditional classroom methods. E-tools represent the language of future generations. In response to COVID-19, the faculty of medical education quickly moved the entire program to electronic formats. Small-group configurations convene online in virtual team environments, and clinical expertise sessions may take place online or may be postponed in certain situations. Examinations have also shifted to electronic setups[2]. More than ever, digital education in problem-based learning, or digital problem-based learning (DPBL), is increasingly being used in education in the health professions. DPBL involves both solely digitally mediated and mixed problem-based learning, incorporating interactive and face-to-face learning. It mandates that Saudi Arabia's educational institutions shift their educational model from embracing technology to changes in instruction and pedagogy[4]. Display quotations of over 40 words, or as needed.

Updating content material may be a boost to the online environment, and virtual activities may seem usable, but the outcome of these changes will require periodic assessment and evaluation. Saudi Arabia's medical institution's preparations should be extensively studied in terms of their technical, technological, and psychosocial capacities and growth to cope with this trend. This transition from the medical school environment to home results in loneliness, increased email usage, and challenges to establish boundaries between work and home that can really affect teachers and students[3].

Therefore, this research paper is intended to explore and assess the changing pattern of the education system affecting the learning style and academic performances of medical students of Saudi Arabia during times of pandemic. This study will not only be appropriate to address the educational issues effectively for medical students of Saudi Arabia during this current crisis but will also help to lay the groundwork for teaching in future disasters and beyond. Hence this study was carried out with an aim to study to explore and assess the impact of the COVID-19 global pandemic crisis on changing educational patterns of medical students in Saudi Arabia.

Materials and methods

Sample and Recruitment

This cross-sectional study was carried out from June to October 2020 among various medical schools all over Saudi Arabia. Presently there are about 37 medical schools with approximately 250-300 students overall in each. With a confidence level of 95% and a population of 10000, the sample size was calculated to be 1200. Following the creation of the questionnaire, the questionnaire was forwarded for review to a biostatistician and a medical education specialist. Pretested questionnaire was distributed in various medical schools situated in Northern, Southern, Western, and eastern regions.

The alpha of Cronbach was determined for the entirety of items in this sample and was suggesting strong internal consistency. A self-administered questionnaire was made accessible online as a weblink to all the students. The study participants included second to six-year students comprising of both males and females. Informed consent was obtained from each participant registered to the survey—the questionnaire contained five sections with a total of 36 items. A total of 24 questions were formulated using the 5-points Likert scale, a total of 3 questions based on Yes/No, remaining 9 were open questions. Ethical approval was sought from the ethics committee, Deanship of scientific research, Majmaah University.

We overlook to assess different parameters that affect medical students during the pandemic time including get the opinion of students regarding online classes, agreement levels of students on live sessions, tools, materials, technical difficulties, agreement level of students on their comfortability with online classes, and distress caused due to COVID 19, testing availability of functioning internet service "networking technology" at home helping you for distance teaching, identify a maximum number of hours one can stay motivated and follow the session, we explore institute's online support and orientation regarding COVID-19 pandemic crisis,

examine the ability of students to concentrate at home while studying, identify different suitable E-Learning method usefulness among medial students, assess different approaches in facilitating learning experience and success and finally examine different between academic year and genders among medical students.

Data analysis

The sample size was computed by using SPSS program version 21.1 for Windows (SPSS, Inc, Chicago, IL, USA). Chi-Square test used in our survey for correlation coefficient to determine the relationship between the various variables. Statistically important is a p-value less than ≤ 0.05. Privacy and confidentiality were maintained throughout the duration of the study.

Results

There were 1021 medical students from various universities across the country who participated in this study; of them, 503 (49%) were males and 518 (51%) females. Most of the students were single 1004 (98%), 9 were married, 5 were separated, and 3 were divorcee. The majority of the students belonged to the western region, 467 (46%) and very less from the northern region 65 (6%). Students from all academic levels were included in the study except the first year. Final-year students were high in the number who responded 289 (28%), followed by fifth-year students 189 (19%), second-year 184 (18%), fourth-year 181 (18%), and least were from 3rd year 178 (17%). The mean age of male participants was 22.40 ± 1.9 and female 21.81 ± 2.1 (**Table I**).

Table II depicts the majority of the students were happy with the teacher's transition from offline classes to online classes. 31% of the students were neutral when asked about the interaction received by the tutors before the launching of online classes. About 50% of the students agreed that 'they know what the teachers expect them to do in their courses' while few students (22%) disagred. A majority of the students (52%) believe that there is too little interaction between teachers and students with the online classes. There was a significant difference in student's opinions observed of the different academic year on their amount of work they have to do at the moment (p- value 0.039). 52% of the students felt that College made an appropriate change when shifting to online study.

The majority of the students (25%) strongly agree and (40%) agree that 'the tools used for distance teaching provided by university learning management system were effective and appropriate. 64% agree that distance teaching tools used by the teachers were easy to understand and use. Few students (7.6%) experienced a lot of technical difficulties during live sessions. About 37% kept neutral while responding to 'Did assignment and homework enhanced their learning' while only 8% of them responded they strongly agree. Overall, 55% responded that they are very much satisfied with the E-learning provided by their institute. About 46% of the students disagree that 'their sleep deprivation negatively affected their study preparedness. 40% agreed that they experienced some sort of psychological distress during the online learning and the Covid19 situation, about 60% distracted by social media, and 45% were distracted by COVID 19 crisis news (**Table II**).

The majority of the students had functioning internet services (80%) at their homes which help them for distance teaching, and 2% did not have internet service. Only 2.4% of the students said they could stay motivated for more than 4 hours and follow the session, and 30% said 'it depends upon the teacher.' 69% said 'their institutes provide them online support and orientation regarding the COVID19 pandemic crisis. About 35% of the student's said 'they are not able to concentrate at home while studying (**Table III**).'

Student's opinions on the usefulness of different E-learning methods were also asked. There was a significant difference of opinion observed between students of different academic years on the use of 'Blackboard learn' P value <0.01. 21% of the 6th year students said 'Not used,' and about 8% of the 5th year students said the use of Blackboard was useless. The majority of the student's found Zoom technology to be a useful tool for E-learning. Of the total 6th year students, 68% of them said 'it is a useful tool. Of the total, 33% of them were either neutral or said 'not used (**Table IV**).' There was a significant difference observed with regard to the use of Microsoft teams (p value <0.01). Only 10% of the

Table I: Sociodemographic characteristics of the study participants.

Characteristics	Frequency	Percent
Gender		
Male	503	49.3
Female	518	50.7
Marital status		
Single	1004	98.3
Married	9	0.9
Separated	5	0.5
Divorced	3	0.3
Current geographic residence		
Western region	467	45.7
Southern region	75	7.3
Central region	273	26.7
Eastern region	141	13.8
Northern region	65	6.4
Academic level		
2nd Year	184	18.0
3rd Year	178	17.4
4th Year	181	17.7
5th Year	189	18.5
6th Year (Final Year)	289	28.3
Total	1021	100.0
Mean Age ± SD		
Male	22.40 ± 1.9	
Female	21.81 ± 2.1	
Total	22.10 ± 2.0	

3rd year students found 'Microsoft teams' useful while it was 28% in 5th year students. There were differences of opinions among students observed with regard to the use of 'Moodle' and 'Email' for the E-learning method with P values <0.01 (**Table IV**).

There was no significant difference between students observed on the usefulness of different approaches in facilitating learning experience except 'Self-study using text and/or video materials provided by the teacher approach' (p-value 0.043) (**Table V**).

Table VI depicts the mean scores of 8 dimensions. There was no statistically significant difference of mean scores of 9 dimensions (Opinion on online classes) and mean scores of 8 dimensions (opinion on live sessions, tools, materials, technical difficulties, etc.) observed in students of different academic years. However, there was a highly significant difference in mean scores observed with regard to opinion on comfortability with online classes and distress caused due to COVID19. Third-year students had high average scores of 3.31±0.51, and fourth-year students had fewer scores of 3.13±0.51 (p -value0.01) (**Table VI**).

Table II: Student's opinion on various aspects (live sessions, tools, materials, technical difficulties, comfortability, and distress due to COVID19.

Dimensions	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree	Total
Student's opinion on online classes						
Overall, I feel the teachers are doing their best to smooth the transition from (offline) classroom teaching to (online) distance teaching under the current circumstances (COVID-19)	50 (4.9%)	88 (8.6%)	177 (17.3%)	425 (41.6%)	281 (27.5%)	1021 (100%)
You are satisfied with interaction received before the commencement (launching) of the online classes by the tutor(s):*	60 (5.9%)	149 (14.6%)	313 (30.7%)	368 (36.0%)	131 (12.8%)	1021 (100%)
I know what the teachers expect me to do in their courses	47 (4.6%)	174 (17.0%)	278 (27.2%)	372 (36.4%)	150 (14.7%)	1021 (100%)
I think there is too little interaction between the teachers and students at the moment	51 (5.0%)	213 (20.9%)	221 (21.6%)	329 (32.2%)	207 (20.3%)	1021 (100%)
I wish I would receive more feedback from the teachers on how much progress I make	44 (4.3%)	121 (11.9%)	220 (21.5%)	374 (36.6%)	262 (25.7%)	1021 (100%)
I feel overwhelmed by the amount of work I have to do at the moment*	81 (7.9%)	155 (15.2%)	257 (25.2%)	293 (28.7%)	235 (23.0%)	1021 (100%)
I think my college made an appropriate change when shifting to online study*	87 (8.5%)	120 (11.8%)	182 (17.8%)	380 (37.2%)	252 (24.7%)	1021 (100%)
I could maintain my concentration on study materials while attending lectures while studying from home	120 (11.8%)	212 (20.8%)	185 (18.1%)	317 (31.0%)	187 (18.3%)	1021 (100%)
I practiced good time management, which helped me achieve my academic goals	94 (9.2%)	161 (15.8%)	243 (23.8%)	337 (33.0%)	186 (18.2%)	1021 (100%)
Student's opinion on live sessions, tools, materials, technical difficulties, etc						
The live session is better than the recorded session	115 (11.3%)	152 (14.9%)	238 (23.3%)	241 (23.6%)	275 (26.9%)	1021 (100%)
Overall, the tools used for distance teaching provided by university learning management system (E-Learning), e.g. (Blackboard Learn, Zoom, Microsoft teams, Webex, Moodle, Email, etc.) are effective and appropriate	47 (4.6%)	69 (6.8%)	238 (23.3%)	409 (40.1%)	258 (25.3%)	1021 (100%)
In general, the distance teaching tools used by the teachers are easy to understand and use	29 (2.8%)	78 (7.6%)	253 (24.8%)	445 (43.6%)	216 (21.2%)	1021 (100%)
I experience a lot of technical difficulties during live sessions	161 (15.8%)	300 (29.4%)	269 (26.3%)	213 (20.9%)	78 (7.6%)	1021 (100%)
In general, the live sessions are too long	42 (4.1%)	238 (23.3%)	338 (33.1%)	259 (25.4%)	144 (14.1%)	1021 (100%)
My academic performance positively influenced by the changes in curriculum due to Covid-19 pandemic	111 (10.9%)	145 (14.2%)	296 (29.0%)	275 (26.9%)	194 (19.0%)	1021 (100%)
Assignments and homework enhanced my learning*	143 (14.0%)	186 (18.2%)	374 (36.6%)	233 (22.8%)	850 (8.3%)	1021 (100%)
Overall, I am satisfied with E- Learning provided by my institute:*	75 (7.3%)	121 (11.9%)	261 (25.6%)	378 (37.0%)	186 (18.2%)	1021 (100%)
Students opinion on their comfortability with online classes and distress caused due to COVID 19						
I have enough sleep hours	71 (7.0%)	171 (16.7%)	191 (18.7%)	318 (31.1%)	270 (26.4%)	1021 (100%)
I have sleep deprivation negatively affect my study preparedness*	159 (15.6%)	309 (30.3%)	253 (24.8%)	225 (22.0%)	75 (7.3%)	1021 (100%)
I experienced some sort of psychological distress since the start of online learning and the Covid19 situation (depressive symptoms, obsessive-compulsive behavior, etc.)*	166 (16.3%)	219 (21.4%)	225 (22.0%)	246 (24.1%)	165 (16.2%)	1021 (100%)
Most likely I am able to study alone at separate room:	34 (3.3%)	74 (7.2%)	143 (14.0%)	417 (40.8%)	353 (34.6%)	1021 (100%)
Most likely i am forced to study at shared room:	263 (25.8%)	365 (35.7%)	207 (20.3%)	131 (12.8%)	55 (5.4%)	1021 (100%)
I become distracted by social media or other entertainment*	54 (5.3%)	127 (12.4%)	216 (21.2%)	362 (35.5%)	262 (25.7%)	1021 (100%)
I become distracted by COVID-19 crisis news	133 (13.0%)	202 (19.8%)	231 (22.6%)	287 (28.1%)	168 (16.5%)	1021 (100%)

Table III: Availability of internet services, motivation, online support, and concentration at home while studying.

Characteristics		Frequency	Percent
Do you have available functioning internet service "networking technology" at home (WIFI, data bundle) helping you for distance teaching?	Yes, Effective Yes, But not effective Not at all effective	819 178 24	80.2% 17.4% 2.4%
Considering the live sessions you have had so far: what is the maximum number of hours you can generally stay motivated and follow the session?	< 1 hour 1 hour 2 hours 3 hours 4 hours > 4 hours I cannot really tell; it depends on the teacher	109 164 188 95 37 25 403	10.7% 16.1% 18.4% 9.3% 3.6% 2.4% 39.5%
My institute provides online support and orientation regarding the COVID-19 pandemic crisis:	Yes No	709 312	69.4% 30.6%
Are you able to concentrate at home while studying?	No, I get distracted Yes, I concentrated well Total	355 666 1021	34.8% 65.2% 100%

Table IV: Usefulness of suitable E-Learning method.

	Useless	Neutral	Not used	Useful	Total
Blackboard Learn					
2nd Year	26 (14.1%)	42 (22.8%)	32 (17.4%)	84 (45.7%)	184 (100%)
3rd Year	29 (16.3%)	28 (15.7%)	20 (11.2%)	101 (56.7%)	178 (100%)
4th Year	28 (15.5%)	37 (20.4%)	17 (9.4%)	99 (54.7%)	181 (100%)
5th Year	15 (7.9%)	43 (22.8%)	29 (15.3%)	102 (54.0%)	189 (100%)
6th Year (Final Year)	37 (12.8%)	68 (23.5%)	61 (21.1%)	123 (42.6%)	289 (100%)
Total	135 (13.2%)	218 (21.4%)	159 (15.6%)	509 (49.9%)	1021 (100%)
Chi-Square, P-value			29.407, 0.003		
Zoom					
2nd Year	8 (4.3%)	38 (20.7%)	33 (17.9%)	105 (57.1%)	184 (100%)
3rd Year	8 (4.5%)	30 (16.9%)	35 (19.7%)	105 (59.0%)	178 (100%)
4th Year	20 (11.0%)	29 (16.0%)	32 (17.7%)	100 (55.2%)	181 (100%)
5th Year	10 (5.3%)	29 (15.3%)	33 (17.5%)	117 (61.9%)	189 (100%)
6th Year (Final Year)	12 (4.2%)	42 (14.5%)	40 (13.8%)	195 (67.5%)	289 (100%)
Total	58 (5.7%)	168 (16.5%)	173 (16.9%)	622 (60.9%)	1021 (100%)
Chi-Square, P-value			20.433, 0.059		
Microsoft teams					
2nd Year	15 (8.2%)	32 (17.4%)	110 (59.8%)	27 (14.7%)	184 (100%)
3rd Year	17 (9.6%)	29 (16.3%)	115 (64.6%)	17 (9.6%)	178 (100%)
4th Year	17 (9.4%)	31 (17.1%)	87 (48.1%)	46 (25.4%)	181 (100%)
5th Year	11 (5.8%)	30 (15.9%)	96 (50.8%)	52 (27.5%)	189 (100%)
6th Year (Final Year)	17 (5.9%)	54 (18.7%)	157 (54.3%)	61 (21.1%)	289 (100%)
Total	77 (7.5%)	176 (17.2%)	565 (55.3%)	203 (19.9%)	1021 (100%)
Chi-Square, P-value			30.830, 0.002		
Webex					
2nd Year	14 (7.6%)	33 (17.9%)	125 (67.9%)	12 (6.5%)	184 (100%)
3rd Year	15 (8.4%)	27 (15.2%)	123 (69.1%)	13 (7.3%)	178 (100%)
4th Year	18 (9.9%)	32 (17.7%)	111 (61.3%)	20 (11.0%)	181 (100%)
5th Year	12 (6.3%)	32 (16.9%)	133 (70.4%)	12 (6.3%)	189 (100%)
6th Year (Final Year)	21 (7.3%)	52 (18.0%)	199 (68.9%)	17 (5.9%)	289 (100%)
Total	80 (7.8%)	176 (17.2%)	691 (67.7%)	74 (7.2%)	1021 (100%)
Chi-Square, P-value			8.486, 0.746		
Moodle					
2nd Year	11 (6.0%)	35 (19.0%)	114 (62.0%)	24 (13.0%)	184 (100%)
3rd Year	12 (6.7%)	34 (19.1%)	121 (68.0%)	11 (6.2%)	178 (100%)
4th Year	21 (11.6%)	29 (16.0%)	105 (58.0%)	26 (14.4%)	181 (100%)
5th Year	10 (5.3%)	38 (20.1%)	133 (70.4%)	8 (4.2%)	189 (100%)
6th Year (Final Year)	37 (12.8%)	53 (18.3%)	164 (56.7%)	35 (12.1%)	289 (100%)
Total	91 (8.9%)	189 (18.5%)	637 (62.4%)	104 (10.2%)	1021 (100%)
Chi-Square, P-value			32.672, <0.001		
Email					
2nd Year	12 (6.5%)	46 (25.0%)	43 (23.4%)	83 (45.1%)	184 (100%)
3rd Year	15 (8.4%)	46 (25.8%)	50 (28.1%)	67 (37.6%)	178 (100%)
4th Year	23 (12.7%)	41 (22.7%)	71 (39.2%)	46 (25.4%)	181 (100%)
5th Year	15 (7.9%)	40 (21.2%)	68 (36.0%)	66 (34.9%)	189 (100%)
6th Year (Final Year)	22 (7.6%)	57 (19.7%)	112 (38.8%)	98 (33.9%)	289 (100%)
Total	87 (8.5%)	230 (22.5%)	344 (33.7%)	360 (35.3%)	1021 (100%)
Chi-Square, P-value			29.571, 0.003		

* Statistically significant if *P* value 0.05

Table V: Usefulness of different approaches in facilitating learning experience and success.

	Ranks					
	First	Second	Third	Fourth	Fifth	Total
Approach 1: Live-over PowerPoint presentations (Virtual classes)						
2nd Year	73 (39.7%)	51 (27.7%)	35 (19.0%)	18 (9.8%)	7 (3.8%)	184 (100%)
3rd Year	80 (44.9%)	46 (25.8%)	30 (16.9%)	10 (5.6%)	12 (6.7%)	178 (100%)
4th Year	79 (43.6%)	51 (28.2%)	27 (14.9%)	13 (7.2%)	11 (6.1%)	181 (100%)
5th Year	91 (48.1%)	33 (17.5%)	30 (15.9%)	21 (11.1%)	14 (7.4%)	189 (100%)
6th Year (Final Year)	120 (41.5%)	79 (27.3%)	50 (17.3%)	19 (6.6%)	21 (7.3%)	289 (100%)
Total	443 (43.4%)	260 (25.5%)	172 (16.8%)	81 (7.9%)	65 (6.4%)	1021 (100%)
Chi-Square, P-value			16.869, 0.394			
Approach 2: Recorded-over PowerPoint presentations (Offline/ Recorded classes)						
2nd Year	60 (32.6%)	57 (31.0%)	38 (20.7%)	10 (5.4%)	19 (10.3%)	184 (100%)
3rd Year	66 (37.1%)	52 (29.2%)	27 (15.2%)	22 (12.4%)	11 (6.2%)	178 (100%)
4th Year	65 (35.9%)	54 (29.8%)	35 (19.3%)	17 (9.4%)	10 (5.5%)	181 (100%)
5th Year	52 (27.5%)	52 (27.5%)	40 (21.2%)	23 (12.2%)	22 (11.6%)	189 (100%)
6th Year (Final Year)	77 (26.6%)	81 (28.0%)	67 (23.2%)	31 (10.7%)	33 (11.4%)	289 (100%)
Total	320 (31.3%)	296 (29.0%)	207 (20.3%)	103 (10.1%)	95 (9.3%)	1021 (100%)
Chi-Square, P-value			23.506, 0.101			
Approach 3: Live session to receive a presentation by the teacher (Seminars)						
2nd Year	56 (30.4%)	56 (30.4%)	45 (24.5%)	18 (9.8%)	9 (4.9%)	184 (100%)
3rd Year	55 (30.9%)	36 (20.2%)	52 (29.2%)	26 (14.6%)	9 (5.1%)	178 (100%)
4th Year	50 (27.6%)	48 (26.5%)	58 (32.0%)	18 (9.9%)	7 (3.9%)	181 (100%)
5th Year	48 (25.4%)	53 (28.0%)	55 (29.1%)	23 (12.2%)	10 (5.3%)	189 (100%)
6th Year (Final Year)	93 (32.2%)	70 (24.2%)	74 (25.6%)	31 (10.7%)	21 (7.3%)	289 (100%)
Total	302 (29.6%)	263 (25.8%)	284 (27.8%)	116 (11.4%)	56 (5.5%)	1021 (100%)
Chi-Square, P-value			14.495, 0.562			
Approach 4: Self-study using text and/or video materials provided by the teacher						
2nd Year	63 (34.2%)	45 (24.5%)	40 (21.7%)	23 (12.5%)	13 (7.1%)	184 (100%)
3rd Year	51 (28.7%)	29 (16.3%)	35 (19.7%)	46 (25.8%)	17 (9.6%)	178 (100%)
4th Year	40 (22.1%)	44 (24.3%)	40 (22.1%)	35 (19.3%)	22 (12.2%)	181 (100%)
5th Year	37 (19.6%)	46 (24.3%)	44 (23.3%)	41 (21.7%)	21 (11.1%)	189 (100%)
6th Year (Final Year)	71 (24.6%)	67 (23.2%)	66 (22.8%)	51 (17.6%)	34 (11.8%)	289 (100%)
Total	262 (25.7%)	231 (22.6%)	225 (22.0%)	196 (19.2%)	107 (10.5%)	1021 (100%)
Chi-Square, P-value			26.849, 0.043			
Approach 5: Assignments and homework						
2nd Year	37 (20.1%)	33 (17.9%)	32 (17.4%)	30 (16.3%)	52 (28.3%)	184 (100%)
3rd Year	23 (12.9%)	26 (14.6%)	33 (18.5%)	26 (14.6%)	70 (39.3%)	178 (100%)
4th Year	27 (14.9%)	37 (20.4%)	34 (18.8%)	33 (18.2%)	50 (27.6%)	181 (100%)
5th Year	14 (7.4%)	39 (20.6%)	29 (15.3%)	33 (17.5%)	74 (39.2%)	189 (100%)
6th Year (Final Year)	36 (12.5%)	46 (15.9%)	59 (20.4%)	53 (18.3%)	95 (32.9%)	289 (100%)
Total	137 (13.4%)	181 (17.7%)	187 (18.3%)	175 (17.1%)	341 (33.4%)	1021 (100%)
Chi-Square, P-value			24.804, 0.073			

* Statistically significant if *p*- value <0.05

Table VI: Comparison of agreement scores between students of the different academic year.

Domain	Academic Year	N	Mean	Std. Dev	F-Value	P-value
Students opinion regarding online classes (Average of 9 variables)	2nd Year	184	3.56	0.48	1.764	0.134
	3rd Year	178	3.43	0.56		
	4th Year	181	3.44	0.56		
	5th Year	189	3.49	0.56		
	6th Year (Final Year)	289	3.44	0.59		
	Total	1021	3.47	0.56		
Students opinion on live sessions, tools, materials, technical difficulties, etc. (Average of 8 variables)	2nd Year	184	3.27	0.48	1.655	0.158
	3rd Year	178	3.30	0.51		
	4th Year	181	3.29	0.53		
	5th Year	189	3.39	0.50		
	6th Year (Final Year)	289	3.33	0.48		
	Total	1021	3.32	0.50		
Students opinion comfortability with online classes and distress caused due to COVID 19 (Average of 7 variables)	2nd Year	184	3.26	0.50	4.169	0.002
	3rd Year	178	3.31	0.51		
	4th Year	181	3.13	0.51		
	5th Year	189	3.18	0.46		
	6th Year (Final Year)	289	3.16	0.48		
	Total	1021	3.20	0.49		

* Statistically significant if *P* <0.05

Discussion

Information technology has gained importance furthermore in the academic arena considering the ongoing pandemic, which has led to the closure of all educational institutions worldwide and thus gave rise to multiple challenges at all levels and stages in education, especially for students[5]. The cross-sectional online survey explored and assessed the impact of the COVID-19 global pandemic crisis on changing educational patterns among 1021 medical

students of various universities in Saudi Arabia. Many participants in the study reported that they were happy with the teacher's transition from offline classes to online classes during Covid-19 circumstances. Several universities worldwide support e-learning as a means of teaching, and it is highly accepted by the learners[6]. Many studies exist on comparing e-learning with face-to-face teaching. In one of the papers presented at a conference on mobile learning in Singapore, it was stated that the e-teaching technique limits the interaction between student and teacher[7]. This finding was in line with our research, where 52 percent of students thought e-teaching had limited contact between student and teacher. With many e-learning benefits, there are still some drawbacks of such as social isolation, lack of student-teacher interaction and communication issues, etc[8].

Analysis of the survey data allows us to state that 64% of students agree that distance teaching tools used by the teachers were easy to understand and use, considering the use of e-learning in the educational process is uniquely effective. As one of the studies suggests, students have a positive attitude towards e-learning, as they find the system easy to use and useful for their course work. And they get several benefits from e-learning; it allows them to organize the learning process in a better way and to use modern teaching tools effectively[9]. Many other studies also indicate numerous reasons for its overall acceptability are its ease of use, flexibility, and better control of the environment, especially applicable in the case of learners[8-10].

Further, findings showed that 55% of respondents reported that they were very much satisfied with e-learning provided by their institute, and 69% of students reported that their institutes provide them online support and orientation regarding the Covid-19 pandemic crisis. The institutional support for the implementation of e-learning has been reported to be important at all levels by the participants. According to some studies, top-down implementation from administrative to user level is an important and more sustainable strategic move[11,12].

Important to note that the analysis of the study reported 40% of medical students agreed that they experienced some sort of psychological distress during the online learning and the Covid-19 situation, and 60% were distracted by social media, and 45% were distracted by the Covid-19 crisis news. These findings suggest a significant impact of Covid-19 crises on student's mental wellbeing, which could be addressed by universities by taking appropriate measures such as organizing online meditation workshops for students.

Furthermore, computer and internet access are the primary learning/teaching instruments for online learners[13]. To test for e-learning readiness along with exposure to technology, the students were asked the related questions. The majority of the students had functioning internet services at their homes which help them for distance learning. It is argued in some studies that the attitude towards e-learning of 'students' can be evaluated in the following dimensions: study habits, skills, motivation, and their time management behaviour[13,14]. It was found that in the present study only 2.4% students stayed motivated for more than 4 hours and followed sessions and 30% said 'it depends upon the teacher,' about 35% of the students said 'they are not able to concentrate at home while studying.' Thus, measuring students' attitudes has an important role in analysing their behaviour. The study findings also reported significant differences of opinions among students of different academic years on the usefulness of different e-learning methods ranging from Blackboard to learn, Zoom, Microsoft teams, WebEx, Moodle, and emails. The majority of 6th-year medical students found Zoom technology a more apt e-learning tool. In one of the studies conducted among physicians actively engaged in ophthalmology-related education, it was noted that during the pandemic, there was a shift to distance learning, with Zoom being the preferred synchronous Tele-education platform, supporting a large number of participants and providing the opportunity to exchange material. The availability of e-learning facilities and institutional academic character were identified as correlated with Tele-education use[15].

The lower level of e-learning readiness using different approaches reported in this study among medical students of Saudi Arabia is contrary to the proposition Rogers 2003, that increase educational status has a positive influence on e-learning readiness. Findings of the study showed self-study using text and/or video materials provided by the teacher as a significant learning method in comparison to virtual classes, recorded sessions, seminars and assignments, and homework. Other studies have similar results to this research, and the reason for this may be that at higher levels of medical school study, students may be more preoccupied with passing exams using the method they are familiar with, which complements the conventional approaches used to the classroom[16]. Nevertheless, medical students showed significant differences as observed with comfortability with online classes and distress caused due to COVID-19. It shows medical students were able to cooperate and are ready to step beyond a predominant reliance on classroom instruction to the e-learning strategy. It is an increasingly common observation in medical education[17,18]. All in all, the findings of this study can be improved as a part of a detailed strategy for most medical schools in the coming years to increase the scope and quality of their e-learning programs[19].

COVID-19 is an infectious disease with high economic and social burden[20-23]. Findings from the current study suggest some important factors to consider when planning

the implementation of e-learning at medical universities in times of severe emergencies such as Covid-19. Factors including economic, gender and cultural issues need to be further explored, particularly when assessing organizational capacity to address changing educational demands[24,25]. Limitations of the validity of the present study that must be highlighted include finding that not all of the medical schools listed had received responses. Furthermore, the option to leave some questions blank meant that the number of answers obtained variated. In addition, the students' geographical and academic backgrounds were considered inhomogeneous, and this may have influenced their understanding and perceptions as a confounding variable in answering the questions. The questions used in the will provide only a brief representation of the different scenarios in individual disciplines at various universities. Finally, the discussion on the implementation of technology in education spotlights largely on students' perspectives rather than on teachers' views.

Conclusion

In a nation such as the Kingdom of Saudi Arabia (KSA), where education is one of the administration's highest priorities, there is a burning need to investigate the expertise of the students on online education. It is extremely necessary to analyze the views of the students and their perspectives on virtual courses, which will be helpful in producing a more enjoyable and productive education. The findings showed acceptable results showing that respective medical universities of Saudi Arabia provided good online support and orientation regarding the COVID 19 crisis, and students were finding distance learning tools easy to use and understand. At the same time, this study showed no significant association of student's opinions on tools, materials, live sessions, degree of program competency, as well as the perceived value of using different e-learning methods in medical education.

Thus, it is concluded that despite gaining immense popularity today, digital technology has not yet been embraced for use in teaching by medical students. Future steps would be taken based on the findings from the study, and further improvement would be implemented to make the learning process easier for medical students. Furthermore, administrative and staff leaders should take the appropriate steps to increase the standards and acceptance level of e-teaching to further improve student learning during the lockdown.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Credit statement

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ORIGINAL

Evaluation of the effectiveness of COVID-19 treatments performed in Iran in comparison with other countries: A review

Evaluación de la efectividad de los tratamientos COVID-19 realizados en Irán en comparación con otros países: una revisión

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Abstract

The treatment of COVID-19 has been one of the most important discussions in the scientific community for the last two years. Coronaviruses have seriously invaded human populations two times before December 2019 in the form of MERS and SARS diseases. Epidemiological findings show that the virus creates different and dangerous variants through new mutations, which make the definitive treatment more difficult. Molecular biologists have stated that as mutations continue, the vaccines would only provide immunity for one year, and the development of new vaccines should be on the agenda. But one of the major problems of developing countries is the lack of facilities such as vaccination, which has caused many problems for the medical staff in these countries. The findings showed that the use of some therapies, such as Remdesivir combined with standard treatment, has shown high therapeutic effectiveness; however, therapeutic side effects such as decreased glomerular filtration rate, decreased lymphocyte count, respiratory failure, and increased blood creatinine levels, have been observed in most patients. Also, paying attention to nutrition and immune-boosting factors can be effective in reducing the risk of contracting the virus.

Keywords: Corona medications, therapeutic efficacy, effectiveness of treatment, Covid-19, Coronavirus.

Resumen

El tratamiento del COVID-19 ha sido uno de los debates más importantes en la comunidad científica durante los dos últimos años. Los coronavirus han invadido gravemente las poblaciones humanas en dos ocasiones antes de diciembre de 2019 en forma de enfermedades MERS y SARS. Los hallazgos epidemiológicos muestran que el virus crea diferentes y peligrosas variantes a través de nuevas mutaciones, que dificultan el tratamiento definitivo. Los biólogos moleculares han afirmado que, al continuar las mutaciones, las vacunas sólo proporcionarían inmunidad durante un año, por lo que el desarrollo de nuevas vacunas debería estar en la agenda. Pero uno de los principales problemas de los países en vías de desarrollo es la falta de instalaciones como la de vacunación, que ha causado muchos problemas al personal médico de estos países. Los resultados mostraron que el uso de algunas terapias, como el Remdesivir combinado con el tratamiento estándar, ha mostrado una gran eficacia terapéutica; sin embargo, en la mayoría de los pacientes se han observado efectos secundarios terapéuticos como la disminución de la tasa de filtración glomerular, la disminución del recuento de linfocitos, la insuficiencia respiratoria y el aumento de los niveles de creatinina en sangre. Asimismo, prestar atención a la nutrición y a los factores de refuerzo inmunitario puede ser eficaz para reducir el riesgo de contraer el virus.

Palabras clave: Medicamentos contra Coronavirus, eficacia terapéutica, eficacia del tratamiento, Covid-19, Coronavirus.

Introduction

Coronaviruses (CoVs) are a group of enveloped viruses that cause various respiratory and gastrointestinal diseases in humans and animals[1]. Human coronaviruses cause one-third of colds in adults and in many cases cause mild diseases, but the new coronavirus (SARS_CoV-2) has become a dangerous virus by inducing new mutations in its genome. The virus binds to the antigens of squamous cells of the respiratory tract and causes pathogenesis[2-4]. The transmission rate of the new coronavirus is very high, and it is now affecting all countries of the world[5,6]. According to the World Health Organization, by mid-May 2021, more than 190 million people worldwide have been infected with the disease, of which about four million have died[7,8].

Age, underlying diseases such as heart failure, diabetes, chronic lung disease, hypertension, cancer, brain disease, kidney disease, liver disease, diabetes are among the underlying risk factors[9-14]. The virus is transmitted through respiratory droplets from sneezing and coughing, and the incubation period of the disease is about 7 to 14 days[15]. Considering the spread of patients and acute complications of the disease, evaluation of effective treatments in highly important.

In the present study, the author tries to provide effective treatment strategies by examining routine treatments inside and outside the country. For this purpose, in May 2021, an electronic research was performed in the scientific databases of Nature, PubMed, Medline and existing valid published articles, using the keywords of Corona medications, Therapeutic efficacy, Effectiveness of treatment, Covid-19, Coronavirus.

Clinical symptoms of Covid-19

The disease may occur with four different severities, namely mild, moderate, severe and critical patients (Acute Respiratory Distress Syndromes, ARDS)[1+]. The most common symptoms at the onset of the disease have been reported to be fever, cough, fatigue or myalgia, sputum, and headache. Among hospitalized patients, 32% develop acute respiratory distress syndrome (ARDS), 32% require intensive care, and 15% die[17,18]. Another study showed that approximately 20 to 30% of hospitalized Covid-19 patients, required intensive care for respiratory support due to pneumonia, of which 4.42% required advanced support of organs with endotracheal intubation and mechanical ventilation[13,19]. Although the virus majorly affects the respiratory and cardiovascular systems, neurological symptoms such as headache, dizziness, decreased sense of smell and taste, and nerve pain have also been observed in patients with severe symptoms[20]. Findings of computerized tomography (CT) scan of the chest also demonstrated bilateral involvement in most patients[21].

Transmission of Covid-19

Two main pathways are identified for the transmission of the coronavirus disease:

1) Direct transmission (through coughing, sneezing and inhalation of respiratory droplets)
2) Contact transmission (through contact with nasal, oral and ocular mucosa)[16].

Studies have shown that respiratory viruses are generally transmitted through respiration, and the coronavirus disease may also be transmitted from human to human through direct or indirect contact with respiratory droplets or through saliva[22]. The volume of the virus in the air is an important issue in the transmission of the virus so that in crowded environments, viruses adhere together as particles and are transmitted in large numbers[23]. New evidence suggests that the coronavirus is most often transmitted through respiratory droplets or microdroplets[24,25]. These cases indicate that attention to air conditioning will play an important role in reducing the risk of infection.

Certainly, paying attention to the factors that reduce the viral population is an important issue in reducing infection in hospitals. Studies show that the survival time of the virus is up to two days in chlorine-free water at 20°C, and this rate is much lower in chlorinated water. Survival of the virus on surfaces also depends on temperature, humidity, and light conditions. The virus is sensitive to sunlight and survives for a short time[26,27].

Common treatments

Domestic and foreign studies on medications and their therapeutic efficacy can be seen in **tables I** and **II**.

Foreign studies

In a study by Khan, Misdary et al.[28] on patients admitted to Robert Wood Johnson Hospital, 92 patients were analyzed, 30 of whom, from the first day of hospitalization, were treated with a standard dosage (10 mg) of oral montelukast once a day, and 62 patients in the control group did not receive the medication. The approved standard treatment of COVID-19 included the use of 400 mg hydroxychloroquine for 5 days and azithromycin. Patients receiving montelukast experienced significantly less clinical deterioration compared with controls (10% vs. 32%, respectively). The findings of this clinical trial showed that montelukast reduces the clinical severity of COVID-19 and could have a clinical effect in reducing the complications of this disease. With further evaluation, montelukast may be a potential treatment for COVID-19 infection[28].

Table I: Covid-19 treatments outside of Iran.

Foreign studies			
Type of treatment	**Study population**	**Treatment efficiency**	**Author(s)**
Montelukast combined with standard treatment	92 patients (30 in the treatment group, 62 in the control group)' the mean age was 67 years in the treatment group, and 59 years in the control group	Montelukast combined with standard treatment	[32]
Lithium carbonate combined with standard treatment	9 patients (6 people in the treatment group, 3 people in the control group). The mean age was 56 years in the treatment group and 65 years in the control group	Zero deaths in the treatment group and 1 death in the control group Decreased CRP, severe reduction in NLR, and decreased PLR	[33]
Tocilizumab (TCZ), a human monoclonal antibody, combined with standard treatment	65 patients (32 people in the treatment group, 32 people in the control group)' the mean age in the treatment group was 65 and in the control group was 60 years	5 deaths in treatment group and 11 in control group	[34]
Remdesivir combined with standard treatment	1062 patients (541 in the treatment group, 521 in the control group), mean age: 58.9±15	Mortality rate was 6.7% in the treatment group and 11.9% in the control group on day 15, and 11.4% in the treatment group and 15.2% in the control group by day 29. The most common unpleasant side effects that were observed in at least 5% of patients included decreased glomerular filtration rate, decreased hemoglobin level, decreased lymphocyte count, respiratory failure, anemia, pyrexia, hyperglycemia, elevated blood creatinine, and elevated blood glucose levels	[35]

In a study by Spuch, López-García et al., the effect of lithium carbonate on nine patients with severe COVID-19 infection was investigated. All patients received hydroxychloroquine for 5 days, and lopinavir-ritonavir as a combination therapy for 14 days. The findings of this study demonstrated that lithium carbonate significantly improved inflammatory activity and immune response in these patients by significantly decreasing the level of C-reactive protein (CRP) in plasma, increasing the number of lymphocytes, and decreasing neutrophil cells, and thus reducing the neutrophil to lymphocyte ratio (NLR); Similar to the NLR, the platelet-to-lymphocyte ratio (PLR) also decreased. It should be noted that lithium carbonate treatment improved all three parameters that were unchanged in the control group and no side effects related to lithium carbonate treatment were reported. All six patients who were treated with lithium carbonate survived, and one of the three patients of the control group died. They suggested that lithium carbonate treatment may be a new method for treating COVID-19 patients[29].

In another study, tocilizumab (TCZ), a human monoclonal antibody that targets the interleukin-6 receptor, was compared with the standard treatment of Covid-19. In all patients, for standard care, hydroxychloroquine 400 mg daily, lopinavir/ritonavir 100/400 mg twice daily, ceftriaxone 2 g for 6 days, azithromycin 500 mg daily, and subcutaneous injection of anticoagulant prophylaxis with enoxaparin 4000 UI once a day, were used. Tocilizumab was injected intravenously at a dose of 400 mg 24 hours after the first injection. On day 28, clinical improvements and mortality rates were not statistically different between the patients treated with tocilizumab and standard treatment. Bacterial or fungal infections were also recorded in 13% of tocilizumab patients and in 12% of standard treatment patients. They stated that there was no significant improvement in patients receiving tocilizumab compared to standard treatment, and in order to assess long-term risks, close monitoring on infectious side effects is required[30].

In a study by Beigel, Tomashek et al., 1062 patients were evaluated, of which 159 were in moderate condition and 903 were in severe condition of the disease (oxygen saturation ≤ 94%, respiration rate ≥ 24 breaths per minute). All patients received a standard care plan. Then, patients were randomly selected to receive Remdesivir (200 mg loading dose on day 1 and then 100 mg daily for up to 9 additional days) or placebo for up to 10 days or until discharge. Their data showed that Remdesivir reduced recovery time in adults, who were hospitalized with Covid-19 and had evidence of lower respiratory tract infection, from 15 days to 10 days. Serious side effects, such as acute respiratory failure, were reported in 131 of 532 patients in the treatment group (24.6%) and in 163 of 516 patients in the control group (31.6%)31.

Domestic studies

In a study by Abbaspour et al., the effect of treatment with sofosbuvir / daclatasvir and ribavirin was investigated; 48 patients were divided into two groups of treatment and control, and the treatment group received sofosbuvir / daclatasvir once a day at a dose of 400.60 mg and ribavirin at a dose of 600 mg twice a day. According to the national guidelines, the control group received hydroxychloroquine (400 mg single dose) and lopinavir/ritonavir (400/100 mg twice daily),

with or without ribavirin (600 mg twice daily). The age group was between 18 and 80 years, and the severity of the disease was moderate (respiratory rate ≥ 24 breaths per minute; arterial O2 saturation < 94%; the manifestation of symptoms 8 days before admission, with consistent findings in chest CT scan). The study period was 21 days for the control group and 24 days for the treatment group. This randomized trial was too small for a definitive conclusion. Signs of improvement and reduced mortality were seen in the sofosbuvir/daclatasvir/ribavirin group. However, there was an imbalance in terms of basic features between different treatment groups. Larger randomized trials should be performed to further investigate this treatment process[36].

Another study examined the effect of convalescent plasma (CP) and standard treatment on Covid-19 patients. Patients were randomly divided into two groups for this clinical trial. Patients in the treatment group received one unit (500 ml) of convalescent plasma on the day of admission in addition to standard care, and the control group received only standard treatments. The mean age was 53.5 ± 10.3 years in the treatment group and 57.2 ± 17 years in the control group and the time of onset of symptoms was less than 7 days. Blood oxygen saturation was ≤ 93%, which was measured in room air. The results showed that the immune response was reduced in the plasma receiving group, but the length of hospital stay and mortality rate were similar in the two study groups[37].

In a study by Sadeghi et al., the effect of treatment with sofosbuvir/daclatasvir along with national standard care (hydroxychloroquine 200 mg twice daily with or without lopinavir/ritonavir 200/ 50 mg twice daily) was investigated. The mean age of patients was 58 years and they were selected from Shariati, Baharloo, Sina (Tehran), and Sayad Shirazi (Gorgan) hospitals. Patients with symptoms of moderate or severe COVID-19 infection were studied (fever above 37.8°C, respiration rate less than 24 breaths per minute, oxygen saturation below 94%, and the onset of symptoms in 8 days or less). The results showed that clinical improvements were observed in 29 of 33 patients (88%) in the treatment group and 22 of 33 patients (67%) in the control group, within 14 days of treatment; the average duration of hospitalization was 6 days for the treatment group and 8 days for the control group. The addition of sofosbuvir and daclatasvir to standard care significantly reduced the length of hospital stay compared to standard care alone. Although fewer deaths were observed in the treatment process, the difference was not statistically significant. Larger-scale trials are required to further investigate this treatment method[38].

In a study of Valizadeh et al. on patients with coronavirus disease, the treatment group received 160 mg of nano-curcumin daily in form of four 40 mg capsules for 14 days, and the control group received placebo capsules. In addition, all subjects in both groups received 300 micrograms of betaferon subcutaneously for up to 5 days, bromhexine 8 mg tablets every 8 hours, and atorvastatin 40 mg daily. Finally, the mortality rate in the nano-curcumin group was 20% (4 out of 20) and in the placebo group was 40% (8 out of 20). This study showed that nano-curcumin, by regulating the inflammatory response, may be used as an innovative therapeutic agent for COVID-19 patients, and might be able to reduce mortality, possibly by modulating cytokines in these patients[39].

The role of nutrition, vitamins, and antioxidants in the treatment

The most important role of vitamins is their positive effect on health and the strengthening of the immune system. Findings in Iran show that vitamins A B, C, D, and E have a positive effect on reducing mortality of COVID-19 patients[43].

B vitamins:

They are a group of vitamins that play a role in the metabolism of all cells. Vitamin B2 deficiency is widely

Table II: Covid-19 treatments inside of Iran.

Domestic studies			
Type of treatment	**Study population**	**Treatment efficiency**	**Author(s)**
Sofosbuvir 400 mg, daclatasvir 60 mg and ribavirin 1200 mg	48 patients (24 patients in the treatment group, 24 patients in the control group)' age range between 18 and 80 years	3 deaths were observed in the control group and no deaths were seen in the treatment group.	[40]
sofosbuvir/daclatasvir along with national standard care (hydroxychloroquine 200 mg twice daily with or without lopinavir 200 mg / ritonavir 50 mg)	66 patients (33 patients in the control group, 33 patients in the treatment group). The average age of patients was 58 years	3 deaths in the treatment group and 5 deaths in the control group	[38]
Study of the effect of convalescent plasma (CP); Donors were recovered individuals in the age range of 20-45 years with an asymptomatic recovery period of at least 2 weeks.	62 patients (in control and treatment groups) in the mean age was 53.5 ± 10.3 in the treatment group and 57.2 ± 17 in the control group	3 deaths in the treatment group and 5 deaths in the control group	[41]
Treatment with nano-curcumin	40 patients (20 in the control group, 20 in the treatment group)' age range between 19 and 69 years.	4 deaths in the treatment group and 8 deaths in the control group	[42]

observed in the elderly in the United States[44]. Also, Vitamin B3 or nicotinamide can boost the ability of immune cells to kill Staphylococcus aureus through a specific myeloid transcription factor and is effective in treatment[45]. In addition, vitamin B3 with a strong anti-inflammatory effect inhibits neutrophil infiltration into the lungs that are damaged due to ventilation[46]. Therefore, B vitamins can be used as a suitable option for reducing harmful microbes and boosting the immune system in selected patients. As mentioned, vitamin B2 deficiency has been observed in the elderly to a large extent, which is a highly important issue for this age group due to their vulnerability to coronavirus disease.

Vitamin D:

Vitamin D modulates adaptive immunity that plays an important role in the detection of viruses[47]. This vitamin regulates inflammatory responses of T helper cells by inhibiting the production of inflammatory cytokines IL-2 and interferon-gamma (INFγ)[48]. Serum vitamin D concentrations, which decrease with age[49], are an important factor in Covid-19 mortality rates in the elderly[14]. Also, vitamin D supplementation increases the expression of genes associated with antioxidants (some enzymes such as glutathione reductase)[50].

One study found that T cell levels were low in many COVID-19 patients and could be increased with vitamin D supplementation. In addition, vitamin D deficiency is associated with an increase in inflammatory cytokines and a significant increase in the risk of pneumonia and viral upper respiratory tract infections[51]. Vitamin D deficiency is associated with increased thrombotic events, which are often seen in patients with coronavirus disease. Also, vitamin D deficiency has been reported to occur more frequently in obese and diabetic patients, who are more likely to die from COVID-19[52, 53].

Therefore, due to the anti-inflammatory properties of vitamin D, it can be considered as a suitable option to reduce inflammation and increase the function of the immune system in treated patients.

Vitamin E:

Vitamin E as an antioxidant by binding to free radicals plays an important role in reducing oxidative stress[54]. Increased oxidative stress is observed in people with severe inflammation. Findings have shown the effective role of vitamin E supplementation along with other vitamins in reducing mortality in patients with coronavirus disease[43]. As a result, the use of antioxidants such as vitamin E in the diet of people exposed to the virus can be effective in boosting their immune systems.

Zinc:

Zinc is an essential substance in cellular functions and the development of the body largely depends on the presence of this substance. The immune system is greatly affected by the level of zinc in the body. Many enzymes and many important cellular proteins involved in biological cycles contain zinc in their structure. Zinc deficiency reduces the function of enzymes that are effective in inflammation and improvement of injuries and chronic diseases. Bone marrow stem cells require zinc to express immune genes and produce immune cells such as B lymphocytes[55-57]. The study of the effect of zinc in patients with coronavirus disease demonstrated that this mineral has been effective in reducing inflammation and cytokine response[58]. Certainly, measurement of zinc levels in patients and addition of zinc supplementation in the diet of patients can have beneficial effects on the prevention and treatment of COVID-19.

Nutrition and antioxidants

Antioxidants have beneficial structures that prevent further intercellular oxidation and inflammation, and this affects the metabolism and better function of cells[16]. Studies have shown that the use of antioxidants as adjunctive therapy in patients with Covid-19 has a beneficial effect on reducing the severity of the disease and improving the condition of patients[59,60]. Free radicals cause cytotoxicity and damage cells. Studies have shown that the use of herbal antioxidants, with a positive effect on the immune system, oxygen delivery, and glutathione levels in patients with lung diseases, reduces the time of mechanical ventilation, length of stay in the intensive care unit, length of hospitalization, and mortality rates; therefore, they can also help patients with coronavirus disease. However, for prescription, effective doses of herbal antioxidants should be considered[61]. Certainly, not all antioxidants provide a 100% recovery for patients with coronavirus disease, but this issue needs to be further investigated.

Immune System

Strengthening the immune system is probably one of the most important factors in improving the disease. The innate immune system is made up of mucus and the body's first defense layers, and the adaptive immune system directly detects pathogens and causes the death of viruses. Many studies have been performed on strengthening the immune system and, as mentioned, vitamins and nutrition are of particular importance in this field[43-54]. Findings show that COVID-19 initially affects the immune system by increasing the inflammatory response, and during the treatment process, attention to reducing the inflammatory response and increasing immune-boosting factors can be effective in reducing the severity of the disease and mortality rate[62].

Research has shown that all people who suffer from certain illnesses, even colds, are exposed to levels of cellular oxidative stress; reducing oxidative stress is an important issue in controlling inflammation, and antioxidants can be highly effective in this field[63-66]. As a result, strategies to reduce cellular stress in patients and the use of antioxidants would certainly be helpful in boosting the immune system and reducing severe cases of the disease. COVID-19[67-69], similar to many infectious diseases[70-80] caused serious morbidity among Iranians. However, diverse treatments have been reported in Iranian investigations[81].

Conclusion

The findings showed that the use of some therapies, such as Remdesivir combined with standard treatment, has shown high therapeutic effectiveness; however, therapeutic side effects such as decreased glomerular filtration rate, decreased lymphocyte count, respiratory failure, and increased blood creatinine levels, have been observed in most patients. Also, paying attention to nutrition and immune-boosting factors can be effective in reducing the risk of contracting the virus.

In addition, due to therapeutic expectations, the study and introduction of new drugs with greater effectiveness should be considered.

Interests conflict

The researchers declare that they have no conflict of interest.

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ORIGINAL

Effectiveness of acceptance and commitment therapy on depression, anxiety and quality of life in women after childbirth in Ardabil

Efectividad de la terapia de aceptación y compromisosobre depresión, ansiedad y calidad de vida en mujeres después del parto en Ardabil

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Abstract

Introduction: Pregnancy is an important event in every woman's life that is associated with conflicting feelings. Acceptance and Commitment Therapy (ACT) is one of the new therapies that has a positive effect on decreasing psychological complications during and after pregnancy. Therefore, the present research aims to investigate the effectiveness of acceptance and commitment therapy on depression, anxiety, and quality of life in women after childbirth.
Methodology: In this quasi-experimental study with a pretest-posttest design with a control group, 40 mothers with delivery of 0 to 6 months admitted to Ardabil health centers in 2018 were investigated. The convenience sampling method was performed and the subjects were randomly divided into two experimental and control groups of 20. Edinburgh Postnatal Depression Scale, Spielberger Anxiety Inventory and Quality of Life Questionnaire (sf-36) were used to collect data. The experimental group underwent acceptance and commitment therapy in a group format for 8 sessions of 2 hours and the control group did not receive any therapy.
Findings: Our results showed that there was a statistically significant difference between the experimental and control groups in scores of depression, anxiety, and quality of life after ACT (P <0.001).
Conclusion: Acceptance and commitment therapy is effective on depression, anxiety, and quality of life in women after childbirth and the results emphasize the importance of using these interventions in depression and anxiety and improving quality of life and providing new horizons in clinical interventions of these women.

Keywords: Depression, anxiety, acceptance and commitment therapy.

Resumen

Introducción: El embarazo es un acontecimiento importante en la vida de toda mujer que está asociado a sentimientos conflictivos. La terapia de aceptación y compromiso (ACT) es una de las nuevas terapias que tiene un efecto positivo en la disminución de las complicaciones psicológicas durante y después del embarazo. Por lo tanto, la presente investigación tiene como objetivo investigar la eficacia de la terapia de aceptación y compromiso sobre la depresión, la ansiedad y la calidad de vida en las mujeres después del parto.
Metodología: En este estudio cuasi-experimental con un diseño pretest-postest con un grupo control, se investigaron 40 madres con parto de 0 a 6 meses ingresadas en los centros de salud de Ardabil en 2018. Se realizó el método de muestreo de conveniencia y los sujetos se dividieron aleatoriamente en dos grupos experimental y de control de 20 sujetos. Se utilizaron la Escala de Depresión Postnatal de Edimburgo, el Inventario de Ansiedad de Spielberger y el Cuestionario de Calidad de Vida (sf-36) para recoger los datos. El grupo experimental se sometió a una terapia de aceptación y compromiso en formato grupal durante 8 sesiones de 2 horas y el grupo de control no recibió ninguna terapia.
Resultados: Nuestros resultados mostraron que había una diferencia estadísticamente significativa entre los grupos experimental y control en las puntuaciones de depresión, ansiedad y calidad de vida después de la TCA (P <0,001).
Conclusión: La terapia de aceptación y compromiso es eficaz en la depresión, la ansiedad y la calidad de vida de las mujeres después del parto y los resultados enfatizan la importancia de utilizar estas intervenciones en la depresión y la ansiedad y en la mejora de la calidad de vida y proporcionan nuevos horizontes en las intervenciones clínicas de estas mujeres.

Palabras clave: Depression, ansiedad, terapia de aceptación y compromiso.

Introduction

Pregnancy is an important event in a woman's life that is associated with two opposite feelings of happiness and anxiety[1]. These dual natural feelings arise as a result of biological, social and psychological changes in women during pregnancy[2]. It has been shown that the birth of a child can have a significant effect on a woman's personal mood. Hence, many women face physiological and hormonal changes as well as the need for psychological adjustment during the pregnancy process and the postpartum period[3]. Postpartum mental health has been identified by the World Health Organization as an important public health issue and it has been reported that at least 1 in 10 women develops serious mental health problems during pregnancy or one year after delivery[4].

Pregnancy-related anxiety is a negative emotion that is associated with a variety of concerns, including concerns about when and where to give birth, maternal health during pregnancy and childbirth, postpartum health, infant health, and birth of an abnormal infant, loss of attractiveness to the spouse and dual feelings about caring for the newborn and the role of[5,6] . According to the WHO reports, approximately 10% of pregnant women and 13% of women who have just given birth struggle with mental health, and in developing countries numbers rise up to 15.6% and 19.8%, respectively[7]. It has also been shown that the prevalence of anxiety in women in the first month after delivery is over 30%, which increases the risk of postpartum depression if it continue[8,9]. Postpartum depression includes a major depression and the simultaneous presence of five symptoms, including physical disorder, insomnia, negative feelings about the infant, lack of enjoyment of life, depressed mood and inability to care for the infant, with at least one of these symptoms being in activities. These symptoms must last for at least two weeks and begin within four weeks after delivery[10,11]. Therefore, any mental disorder of mothers has a negative effect on the quality of life and health of family, primarily children, and the daily needs of children and the level of care required such as breastfeeding and attachment of mother and baby may be affected by mental disorder[8,12].

Therapists have used various psychotherapies to reduce mental disorders, including depression, anxiety, and consequently quality of life, along with pharmacotherapy. However, in the last decade, according to numerous reports on the remarkable effectiveness of mindfulness-based therapies, attention has turned to these therapies. One of these mindfulness-based therapies is the Acceptance and Commitment Therapy (ACT) approach. This therapy helps the individual to cope with stressful situations by increasing mindfulness, cognitive distancing (observation of thoughts) and creating a commitment to active involvement in the outside world and striving for a meaningful and authentic life with the aim of increasing psychological flexibility[13,14].

In ACT, the patient is helped to accept the pain caused by unpleasant thoughts and feelings and promises that pain is an inevitable aspect of life and tries to prevent suffering from pain as a more unpleasant feeling. What sets ACT apart from other therapies is the use of simile and metaphor, which make therapy sessions more interactive and dynamic for patients[15].

Therefore, according to reports that this approach is effective on many disorders such as depression and anxiety and improving the quality of life, the present research aims to investigate the effectiveness of acceptance and commitment therapy on depression, anxiety, and quality of life in women after childbirth.

Materials and methods

Selection of patients

In this quasi-experimental study, which was in the form of two groups (one experimental group and one control group) with pre-test and post-test, all women in Ardabil province (0-6 months after delivery) admitted to Ardabil health centers in 2018 were investigated. The independent variable in this study was acceptance and commitment therapy (ACT) and the dependent variables were depression, anxiety, and quality of life. Convenience sampling method was used to obtain research samples. The statistical sample size included 40 people, 20 of whom were randomly investigated in the experimental group and 20 in the control group. To conduct research, first, the necessary permits were obtained from Ardabil University of Medical Sciences, then we randomly referred to several health centers in Ardabil.

The study groups were provided with questionnaires. Then, the experimental group underwent acceptance and commitment therapy (ACT) as a group during 8 weekly sessions and one 2-hour session (**Table I**). The control group also waited for therapy after the end of the two-month therapy period for the intervention group and did not undergo any intervention in this two-month period. After the end of the therapy period, the intervention group answered research questionnaires and at the end of each therapy session, a summary of that session was again given to the subjects.

Measuring tools

Edinburgh Postnatal Depression Scale

Edinburgh Depression consists of 10 questions on a 4-point scale that assesses a person's mental state over the past 7 days. The questionnaire was developed by Cox in 1987 in 10 items to diagnose postnatal depression. With a score of 10 or higher for the assessment of postnatal depression, the Edinburgh Scale has a sensitivity of 84% -100% and a specificity of 82% -84%. The reliability of the Postnatal Depression Scale was 93% by retest method.

Table I: Acceptance and commitment therapy sessions in the intervention group.

Session 1
Getting familiar with group members and establishing a therapeutic relationship, introducing members to the research topic, discussing the limits of secrecy, examining depression, anxiety and quality of life of each subject after childbirth, including the duration of illness and the therapies used, general assessment and examination of disturbing thoughts and feelings in group members, measuring ways to control these thoughts and feelings, introduction to hopelessness, giving assignments, answering questionnaires.
Session 2
Feedback from the first session, reviewing the previous session assignment and discussing it, continuing creative hopelessness, evaluating the modern and outside world in ACT, creating the tendency to abandon the dysfunctional program of change, understanding that control is the problem, not the solution, and expressing the introduction of an alternative to control, i.e. tendency.
Session 3
Feedback from the second session and reviewing the reaction to the previous session, continuing the topic of tendency using metaphors and allegories of ACT, introducing values and identifying values of individuals and relating and understanding the concept of tendency along with the concept of values, giving assignment
Session 4
Feedback from the third session and reviewing the reaction to the previous session, evaluating the values of each individual, specifying values, goals, actions and internal and external obstacles and deepening these concepts, introduction to the concept of defusion, giving assignment.
Session 5
Feedback from the fourth session and reviewing the reaction to the previous session, understanding fusion and defusion using ACT metaphors and allegories, and performing experimental exercises to understand the concept of defusion, introducing mindfulness, and performing one of the mindfulness exercises, giving assignment.
Session 6
Feedback from the fifth session and reviewing the reaction to the previous session, introducing the types of fusion, self-conceptualized concept and teaching how to defuse from it, pointing to values and examining the compliance score, performing one of the mindfulness exercises.
Session 7
Feedback from the sixth session and reviewing the reaction to the previous session, introduction to the fusion with the life story, mindfulness and emphasis on being in the present, pointing to values and the concept of commitment to values.
Session 8
Feedback from the seventh session and reviewing the reaction to the previous session, examining the concept of self-observer and summarizing the previous sessions and emphasizing the main processes of acceptance and commitment therapy, i.e. acceptance, defusion, self as context, being in the present, values and committed action.

Spielberger State-Trait Anxiety Inventory

The Spielberger State-Trait Anxiety Inventory, known as the STAI, includes separate self-assessment scales to measure both state and trait anxiety. The state anxiety scale (STAI Form Y-1) consists of twenty statements that evaluate the person's feelings feels at this moment and the response language. The trait anxiety scale (STAI Form Y-2) consists of twenty statements that evaluate the person's general and regular feelings. Regarding the validity of this questionnaire on 150 patients undergoing surgery, the reliability of 97% was reported that the validity and reliability of these studies are the basis of the present research.

Quality of Life Questionnaire (sf-36)

This scale has 36 questions that consist of eight subscales and each subscale consists of 2 to 10 items. The eight subscales of this questionnaire are: physical functioning (PF), role disorder due to emotional health (RE), energy/fatigue (EF), emotional well-being (EW), social functioning (SF), pain (P) and general health (GH). It is also obtained from the integration of subscales into the general scale called physical health and mental health. In this questionnaire, a low score indicates a lower quality of life and vice versa. The validity and reliability of this questionnaire were evaluated in the study of determining the reliability and validity of the Persian version of the standard instrument (SF-36). Reliability test was carried out using the statistical method of internal consistency on the questionnaire scale by determining the Cronbach's alpha coefficient. The coefficient value of 0.7 and higher was considered appropriate. The validity test was carried out using the statistical method of known groups comparison. Convergence validity test was carried out to evaluate the measurement hypotheses using the correlation of each question with its hypothesized scale. The Pearson correlation coefficient value of 0.4 or higher was considered desirable.

Data analysis

Data were analyzed by SPSS software version 25 (version 25, SPSS Inc., Chicago, IL). Frequency, relative frequency and central mean index were used for descriptive statistics, and analysis of covariance (ANCOVA) was used to compare quantitative and qualitative variables in the two groups. Finally, P less than 0.05 was considered statistically significant.

Results

The demographic results of our study showed that in the experimental group most patients (14 patients, 70%) had associate and bachelor's degrees, and in the control group 80% (18 patients) had diploma and lower education. Also, the frequency distribution based on the month of delivery showed that in the experimental group 60% of patients were in the fourth month and more of delivery, and in the control group 50% of patients were in the first month of delivery (**Table II**).

According to the results of **table III**, the mean and (standard deviation) scores before the intervention and after the intervention were evaluated for the experimental group and the control group related to quality of life, depression and anxiety scores.

One of the assumptions of the analysis of covariance is the normal distribution of data. Kolmogorov-Smirnov test was used to test this hypothesis.

The results of this test in **table III** to evaluate the assumption of normality of data distribution indicate that the scores of quality of life, postnatal depression, and anxiety follow the assumption of normality (P> 0.05).

Also, according to **table IV**, mental health and social adjustment were not significant in any of the research scales in Levin test; therefore, it can be said that both groups were homogeneous in terms of variance before the intervention (P> 0.05).

Based on the results of univariate analysis of covariance in **table V**, there was a statistically significant difference between the experimental and control groups in scores of postnatal depression (P <0.000, F=7.057), trait anxiety (P <0.000, F=58.55), state anxiety (P <0.000, F=19.40), and quality of life of women (P <0.000, F=16.13) after ACT.

The results of **table VI** also showed that there was a statistically significant difference between the experimental and control groups in the scores of depression, anxiety and quality of life after ACT (P <0.000, F=22.97).

Table II: Frequency distribution of studied samples in terms of education and month of delivery.

Variables		Experimental group		Control group	
		N	%	N	%
Education	Diploma and lower	2	10	18	80
	Associate and Bachelor	14	70	2	10
	Master and above	4	20	70	0
	Total	20	100	20	100
Month of delivery	1	0	0	10	50
	2	5	25	4	20
	3	3	15	1	5
	4 and above	12	60	5	25
	Total	20	100	20	100

Table III: Mean and standard deviation for scores of quality of life, and postnatal depression and anxiety.

Type of training Scale/subscales	Before intervention		After intervention	
	Experimental group Mean Standard deviation	Control group Mean Standard deviation	Experimental group Mean Standard deviation	Control group Mean Standard deviation
Quality of life	75/76 (24/3)	55/84 (24/1)	4/ 93(88/4)	25/ 80(37/1)
Postnatal depression	4/ 20(01/3)	65/17 (42/6)	55/ 13(36/3)	2/16 (93/2)
State anxiety	75/ 70 (94/9)	6/ 41(25/11)	6/ 65(17/13)	95/ 59(82/8)
Trait anxiety	6/ 64(25/11)	2/ 16(56/8)	25/ 60(31/8)	1/ 57(12/5)

Table IV: Evaluating the normality distribution and evaluating the homogeneity of variances of the studied variables.

Subscales		Variable			
		Quality of life	Postnatal depression	State anxiety	Trait anxiety
Kolmogorov-Smirnov test	Statistic	46/1	886/0	669/0	922/0
	Df	40	40	40	40
	P-value	028/0	416/0	763/0	363/0
Subscales	LLevene's Statistic	08/22	6594/0	27/2	93/3
	df1	1	1	1	1
	df2	38	38	38	38
	P-value	451/0	1644/0	522/0	0/054

Table V: Evaluating the effect of ACT on depression, trait and state anxiety, and quality of life in women.

Variables	Source of changes	Sum of squares	Degrees of freedom	Mean square	F	Sig. level	Effect size
Postnatal depression of women	Pre-test Group effect Error effect	22/70 625/8850 15/378	1 1 38	22/70 625/8850 95/9	7/057 889/39 -	0/000 0/000 -	0/15 0/95 -
Trait anxiety	Pre-test Group effect Error effect	3080/020 93412/2 1998/750	1 1 38	3080/020 934122/2 52/59	58/55 1/77 -	0/000 0/000 -	0/606 0/97 -
State anxiety	Pre-test Group effect Error effect	2356/22 97131/025 4614/75	1 1 38	2356/22 97131/025 121/414	19/40 799/13 -	0/000 0/000 -	0/328 0/95 -
Quality of life of women	Pre-test Group effect Error effect	22/301543 22/1729 55/4026	1 1 38	22/301543 22/1729 1496/105	2/86 16/13 -	0/000 0/000 -	0/98 0/30 -

Table VI: Evaluating ACT on depression, anxiety and quality of life.

Source of changes	Value	Degree of freedom	Error degree of freedom	F	Sig. level	Effect size
Pillai's trace	0/657	3	36	22/97	0/000	0/657
Lambda trace	0/343	3	36	22/97	0/000	0/657
Hoteling's trace	1/914	3	36	22/97	0/000	0/657
Largest root	1/914	3	36	22/97	0/000	0/657

Discussion

Pregnant women experience various types of fear, the most important of which is harm to the infant[16,17]. This perception is very stressful for pregnant women and it seems that ACT can be a good solution for this group of women with anxiety-provoking thoughts. Cognitive science can explain the failure of women to overcome these fears because people's thoughts and behaviors are so intertwined that the issue eventually distances from the present moment and its values[18]. Therefore, the present study was conducted to evaluate the therapeutic effects of ACT on depression, anxiety and quality of life in women after childbirth.

The results of our study showed that there was a statistically significant difference between the experimental and control groups in the scores obtained from quality of life, depression and anxiety in ACT.

According to research on improving the quality of life after ACT, Eilenberg et al[19], Vakilian et al.[15] and Stenhoff et al.[20] had a similar result to the present study. It has been shown that many changes occur during pregnancy and postpartum period in the physical, mental, social health dimensions and in general in the quality of life of women. Women face many physical and mental disorders in the postpartum period. Approximately 40% of pregnant women (50) million people each year experience health problems during pregnancy or after childbirth, and 11% suffer from long-term or serious complications that sometimes accompany them for the rest of their lives. Significant changes in the physical and mental health of women in the postpartum period are associated with a decrease in their quality of life in this critical period[21]. According to studies, ACT training improves the quality of life in terms of physical functioning, physical role, bodily pain, general health, vitality, social functioning, emotional role playing, and emotional well-being. Regarding the justification of these changes, it can be said that mindfulness means paying attention to the present in specific, purposeful and judgment-free ways, in the sense that without judging and without commenting on what is happening, one experiences being in the moment and everything that exists now, pure reality without explanation. The basis of mindfulness is derived from Buddhist meditation practices that increase the capacity for continuous and intelligent attention and awareness that goes beyond thought. Therefore, this attention to the present and its acceptance increases the quality of life[22,23]. On the other hand, most women experience mood swings after childbirth due to physical and chemical changes in the body, which in turn leads to a lack of enjoyment of life in these women, which reduces the feeling of pleasure and quality of life. As a result of ACT training, people become aware of experiencing the present and understand that this condition is due to physical and chemical changes in the body and physical balance will be established over time, this awareness in turn increases the quality of life[24,25].

Furthermore, the results of a study by Hosseini et al.[25], Dindo et al.[26] and Strosahl et al.[27] on the effects of ACT on postpartum depression were similar to those of our study. Similar studies such as Bonacquisti et al.[28] and Vakilian et al.[15], like our study, showed the improving effects of ACT on anxiety.

In order to explain the findings, it can be stated that ACT increases the psychological flexibility of mothers with postpartum depression. Therefore, with the increase of flexibility in mothers after childbirth, mood swings, etc. are easily accepted. In fact, the goal of this therapy is to increase one's behavioral capacity, not to decrease the symptoms of the disorder, which is called psychological flexibility[29,30]. ACT interventions, on the other hand, target changes in avoidance patterns, and during the interventions, the reduction of experimental avoidances mediates changes in depression symptoms. Avoidance is defined as the attempt to escape from depressing thoughts and memories that are brought to the awareness of a depressed person through this therapy. In this therapy, acceptance exercises and discussions about the values and goals of the individual all reduce postpartum depression. This therapy taught people how to let go of their avoidance beliefs and accept them instead of trying to control them. Although experiential avoidance has a reducing effect on unpleasant experiences in the short term, it has many destructive effects in the long term and can lead to lack of flexibility and functional impairment.[31-33.]

Regarding the effects of ACT on anxiety, it can be said that considering that anxious people have a lot of rumination and also thoughts about the future make them anxious, ACT is what makes an individual ability to leave the stage of struggling with anxiety. ACT also increases moment-by-moment awareness of the five senses, thoughts, emotions, and events created in the mind, and gradually facilitates the ability to develop this "disconnection" with thoughts, emotions, and bodily feelings. One learns that s/he can regard them as aspects of experience rather than as acquired reality. one can also see that thoughts are not reality and are only thoughts[19,34].

In general, despite the effective results of the present study on improving the mental state of mothers after childbirth, our study also had some limitations. One of the limitations was that the present study was cross-sectional, which raises limitations in interpretation and etiology of the studied variables. Also, in the present study, following the persistence of the ACT effect, checking the honesty of respondents' answers to the questionnaires and not generalizing the results to other people were other limitations. Finally, given the high rate of depression and anxiety among women after childbirth,

it is suggested to consider the results of this research in order to treat depression and anxiety and increase their quality of life and use it in counseling and psychotherapy sessions. It is also suggested that future studies investigate the role of other variables such as gender and genetic differences and the rate of hormonal changes in women after and before childbirth. Put together, it is important to observe health care management in Iran[35-40].

Conclusion

ACT can be a good option to improve depression, anxiety and quality of life in women after childbirth and can be an effective treatment for depression and anxiety and improve quality of life and provide new horizons in the clinical interventions of these women.

Interests conflict

The researchers declare that they have no conflict of interest.

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ORIGINAL

Effect of vitamin D supplement on glycemic control in gestational diabetes

Efecto del suplemento de vitamina D sobre el control glucémico en diabetes gestacional

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Abstract

Introduction: Gestational diabetes mellitus (GDM) is a pregnancy complication characterized by intolerance to carbohydrates and metabolic diseases. Vitamin D supplement prescription has been shown to be effective on glycemic control and other pregnancy outcomes. Therefore, this study aimed to investigate the effect of high dose of vitamin D supplement on glycemic control in pregnancy and its effect on reducing other adverse outcomes of pregnancy.

Methods: The study was conducted on 40 pregnant women in the first trimester who had impaired glucose tolerance test by the randomized clinical trial method. Subjects were divided into two groups. Simultaneously with the regimen, the intervention group was given a higher dose of vitamin D and the control group received vitamin D routinely. Then, HbA1c level, fasting blood sugar, fasting serum insulin, and insulin resistance were measured at the beginning and 6 weeks later. Patients were followed up for pregnancy complications until the end of pregnancy.

Results: Fasting blood sugar, HbA1C, serum insulin level, and HOMA-IR level after receiving vitamin D in the case group were less than the control group, which were significantly different (p.v <0.001). Cases that required insulin therapy and preterm labor were higher in the control group, but it was not significant. There were no significant differences in other outcomes of pregnancy. The level of vitamin D in umbilical cord blood was higher and significant in the case group (p.v <0.001) but there was no significant difference with pregnancy complications in the two groups.

Conclusion: Our study showed that administering a dose higher than the current vitamin D recommendation in pregnancy can help prevent gestational diabetes and its adverse outcomes.

Keywords: Gestational diabetes, vitamin D, supplement, pregnancy outcomes, glucose.

Resumen

Introducción: La diabetes mellitus gestacional (DMG) es una complicación del embarazo caracterizada por la intolerancia a los hidratos de carbono y las enfermedades metabólicas. Se ha demostrado que la prescripción de suplementos de vitamina D es eficaz para el control glucémico y otros resultados del embarazo. Por lo tanto, este estudio tenía como objetivo investigar el efecto de una dosis alta de suplemento de vitamina D en el control glucémico en el embarazo y su efecto en la reducción de otros resultados adversos del embarazo.

Métodos: El estudio se llevó a cabo en 40 mujeres embarazadas en el primer trimestre que tenían una prueba de tolerancia a la glucosa alterada por el método de ensayo clínico aleatorio. Los sujetos se dividieron en dos grupos. Al grupo de intervención se le administró una dosis más alta de vitamina D y el grupo de control recibió vitamina D de forma rutinaria. A continuación, se midieron el nivel de HbA1c, la glucemia en ayunas, la insulina sérica en ayunas y la resistencia a la insulina al principio y 6 semanas después. Se realizó un seguimiento de las pacientes para detectar complicaciones del embarazo hasta el final del mismo.

Resultados: La glucemia en ayunas, la HbA1C, el nivel de insulina sérica y el nivel HOMA-IR después de recibir vitamina D en el grupo de casos fueron menores que en el grupo de control, que fueron significativamente diferentes (p.v <0,001). Los casos que requirieron terapia de insulina y parto prematuro fueron mayores en el grupo de control, pero no fue significativo. No hubo diferencias significativas en otros resultados del embarazo. El nivel de vitamina D en la sangre del cordón umbilical fue mayor y significativo en el grupo de casos (p.v <0,001), pero no hubo diferencias significativas con las complicaciones del embarazo en los dos grupos.

Conclusión: Nuestro estudio demostró que la administración de una dosis superior a la recomendación actual de vitamina D en el embarazo puede ayudar a prevenir la diabetes gestacional y sus resultados adversos.

Palabras clave: Diabetes gestacional, vitamina D, suplemento, resultados del embarazo, glucosa.

Introduction

Gestational diabetes mellitus (GDM) is a common medical complication of pregnancy that is defined as "diabetes diagnosed in the second or third trimester of pregnancy where diabetes is not overt"[1,2]. It is estimated that approximately 7% of all pregnant women in the United States have GDM, but its prevalence is between 1% and 4% of all pregnancies worldwide, depending on the study population and diagnostic criteria[3,4]. Various factors such as old age during the first pregnancy, stressful living conditions, a sedentary lifestyle with low physical activity, and poor diet affect the incidence of this complication and lead to an increased risk of GDM [5]. Recent studies have shown that calcium and vitamin D supplements for patients with GDM may affect pregnancy outcomes[6,7].

Vitamin D has been one of the most important topics in the medical world for the last decade due to its numerous effects on human health[8-10]. This vitamin has important and multifaceted effects beyond the effects of the skeletal system. Some of the activities of this vitamin during pregnancy are the effect on fetal skeletal growth and development, regulating calcium transfer from the placenta, modulating immune reactions during placental implantation and its effect on fetal development and brain development[11,12]. Several studies have shown that the 25-hydroxyvitamin D level is significantly lower in patients with diabetes than in healthy individuals[13-15]. Many studies show that pregnant women are at higher risk for vitamin D deficiency due to the increased need of the fetus due to rapid growth and calcification of bones in the third trimester[16-18]. Also, according to studies, there is a high prevalence of vitamin D deficiency in newborns and their mothers in Iran[19].

The appropriate dose of vitamin D during pregnancy is unknown, although it appears to be greater than the current dietary reference intake of 200–400 IU/d. In 2010, the FDA estimated the appropriate amount of vitamin D during pregnancy at 600 IU/d[20,21]. Several studies have shown that more than 1000IU of vitamin D is required to reach the normal level of 25OHD[22,23]. The Endocrine Society has recommended daily intake of vitamin D at a dose of 1500-2000 IU to reach the level of 30 ng/ml from 25OHD[24]. However, one study found that with a daily intake of 4,000 IU, approximately 83% of women reached a minimum serum level of 32 ng/ml at the time of delivery and suggested that 4,000 IU was the appropriate dose for pregnant women[25,26].

There are few studies on the effect of vitamin D supplement on maternal and fetal pregnancy outcomes. A number of observational studies have been conducted, but there are few interventional studies to evaluate the effect of vitamin D supplement on blood glucose metabolism, gestational diabetes, preeclampsia, intrauterine growth retardation, intrauterine fetal death, and macrosomia. Therefore, the present study aimed to investigate the effect of high dose of vitamin D supplement (50,000 oral units) on blood sugar control in pregnant women and also its effect on outcomes such as preeclampsia, intrauterine growth retardation, intrauterine fetal death, and macrosomia.

Materials and methods

Selection of patients

In this randomized clinical trial study, 40 pregnant women with impaired glucose tolerance test in the first trimester of pregnancy during 2014-2015 in the city of Kerman were investigated.

Inclusion criteria were women over 18 years of age, gestational age of 8 to 13 weeks, and exclusion criteria were patients with renal or hepatic insufficiency, alcoholism, malabsorption, hypo or hyperparathyroidism, malignancies, use of effective drugs on vitamin D metabolism, previous use of vitamin D supplements, and a history of previous diabetes.

This study was presented in the Ethics Committee of Kerman University of Medical Sciences and was approved with the number 1394.203. Also, it was registered in IRCT with the code N12015122725725. Therefore, at first, the objectives, nature, and the research process were explained to the sample and their consent to participate in the research was obtained. The sample was assured that their information would be kept confidential and reminded that the results of the research would be made available to them if they wished. The sample was also reassured that they could leave the research at any stage of the research if they did not wish to continue and be referred to a psychiatrist if they needed medical treatment.

Method of implementation

The diagnosis of gestational diabetes was made according to the criteria of the American Diabetes Association (ADA) [25]. A two-hour diabetes screening test (GTT) was performed by prescribing 75 grams of glucose 75 g of glucose. First, fasting blood sugar was measured and after consuming 75 grams of glucose, 4 cc of blood was taken from each patient twice one and two hours later, and blood glucose was measured one and two hours later.

Values of FBS<92 /BS1hpp <180 / BS2hpp <153 were considered normal. Patients who had an abnormal test in the above three cases were considered to have an impaired test, which HbA1C and serum insulin were measured immediately from the stored serum of them. HbA1C level <6 normal and fasting serum insulin level less than 5 µU/ml were considered normal. Sampling continued until reaching the sample size of 40 people (impaired test).

Subjects with impaired tests were divided into intervention and control groups by simple randomized method. In both groups, the amount of insulin resistance was calculated by homeostasis model assessment (HOMA-IR). Both groups were on a diet. Simultaneously with the diet, the intervention group received 50,000 IU of oral vitamin D (one pearl) up to three doses once every two weeks, and the control group routinely received up to 28,000 IU of vitamin D during the same period. 2 weeks after the last dose of vitamin D, serum HbA1c, fasting serum insulin, fasting blood sugar were measured and HOMA-IR was calculated. Then patients were followed up until the end of pregnancy in terms of pregnancy complications including intrauterine fetal demise (IUFD), intrauterine growth restriction (IUGR), large for gestational age (LGA) infant, preeclampsia (BP>=140/90 and proteinuria), preterm delivery less than 37 weeks of gestation, and the need for insulin regimen therapy. After delivery, 5 cc blood of umbilical cord was taken to check the level of vitamin D, and the relationship between the level of vitamin D in the umbilical cord blood and pregnancy complications such as preeclampsia, intrauterine fetal demise, intrauterine growth retardation was investigated.

Data analysis

Data were analyzed by SPSS software version 25 (version 25, SPSS Inc., Chicago, IL). Frequency, relative frequency and central tendency of mean were used for descriptive statistics and chi-square and t-tests were used to compare quantitative and qualitative variables in the two groups. Finally, P less than 0.05 was considered statistically significant.

Results

In this study, 254 pregnant women underwent diabetes screening. Of these, 40 had impaired glucose tolerance test that were divided into case and control groups.

The mean serum level of fasting blood sugar in the case group was significantly lower than the control group. The level of fasting serum insulin and hemoglobin A1C in the case group was much lower than the control group. The level of HOMA-IR in the case group was clearly different and lower than the control group. These findings confirm the statistically significant difference between the two groups (p <0.001) (**Table I**).

Also, the mean level of vitamin D in umbilical cord blood at delivery in the case group was clearly higher than the control group, which was a statistically significant difference (p <0.001).

The frequency of need for insulin regimen therapy was investigated in the two groups. 3 patients (15%) in the case group and 7 patients (35%) in the control group needed insulin regimen due to lack of blood sugar control or diet and vitamin D supplement. There was no statistically significant difference between the two groups in the frequency of need for insulin regimen.

In terms of delivery status, our results showed that 19 term deliveries (95%) were performed in the case group and 15 term deliveries (75%) were performed in the control group, resulting in 1 preterm delivery (5%) in the case group and 5 preterm deliveries (25%) in the control group. There was no significant difference between the two groups in terms of delivery status (**Figure 1**).

Pregnancy complications between the two groups also showed that no intrauterine fetal death (IUFD) was seen in the case group but one case was observed in the control group. Preterm labor pain (PLP) was reported in two patients in the case group and six patients in the control group. Intrauterine growth restriction (IUGR) was not seen in the case group but one case was observed in the control group. Large for gestational age (LGA) infants were seen in one case in the case group and in four cases in the control group. Preeclampsia (PIH) was not seen in the case group but was reported in three subjects in the control group. There was no significant difference between the two groups in terms of pregnancy complications (**Figure 2**).

Table I: Comparison of serum levels of serum insulin, hemoglobin A1C, fasting blood sugar, and HOMA-IR.

	Groups		
	Case	Control	p.v*
Fasting blood sugar before regimen	107.50±11.85	107.75 ± 15.19	0.254
Fasting blood sugar after regimen	93.40±6.47	76.65±7.74	0.001>
HOMA-IR before regimen	7.04 ±1.82	6.14 ±2.35	0.187
HOMA-IR after regimen	6.39±1.76	2.94 ±1.35	0.001>
Hemoglobin A1C levels before regimen	6.68±1.01	5.92±1.12	0.038
Hemoglobin A1C levels after regimen	6.43±0.92	5.02±0.83	0.001>
Insulin levels before regimen	26.34±5.33	23.17±8.52	0.166
Insulin levels after regimen	26.90±5.65	15.68±7.36	0.001>
Vitamin D levels in umbilical cord blood	13.33±4.60	21.35±15.39	0.001>

Figure 1: Comparison of the frequency of delivery status in the case and control groups.

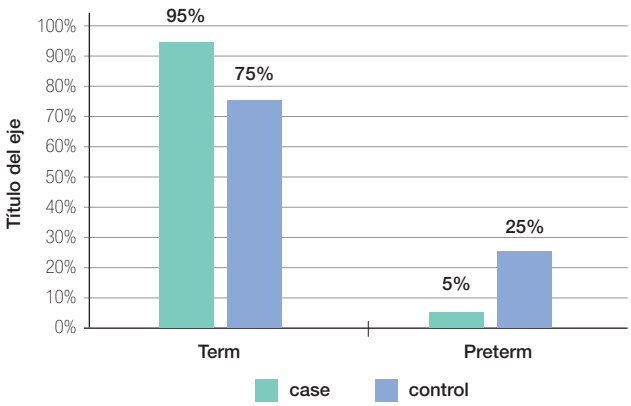
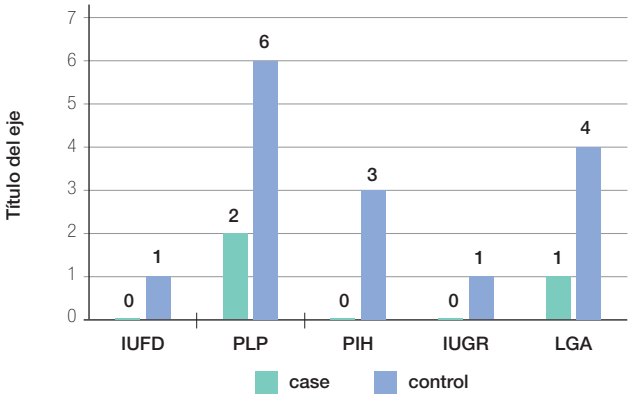


Figure 2: Comparison of pregnancy complications in the case and control groups.



The level of vitamin D in umbilical cord blood was not significantly different in any of the groups based on pregnancy complications (**Tables II** and **III**).

Table II: Comparison of vitamin D levels in umbilical cord blood and pregnancy complications in the case group.

	No	Yes	p.v*
Intrauterine fetal death	30.05±2.67	26.11±5.97	30.05±2.67
Preterm delivery	16.19± 30.77	21.12 ± 35.50	0.692
Preeclampsia	13.42 ±4.71	11.06±0	0.710
Intrauterine growth restriction	13.42 ±4.71	11.06±0	0.710
Large for gestational age infant	14.97± 32.35	0± 10.20	0.166

Table III: Comparison of vitamin D levels in umbilical cord blood and pregnancy complications in the control group.

	No	Yes	p.v*
Intrauterine fetal death	13.42±4.71	11.06±0	0.710
Preterm delivery	13.60±4.08	12.70±6.04	0.698
Preeclampsia	13.74±4.83	11±2.17	0.354
Intrauterine growth restriction	13.53±4.63	9.5±0	0.407
Large for gestational age infant	4.97± 13.08	2.94 ±14.35	0.635

Discussion

It has been shown that the need for vitamin D and calcium during pregnancy and lack of proper nutrition at this important time in life may increase the risk of GDM[27]. The results of several meta-analyses have shown that there is a significant inverse relationship between serum 25-(OH) D concentration and GDM risk[28,29]. Several mechanisms have been proposed for the association between vitamin D and type II diabetes. These mechanisms are associated with diabetes and vitamin D in three ways and affect insulin secretion, peripheral tissue resistance to insulin, and inflammation[30]. Therefore, the present study aimed to investigate the effect of vitamin D supplement on glycemic control in GDM.

The results of the present study showed that the level of fasting serum insulin, hemoglobin A1C and HOMA-IR levels in the case group were lower than the control group. Meanwhile, the mean level of vitamin D in umbilical cord blood at delivery was higher in the case group than the control group, but there was no significant difference with pregnancy complications in the two groups. Also, in statistical studies, there was no significant difference between the two groups in terms of pregnancy complications.

Cross-sectional studies have shown an association between maternal vitamin D levels and impaired glucose metabolism in pregnant women[31-33]. Wang et al. also reported that vitamin D supplement in women with GDM may improve glycemic control and reduce adverse outcomes for mother and infant[34]. Ojo et al. also reported in a systematic review study that vitamin D supplement has the potential to increase blood sugar control in women with GDM. However, they reported that due to the limited number of studies in meta-analysis, the conclusion should be interpreted with caution and further studies are required to fully understand the exact mechanism of the effect of vitamin D on glucose metabolism[35]. However, no such association was found in the study of Pleskacovu[36]. The results of our study showed the effect of vitamin D on decreasing fasting blood sugar and hemoglobin A1C, but the need for insulin therapy did not differ significantly between the two groups. It has been shown that normal pregnancy requires increased insulin secretion due to increased insulin resistance, and women with impaired insulin secretion are at risk for developing gestational diabetes[37].

Animal studies have shown that vitamin D deficiency impairs the function of pancreatic B cells[38]. The effect of vitamin D on pancreatic B cell function and insulin resistance has also been shown in human studies[39]. In some studies, vitamin D deficiency has been reported to be more common in pregnant women with gestational diabetes than in normal individuals[40,41]. In the of study Lau, vitamin D deficiency was indirectly associated with poor glycemic control and recommended measuring vitamin D levels before or during pregnancy and recommending treatment with vitamin D[42]. The study of Alzaim had similar results and recommended the prescription of vitamin D supplement[43]. Zhang et al. also reported that women with vitamin D deficiency during early pregnancy had a 3.7-fold increased risk of developing GDM compared with those who were vitamin D replete[44]. In these studies, which showed negative results of vitamin D deficiency and gestational diabetes, none of them investigated the results of prescribing vitamin D supplement on developing and controlling glucose.

There are several studies on non-pregnant patients that have investigated the effect of vitamin D supplement on the incidence of diabetes[45]. However, few studies have investigated the effect of vitamin D supplement on glucose metabolism in pregnancy. In the study of Rodniki on 12 pregnant women with GDM, administration of 1,25 dihydroxyvitamin calciferol reduced fasting blood sugar[46]. In the study of Soheilikhah, pregnant women

were treated with three doses of vitamin D (200 IU daily, 50,000 IU monthly, and 50,000 IU every two weeks) from the beginning of pregnancy to delivery. There was a significant improvement in the HOMA-IR index at the end of pregnancy compared to the beginning of pregnancy in the group receiving 50,000 IU of vitamin D every two weeks, which was consistent with our study. However, in the study of Soheilikhah, vitamin D supplement had no effect on fasting blood sugar[47]. But in our study, fasting blood sugar and hemoglobin A1C were significantly reduced in people who took vitamin D supplement. In another study by Asemi et al., vitamin D supplement with a dose of 50,000 IU every 21 days was administered in GDM that improved fasting blood sugar and HOMA-IR index[48], which was consistent with our study. Vitamin D in umbilical cord was not investigated in these studies. In the study of Yap et al., pregnant women with GDM received vitamin D supplement at a dose of 5,000 IU or 400 IU per day. In this study, taking the supplement in the two groups had no effect on fasting blood sugar HOMA - IR, and pregnancy complications such as gestational hypertension, preeclampsia and preterm delivery were not different in the two groups, which was consistent with our study. Furthermore, vitamin D levels in umbilical cord were higher in those who received higher doses of the vitamin, and in our study, vitamin D levels in umbilical cord were higher in those who received vitamin D supplement, although it had no association with obstetric complications[49]. In the study of Mojibian et al. patients were treated with vitamin D 5000 IU daily and a group with 50,000 IU every two weeks, obstetric complications such as preeclampsia, gestational hypertension, preterm delivery, and low birth weight did not differ between the two groups, which was consistent with our study. Also, in their study, those who received higher doses of vitamin D were less likely to develop gestational diabetes[50,51].

However, vitamin D can reach to the body using diverse food sources, but the risk of foodborne diseases is another important issue[52-55]. According to the results of this study and previous studies, it can be concluded that vitamin D deficiency in pregnancy is one of the factors affecting gestational diabetes in addition to other known factors such as race, age, BMI, family history of diabetes, and etc. Also, prescribing vitamin D with a high dose in pregnancy can help better control blood sugar and possibly reduce the need for insulin therapy. However, studies with a larger sample size in which the type of treatment has also been investigated are recommended for better conclusions.

Conclusion

In our study, those who received higher doses of vitamin D were less likely to need insulin therapy than those who received vitamin D routinely. However, there was no statistically significant difference that had not been investigated in other studies.

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Interests conflict

The researchers declare that they have no conflict of interest.

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ORIGINAL

The effect of inflammation in MIA-induced osteoarthritis on physiological cardiovascular function in male rats

El efecto de la inflamación en la osteoartritis inducida por MIA sobre la función cardiovascular fisiológica en ratas macho

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Abstract

This study investigates the effect of inflammation in MIA-induced osteoarthritis on cardiovascular physiological function in male rats Osteoarthritis (OA) is the most common joint disease in adults worldwide and osteoarthritis of the knee is the most common type. The most common symptom of osteoarthritis is joint pain. Osteoarthritis is a common degenerative disorder of articular cartilage, accompanied by hypertrophic changes in the subchondral bone, which causes inflammation of the surrounding tissues. Studies have shown that systemic and chronic inflammation can increase the risk of cardiovascular disease. Because synovial inflammation is involved in the early stages of OA, one of the side effects of OA is CVD. OA is associated with mild to moderate pain symptoms and the first line of treatment for this disease is the use of nonsteroidal anti-inflammatory drugs (NSAIDs) such as celecoxib. However, the dangerous side effects of NSAIDs in the development of cardiovascular disease in these individuals limit the long-term use of NSAIDs. Using alternative methods such as the use of herbs can prevent side effects. Among these plants is Papaver rhoeas with the scientific name (Papaver rhoeas L.) which has anti-inflammatory properties and is effective in vascular congestion.

Keywords: Papaver rhoeas, osteoarthritis, inflammation, cardiovascular disease, celecoxib.

Resumen

Este estudio investiga el efecto de la inflamación en la osteoartritis inducida por MIA sobre la función fisiológica cardiovascular en ratas macho. La osteoartritis (OA) es la enfermedad articular más común en adultos en todo el mundo y la osteoartritis de rodilla es el tipo más común. El síntoma más común de la osteoartritis es el dolor articular. La osteoartritis es un trastorno degenerativo común del cartílago articular, acompañado de cambios hipertróficos en el hueso subcondral, que causa inflamación de los tejidos circundantes. Los estudios han demostrado que la inflamación sistémica y crónica puede aumentar el riesgo de enfermedad cardiovascular. Debido a que la inflamación sinovial está involucrada en las primeras etapas de la OA, uno de los efectos secundarios de la OA es la ECV. La OA se asocia con síntomas de dolor leve a moderado y la primera línea de tratamiento para esta enfermedad es el uso de medicamentos antiinflamatorios no esteroideos (AINE) como celecoxib. Sin embargo, los peligrosos efectos secundarios de los AINE en el desarrollo de enfermedades cardiovasculares en estas personas limitan el uso a largo plazo de los AINE. El uso de métodos alternativos, como el uso de hierbas, puede prevenir efectos secundarios. Entre estas plantas se encuentra la anémona silvestre de nombre científico (Papaver rhoeas L.) que tiene propiedades antiinflamatorias y es eficaz en la congestión vascular.

Palabras clave: Extracto acuoso alcohólico de anémona salvaje, osteoartritis, inflamación, enfermedad cardiovascular, celecoxib.

Introduction

New evidence suggests that inflammation is a major mediator of joint pathology in osteoarthritis and that NF κ-B signaling pathway regulation plays an important role in causing this inflammation[1&2]. The proinflammatory cytokines involved in osteoarthritis are TNF-α and β1-IL, which are considered to be the main problem[3]. TNF-α, which is derived from damaged endothelial cells, also causes inflammation in the walls of blood vessels and regulates leukocyte activity, leading to the maturation and release of cytokines and chemokines[4]. On the other hand, there is a lot of evidence that inflammatory markers play an important role in the formation of atherogenesis and arterial thrombosis. Studies have also shown that systemic inflammation can increase the risk of CVD. Chronic inflammation is another risk factor for CVD. Chronic inflammation is one of the risk factors for cardiovascular disease (CVD). Since synovial inflammation plays a role in the initial stages of osteoarthritis (OA), therefore, the side effects of OA are the incidence of CVD. One of the most appropriate methods for treating this disease is the use of medicinal herbs such as Papaver Rhoeas that have effect in blood pressure modifying[5]. Because synovial inflammation is involved in the early stages of OA, one of the side effects of OA is CVD[6]. Cardiovascular diseases include ischemic heart disease, congestive heart failure, transient ischemic attacks, and stroke[7].Several studies have shown that the inflammatory reflex is associated with an increased risk of atherosclerosis 8. Epidemiological studies have also shown an association between increased levels of inflammatory markers and a high prevalence of CVD9.

Steroid anti-inflammatory drugs, including cyclooxygenase 2 inhibitors (celecoxib or celebrex), which are recommended as first-line treatment for OA, are associated with an increased risk of CVD. Study in 2014 found that taking NSAIDs increases the risk of myocardial infarction, stroke, hypertension, heart failure, and atrial fibrillation10. To date, much information has been obtained about the cardiovascular toxicity of NSAIDs, and often conflicting results have been obtained, especially for aspirin and naproxen, as well as similar results for patients taking ibuprofen[11&12]. To date, clinical research on the effect of NSAIDs in patients with cardiovascular disease has been limited to experimental studies with flurbiprofen, meloxicam, and parecoxib / valdecoxib.

The mechanism of cardiovascular effects of aspirin, naproxen and other non-selective NSAIDs and COX-2 inhibitors is still debated. Although non-selective NSAIDs inhibit both COX-1 and COX-2, selective COX-2 inhibitors, including lumiracoxib, have no effect on COX-1 at therapeutic concentrations. The initial hypothesis explaining the increased risk of cardiovascular disease associated with COX-2 inhibitors is that the inhibitor of this enzyme causes an imbalance resulting in platelet aggregation due to COX-1, while in COX-2-dependent prostacyclin is inhibited by endothelial cells that can affect blood vessels[13].

Inhibition of COX by NSAIDs reduces the effect of systemic vasodilation on prostaglandins such as PG I2, PG E2, and group (CINOD), which are prescribed to treat patients with OA and are more widely used to reduce the complications of CVD than NSAIDs.[14] Extensive clinical and experimental evidence suggests that NSAIDs and COX-2 inhibitors may cause vasoconstriction[15]. Due to the tendency of people to use herbal medicines and also to reduce the cardiovascular effects of OA chemotherapy drugs, so the use of alternative methods such as the use of medicinal plants seems necessary, including Papaver rhoeas plants. Papaver rhoeas (scientifically named Papaver rhoeas L.) is a dark poppy plant 77 and has a variety of alkaloids and has a family affinity and similar effects with poppy[16]. Due to the very small amounts of morphine in the extract of this plant, it is called “harmless opium”[17]. So far, various medicinal properties of this plant have been reported.

The active ingredients in Papaver rhoeas cracking include: papaverine, radin, radic acid, papauric acid[18], roagenin and anthocyanin. Papaverine is one of the opium alkaloids that is used in the treatment of clogged arteries, especially the coronary arteries. It has also been used in a wide range of treatments for diseases such as inflammation[18], labor pain and pain relief and as a sedative and sedative. In addition, it is useful in the treatment of urinary incontinence and pruritic fever[19]. Another major herb is anthocyanin, which has the ability to reduce the risk of CVD[20] and to improve platelet function and antithrombotic effects. Endothelial dilation, improvement of arterial stiffness and protective effect on the heart[21] by suppressing hypertrophy Phosphorylation of protein kinase C and activation of Akt protein kinase B. Study in 2017 also showed that anthocyanins have anti-inflammatory properties, and high anthocyanin consumption is associated with decreased levels of proinflammatory cytokines, such as C-reactive protein (CRP) and the regulation of inflammatory mediators. Other effects of anthocyanins on inflammation include:[22]. The effect of cholinergic and nitrogenic systems in osteoarthritis is as follows.

Because acetylcholine (Ach), the main neurotransmitter of the vagus nerve, is a major mediator of the cholinergic anti-inflammatory pathway and nicotinic receptor α7 (α7nAChR) is present in the synovial tissue of the knee joint of patients with OA, local acetylcholine production can be used to regulate arthritis. Attributed to the cholinergic anti-inflammatory pathway which inhibits the production of inflammatory cytokines, such as IL-6, TNF-α, and the matrix metalloproteinase 9[23].

Stimulation of articular chondrocytes by IL-1β or TNF-α to transmit NF-κB p65 nucleus also includes a wide range of

catabolic genes such as nitric oxide synthase (iNOS) and COX-2 in chondrocytes, which lead to the production of proteases. Destructive attenuation of the extracellular matrix[24] However, studies have shown that systemic treatment with nicotine agonists reduces the severity and prevalence of osteoarthritis in mice. The most important effect of the cholinergic system in the circulatory system is the regulation of heart rate, which is applied through the parasympathetic fibers in the vagus nerves, which significantly reduces the heart rate and reduces the contractile strength of the heart. Acetylcholine released from nerve terminals by M2 muscarinic receptors opens a bunch of potassium channels and increases potassium excretion and hyperpolarization of nodes that produce action potential in the heart. The cholinergic system does not expand much in the arteries, and in the skeletal muscle and coronary arteries of the endocrine vessels, it causes a nitric oxide-dependent relaxant effect[25].

Preparation and maintain of rats

The present study is experimental and of a fundamental type. In this study, according to the regulations of the Medical Ethics Committee, 70 adults male Wistar rats in 14 groups of 5 with a weight range of 100 to 200 grams were purchased from Razi Serum Institute of Shiraz. In the animal house of Shiraz University, Faculty of Science, under light-controlled conditions, the dark cycle of light and food was maintained so that 12 hours before the start of the experiment, their access to food was cut off but they had free access to water.

Preparation of extract

First of all the leaves of Papaver rhoeas, Osteoarthritis, Inflammation, Cardiovascular Disease, Celecoxibwere collected from the cities around Shiraz and transferred to the Faculty of Science by the professor of botany of the Faculty of Science of Shiraz University, were scientifically identified. Then the collected plant was healthy in a shady environment without dry moisture and by Electric powder mill was transferred to human 1800 ml to prepare the extract and then enough 70% ethanol was added to it and it remained in the same condition for 12 hours. After 12 hours, the solution was filtered on the surface of the powder with a funnel filter paper and transferred to Petri dishes and placed in an incubator at 37°C for 12 hours to dry completely and become a powder.

Preparation of extract in oral and injectable groups

For this purpose, first the required dose for each mouse was calculated according to its weight. The weight calculated by the scales was then weighed, then 300 µl of solvent was added and dissolved on a vortex machine. In the oral groups, the extract at doses of 100, 200 and 400 mg / kg was given to the animal by gavage for 2 weeks, and in the injected groups, the extract was injected through a venous cannula on the day of surgery.

Osteoarthritis Induction Method

The animal was initially anesthetized by intraperitoneal injection of urethane (1.2 mg / kg) and osteoarthritis was induced in the knee joint of 35 30-day-old rats injected with monosodium iodoacetate (MIA; sigma-ALDRICH, USA). For this purpose, first the animal's right knee joint was sterilized with 100% ethanol and after induction of cartilage defect by injecting 1 mg of monosodium iodostat in 50µL (as a single dose containing 1 mg of MIA in 0.9% saline) by a The G 27 sterile needle was inserted into the longitudinal groove of the right knee joint at maximum flexion. Of course, in situations where no damage was done to the subchondral bone[26].

Surgical protocol and prescription of drugs

Thirty days after the MIA injection, animals whose access to food but had free access to water were excluded 12 hours before the start of the experiment. The surgical procedures are as follows: Each animal in the experimental groups was anesthetized by intraperitoneal injection of urethane (1.2 mg / kg) and then a tracheostomy was performed to prevent aspiration and suffocation during anesthesia. Cannulation was performed to access the femoral arteries. The venous cannula was used for injections during the test and the arterial cannula was connected to the power lab, which recorded the mean arterial pressure, systolic pressure, diastolic pressure, and heart rate as follows:

Prescription of Drugs

After surgery, the animal was rested for one hour to relieve the effects of surgical stress and keep the animal in a stable position. A total of 70 adult male Wistar rats were randomly divided into 14 groups of 5 with a weight range of 150-100 g and in all groups, cardiac parameters were recorded and then blood plasma of all samples for troponin, Tnf-alfa and CK was collected.

Group receiving injectable and oral extract of Papaver rhoeas

In the injection group: At first, the blood pressure of the animals in this group was recorded for 30 minutes without receiving any treatment. Then 300 µl of solvent extract was injected intravenously over 15 seconds and blood pressure was recorded. After blood pressure returned to normal, 300 µl of Papaver rhoeas, Osteoarthritis, Inflammation, Cardiovascular Disease, Celecoxibextract

at a dose of 2 mg / kg (equivalent to 0.005 gr / kg of extract powder), dose of 5 mg / kg (equivalent to 0.01 g / kg of extract powder), dose of 10 mg / kg (equivalent 0.025 extract powder) and a dose of 25 mg / kg (equivalent to 0.07 g / kg extract powder) were injected and blood pressure was recorded.

In the oral group: After creating the OA model (by MIA injection), Papaver rhoeas extract was gavaged for two weeks, so that in the experimental groups, different doses of Papaver rhoeas extract were 100 mg / kg (equivalent to 0.23 gr / kg). Extract powder), dose 200 mg / kg (equivalent to 0.46 g / kg extract powder), dose 400 mg / kg (equivalent to 0.1 g / kg extract powder) and in the positive control group, Celebrex (10 mg / kg) in 300 microliters of solvent (water and alcohol Percent 70) Was dissolved and given to the animals by gavage. Blood pressure was recorded on day 30 similar to the injection group.

Measuring research variables

How to measure blood pressure changes

For this purpose, cannulation was performed to access the femoral arteries. The venous cannula was used for injections during the experiment and the arterial cannula was connected to the power lab, which recorded the mean arterial pressure, systolic, diastolic and heart rate. This device is equipped with an A-to-D system that converts and records analog data into numbers.

Method of measuring the weight of a mouse foot

Measure the volume of edema by placing the right foot (with OA by injection of MIA and the left foot (healthy) of the animal up to the wrist (to measure the difference in weight between the two feet) in a water container placed on a scale and record the weight of the rat's foot in Days (1,7,14,21,28) (Xu.et al, 2017) and the weight distribution of rats were calculated

Method of measuring knee thickness

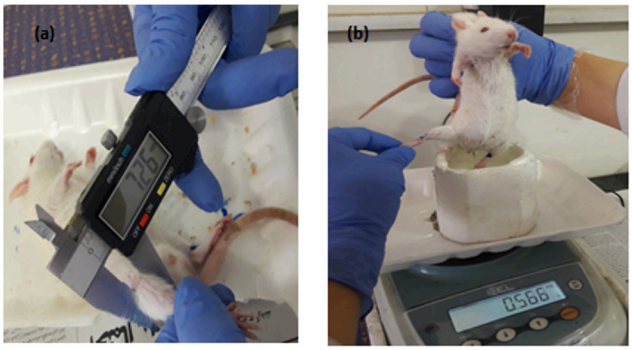
Knee thickness in rats with osteoarthritis was assessed using a caliper with an accuracy of 0.02 mm and was evaluated on days (1,7,14,21,28). According to Janet's description, the animal's knee diameter was scored this way.

1 / 0-2 mm score (01)
1 / 2-0 / 4 score (02)
1 / 4-6 score (03)
1 / 6-8 score (04) (Janet et al., 2004)

Creatine kinase (ck) measurement method

ELISA Kits were used to analyze creatine kinase (coat number: CUBEK06774). CK enzyme contains CK-M isoenzyme, which produces CK-MB and CK-MM isoenzymes. Measurement of CK-MB activity is a test. It is completely dedicated to diagnosing heart muscle damage and thus diagnosing and evaluating a heart attack.
TNF-α: A cytokine is a polypeptide made by monocytes

Figure 1: a) Measurement of rat knee thickness b) Weight measurement of rat foot with osteoarthritis.



and macrophages. This factor plays an important role in many diseases, including inflammatory diseases. The body responds to stimuli such as infection or tissue damage. This factor creates inflammation and this factor leads to the activation of neutrophils and changes in the permeability of vascular endothelial cells. To measure TNF-α by ELISA solid phase sandwich method 1 and the kit made by the French company Diaclone (coat number: 872.010 .001) was used.

Troponin measurement method

ELISA Kits (coat number: MBS727624) were used for troponin analysis.

Information analysis method

Data were analyzed using SPSS software using Independent T-test to examine the differences between groups and Paired sample T-test to examine the differences between different stages of a group with $p < 0.05$ as a significant level. Was analyzed.

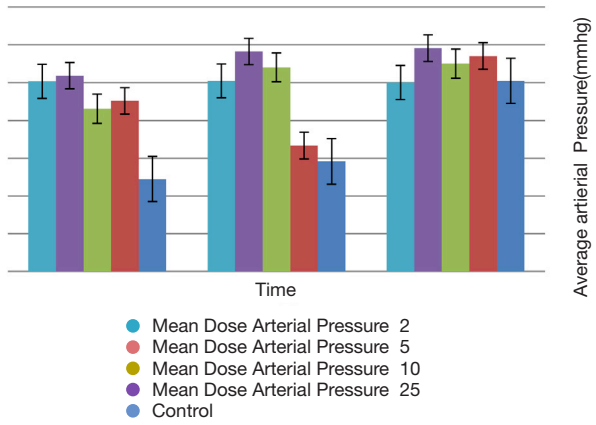
Research Findings

In this study, in order to evaluate the obtained data, first the initial results of the data have been reported through statistical indices of mean and standard deviation of mean. Through one-way analysis of variance and pairwise comparison tests by LSD method, we investigated the differences between the experimental groups. Significance level was considered $P < 0.05$ and all statistical methods were performed using SPSS software version 19.

Hypothesis 1
Determining the effective dose of Papaver rhoeas extract injection:

Mean arterial pressure in response to different doses of Papaver rhoeas extract in both control and experimental groups in the injection group (doses 2, 5, 10 and 25 mg / kg) As shown in Chart 1, among the different doses tested, in response to the injected extract at a dose of 5 mg / kg, the fastest arterial pressure drop was observed, which returned to the optimal position compared to the control group over time.

Figure 2: Comparison of mean arterial pressure changes (Beat / min) in response to different doses of Papaver rhoeas extract in the injected group compared with the control group. a indicates a significant difference between the extract group and the control group and control P = 0.000. b indicates no significant difference between control and control group P≤0.05.



Hypothesis 2
Cardiovascular effect of effective dose of Papaver rhoeas injectable extract:

Mean arterial pressure, systolic, diastolic and heart rate in the presence of 5 mg / kg injection of Papaver rhoeas extract. According to Chart 2 and 3, in the group receiving Papaver rhoeas extract, systolic, diastolic pressure and mean arterial pressure in the experimental mode were significantly reduced compared to the control and control modes.

Figure 3: Mean arterial pressure, systolic, diastolic and heart rate in the presence of 5 mg / kg injection of Papaver rhoeas extract. According to Chart 2 and 3, in the group receiving Papaver rhoeas extract, systolic, diastolic pressure and mean arterial pressure in the experimental mode were significantly reduced compared to the control and control modes.

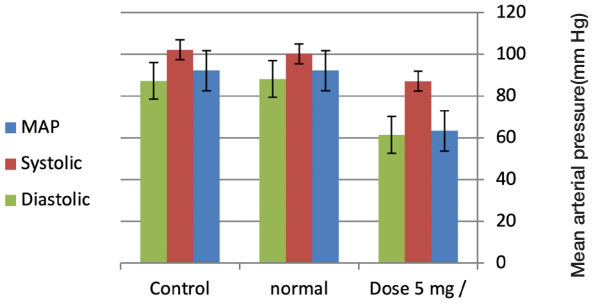
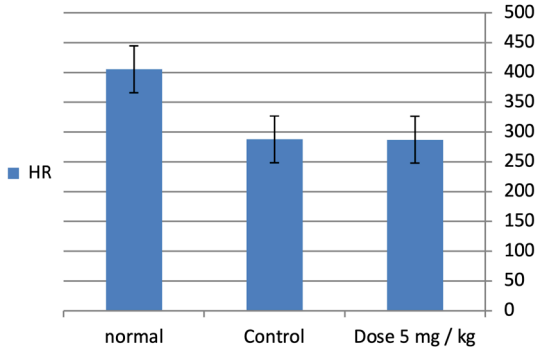


Figure 4: Comparison of heart rate in control, solvent and 5 mg / kg dose groups of Papaver rhoeas extract injection. a indicates a significant difference between the group receiving the extract and the control group and control P = 0.000
b indicates no significant difference between control and control group P≤0.05.



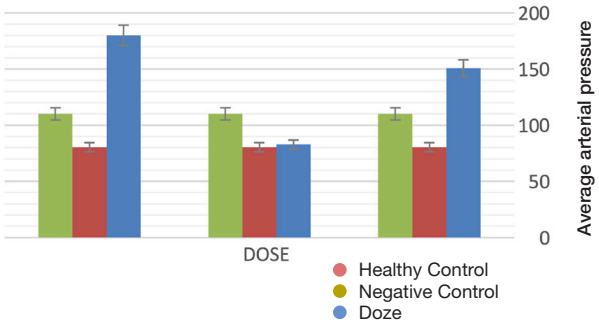
Discussion

Hypothesis 1: Determining the effective dose of oral extract of Papaver rhoeas.

Mean arterial pressure in response to different doses of Papaver rhoeas extract in both control and experimental groups in the oral group (200, 100 and 400) mg/kg

As shown in **Figure 5**, between different doses tested, the mean arterial pressure in response to the oral extract at a dose of 200 mg / kg had a significant decrease compared to the negative control group and doses of 100 and 400 (mg/kg).

Figure 5: Comparison of changes in blood pressure in response to different doses of Papaver rhoeas extract in the oral group compared with the control and negative control groups. a: Indicates a significant difference between the experimental and negative control groups P <0.05
b: Indicates the difference in meaning between in the experimental and healthy control groups P <0.05.



Hypothesis 2: Cardiovascular effects of oral anemone extract

Systolic, diastolic pressure, mean artery and heart rate in the presence of 200 mg / kg oral extract of Papaver rhoeas. As you can see in **table I**, mean arterial mean pressure, systolic pressure, and diastolic pressure are significantly lower in the 200-dose group compared with the orthosis or OA (negative control) group. Also, all parameters of mean arterial pressure, systolic pressure, diastolic pressure and heart rate (**Figure 6**) increased in the negative control group compared to the control group.

Figure 6: Comparison of systolic and diastolic blood pressure and mean arterial pressure (mmHg) of control, solvent and 200 mg/kg dose groups of injected Papaver rhoeas extract

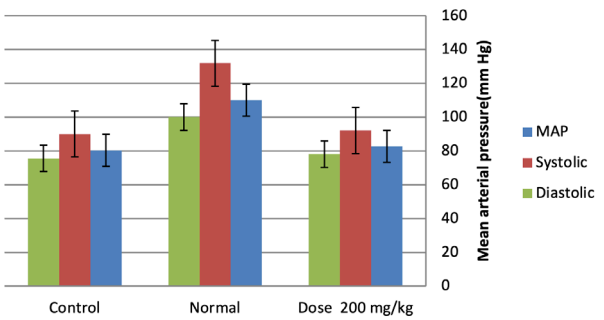


Table I: Comparison of systolic, diastolic blood pressure and mean arterial pressure (mmHg), heart rate (Beat / min) in control groups (healthy), with (negative control) and rats with OA receiving a dose of 200 oral anemone extract Papaver rhoeas (N = 5)
a: shows a significant difference between the negative control group and the control group P <0.05
b: shows a significant difference between the 200-dose group and the negative control group P <0.05.

Parameters / Group	Heart beat	Average arterial pressure	Systolic pressure	Diastolic pressure
Control	364.39±25.81	110.07±5.75	131.9±4.76	100.10±3.88
With OA (negative control)	364.39±12.41	110.07±5.46	131.9±5.55[a]	100.10±4.88
	316.97±27.21	82.75±7.36[b]	92.09±5.44[b]	78.09±3.88

The Effect of Papaver rhoeas on the Improvement of Cardiovascular Complications Caused by Osteoarthritis

Measurement of Rat knee Diameter and Weight

The effect of Celebrex and oral extract of Papaver rhoeas at a dose of 200 mg / kg on knee inflammation has been investigated in **table II**.

According to the table, rat knee diameter (right foot) in the experimental group receiving Celebrex

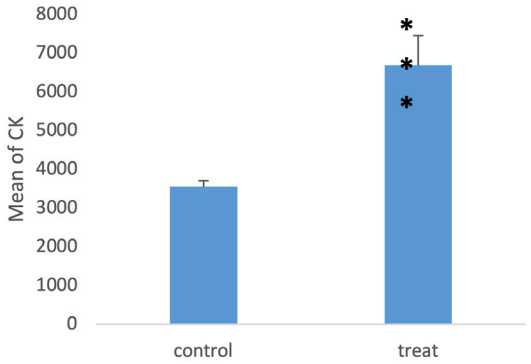
From day 1 to day 14 and then on day 21 compared to the control group (left foot) had a similar amount. And rat knee weight from day 1 to 7 and then on day 14 had a similar amount compared to the control group.

Creatine Kinase (CK) Assay Results

To measure the level of creatine kinase (CK) in rat serum according to different concentrations of standard solutions and their absorption, draw a standard diagram and then using a standard diagram (**Figure 7**), the concentration (CK) of each the sample was identified using its adsorption rate.

The mean of the control group was 3552.17 2. 162.331 and the mean of the experimental group was 6691.8 76 766.025 and the independent t-test in unequal variance showed that the difference between the mean observed between the two groups was significant (p = <0.0001) Has increased significantly.

Figure 7: Standard curve of creatine kinase



TNF-α assay results

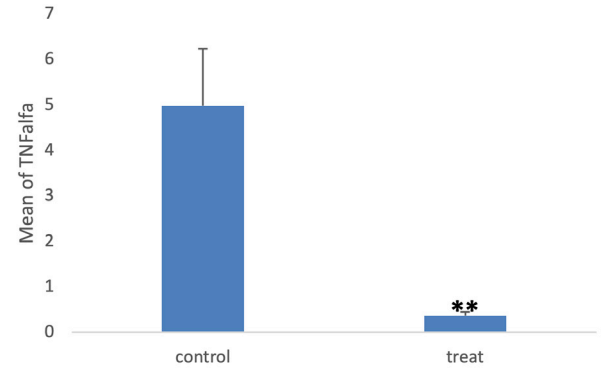
To measure the amount of TNF-α in the rat knee joint according to the different concentrations of standard solutions and their absorption, draw a standard diagram and then using a standard diagram (**Figure 8**), the concentration of TNF-α for each sample using Its absorption was determined.

The mean of the control group was 4.98 1. 1.25 and the mean of the experimental group was 0.085 ± 0.364 and the independent t-test in unequal variance showed that the mean difference between the two groups was significant (p <0.0001) Significance has decreased. (**Figure 9**).

Table II: Table of diameter and weight of rat knee in Celebrex group and dose 200 mg / kg
Paired t-test results were used for all comparisons.
a: Indicates significant difference between right and left foot diameters, P <0.05
b: Indicates significant difference between right and left foot weights, P <0.05

Group		Day	-1	1	7	14	21
Control	(ml) Knee diameter	right left	6.05±0.40 6.03±0.26	6.08±0.31 6.03±0.16	6.04±0.33 6.07±0.15	6.03±0.20 6.04±0.10	6.04±0.28 6.01±0.14
	Weight of Knee	right left	1.49±0.50 1.44±0.33	1.47±0.44 1.48±0.34	1.44±0.33 1.44±0.31	1.48±0.31 1.42±0.41	1.46±0.33 1.43±0.44
Arthritis control	Weight of Knee (ml)	right left	6.05±0.40 6.03±0.26	6.08±0.31 6.03±0.16	6.04±0.33 6.07±0.15	6.03±0.20 6.04±0.10	6.04±0.28 6.01±0.14
	Weight of Knee	right left	1.49±0.50 1.44±0.33	1.47±0.44 1.48±0.34	1.44±0.33 1.44±0.31	1.48±0.31 1.42±0.41	1.46±0.33 1.43±0.44
Selberks	(ml) Knee diameter	right left	6.08±0.21 6.09±0.22	6.16±0.30[a] 6.08±0.17	7.01±0.30[a] 6.35±0.14	6.86±0.22[a] 6.34±0.13	6.23±0.26 6.21±0.15
	Weight of Knee	right left	1.46±0.34[b] 1.45±0.44	1.47±0.54[b] 1.49±0.54	1.73±0.43 1.54±0.41	1.82±0.41 1.62±0.40	1.64±0.43 1.49±0.42
200 Doze/kg	(ml) Knee diameter	right left	6.10±0.33 6.08±0.26	6.19±0.20 6.09±0.27	7.14±0.25 6.30±0.27	6.79±0.22 6.31±0.26	6.47±0.19 6.13±0.25
	Weight of Knee	right left	1.48±0.54[b] 1.36±0.04	1.48±0.40 1.35±0.18	1.79±0.37 1.46±0.17	1.81±0.37 1.52±0.19	1.60±0.38 1.44±0.18

Figure 8: TNF assay results

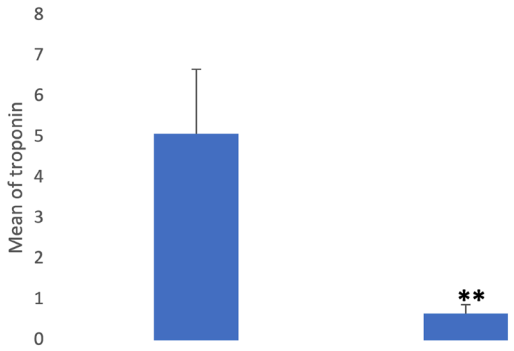


8. Tropenin assay results

To measure the amount of troponin in the rat knee joint according to different concentrations of standard solutions and their absorption, draw a standard diagram and then using a standard diagram (**Figure 9**), the concentration of troponin for each sample using its absorption was found.

The mean of the control group was 5.08 1.5 1.592 and the mean of the experimental group was 0.223 ± 0.651 and the independent t-test in unequal variance showed that the mean difference between the two groups was significant (p = 0.018) and the amount of troponin in the experimental group was significant. Significance has decreased.

Figure 9: Troponin assay results



Conclusion

The results of this study showed that Papaver rhoeas extract can significantly inhibit the OA process in rats with arthrosis of monosodium iodostat (especially at a dose of 200 mg/kg) and reduce edema and foot weight in infected rats. Oral extract of Papaver rhoeas showed that anthocyanin (active substance in Papaver rhoeas) had an anti-inflammatory effect through the mechanism of action in inhibiting the activity of inflammatory cells and proinflammatory cytokines in monosodium iodoacetate mice. Also, the decrease in creatine kinase-MB level in coronary fluid in the group receiving Papaver rhoeas confirms that the presence of anthocyanin can reduce the risk of CVD and cause endothelial dysplasia and by increasing the phosphorylation of hypertrophy protein kinase C and activation of protein kinase B Improves vascular stiffness, which has a protective effect on the heart. since the Papaver rhoeas used in this study has been shown in previous studies to significantly reduce the proliferation of monkey kidney cancer cell line (IC50 7.80 = µg / ml) and the effect of extract inhibition on DPPH radical (74.7) 5 µg / ml) The extract also had a phenolic content higher than the flavonoid content, which makes its use relatively safe. On the other hand, hypertension (moderate arterial pressure, systolic and diastolic pressure) can be related to vagal nerve activity, which causes There is a significant reduction in heart rate and decreased contractile strength of the heart[9]. Also, the serological findings of the present study showed that troponin levels decreased with the consumption of Papaver rhoeas. On the other hand, acetylcholine released from nerve terminals through muscarinic M2 receptors causes the opening of a group of potassium channels and increases potassium outflow and hyperpolarization of nodes that produce action potential in the heart. There is also a nicotinic receptor (α7 (α7nAChR) in synovial tissue. It has been shown for synovial tissue in the knee joint of patients with OA that it can produce local acetylcholine in arthritis attributed to the cholinergic system[27]. Which inhibits the production of inflammatory cytokines[23&28].

Stimulation of articular chondrocytes by IL-1β or TNF-α to transport p65 NF-κB nuclei also involves a wide range of catabolic genes such as nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) in chondrocytes, leading to the production of proteases. Destroys and weakens the extracellular matrix[29]. In this study, Papaver rhoeas reduced TNF-α in rat knee joint, which is in line with the study[30] on the other hand, epidemiological studies have shown that there is a relationship between increased levels of inflammatory markers and high prevalence of CVD. Based on the obtained results, it can be said that in the rats receiving the effective dose, the least joint damage and the best physiological function of the heart were observed.

Interests conflict

The researchers declare that they have no conflict of interest.

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ORIGINAL

The effect of *Cannabis sativa* on memory, apoptotic genes and inflammatory cytokines in rat

El efecto del Cannabis sativa sobre la memoria, los genes apoptóticos y las citoquinas inflamatorias en la rata

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Abstract

Objectives: *Cannabis sativa* L. has important ingredients of delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD). CBD is non-psychotropic, but THC is psychotropic responsible for making people feel "high". This study investigated changes in memory, apoptosis and inflammatory cytokines following *C. sativa* use in experimental rats.

Methods: Forty-five Wistar rats were randomly divided to 3 equal groups of experimental receiving cannabis subcutaneously (2 mg/kg in 0.6 mL volume) for 3 weeks, sham receiving ethanol identically (0.6 mL), and control receiving normal saline similarly (0.6 mL). The animals' spatial memory was assessed for 3 weeks using mean percentage of alternation and number of entries in a Y-maze to confirm cannabis effect on the brain. Real-time PCR was conducted for expression analysis of primer pairs for Bax and Bcl-2 genes in response to cannabis. Changes in inflammatory cytokines of IL-1, IL-6, IL-10, TNFα, INFγ, superoxidase dismutase (SOD) and malondialdehyde (MDA) were assessed following cannabis use.

Results: Significant reduction in memory and expression of Bcl-2 genes and increase in expression of Bax and inflammatory cytokines of IL-1, IL-6, IL-10, TNFα, INFγ and SOD were noted following cannabis use.

Conclusions: Based on our findings and reduction in memory and expression of Bcl-2 gene, and increase in expression of Bax gene and inflammatory cytokines following cannabis use, the paramount public health importance of cannabis use, when targeted for medical purposes should come into consideration.

Keywords: *Cannabis sativa*, Memory, Apoptosis, Inflammation.

Resumen

Objetivos: El *Cannabis sativa L.* tiene importantes ingredientes de delta-9-tetrahidrocannabinol (THC) y cannabidiol (CBD). El CBD no es psicotrópico, pero el THC es psicotrópico, responsable de hacer que las personas se sientan "colocadas". Este estudio investigó los cambios en la memoria, la apoptosis y las citoquinas inflamatorias tras el uso de *C. sativa* en ratas experimentales.

Métodos: Cuarenta y cinco ratas Wistar fueron divididas aleatoriamente en 3 grupos iguales de experimentación que recibieron cannabis por vía subcutánea (2 mg/kg en 0,6 mL de volumen) durante 3 semanas, de simulación que recibieron etanol de forma idéntica (0,6 mL) y de control que recibieron solución salina normal de forma similar (0,6 mL). Se evaluó la memoria espacial de los animales durante 3 semanas utilizando el porcentaje medio de alternancia y el número de entradas en un laberinto en Y para confirmar el efecto del cannabis en el cerebro. Se realizó una PCR en tiempo real para el análisis de la expresión de los pares de cebadores para los genes Bax y Bcl-2 en respuesta al cannabis. Se evaluaron los cambios en las citoquinas inflamatorias de IL-1, IL-6, IL-10, TNFα, INFγ, superoxidasa dismutasa (SOD) y malondialdehído (MDA) tras el consumo de cannabis.

Resultados: Se observó una reducción significativa de la memoria y la expresión de los genes Bcl-2 y un aumento de la expresión de Bax y de las citoquinas inflamatorias de IL-1, IL-6, IL-10, TNFα, INFγ y SOD tras el consumo de cannabis.

Conclusiones: Basándonos en nuestros hallazgos y en la reducción de la memoria y la expresión del gen Bcl-2, y el aumento de la expresión del gen Bax y de las citoquinas inflamatorias tras el consumo de cannabis, debe tenerse en cuenta la importancia primordial del consumo de cannabis para la salud pública, cuando se destina a fines médicos.

Palabras clave: *Cannabis sativa*, Memoria, Apoptosis, Inflamación.

Introduction

Cannabis plant with scientific name of *Cannabis sativa L*. has important ingredients of delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), while CBD is non-psychotropic part and THC a psychotropic chemical responsible for making people feel "high". Cannabinoids are endogenous lipid-based retrograde neurotransmitters that produce endocannabinoids in the body bound to cannabinoid receptors [G-protein coupled receptors of cannabinoid receptor type 1 (CB1R) and cannabinoid receptor type 2 (CB2R)] expressed throughout central and peripheral nervous system. CB1R receptors are noted in excitatory glutamatergic neurons and inhibitory GABA-ergic neurons mostly prevalent in hippocampus, basal ganglia, frontal cortex, cerebellum, hypothalamus, spinal cord and peripheral nervous system. CB2R receptors are mostly visible on hematopoietic, immune and glial cells expressed in the periphery under normal healthy condition, but in conditions of disease or injury, an upregulation can happen within the brain in unhealthy conditions. So THC and CBD are mostly responsible for the therapeutic potentials of cannabis and cannabinoids, even, THC in cannabis and cannabinoid makes the consumers to feel "high" that can limit their clinical use[1,2].

Smoking was reported as the most common route of cannabis administration over the past few decades that can cause an increase in THC and a decrease in cannabidiol leading to an increase in the persistence of neuroanatomic changes in the brain during adolescence[3]. There are conflicting results for dopamine release after cannabis use. Acute THC administration was demonstrated to elicit striatal dopamine release in animals[4] and humans[5], but others reported no evidence for THC-induced dopamine release[6], because THC induces quantitatively less dopamine release in comparison to other psychostimulants such as amphetamine or methylphenidate[7].

Cannabis was illustrated to have benefit in various neuropsychiatric disorders including anxiety, psychosis, autism spectrum disorder, neuropathic pain, cancer pain, multiple sclerosis, migraine, Parkinson disease, Alzheimer disease, Huntington disease, epilepsy, hypoxic-ischemic injuries, and HIV, as well as chronic cardiovascular and respiratory effects. Also, adverse events such as diarrhea and somnolence may occur following cannabis use[1,2,7].

Erectile dysfunction is the most common male sexual disorder after cannabis use[8]. Regular marijuana use can have neurotoxic effects leading to disruptions in the brain development and significantly change neuro-developmental trajectories, neurochemical communication and genetic expression of neural development9. Chronic cannabis use can increase the risk of developing substance use disorders, and influence motivation, cognitive and executive function and emotion processing[7,10,11].

Cannabis is the most commonly used substance of abuse in the United States after alcohol and tobacco and its use has a global increasing trend along with the progressive legalization of both recreational and medical cannabis, despite the various health effects of this substance[2,12]. Neuropsychological studies revealed considerable understanding of the effects of cannabis on the brain due to advances in neuroimaging providing the chance to track neuronal activation, neuroanatomic changes, and metabolic and neurotransmitter activity during brain development[13].

With worldwide increases in cannabis use and decreases in perceived risk, it is necessary to reevaluate its adverse effects especially on nervous system[14] and the brain as the mostly target organ after administration of cannabis. A suppressive effect of THC on secretion of different cytokines by cultured murine spleen cells was previously reported[15]. THC at doses of 5-100 mg/kg was demonstrated to decrease the plasma concentration of interferon-alpha and –beta[16], while the immunomodulatory concentrations of used THC were more than physiological range of THC (1-100 ng/ml) observed in plasma of human marijuana smokers[17].

Watzl et al.[18] showed that CBD suppressed the secretion of IL-1, TNF and IFN, and THC the release of IFN. So this study was carried out to assess changes in memory, apoptotic genes and inflammatory indicators of malondialdehyde (MDA), superoxidase dismutase (SOD), interleukins of IL-1, IL-6, IL-10, tumor necrosing factor alpha (TNFα), and interferon-gamma (INFγ) following *C. sativa* use in experimental rats.

Methods

Preparation of *C. sativa*

C. sativa L. was donated by Shiraz Islamic Azad University herbarium in Shiraz, Iran. The whole plant was left at room temperature in shadow to be dried and then changed to powder (particles not greater than 1.8 inch). The maceration method was applied for extraction. In brief, the powder was soaked in a closed container containing 70% ethanol for 2-4 days, was later shaken twice per day, was filtered and was separated by a rotary evaporator. The extract was put in oven at 40°C to be dried. To reach the requested concentration for the research, the dried extract was finally dissolved in distilled water.

Animals and grouping

Forty five male 8 weeks old Wistar rats (200-220 g) were purchased from Shiraz University of Medical Sciences, Shiraz, Iran and kept at 22±1°C with 12 h light/dark cycle, and had free access to water and food and were allowed to accommodate to their condition before the experiments. The study was approved in Ethics Committee of Shiraz Islamic Azad University (7-E-IR-

MIAU.REC.80-B-1397), and all experiments were carried out based on guidelines of Iran Veterinary Organization.

Rats were randomly divided to three equal groups. The experimental group received daily subcutaneous administration of 2 mg/kg of the cannabis for three weeks in 0.6 mL volume. The sham group was injected identically with equal volume of 70% ethanol and the control group received distilled water similarly. All experiments were undertaken between 08:00 and 12:00 AM.

The memory Y-maze test

The Y-maze was used to assess animals' spatial memory as described before[19]. Briefly, Y-maze possess three similar 16 arms, while the maze floor involves soiled animal bed. Animals were investigated in dark phase of their cycle. First test included blockage of one arm with black Plexiglas considered as the 'Novel' arm in the second test. The other remaining arm was the 'Start' arm and the last arm was the 'Other', and all arms were randomized between animals. The rats were allowed to explore the start and other arms for 15 minutes as acquisition trial. Quantification of the entries into an arm was recorded when the rat entered 10 cm of a given arm. After the first assessment, the rats returned to their cage. After 4 hours, the animals were transferred in the same start arm as first testing was undertaken.

The arm that was previously blocked was available in the second test and the animals were allowed to explore all arms for 5 minutes. In the second trial, first arm entrance between the novel and other arm was designated as the First Choice denoting to the percentage of rats with recognition of the novel arm-arm discrimination memory. The time spent in each arm for each minute was quantified and recorded (Dwell Measure) to indicate the inspective exploratory behaviors. The number of entries made into each arm for each minute was quantified and recorded (Entry Data) to depict the inquisitive behavior of responses to novelty. The interaction on Dwell and/or Entry data between arm choice, exposure and period time of injection showed the spatial recognition memory of the previously unvisited arm. Arm entry was completed after location of the entire tail was within the arm. Alternation was defined as successive entries into the three arms on overlapping triple sets.

Quantitaive real time PCR

To quantify expression of Beta-2 microglobulin (B2m), Bax, and Bcl-2 genes, brain tissue was harvested for total cellular ribonucleic acid (RNA) extraction 1 to 3 weeks after treatment of the cells to cannabis using an RNA extraction kit (Cinna Gen Inc., Tehran, Iran). The ratio of optical density (A260/A280 and A260/A230) was assessed using a Nanodrop™ spectrophotometer (Nanodrop; Thermo Fisher Scientific Inc., USA), the quantity and quality of obtained RNA were determined. The cDNA was synthesized using 1000 ng total RNA in a first strand complementary DNA (cDNA) synthesis reaction applying the Revert Aid™ first strand cDNA synthesis kit (Thermo Fisher Scientific Inc., USA). The Bax and Bcl-2 genes were target and B2m was the housekeeping gene and an endogenous control. The sequences of the genes were determined using NCBI database and primer sets were designed by primer3 software (**Table I**).

Table I: Primers used in the present study.

Genes	Primer Sequences	Sizes (bp)
Bax	Forward: 5'-CTGCAGAGGATGATTGCTGA-3' Reverse: 5'-GATCAGCTCGGGCACTTTAG-3'	174
Bcl-2	Forward: 5'-ATCGCTCTGTGGATGACTGAGTAC-3' Reverse: 5'-AGAGACAGCCAGGAGAAATCAAAC-3'	134
B2m	Forward: 5'-CGTGCTTGCCATTCAGAAA-3' Reverse: 5'-ATATACATCGGTCTCGGTGG-3'	244

Abbreviation: bp, base pair.

Real time-polymerase chain reaction (PCR) was carried out using SYBR Green I as reporter dye and Step One Real time-PCR reactions (Applied Biosystems, USA). In each reaction, 200 nM of each primer was used for targeting the specific sequence. The PCR conditions were set as 10 min at 94°C followed by 40 cycles of 15 s at 94°C, 60 s at 60°C, and melting curve analysis ramping of 65-95°C. The amplification signals of different samples were normalized to B2m cycle threshold (Ct), and then the 2-delta delta cycle threshold (2-DDCt) method was applied to compare mRNA levels of various groups, which represented a fold-change in data analysis[20].

Assessment of inflammatory cytokines

A blood sample was provided in each group on days 7, 14 and 21 after interventions by cardiac puncture in tubes with heparin sodium for hematological tests and in serum-separated tubes for biochemical parameters. The coagulated blood was left to clot at room temperature for 30 min, and was latter centrifuged at 3600× g for 15 min. The following parameters were determined by commercial kits (Merck, Germany): IL-1, IL-6, IL-10, TNFα, INFγ, superoxidase dismutase and MDA.

Statistical analysis

Data were shown as mean±SEM (tandard error of the mean) and analyzed using statistical package for the social sciences software (SPSS, Version 20, Chicago, IL, USA). One-way Analysis of variance (ANOVA) and Post-hoc Tukey's were used for comparison. P values less than 0.05 were considered statistically significant.

Results

The memory Y-maze test

Regarding behavioral alteration when the groups were compared after 1, 2 and 3 weeks of cannabis use; a significant difference was noted between the groups ($P \leq 0.01$, $P \leq 0.01$, $P \leq 0.001$, respectively) revealing spatial

memory impairment following cannabis administration (**Figure 1**). Regarding the number of entries when comparison between the groups was conducted after 1, 2 and 3 weeks of cannabis use, a significant statistical difference was visible after one ($P \leq 0.01$), two ($P \leq 0.05$) and 3 weeks ($P \leq 0.01$) denoting to an impairment in spatial memory following cannabis use (**Figure 2**).

Figure 1: Comparison of the effect of cannabis on mean percentage of behavioral alterations between the control, sham and the experimental groups; 1, 2 and 3 weeks after interventions (P = 0.01, P = 0.01, P = 0.001, respectively).

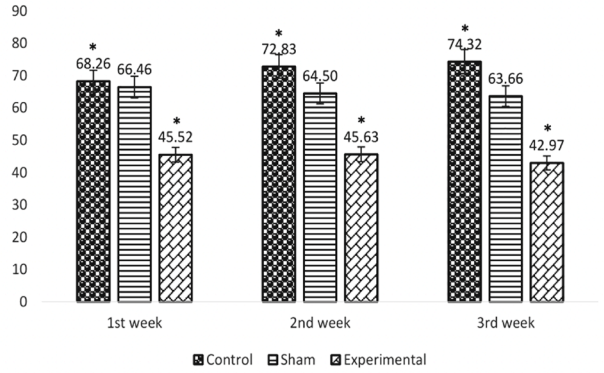


Figure 2: Comparison of the effect of cannabis on mean number of entries by rats between the control, sham and the experimental groups; 1, 2 and 3 weeks after interventions (P = 0.01, P = 0.05, P = 0.01, respectively).

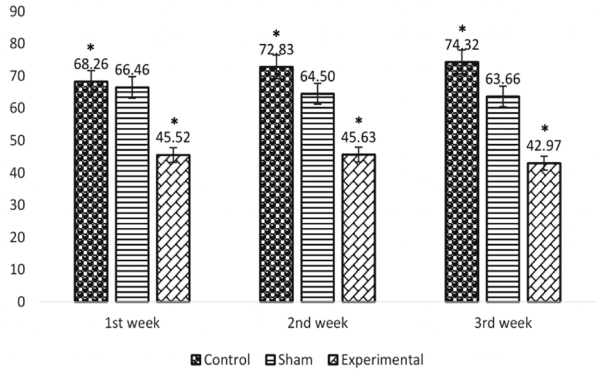
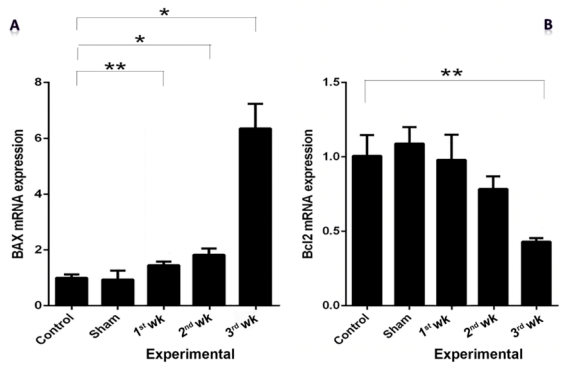


Figure 3: Using real-time quantitative PCR and assessment of the effect of Cannabis on various genes: (A). Bax (*P = 0.0003) (**P = 0.01) vs. control, (B). Bcl-2 (**P = 0.003) vs. control.



Quantitaive real time PCR

Regarding the expression of apoptotic genes, cannabis resulted to an increase in Bax expression (P = 0.0003, P = 0.01), and a decrease in Bcl-2 expression (P = 0.003) (**Figure 3**).

Assessment of inflammatory cytokines

Regarding MDA level, no significant changes were noted following cannabis use ($P > 0.05$). For SOD level, there were significant modification between sham and control group (P = 0.02) and between control and cannabis group after two (P = 0.01) and 3 (P = 0.03) weeks illustrating an increasing trend. Regarding IL-1, IL-6, and IL-10, there were significant modification between sham and control group (P = 0.0001) and between control and cannabis group after one (P = 0.0001), two (P = 0.0001) and 3 (P = 0.0001) weeks revealing a rising trend. The changes between sham and control group and between control and cannabis group after one, two and 3 weeks were also statistically significant ($P < 0.05$) demonstrating an increase. Totally, an increase was noted in IL-1, IL-6, IL-10, TNFα, INFγ and SOD following cannabis use, but MDA illustrated no significant change following cannabis use (**Table II**).

Discussion

C. sativa plant with the major psychoactive constituent of Δ-9 tetrahydrocannabinol (THC) is the most widely cultivated, trafficked and consumed substance among approximately 147 million people annually, consisting 2.5% of the world population[21]. Although cannabis is used for therapeutic purposes and has wide-ranging potential uses in medicine, with increasing legalization, still the adverse events in central nervous system and other health outcomes limit its adoption. In this study we showed an increase in IL-1, IL-6, IL-10, TNFα, INFγ and SOD following cannabis use, but MDA did not show any significant changes following cannabis use.

Similar to our findings, a suppressive effect of THC on secretion of different cytokines by cultured murine spleen cells was previously reported[15]. THC at doses of 5-100 mg/kg was demonstrated to decrease the plasma concentration of interferon-alpha and –beta[16], while the immunomodulatory concentrations of used THC were more than physiological range of THC (1-100 ng/mL) observed in plasma of human marijuana smokers[17]. It was shown that CBD suppressed the secretion of IL-1, TNF and IFN, and THC the release of IFN[18].

We showed that tumor necrosis factor secretion was affected by cannabis. It was already reported that murine macrophage phagocytosis was impaired by THC concentrations above 5 pg/mL[15]. Animal and human studies revealed that THC at physiological levels of 2.5 ~g/mL had no effect on NK cell activity *in vivo* and *in*

Table II: Changes in hematological variables following cannabis use.

Variable \ Group	Control (Mean ± SD)	Sham (Mean ± SD)	Cannabis 1 week (Mean±SD)	Cannabis 2 weeks (Mean ± SD)	Cannabis 3 weeks (Mean ± SD)
MDA **P value**	31.50 ± 2.12 N/A	19.66 ± 6.02 0.12	20.66 ± 3.05 0.18	18.75 ± 4.57 0.07	21.50 ± 5.80 0.193
Super Oxidase Dismutase **P value**	325.00 ± 35.35 N/A	409.66 ± 51.43 0.02	427.00 ± 8.71 0.01	426.50 ± 11.03 0.01	409.00 ± 19.18 0.029
IL-10 **P value**	325.00 ± 35.35 N/A	493.33 ± 4.93 0.0001	502.66 ± 5.50 0.0001	476.50 ± 18.06 0.0001	480.75 ± 9.53 0.0001
INFγ **P value**	136.00 ± 15.55 N/A	447.66 ± 25.10 0.0001	204.66 ± 8.32 0.03	406.75 ± 16.56 0.0001	575.75 ± 27.98 0.0001
TNF **P value**	647.50 ± 67.17 N/A	1291.66 ± 175.61 0.0001	948.00 ± 22.51 0.05	1058.50 ± 119.32 0.006	1321.50 ± 58.54 0.0001
IL-6 **P value**	11.00 ± 1.41 N/A	61.33 ± 10.69 0.0001	43.66 ± 1.52 0.0001	49.50 ± 1.73 0.0001	59.25 ± 3.30 0.0001
IL-1 **P value**	337 ± 11.31 N/A	944.66 ± 93.24 0.0001	744.00 ± 29.51 0.0001	814.50 ± 35.45 0.0001	930.75 ± 45.38 0.0001

vitro[22,23], while in vitro concentrations of THC above 5 pg/mL could decrease the NK cell activity[24,25], which was a dose-dependent modulation for IFN in another study[18]. No effect was noted no effect on IFN release compared with the control[26], but at concentrations more than 5 pg/mL THC, the release of interferon-alpha (IFN-α) and interferon-beta (IFN- β) was suppressed[15,18,26].

Cannabis use was demonstrated to be associated with a potentially beneficial decrease in systemic inflammation and immune activation such as IL-6 and TNFα in the context of antiretroviral-treated HIV infection[27]. Several studies illustrated the anti-inflammatory activity of CBD in cell lines and animal models of skin inflammation[28-30]. Sangiovanni et al.[29] showed that cannabis can inhibit the release of mediators of inflammation involved in wound healing via impairment of the NF-κB pathway and inhibiting the TNFα-induced NF-κB-driven transcription and inhibition of the release of IL-8 and MMP-9 in HDF and HaCaT cell lines. It was noted that cannabinoid compounds mitigated inflammation associated with alcohol use including circulating levels of the pro-inflammatory cytokines interleukin 6 (IL-6), IL-8, and IL-1β in the blood[31]. Our findings showed a decrease in expression of Bcl-2 and an increase in expression of Bax genes which were also confirmed by other researchers too[32-35].

Conclusions

In summary, based on our findings revealing a reduction in memory and expression of Bcl-2, an increase in expression of Bax and inflammatory cytokines of IL-1, IL-6, IL-10, TNFα, INFγ and superoxidase dismutase, we can conclude that changes in memory, apoptotic genes and inflammatory indicators following cannabis use emphasize paramount importance of cannabis when targeted for medical use. The results can be added to the literature regarding its public health issues.

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Conflict of interests

The authors have no conflict of interest.

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ORIGINAL

COVID-19 outbreak- Beliefs and practices among dental professionals of Riyadh, Saudi Arabia-A Cross-sectional study

Brote COVID-19 - Creencias y prácticas entre los profesionales de la odontología de Riyadh, Arabia Saudí - Estudio transversal

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Abstract

Background: Covid-19 virus has caused unparalleled hastening of infection transmission to healthcare workers including dental professionals worldwide. This study examined dental professional's knowledge, awareness, and practice during the Covid-19 outbreak in Riyadh.
Materials and methods: A cross-sectional study was conducted among dental professionals of government and private dental hospitals and medical centers in the Riyadh region through an electronic survey. A self-designed questionnaire designed in English and comprised of a series of questions pertaining to socio-demographic characteristics, the awareness of dental professionals towards COVID-19, and infection control in dental clinics. Knowledge, awareness, and practice scores were considered as primary outcome variables. The data were imported into SPSS and the p-value was set at < 0.05 as significant statistically.
Results: Out of 381, 171 (44.88%) were aged >45 years and the respondents were predominantly females 247 (64.83%) compared to males134 (35.17%). More than half of the respondents were dentists 234 (61.42%) and 258 (67.72%) having experience of >10 years. Most of the respondents 270 (70.90%) were practicing under COVID-19 guidelines. Age >45 years, females, dental profession, years of working experience, and dental professionals working in a military hospital under the government sector were statistically significant (p<0.001) for good knowledge, awareness, and practice scores.
Conclusion: Dental professionals of Riyadh had excellent knowledge, positive awareness, and good practices regarding COVID-19 measures to be taken in dental clinics.

Keywords: Coronavirus, knowledge, practice, dental professionals, infection control, beliefs.

Resumen

Antecedentes: El virus Covid-19 ha causado una aceleración sin precedentes de la transmisión de la infección a los trabajadores sanitarios, incluidos los profesionales dentales, en todo el mundo. Este estudio examinó los conocimientos, la concienciación y la práctica de los profesionales dentales durante el brote de Covid-19 en Riyadh.
Materiales y métodos: Se llevó a cabo un estudio transversal entre los profesionales dentales de hospitales dentales y centros médicos gubernamentales y privados de la región de Riyadh mediante una encuesta electrónica. Se utilizó un cuestionario de diseño propio, redactado en inglés y compuesto por una serie de preguntas relativas a las características sociodemográficas, la concienciación de los profesionales de la odontología respecto al COVID-19 y el control de la infección en las clínicas dentales. Las puntuaciones de conocimiento, concienciación y práctica se consideraron variables de resultado primarias. Los datos se importaron al SPSS y el valor p se fijó en < 0,05 como significativo estadísticamente.
Resultados: De un total de 381, 171 (44,88%) tenían más de 45 años y entre los encuestados predominaban las mujeres, 247 (64,83%), frente a los hombres, 134 (35,17%). Más de la mitad de los encuestados eran dentistas 234 (61,42%) y 258 (67,72%) tenían una experiencia de más de 10 años. La mayoría de los encuestados, 270 (70,90%), ejercían según las directrices COVID-19. La edad >45 años, el sexo femenino, la profesión de odontólogo, los años de experiencia laboral y los profesionales de la odontología que trabajaban en un hospital militar del sector gubernamental fueron estadísticamente significativos (p<0,001) para las puntuaciones de buen conocimiento, concienciación y práctica.
Conclusión: Los profesionales de la odontología de Riyadh tenían un conocimiento excelente, una concienciación positiva y buenas prácticas en relación con las medidas de COVID-19 que deben adoptarse en las clínicas dentales.

Palabras clave: Coronavirus, conocimiento, práctica, profesionales dentales, control de la infección, creencias.

Introduction

Severe Acute Respiratory Coronavirus 2 (SARS-CoV-2) causes COVID-19 disease which appeared first among patients visiting the wet market, that contains some wildlife species in Wuhan City, Hubei Province of China, in December 2019. Since then, large outbreaks are being reported in other Chinese Provinces and many nearby countries eventually spreading across the globe[1]. On 30 Jan 2020, the World Health Organization (WHO) International Health Regulation (IHR) emergency committee declared the disease a Public Health Emergency of International Concern (PHEIC) due to its novel nature and spreading rapidly nationally and internationally. On 11 March 2020, WHO declared it as a worldwide Pandemic. A citizen of Saudi returning from Iran through Bahrain was tested positive for Covid-19 and on the 2nd of March 2020, the Ministry of Health reported it as the first case in Saudi Arabia[2].

Saudi Ministry of Health has recommended following social distancing and adopting sanitary habits and also to self-quarantine for 14 days if an individual has arrived from outside the kingdom. The classical routes of transmitting coronavirus include direct droplets while coughing, sneezing, and contact with oral, nasal, and eye mucous membranes[3]. General population can get anxious and create ruckus during epidemics and pandemics due to less knowledge about the emerging disease. Awareness, Attitude, and practice have been studied in many previous epidemics such as swine influenza, Middle East Respiratory Syndrome (MERS), and Dengue fever. The spread and transmission of viruses can be reduced by being aware of the disease and having positive attitudes and practices to stop the progression of the virus further[4].

Among the infected individuals with covid-19, healthcare professionals represent 9% due to close interaction with patients with covid-19. Due to the direct exposure to saliva and blood, dental practitioners are also at high risks of contracting COVID-19. To "flatten the curve" during this first outbreak, many countries have issued quarantine measures, and for time being dentists have been instructed to provide emergency treatments only[5].

Occupational Safety and Health Administration (OSHA), specified dental professionals at high-risk exposure category for nosocomial infection, due to droplets/ aerosols generated during dental procedures[6]. Likewise, the New York Times in March 2020 in their work entitled "The worker who faces the greatest coronavirus risk", mentioned dental professionals as utmost exposed workers, compared to nurses and general physicians[7]. To decrease the risk of contamination and spread from COVID-19, dental health care workers should take appropriate measures for preventing and entertain a high level of awareness regarding COVID-19[8]. In countries/ regions affected by COVID-19, infection control protocols for dental practices should be implemented on an urgent basis by following guidelines recommended by the Centers for Disease Control and Prevention (CDC), the American Dental Association (ADA), and WHO for dentists and dental staff to control the spread of COVID-19[9,10] Infection and transmission from droplets/ aerosols generated during dental procedures in dental clinics and hospitals can be prevented by taking personal precautions (mask, goggles, face shields, and protective outerwear, etc.) by the dental professionals[11].

In a Cross-sectional study conducted by Kamran et al.[12] in Pakistan, most of the dentists were aware of the CDC guidelines and designation of dentist and level of awareness had a potential correlation ($p = 0.01$). Further study by Nasser et al.[13] among Lebanese dentists who had good knowledge (91.3%), and good practice (58.7%) regarding COVID-19. Another cross-sectional study by Ruba et al.[14] among Dentists reported having satisfactory knowledge and a positive attitude towards COVID-19.

Though cases of coronavirus transmission in a dental setting were not reported in Saudi Arabia, dental professionals should always upgrade themselves regarding hazards challenging their current practice. In Riyadh, there is no empirical data regarding dental professional's knowledge, awareness, and practice during COVID-19. Therefore, evaluating their knowledge is crucial in identifying the existing gaps. With this background, the present study aimed to assess dental professionals' knowledge, awareness, and practice during the Covid-19 outbreak in Riyadh, Saudi Arabia.

The aim of the study was to assess the knowledge, awareness, and practice of dentists toward Covid-19 in Riyadh, Saudi Arabia,

Materials and methods

Study design: A Cross-sectional study employed using a self-reported questionnaire.
Source population: The source population comprised dental health care professionals in the Riyadh region of Saudi Arabia.
Study population: The study population comprised registered dental professionals which include dentists, dental hygienists, and assistants who are registered under the Saudi council of health specialists.
Study setting: The present study was an electronic survey conducted among dental professionals via a link attached to a mass e-mail distribution.
Study period: 4 months from 20 December 2020 to March 20. 2020
Sample size: The sample size was 387
Sampling technique: Non-probability convenience sampling
Sample size calculation:
The sample size is calculated based on the proportion of

awareness of COVID_19 from a study by Yousuf et al.[15] and using the formula of

$$\frac{z^2\, p(1-p)}{d}$$

Z = Standard normal variate at 5% type 1 error = 1.96
P = 0.70
D = maximum acceptable error=0.05

$$\frac{(1.96)2x\ 0.70(1\_0.70)}{0.05x0.05} = 323$$

Non response rate = 20%
Estimated sample size = 323+64 = 387

Ethical and informed consent: Ethical permission was obtained from Institutional Review Board (IRB) in the Riyadh region. Electronic informed consent was obtained from all the participants to avoid anonymity and voluntary participation. They were explained in detail the information present in the questionnaire.

Inclusion criteria:
- Registered dentists, dental assistants, hygienists working at government and private hospitals, clinics and, medical centers,

Exclusion criteria:
- Not completed the questionnaire in the given period.
- Whose contact information was missing.

Data collection: The questions on the survey were developed after reviewing pertinent literature and the international guidelines. A self-designed questionnaire was designed in English and comprised of a series of questions pertaining to socio-demographic characteristics, the awareness of dental professionals towards COVID-19, and infection control in dental clinics. The questionnaire was delivered to the study subject via email and What's App (social media application through Google forms link.

Components of the questionnaire:
-The survey was structured multiple-choice questionnaire divided into sections:
- Section 1: Dental professionals demographic and profession-related characteristics (gender, age, type of dental professionals, years of practice, workplace.)
- Section 2: questions related to dental professionals knowledge and awareness COVID-19 (incubation period, the symptoms of the disease, the mode of transmission of COVID-19, and infection control measures for preventing COVID-19 e.g hygiene practices, etc

Validity and reliability of questionnaire:
- A specialist in infectious and communicable diseases was consulted to verify the content of the questionnaire.
- The questionnaire was pre-tested for validity and reliability.

Study variables: Knowledge, awareness, and practice scores were considered as primary outcome variables. Age, gender, dental profession, years of working and working sector were considered as explanatory variables.

Statistical analysis: Data collection and entry were done in Microsoft excel and was analyzed using SPSS[16] package version 25. Descriptive statistics were presented as means and standard deviations (SD) for continuous variables and frequency and percentages for categorical variables. A Chi-square test was used to check the association between KAP scores and socio-demographic factors. A P-value of less than 0.05 was considered significant.

Results

The final analysis included 381 respondents.

Respondents characteristics

Table I shows respondents' socio-demographic data of which the majority of 171 (44.88%) participants were aged >45 years, and were predominantly females 247 (64.83%) compared to males 134 (35.17%). More than half of the respondents were dentists 234 (61.42%). The study consisted of a majority of 361 (94.75%) working in the government sector (military hospital, Universities clinics, or ministry health center) and 258 (67.72%) having experience of >10 years.

Knowledge about the COVID-19 Infection

Table II represents the dental professional knowledge regarding COVID-19 and almost 268 (70.3%) had good knowledge about the Incubation Period, Symptoms, and Mode of Transmission of the COVID-19 Infection. The mean total knowledge score was 10.84. When asked about the incubation period, 122 (32.0%) participants have reported the correct answer. The majority 377 (99.0%) responded to fever and cough as prodromal symptoms of Covid-19. In addition, the majority 373 (97.9%) were known modes of transmission.

Awareness for Preventing COVID-19 Transmission

Table III shows the dental professional awareness regarding COVID-19. Out of the 381 dental professionals, the majority 215 (56.40%) dental professionals were aware of preventing COVID-19 Transmission in Dental Clinics. The mean total awareness score was 6.62. When they were asked about, Personal Protective Equipment's (PPE) worn during Aerosol generating procedures GP, 243 (63.78%) respondents were aware of PPE importance. Almost all dentists366 (96.1%) reported that importance of physical distancing, hand hygiene, universal masking, and respiratory etiquette to decrease the possibility of transmitting infections to patients and themselves.

The practice of COVID-19 guidelines.

Table IV reports the dental professional practice during COVID-19. Out of the 381 dental professionals, the majority 270 (70.90%) we're practicing under COVID-19 guidelines. The mean total practice score was 14.90. The majority of the dental professional reported that cleaning hands frequently, cleaning and disinfecting surfaces in contact with suspected patients, and wearing personal protective equipment can help in preventing transmission of COVID-19 (**Table IV**).

Association of knowledge, awareness, and practice scores with demographic data

Table V shows the level of knowledge, awareness, and practice as per socio-demographic factors. The levels of knowledge, awareness, and practice scores were significantly associated ($p<0.001$) for >45 years age, females, dental profession, years of working experience, dental professionals working in a military hospital under government sector.

Table I: Summary of demographic parameter.

Demographic parameter	Summary
Age	
25-35	79 (20.73%)
> 35-45	131 (34.38%)
> 45	171 (44.88%)
Gender	
Female	247 (64.83%)
Male	134 (35.17%)
Type of dental professional	
Dentist	234 (61.42%)
Dental assistant	100 (26.25%)
Dental hygienist	36 (9.45%)
Others	11 (2.89%)
Years of experience	
> 10 years	258 (67.72%)
> 5 years-10	73 (19.16%)
up to 5 years	50 (13.12%)
Which sector do you work	
Private	20 (5.25%)
Governmental	361 (94.75%)
Which government facility	
Military hospital	187 (49.08%)
Ministry of health	97 (25.46%)
Universities clinics	77 (20.21%)
Others	20 ()5.25%

Table II: Summary of knowledge regarding COVID 19.

Knowledge parameters	Correct answer
What is the incubation period days of Covid 19 Infection	122 (32.0%)
Symptoms of Covid 19 infection include Fever	377 (99.0%)
Cough	374 (98.2%)
Short of breath	371 (97.4%)
May present without symptoms	345 (90.6%)
Diarrhea	320 (84.0%)
Running nose	298 (78.2%)
Skin rash	174 (45.7%)
What is the mode of transmission of Covid 19 infection?	
Droplet (Coughing and Sneezing)	373 (97.9%)
Close contact with others(handshaking, hugging)	364 (95.5%)
Contact with surfaces (doorknobs and tables)	354 (92.9%)
Airborne (airplane travel)	294 (77.2%)
Can dental health professional get infected by an asymptomatic patient	363 (95.28%)
Mean total Knowledge Score	10.84 ± 1.56
Poor knowledge (<11)	113 (29.7%)
Good knowledge (>=11)	268 (70.3%)

Table III: Summary of Awareness of COVID 19.

Awareness	Correct answer
Personal Protective Equipment's (PPE) that should be worn by a dental health professional during AGP	243 (63.78%)
Since the dentist is always physically close to the patient, he needs to wear a high efficient respirator (e.g N 95) all the time during his work in the dental clinic	61 (16.01%)
What are the points that we should follow to decrease the chance of transmission of Covid-19 between HCWs?	
• Physical distancing	366 (96.1%)
• Hand hygiene	366 (96.1%)
• Universal masking	344 (90.3%)
• Respiratory etiquette	294 (77.2%)
It is acceptable to clean and disinfect the face shield or protective goggles during extended use and reuse and dispose of only when it is damaged or difficult to see through	141 (37.01%)
It is possible to use the same high-efficiency respirator (N95) or other personal protective equipment PPE by more than one health worker	356 (93.44%)
According to your opinion, Covid-19 is Serious respiratory infection. Routinely mild respiratory infection	352 (92.39%)
Mean total awareness score	6.62 ± 1.07
Poor awareness (<7)	166 (43.60%)
Good awareness (>=7)	215 (56.40%)

Table IV: Summary of practice related questions.

	Correct answer
Can the female dental professional wear (niqab) instead of the surgical mask as preventive measures for COVID 19	346 (90.8%)
Are medical glasses considered as a substitute for face shield or googles	188 (49.3%)
The correct sequence of donning wearing of PPE	287 (75.33%)
The correct sequence of doffing take off the PPE	77 (20.21%)
To save resources, we can use the surgical gloves for more than one patient or wash and disinfect them to be reused	357 (93.70%)
Measures for prevention of COVID 19 transmission in dental clinics include	
Frequently clean hands by using soap and water or alcohol-based hand rub	371 (97.4%)
Personal protective equipment such as dental goggles, masks, and gloves.	361 (94.8%)
Routinely clean and disinfect surfaces in contact with known or suspected patients	354 (92.9%)
Wearing a surgical mask directly on the face then high-efficiency respirators like N95 over it.	265 (69.55%)
How can we reduce the exposure to patients' fluids or secretions while providing dental care in dental clinics?	
Use of high-speed suction devices	348 (91.3%)
Use of rubber dam inside the patient's mouth	347 (91.1%)
Reducing the follow-up visits for the patient unless necessary	343 (90.0%)
Arranging seating in the waiting area to a safe distance of at least one meter	331 (86.9%)
Use of absorbent materials such as sterile cotton or gauze	305 (80.1%)
Use of manual filling or scaling tools instead of the high-speed handpiece or ultrasonic	303 (79.5%)
Personal and clinic hygiene practices include	
Clean hand with an alcohol-based rub or soap and water	377 (99%)
Disinfecting the lab work area every day	353 (92.7%)
Thoroughly cleaning the chairs saliva ejector with disinfectant	347 (91.1%)
Routinely clean and disinfect clinic surfaces every three days	298 (78.2%)
Fumigation of dental operatory once a week	297 (78.0%)
Total Practice Score	14.90 ± 1.90
Poor practice (<15)	111 (29.10%)
Good practice (>=15)	270 (70.90%)

Table V: Comparison of demographic parameters between Total knowledge score, awareness score, and practice score (N=381).

		Total knowledge score		Total awareness score		Total practice score	
		Poor (<11)	Good (>=11)	Poor (<7)	Good (>=7)	Poor (<15)	Good (>=15)
Age	25-35 (N=79)	39 (49.37%)	40 (50.63%)	39 (49.37%)	40 (50.63%)	36 (45.57%)	43 (54.43%)
	>35 -45 (N=131)	43 (32.82%)	88 (67.18%)	51 (38.93%)	80 (61.07%)	36 (27.48%)	95 (72.52%)
	>45 (N=171)	31 (18.13%)	140 (81.87%)	76 (44.44%)	95 (55.56%)	39 (22.81%)	132 (77.19%)
	***p* value**	**<0.001**		0.320		**<0.001**	
Gender	Female (N=247)	57 (23.08%)	190 (76.92%)	110 (44.53%)	137 (55.47%)	70 (28.34%)	177 (71.66%)
	Male (N=134)	56 (41.79%)	78 (58.21%)	56 (41.79%)	78 (58.21%)	41 (30.6%)	93 (69.4%)
	***p* value**	**<0.001**		0.606		0.643	
Type of dental professional	Dental assistant (N=100)	22 (22%)	78 (78%)	37 (37%)	63 (63%)	35 (35%)	65 (65%)
	Dental hygienist (N=36)	4 (11.11%)	32 (88.89%)	26 (72.22%)	10 (27.78%)	5 (13.89%)	31 (86.11%)
	Dentist (N=234)	82 (35.04%)	152 (64.96%)	97 (41.45%)	137 (58.55%)	65 (27.78%)	169 (72.22%)
	Others (N=11)	5 (45.45%)	6 (54.55%)	6 (54.55%)	5 (45.45%)	6 (54.55%)	5 (45.45%)
	***p* value**	**0.004**		**0.002**		**0.025**	
Years of experience	Up to 5 years (N=50)	25 (50%)	25 (50%)	24 (48%)	26 (52%)	25 (50%)	25 (50%)
	> 5 Years-10 (N=73)	19 (26.03%)	54 (73.97%)	33 (45.21%)	40 (54.79%)	18 (24.66%)	55 (75.34%)
	>10 years (N=258)	69 (26.74%)	189 (73.26%)	109 (42.25%)	149 (57.75%)	68 (26.36%)	190 (73.64%)
	***p* value**	**0.003**		0.718		**0.002**	
Which sector do you work	Governmental (N=361)	108 (29.92%)	253 (70.08%)	158 (43.77%)	203 (56.23%)	104 (28.81%)	257 (71.19%)
	Private (N=20)	5 (25%)	15 (75%)	8 (40%)	12 (60%)	7 (35%)	13 (65%)
	***p* value**	0.639	0.741	0.553			
Which Government Facility	Military hospital (N=187)	50 (26.74%)	137 (73.26%)	83 (44.39%)	104 (55.61%)	56 (29.95%)	131 (70.05%)
	Ministry of health (N=97)	25 (25.77%)	72 (74.23%)	46 (47.42%)	51 (52.58%)	27 (27.84%)	70 (72.16%)
	Universities Clinics (N=77)	33 (42.86%)	44 (57.14%)	29 (37.66%)	48 (62.34%)	21 (27.27%)	56 (72.73%)
	Others (N=20)	5 (25%)	15 (75%)	8 (40%)	12 (60%)	7 (35%)	13 (65%)
	***p* value**	**0.044**		0.608		0.896	

Discussion

Several infectious diseases have been treated the human health[17-22]. SARS-COVID disease caused higher morbidity and mortality in the last century[23-26]. The present study examined dental professional's knowledge, awareness, and practice during the COVID-19 outbreak in Riyadh, Saudi Arabia. Out of 381, 171 (44.88%) were aged >45 years and the respondents were predominantly females 247 (64.83%) compared to males134 (35.17%). More than half of the respondents were dentists 234 (61.42%) and 258 (67.72%) having experience of >10 years. Most of the respondents 270 (70.90%) were practicing under COVID-19 guidelines. Age >45 years, females, dental profession, years of working experience, and dental professionals working in a military hospital under the government sector were statistically significant (p<0.001) for good knowledge, awareness, and practice scores.

The current study revealed that 381 dentists participated and submitted the form. This optimum number was filled by working and non-working dental professionals since it was distributed electronically. This finding can be compared to a similar KAP study by Duruk et al.[11] where 1,454 participants out of (n=1,958) responded to the survey considering the COVID-19 outbreak as a worrisome issue to be looked into.

Increasing age has a potential impact on the knowledge of dental health professionals about COVID-19. This can be compared to a countrywide survey in Saudi Arabia by Abdurrahman et al. 27 regarding knowledge, attitude, and practice of health care professionals, where the middle and elderly age group were more knowledgeable when compared to a younger age. Most of the respondents 247 (64.83%) were females compared to males 134 (35.17%). This finding can be compared to a pilot study by Cintia et al.[28] where out of 400 dentists, (64.5%) were women and 27% were in the age group of 36-45 years.

In the present study majority of dental health professionals, 361 (94.75%) were working in the government (public) sector (military hospital, or ministry health center) and 258 (67.72%) having experience of >10 years. This finding is contrary to De Stefani et al. 29 where more than 90% of the respondents were working as private practitioners, confirming that the National Healthcare System and University Departments of Italy offered a lesser part of dental treatments. (6.10%).

Important in this study is that dental professionals had excellent knowledge about the Incubation Period, Symptoms, and Mode of Transmission of the COVID-19

Infection which was significant statistically ($p<0.001$). This finding was very much similar to a study in Turkey by Fatih et al.[30] where the results showed satisfactory knowledge regarding COVID-19 etiology and symptoms. In the present study, the majority 377 (99.0%) reported fever and cough as prodromal symptoms of COVID-19 and were aware of modes of transmission. This finding is in contrast to Quadri et al.[31] where dental health care workers in Saudi Arabia had adequate knowledge regarding COVID-19 symptoms of common cold/flu.

Dental professionals are first-line providers of dental emergency care and should be well prepared to tackle any emergency related to oral and maxillofacial infections from localized dentoalveolar abscesses to deep-neck space infections or more severe cases of necrotizing fasciitis[32]. Considering the present situation, WHO labeled emergency dental procedures must be given priority until the COVID-19 outbreak subsides. Guidelines released by the Ministry of health and infection prevention and control department of Saudi Arabia should be circulated among all registered dental professionals during COVID-19 pandemic so that the dental professionals have information and awareness regarding disease management approaches. In response to an epidemic or pandemic, these guidelines should be implemented and practiced by covering a wider range of programs that focus on education and personal counseling of health care professionals.

The major strength of this study is that it addressed a very crucial problem faced by all dental health care professionals in many countries across the globe during this pandemic.

The main limitation of the study is its design which is Cross-sectional in nature and hence a temporal relationship cannot be established. The data was collected briefly in less time, due to the advancing pandemic. There might be recall bias in the study as it was based on self-reported information. The answers given by the respondents may differ evolving research and potential therapy of COVID-19. The guidelines provided by each country are different and so are the precautions taken by a specific country that might affect the survey outcome. Hence, the findings should be generalized cautiously. Further, longitudinal studies are recommended that provide cause and effect relationships between demographic factors of dental professionals and their level of knowledge, awareness, and practice during the Covid-19 outbreak.

Conclusion

In conclusion, it can be said that dental professionals, had ample knowledge about COVID-19 in terms of the incubation period, symptoms, mode of transmission, and prevention of disease. Awareness on using PPE (personal protective equipment) handwashing, making, and hygiene protocols were specific and clear. Guidelines released by the Ministry of health and infection prevention and control department of Saudi Arabia had an essential part in spreading information about COVID-19 to health care and dental health care professionals which they practice on day to day basis since the pandemic. The study recommends comprehensive training programs by the infection prevention and control department during and even after the outbreak to provide scientifically proven clinical awareness among all health care professionals and other associated clinical and non-clinical staff.

Conflict of interests

The authors have no conflict of interest.

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ORIGINAL

Investigating smell and taste disorders in COVID-19 patients referred to public hospitals in Arak, Iran in 2020

Investigación de los trastornos del olfato y el gusto en los pacientes de COVID-19 remitidos a los hospitales públicos de Arak (Irán) en 2020

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Abstract

Introduction: The 2019 Coronavirus (COVID-19) pandemic has caused widespread disasters around the world. There is growing evidence that suggests olfactory and taste disorder is observed in COVID-19 patients. Anosmia and taste disorders can occur alone or with other symptoms of COVID-19, such as a dry cough. However, the pathogenic mechanism of anosmia and its clinical features in patients with COVID-19 is still unclear.
Methods: This retrospective cross-sectional study was conducted in Arak, Markazi province, in public hospitals in 2020. A total of 54 patients referred to Arak public hospitals were included in the study after examining their inclusion and exclusion criteria and performing PCR tests. Patients were divided into symptomatic and asymptomatic groups. In the symptomatic group, based on the severity of the disease, patients were divided into three groups: 1- Moderate patients with high fever and moderate respiratory symptoms, 2- Severe patients with shortness of breath, 3- As bad as it can be patients with respiratory failure, septic shock or dysfunction in multiple organs. Demographic information, including age, gender, recent travel experience, symptoms (fever, myalgia, cough, shortness of breath, fatigue, sore throat, anosmia, diarrhea, etc.), past nasal and paranasal diseases, smoking history, and disease severity was obtained from the positive patient. The present study data were collected through three questionnaires on approximate time of onset, the interval of symptoms, associated clinical symptoms, and severity of changes.
Results: Out of 54 patients in the study, the frequency of anosmia in asymptomatic, moderate, severe, and as bad as it can be grouped was 11% (n=6), 9% (n=5), 20% (11), and 59% (n=32), respectively. The frequency of taste disorder in these groups was 28% (n=15), 17% (9), 17% (n=9) and 39% (n=21), respectively. Productive cough (93%), constipation (98%), and confusion (93%) were the most common symptoms observed in patients with smell and taste disorders. The Chi-Square Independence T test results and Fisher exact test showed that the clinical sign of anosmia was significantly related to taste disorder. The interval between different disease severity groups with anosmia and taste disorder did not show a significant difference.
Conclusion: In the present study, the severity of the disease was associated with the manifestations of anosmia and taste disorders, so that in severe cases, a higher percentage of patients with two disorders also showed other symptoms of the disease, especially cough, constipation, and confusion. Further clinical studies are needed to determine the exact correlation, pathogenesis, prognosis, and association between the severity of the disease and smell and taste disorders worldwide.

Keywords: COVID-19, clinical signs, epidemiology, smell disorder, taste disorder.

Resumen

Introducción: La pandemia de Coronavirus (COVID-19) de 2019 ha causado desastres generalizados en todo el mundo. Cada vez hay más pruebas que sugieren que se observan trastornos olfativos y gustativos en los pacientes con COVID-19. La anosmia y los trastornos del gusto pueden ocurrir solos o con otros síntomas de COVID-19, como la tos seca. Sin embargo, el mecanismo patogénico de la anosmia y sus características clínicas en los pacientes con COVID-19 aún no está claro.
Métodos: Este estudio transversal retrospectivo se realizó en Arak, provincia de Markazi, en hospitales públicos en 2020. Un total de 54 pacientes remitidos a los hospitales públicos de Arak fueron incluidos en el estudio tras examinar sus criterios de inclusión y exclusión y realizar pruebas de PCR. Los pacientes se dividieron en grupos sintomáticos y asintomáticos. En el grupo sintomático, en función de la gravedad de la enfermedad, los pacientes se dividieron en tres grupos: 1- Pacientes moderados con fiebre alta y síntomas respiratorios moderados, 2- Pacientes graves con dificultad respiratoria, 3- Pacientes graves con insuficiencia respiratoria, shock séptico o disfunción en múltiples órganos. Se obtuvo información demográfica, como la edad, el sexo, la experiencia de viaje reciente, los síntomas (fiebre, mialgia, tos, disnea, fatiga, dolor de garganta, anosmia, diarrea, etc.), las enfermedades nasales y paranasales anteriores, los antecedentes de tabaquismo y la gravedad de la enfermedad del paciente positivo. Los datos del presente estudio se recogieron mediante tres cuestionarios sobre el momento aproximado de inicio, el intervalo de los síntomas, los síntomas clínicos asociados y la gravedad de los cambios.
Resultados: De los 54 pacientes del estudio, la frecuencia de anosmia en los grupos asintomático, moderado, severo y tan malo como se puede agrupar fue del 11% (n=6), 9% (n=5), 20% (11) y 59% (n=32), respectivamente. La frecuencia del trastorno del gusto en estos grupos fue del 28% (n=15), 17% (9), 17% (n=9) y 39% (n=21), respectivamente. La tos productiva (93%), el estreñimiento (98%) y la confusión (93%) fueron los síntomas más comunes observados en los pacientes con trastornos del olfato y del gusto. Los resultados de la prueba T de independencia de Chi-cuadrado y la prueba exacta de Fisher mostraron que el signo clínico de la anosmia estaba significativamente relacionado con el trastorno del gusto. El intervalo entre los distintos grupos de gravedad de la enfermedad con anosmia y trastorno del gusto no mostró una diferencia significativa.
Conclusiones: En el presente estudio, la gravedad de la enfermedad se asoció con las manifestaciones de la anosmia y los trastornos del gusto, de modo que en los casos graves, un mayor porcentaje de pacientes con dos trastornos mostraba también otros síntomas de la enfermedad, especialmente tos, estreñimiento y confusión. Se necesitan más estudios clínicos para determinar la correlación exacta, la patogénesis, el pronóstico y la asociación entre la gravedad de la enfermedad y los trastornos del olfato y el gusto en todo el mundo..

Palabras clave: Coronavirus, conocimiento, práctica, profesionales dentales, control de la infección, creencias.

Introduction

In December 2019, a pneumonia-like viral disease first emerged in Wuhan, China. Then, it spread rapidly to more than 200 countries worldwide, resulting in more than 178 million confirmed cases and 3 million deaths worldwide, based on a report of the World Health Organization in June 2021[1]. The World Health Organization named this new virus severe acute respiratory syndrome coronavirus (SARS-CoV-2), and it named the disease caused by coronavirus disease COVID-19 in 2019. The COVID-19 pandemic is considered the most severe global health crisis since the outbreak of the flu in 1918[2]. On February 19, 2020, two patients were diagnosed with COVID-19 in Qom, Iran, and after a short time, the disease spread rapidly to neighboring provinces, such as Tehran, Markazi, Isfahan, and Khorasan Razavi, and later to 31 provinces of Iran[3]. People infected with SARS-CoV-2 have a wide range of clinical symptoms, from asymptomatic to severe disease. The disease's signs and symptoms include fever, cough, fatigue, sore throat, chest pain, shortness of breath, myalgia, headache, abdominal pain, and diarrhea. In more severe cases, the infection can cause pneumonia, acute respiratory syndrome, kidney failure, and even death[4]. One of the most important unknown characteristics of COVID-19 is the duration of clinical symptoms. In the early stages of the disease, experts believe that the recovery time in mild cases is 1-2 weeks, but in many patients, symptoms of 8 to 10 weeks or even more have been reported.

In some cases, early symptoms are replaced with long-term complications such as lung or heart damages[5]. Observational studies have reported that the elderly and people with underlying respiratory and cardiovascular diseases are at greater risk for the disease, and most patients with the disease have underlying diseases such as hypertension and cardiovascular disorders, diabetes, cancer, and chronic kidney disease and mortality rate in these people is higher than that of other patients. However, severe forms of the disease are observed in younger adults with no previous history of the disease[6]. One of the extrapulmonary symptoms of COVID-19 is smell disorder, including anosmia and hypoxemia, which is more common in adults with up to 40% infection with viruses infecting the upper respiratory tract.

Different possible hypotheses have been proposed to justify this clinical sign, including damage caused by SARS-CoV-2 to the surface of the olfactory neuroepithelium in the roof of the nasal cavity or the central olfactory pathways[7]. COVID-19 patients can develop sudden anosmia without any other symptoms or, more commonly, other mild symptoms before the onset of anosmia, such as a dry cough. In a retrospective study conducted by Klopenstein et al., 54 (47%) out of 114 COVID-19-approved patients showed anosmia. This study also revealed that patients generally develop anosmia 4.4 days after the onset of SARS-CoV-2 infection with a duration of 8.96 days, and 98% of patients can recover within 28 days[8]. Since smell affects the sense of taste, people with COVID-19 may also experience a loss of sense of taste[9]. Sudden, severe, and isolated loss of sense of smell or taste, in the absence of other inflammatory manifestations of the upper airways such as allergic rhinitis, chronic rhinosinusitis, nasal polyposis, inform physicians on the possibility of developing COVID-19. Evaluation of smell and taste disorders with analog visual scale or smell or taste test in hospital or telemedicine to prevent infection facilitates early diagnosis of infected patients and reduces SARS-CoV-2 transmission[10]. Thus, given the high prevalence and importance of this emerging disease that has become a global crisis and its unknown dimensions and effects on body organs and considering the importance of two clinical findings of taste and smell disorders, the present study was conducted to evaluate smell and taste disorders in COVID-19 patients referred to public hospitals in Arak in 2020 to better understand this disease and contribute to achieving diagnostic and therapeutic goals.

Materials and methods

Study design

This retrospective cross-sectional study was conducted in public hospitals in Arak, Markazi province, Iran, in 2020. Patients with COVID-19 infection approved by PCR (polymerase chain reaction) pharyngeal swabs were included in the study. PCR swabs were tested for coronavirus in the pathology laboratory of Arak. This study was a retrospective analysis of anosmia and taste disorder in COVID-19 patients. PCR of pharyngeal swabs for the diagnosis of COVID-19 is routinely performed at this center and worldwide, so no ethical consideration is made in this study.

Study group

Individuals with incomplete data, previous anosmia or taste disorder, psychological disorders, and inaccessible subjects were excluded. Patients were divided into symptomatic and asymptomatic groups, and patients in the symptomatic group were divided into three groups based on the severity of the disease: 1- Moderate patients complained of fever with high temperature and moderate respiratory symptoms. Pneumonia findings were observed in chest radiography. Two severe patients with shortness of breath, the respiration rate of 30 per minute, blood oxygen saturation of 93%, CT scan findings with at least 50% increase in penetration volume.

Three critical patients with respiratory failure, septic shock, or dysfunction in multiple organs. Demographic data, including age, gender, recent travel experience, symptoms (fever, myalgia, cough, shortness of breath, fatigue, sore throat, anosmia, diarrhea, etc.), past nasal

and paranasal diseases, smoking history, and disease severity was taken from a positive patient. The research data were obtained through three questionnaires on approximate time of onset and interval of symptoms, the associated clinical symptoms, and severity of changes.

Statistical analysis

The Shapiro-Wilk test was used to determine whether the data follow the normal distribution. Student-t and Mann-Whitney U tests were used for parametric and non-parametric data, respectively. For classification of variables, chi-square, Fisher exact test, and Fisher-Freeman Halton tests were used. Spearman test was used for correlation. IBM-SPSS version 22 statistical software was used for data analysis. If P-value is less than 0.05, a statistically significant difference was considered.

Results

Frequency of patients in different groups of disease severity

The results of the Chi-Square test (Goodness of fit test) show that for anosmia patients, the frequencies of patients in different groups of disease severity are significantly different (P-value 0.000 <0.05). However, for the taste change patients, this difference does not show a difference at the significance level of 0.05. In general, the results show that anosmia patients are more in the as bad as it can be severe group. **Table I** shows the frequency of anosmia and taste change in patients in different disease severity groups.

The severity of disease in patients with anosmia and taste disorders

The results of Chi-Square, Independence Test, and Fisher exact test show that anosmia disease has a significant relationship with taste change disease, so that Spearman correlation coefficient with a value of 0.451 indicates that as the severity of anosmia increases and goes toward as bad as it can be, the severity of taste change will also increase and will go towards as bad as it can be. As shown in the table, out of 32 anosmia patients with severity of as bad as possible, 20 patients had taste change with severity of as bad as it can be. **Table II** shows the frequency of taste change in patients in different disease severity groups based on the severity of anosmia disease groups.

The interval between different groups of disease severity

Table III shows the interval comparison results using the Kruskal-Wallis test for anosmia and taste change. The interval between different disease severity groups for anosmia and taste change did not show a significant difference.

Clinical symptoms in different groups of disease severity

Out of 37 patients with fever and anosmia, 24 were in the "as bad as it can be" group, and 11 were in the severe group. **Table IV** shows the frequency of symptoms in different groups of disease severity. Significant results of the Chi-Square Independence Test, Fisher exact test, have been presented. Significance at the level of 0.05 indicates the relationship between symptoms and different severities of the disease.

Discussion

Several infectious diseases have been treated the human health (10-15). SARS-COVID disease caused higher morbidity and mortality in the last century[16-19].

Smell and taste disorders are associated with a wide range of viral infections. These sensory disorders are a

Table I:

	Severity					
	None	Moderate	Severe	As bad as it can be	Total	P value
Anosmia; n (%)	6 (11%)	5 (9%)	11 (20%)	32 (59%)	54	0.000
Taste change; n (%)	15 (28%)	9 (17%)	9 (17%)	21 (39%)	54	0.067

Table I:

	Severity				
	None	Moderate	Severe	As bad as it can be	P value
Taste change; median interval (IQR)	-	7 (7-14)	17 (16-17)	17 (7-20)	0.211
Taste change; median interval (IQR)	-	14 (14-14)	17 (9-17)	15.5 (7-20.5)	0.725

IQR = interquartile range

Table I:

		Anosmia severity				Total	P value	Correlation (Spearman)
		None	Moderate	Severe	As bad as it can be			
Taste change severity; (within Anosmia severity, n (%)	None Moderate Severe As bad as it can be	4 (66.7%) 0 (0.0%) 2 (33.3%) 0 (0.0%)	0 (0.0%) 4 (80.0%) 0 (0.0%) 1 (20.0%)	3 (27.3%) 5 (45.5%) 3 (27.3%) 0 (0.0%)	8 (25.0%) 0 (0.0%) 4 (12.5%) 20 (62.5%)	15 (27.8%) 9 (16.7%) 9 (16.7%) 21 (38.9%)	0.000	.451**
Total		6 (100.0%)	5 (100.0%)	11 (100.0%)	32 (100.0%)	54 (100.0%)		

**. Correlation is significant at the 0.01 level (2-tailed).

Table I:

		Anosmia severity					
		None, (n= 6; 11%)	Moderate, (n= 5; 9%)	Severe, (n=11; 20%)	As bad as it can be, (n= 32; 59%)	Total	P value
Nasal_congestion	No	6 (100%)	5 (100%)	5 (45%)	26 (81%)	42 (78%)	0.027
	Yes			6 (55%)	6 (19%)	12 (22%)	
Fatigue	No	4 (67%)			13 (41%)	17 (31%)	0.004
	Yes	2 (33%)	5 (100%)	11 (100%)	19 (59%)	37 (69%)	
Dry_caugh	No		5 (100%)	3 (27%)	19 (59%)	27 (50%)	0.001
	Yes	6 (100%)		8 (73%)	13 (41%)	27 (50%)	
Productive_caugh	No	6 (100%)	5 (100%)	8 (73%)	31 (97%)	50 (93%)	0.100
	Yes			3 (27%)	1 (3%)	4 (7%)	
Fever	No	4 (67%)	5 (100%)		8 (25%)	17 (31%)	0.000
	Yes	2 (33%)		11 (100%)	24 (75%)	37 (65%)	
Dyspnea	No	2 (33%)	4 (80%)	8 (73%)	11 (34%)	25 (46%)	0.062
	Yes	4 (67%)	1 (20%)	3 (27%)	21 (66%)	29 (54%)	
Headeche	No	4 (67%)	1 (20%)	5 (45%)	12 (38%)	22 (41%)	0.447
	Yes	2 (33%)	4 (80%)	6 (55%)	20 (63%)	32 (59%)	
Chest_pain	No	6 (100%)		11 (100%)	23 (72%)	40 (74%)	0.000
	Yes		5 (100%)		9 (28%)	14 (26%)	
Sore_throat	No	6 (100%)	5 (100%)	6 (55%)	20 (63%)	37 (69%)	0.086
	Yes			5 (45%)	12 (38%)	17 (31%)	
Body_pain	No	6 (100%)	5 (100%)		15 (47%)	26 (48%)	0.000
	Yes			11 (100%)	17 (53%)	28 (52%)	
Low_appetite	No	6 (100%)	5 (100%)	8 (73%)	7 (22%)	26 (48%)	0.000
	Yes			3 (27%)	25 (78%)	28 (52%)	
NandV	No	6 (100%)	5 (100%)	8 (73%)	24 (75%)	43 (80%)	0.429
	Yes			3 (27%)	8 (25%)	11 (20%)	
Diarrhea	No	6 (100%)	5 (100%)	11 (100%)	13 (41%)	35 (65%)	0.000
	Yes				19 (59%)	19 (35%)	
Constipation	No	6 (100%)	5 (100%)	11 (100%)	31 (97%)	53 (98%)	1.000
	Yes				1 (3%)	1 (2%)	
Confusion	No	6 (100%)	5 (100%)	8 (73%)	31 (97%)	50 (93%)	0.100
	Yes			3 (27%)	1 (3%)	4 (7%)	

Table I:

		Taste change severity					
		None, (n= 15; 28%)	Moderate, (n= 9; 17%)	Severe, (n=9; 17%)	As bad as it can be, (n= 21; 39%)	Total	P value
Nasal_congestion	No	8 (53%)	9 (100%)	4 (44%)	21 (100%)	42 (78%)	0.000
	Yes	7 (47%)		5 (56%)		12 (22%)	
Fatigue	No	8 (53%)		4 (44%)	5 (24%)	17 (31%)	0.025
	Yes	7 (47%)	9 (100%)	5 (56%)	16 (76%)	37 (69%)	
Dry_caugh	No	6 (40%)	4 (44%)		17 (81%)	27 (50%)	0.000
	Yes	9 (60%)	5 (56%)	9 (100%)	4 (19%)	27 (50%)	
Productive_caugh	No	15 (100%)	9 (100%)	6 (67%)	20 (95%)	50 (93%)	0.033
	Yes			3 (33%)	1 (5%)	4 (7%)	
Fever	No	7 (47%)	4 (44%)	2 (22%)	4 (19%)	17 (31%)	0.246
	Yes	8 (53%)	5 (56%)	7 (78%)	17 (81%)	37 (69%)	
Dyspnea	No	3 (20%)	9 (100%)	4 (44%)	9 (43%)	25 (46%)	0.001
	Yes	12 (80%)		5 (56%)	12 (57%)	29 (54%)	
Headeche	No	4 (27%)	5 (56%)	2 (22%)	11 (52%)	22 (41%)	0.235
	Yes	11 (73%)	4 (44%)	7 (78%)	10 (48%)	32 (59%)	
Chest_pain	No	15 (100%)	5 (56%)	7 (78%)	13 (62%)	40 (74%)	0.016
	Yes		4 (44%)	2 (22%)	8 (38%)	14 (26%)	
Sore_throat	No	11 (73%)	4 (44%)	7 (78%)	15 (71%)	37 (69%)	0.464
	Yes	4 (27%)	5 (56%)	2 (22%)	6 (29%)	17 (31%)	
Body_pain	No	8 (53%)	4 (44%)	4 (44%)	10 (48%)	26 (48%)	1.000
	Yes	7 (47%)	5 (56%)	5 (56%)	11 (52%)	28 (52%)	
Low_appetite	No	7 (47%)	9 (100%)	6 (67%)	4 (19%)	26 (48%)	0.000
	Yes	8 (53%)		3 (33%)	17 (81%)	28 (52%)	
NandV	No	11 (73%)	9 (100%)	6 (67%)	17 (81%)	43 (80%)	0.335
	Yes	4 (27%)		3 (33%)	4 (19%)	11 (20%)	
Diarrhea	No	7 (47%)	9 (100%)	9 (100%)	10 (48%)	35 (65%)	0.001
	Yes	8 (53%)			11 (52%)	19 (35%)	
Constipation	No	15 (100%)	9 (100%)	9 (100%)	20 (95%)	53 (98%)	1.000
	Yes				1 (5%)	1 (2%)	
Confusion	No	15 (100%)	9 (100%)	6 (67%)	20 (95%)	50 (93%)	0.033
	Yes			3 (33%)	1 (5%)	4 (7%)	

common problem during the COVID-19 epidemic crisis. SARS-CoV in a mouse model showed external infiltration through the olfactory bulb. In addition, the angiotensin-converting enzyme receptor 2, used by SARS-CoV-2 to bind to and penetrate cells, is widely expressed in oral mucosal epithelial cells[20]. These findings can explain the underlying pathogenetic mechanism of taste and smell disorders in SARS-CoV-2 infection. Smell and taste disorders are the first and only complaint in 10% of people, and 19% experience it before other classic symptoms such as fever and cough. Also, 25% of children have only smell and taste disorders at admission[21]. Therefore, these disorders are early signs of COVID-19 disease and are essential for screening and controlling the infection. The present study used a questionnaire for diagnosing patients with anosmia, taste disorder, or both. The results of this study showed that the frequency of anosmia in asymptomatic, moderate, severe, and as bad as it can be grouped were 11%, 9%, 20%, and 59%, respectively, and taste disorder in these groups were 28% and 17%, 17%, and 39%, respectively.

It has previously been reported that COVID-19-induced anosmia is associated with a mild course of the disease. One study showed that the percentage of anosmia in hospitalized patients (26.9%) was lower than in non-hospitalized patients (66.7%). In a study on 3191 patients with mild COVID-19, 15.3% had anosmia or taste disorders[22]. Leichen et al. conducted a study on 417 cases with mild to moderate disease and showed that smell disorder was present in 88% of cases and anemia was the primary symptom in 11.8% of cases[23]. A similar study conducted by Kaye et al. on 237 cases showed that anosmia was present in 73% of cases during the disease, while 26.6% of cases were initially associated with anosmia[24]. As a result, the results of this study are somewhat inconsistent with previous results. The most common symptoms of COVID-19, including fever, cough, and headache, can be observed in other non-specific viral upper respiratory tract infections. In the present study, productive cough (93%), constipation (98%), and confusion (93%) were the most common symptoms observed in patients with smell and taste disorders. Dysfunction of these two functions may begin before, after, or at the same time as these clinical signs, or it may be the only symptom. There was a significant relationship between the symptoms of the disease and different severities of the disease in patients with anosmia and taste disorders. For example, out of 37 patients with fever and anosmia, 24 were in the "as bad as it can be" group, and 11 were in the severe group. In the study conducted by Klein et al., headache, fever, dry cough, and muscle pain accounted for 38% to 43% of cases associated with taste and smell disorders.

Moreover, fatigue was the second common symptom observed in these patients. In the results of a study conducted by Klein, it manifested as a primary symptom in 80% of patients who experienced it (14% of all patients), while in previous studies, fatigue was observed at higher rates (36%-46% of patients)[25].

Conclusion

Based on the present study results, the association of headache, fever, dry cough, muscle pain, and fatigue with smell and taste disorders was 59%, 65%, 50%, 52%, 69%, respectively, which has a high percentage compared to previous studies. Anosmia or taste disorder in a patient with COVID-19 is uncomplicated in the early days, but it requires a comprehensive evaluation of central nervous system involvement. Since smell disorder may affect patients' quality of life, further clinical studies are needed to determine the exact correlation, pathogenesis, prognosis, and any association between disease severity and smell disorder worldwide. In the absence of other respiratory disorders, such as allergic rhinitis and acute rhinosinusitis or chronic rhinosinusitis, anosmia, hypoxemia, and taste disorders, physicians should be informed on the possibility of COVID-19 infection, and serious attention should be paid to isolation and testing these individuals.

Conflict of interests

The authors have no conflict of interest.

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ORIGINAL

Frequency of burns and its causes in Kermanshah, Iran

Frecuencia de las quemaduras y sus causas en Kermanshah, Irán

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Abstract

Introduction: Burn is one of the public health problems and one of the major causes of death in Iran, which causes many physical and psychological disabilities. The aim of this study was to investigate Frequency of burns and its causes in Kermanshah province.
Methods: This is a descriptive -analytical cross-sectional study. Data were obtained from the burn data record center of Kermanshah province. 490 patients were studied in this research. A designed checklist was used for data collection. Data analysis was performed using SPSS 22.
Results: The mean age of patients was 17.01 years. Most burns (28.6% of the patients) were caused by oil and gasoline. 65.5% of patients had 25% to 50% burning rate. Remedial measures taken for 44% (44.1%) of patients were debridement.
Conclusion: Since burn is more prevalent in childhood and adolescence, it is necessary to provide policy interventions and required trainings to this at-risk group to prevent burn incidence.

Keywords: Burn incidence, Burn etiology, Kermanshah.

Resumen

Introducción: Las quemaduras son uno de los problemas de salud pública y una de las principales causas de muerte en Irán, que provoca muchas discapacidades físicas y psicológicas. El objetivo de este estudio fue investigar la frecuencia de las quemaduras y sus causas en la provincia de Kermanshah.
Métodos: Se trata de un estudio transversal descriptivo-analítico. Los datos se obtuvieron del centro de registro de datos de quemaduras de la provincia de Kermanshah. Se estudiaron 490 pacientes en esta investigación. Se utilizó una lista de comprobación diseñada para la recogida de datos. El análisis de los datos se realizó con el programa SPSS 22.
Resultados: La edad media de los pacientes fue de 17,0 años. La mayoría de las quemaduras (28,6% de los pacientes) fueron causadas por aceite y gasolina. El 65,5% de los pacientes tenían entre un 25% y un 50% de quemaduras. Las medidas correctoras adoptadas en el 44% (44,1%) de los pacientes fueron el desbridamiento.
Conclusiones: Dado que las quemaduras son más frecuentes en la infancia y la adolescencia, es necesario proporcionar intervenciones políticas y la formación necesaria a este grupo de riesgo para prevenir la incidencia de quemaduras.

Palabras clave: Incidencia de las quemaduras, etiología de las quemaduras, Kermanshah.

Introduction

Burn is one of the main and common health problems throughout world especially in the developing countries. According to International Society for Burn Injuries, burn is defined as disruption of a part or all cell layers in skin as the result of contact with hot liquid or solid materials. Generally, 195.000 cases of death occur annually due to burn throughout the world. Burn is of the most important accidents and disasters that relates to the human health that took more attention because of the severe complications and the number of mortality[1]. Burn is the tissue injury because of the heat, chemical or electrical contact that leads to the change in protein, edema, and reduction in intravascular liquid volume. Burns are always considered as one of the most destructive damage. Not only do they lead to death and disability, they have major psychological and economic consequences and long-term severe physical complications[2]. The severity of injury varies from a superficial injury to the full-thickness injuries that threaten life. Psychological problems and deformation physical changes such as scars, contractures and organs' removal are often the consequences of burns so the burns are of the most expensive damage in terms of economic matters[3]. In Iran, burns' damage is highly prevalent and leads to death because 8 people die per day due to burn. Burns are the third factor of mortality followed by driving accidents and trauma[2]. However, compensation of losing physical performance or psychological damage and beauty defects is not computable[4] and it brought about a big challenge for Iran's health system in case of treatment and rehabilitation of patients[5]. Although the recent developments saved many lives, many patients are in pain of its complications[6]. Annually, more than 11 million people face burn with the severity that requires medical intervention. WHO (2011) reported that more than 300.000 people die in the world because of burn complications[7]. In addition, 1.250.000 people experience burn in the U.S. that need medical care. About 50.000 of them are admitted in the hospitals and it costs 7 B$[8]. The statistics in Iran indicate that 2749 people were admitted in Shahid Motahhari Burn Treatment Center in 2008 and it reached 1929 patients during March 2009 to December 2009, a considerable extent[9]. A study on 2257 burns in Chaharmahal and Bakhtiari Province in 2012 showed 55.57% female and 44.43 % male burns[10]. In Feck's study, the average amount of burn was 9%; the most dangerous groups were men, dark skin and youth being burnt during work[11]. Lie reported internal organ disorder, severe infections, and respiratory damage as the most prevalent causes of death due to burn[12]. Faramarzi et al. (2012) reported that many burns are unintentional and the average age was 36[13]. Soltan Dallal et al conducted an epidemiological analysis of burn in Motahhari Hospital and concluded that the most common cause of burn is the hot liquids and pseudomonas is diagnosed as the most important microbial factor[14].

The aim of this study is the epidemiological and etiological analysis of burn among patients referred to Specialized Burn Hospital in Kermanshah town where is the only burn treatment center in the province in order to identify the precautionary scales and reduce the wide spectrum of mortality due to burns.

Materials and methods

The present study is a descriptive-analytical-cross-sectional one and deals with 490 cases of patients suffered from burn during 2012-2015 in Kermanshah Emam Khomeini Hospital. Through census sampling, the statistical population includes all patients with burn that referred Kermanshah Emam Khomeini Burn Treatment Center. The research setting is Kermanshah Emam Khomeini Hospital where is the only burn treatment center in Kermanshah Province. To gather the information, a twofold checklist used which included demographic information such as age, sex, education level and occupation; geographic information such as province, city and region of residence; and information on burn such as burn severity and degree, burn percentage and regions, burn cause, and finally the clinical consequences for patients. To collect the data, the comprehensive program of recording burn information in Emam Khomeini Hospital, analysis of patients' cases, interview with patients and telephone contact with patients were utilized. Data analysis was conducted with SPSS®-16. Statistical tests on descriptive analysis such as mean, standard deviation, and frequency were used to describe the variables. Chi-2 test was used for information analysis. In this study, p-value < 0.05 is significant.

Results

Table I shows the absolute Frequency and Relative Frequency Percentage of demographic variables in patients.

Table I: Absolute Frequency and Relative Frequency Percentage of demographic variables in patients.

Variables		Absolute Frequency (Relative Frequency Percentage)
Gender	Man Female	276(56.3%) 214(43.7%)
Education	Illiterate Subdivision Academic	318(64.9%) 157(32%) 15(3.1%)
Job	Unemployed Housewife Employee Free	272(55.5%) 132(26.9%) 20(4.1%) 66(13.5%)
Economic situation	Weak Medium Good	167(34.1%) 281(57.3%) 42(8.6%)
Age	less than 15 years 15-30 years 30-45 years Over 45 years	286(58.4%) 92(18.8%) 56(11.4%) 56(11.4%)

In this study, information related to 490 burn patients was analyzed. Their average age is 17.01 years old with standard deviation of 20.28 years old and age range between 1 and 87 years old. The admission average is 4.86 days with standard deviation of 6.70. The admission period varied from 1 day to 80 days. 56.3% of patients were men. 56.3% of patients were women. 58.4% of patients were under 15 years old. 55.5% of patients were illiterate. 57.3% of patients were in medium economic condition.

According to **table II**, the results showed that 28.6% of burns occurred with oil and gasoline, 14.5% with gas, and 29.2% with alcohol. Additionally, 55.3% of burns were less than 25% severity and 65.5% of them were between 25% and 50% severity. 32.2% of burns were degree 1 and 23.9% of them were a combination of degrees 2, 1 and 3 burns.

Table I: Absolute Frequency and Relative Frequency Percentage of demographic variables in patients.

Variables		Absolute Frequency (Relative Frequency Percentage)
Burning agent	Oil and gasoline	140(28.6%)
	Gas	71(14.5%)
	Acid	3(0.6%)
	Electricity	8(1.6%)
	Alcohol	143(29.25)
	Hot object and hot object	72(14.7%)
	Others	53(10.8%)
Percentage of burns	25%≤	271(55.3%)
	20-50%	130(26.53%)
	50-75%	59(12.04%)
	75%≥	30(6.13%)
Degree of burn	grade 1	158(32.2%)
	Grade 2	17(3.5%)
	Grade 3	149(30.4%)
	Grades 1 and 2	21(4.3%)
	Grades 1 and 3	8(1.6%)
	Grade 2 and 3	20(4.1%)
	Grades 1, 2 and 3	117(23.9%)

Fasciotomy was used for 39.6% of patients. Scarotomy was used for 41% of patients. Debridement was used for 44.1% of patients. In addition, 98.6% of patients were administered medications such as antibiotics, analgesics, and supplementary treatments. 3.1% of patients used tourniquet; 80.6% used massage; 38.4% used weights; 81.6% used position therapy; and 81.6 % used respiratory physiotherapy. Psychological interview was done 25.9% of cases. Finally, the number of mortality was reported 6.9% among burn patients (**Table III**).

Table III: Absolute Frequency Distribution and Relative Frequency Percentage Treatment for patients.

Variables		Absolute Frequency (Relative Frequency Percentage)
Fasciotomy	Yes	194(39.6%)
	No	294(60.4%)
Scartomy	Yes	201(41%)
	No	289(59%)
Debrideman	Yes	216(44.1%)
	No	274(55.9%)
Drug treatment	Antibiotics	4(0.8%)
	Painkiller	2(0.4%)
	Reinforcement treatments	1(0.2%)
	All three	483(98.6%)
Splinting	Yes	15(3.1%)
	No	475(96.9%)
Massage	Yes	395(80.6%)
	No	95(19.4%)
Use Weights	Yes	188(38.4%)
	No	302(61.6%)
Therapy Position	Yes	400(81.6%)
	No	90(18.4%)
Respiratory Physiotherapy	Yes	400(81.6%)
	No	90(18.4%)
Psychological Interview	Yes	127(25.9%)
	No	363(74.1%)
Post-treatment status	Discharge after treatment	456(93.1%)
Actions taken	Deceased	34(6.9%)

According to **table IV**, the results of Pearson's correlation coefficient test showed there is not significant relationship between sex of patients and burn factor and the burn degree ($p>0.05$). Meanwhile, the results of this test showed a significant relationship between sex and burn percentage ($p=0.001$). The results of Pearson's test manifested an inverse and significant relationship between education and burn cause ($p=0.001$). There is a direct and significant relationship between the burn percentage and burn degree ($p<0.05$). In addition, the findings set a direct and significant relationship between the economic situation and burn cause ($p=0.004$). Meanwhile, there is an inverse and significant relationship between burn percentage and burn degree ($p<0.05$). There is an inverse and significant relationship between age and burn cause ($p=0.001$). Pearson's test showed that there is a direct and significant relationship between age and burn percentage as well as burn degree ($p<0.05$).

Table III: Absolute Frequency Distribution and Relative Frequency Percentage Treatment for patients.

Variables	Burning agent		Percentage of burns		Degree of burn	
	P-value	r	P-value	r	P-value	r
Gender	0.28	-0.049	0.001	0.275	0.221	0.055
Education	0.001	-0.335	0.001	0.169	0.001	0.463
Job	0.001	-0.318	0.001	0.105	0.001	0.305
The economic situation	0.004	0.129	0.001	-0.247	0.001	-0.476
Age	0.001	-0.371	0.001	0.209	0.001	0.469

Discussion

Burn is an irreparable incident that has many physical, psychological, social and economic consequences, but in half of the cases, this incident and its complications can be prevented[1]. The available information is obtained from the study of 490 cases of patients admitted to Imam Khomeini Hospital in Kermanshah form 2012 to 2016. In the present study, the mean age of patients was 17.2 years, ranging from 1 to 87 years. 58.4% of patients were younger than 15 years. The age distribution of this study is similar to that of other studies, especially from childhood to middle age[8,9]. But in the US studies, elderly hospitalization rates were reported to be 16%, respectively[10]. In this study, the low rates of hospitalization in the elderly can be attributed to the cultural and religious context of the community in terms of maintaining and protecting the elderly in the family environment and consequently reducing the risk of exposure to the contributing factors to burn. On the other hand, the prevalence of burns in different age groups can be associated with the behavioral and developmental patterns of people of different ages. For example, lack of awareness and attention to hazardous substances in children plays an important role in the incidence of burns at this age. Increased incidence of burns in young adults is also justified by having an active life, exposure to work and home accidents as well as specific cultural and psychological issues of these ages[11]. Therefore, the need to implement training programs to prevent and reduce risk factors, especially in children and adolescent burn incidence, and to make the home environment safer is felt more than ever.

Burns were higher in men than in women, and these results have been obtained in other studies[12-14] as well. The higher incidence of burns in men can be attributed to their higher presence in work and hazardous occupations. The results of the present study showed that the majority of burns were caused by gasoline, oil and alcohol. Flame burns in Tehran and Hamadan were also reported as the most common cause of burns[15,16], while hot liquids were the most common cause in Yazd[17]. The present study showed that most of the patients were unemployed and with moderate economic status. The study of Moghsoudi et al. revealed that social factors are the main cause of the increase in burns in Iran. Most burns are due to internal accidents and can be prevented. Therefore, training programs can reduce the incidence of burn injuries[18]. The depth of burn in the present study was higher than the first degree. In a study in Turkey, 48.7% of burns were reported to be of full thickness[19]. Since the depth of burn depends on factors such as the burned area, the burner (burning agent), the contact time, and the burn mode, the burn depth has also been reported differently in different centers. The average length of hospital stay was approximately 2 days. The average length of stay in Turkey was 25 days, in Tehran was 12 and 16.7 days, in Portugal was 15.5 days, and in Kuwait was reported to be 38 days[19-22]. Since the length of hospital stay depends on factors such as quality and quantity of care and treatment, extent and depth of burns, age, etc., it is observed that the length of hospitalization in general as well as in the living and dead patients in the study is shorter than that of some similar studies, which can be due to patients not being scheduled for surgery, first degree burns in most patients, etc. The duration of hospitalization in children was shorter than in adults, which may be due to lesser extent of burns in these patients. In terms of remedial measures taken, debridement was performed for most patients. Most patients also received pharmacological treatments including antibiotics, analgesics, and booster treatments. In most patients, massage, position therapy, and respiratory physiotherapy were used. 38.8% of patients and 35.6% of patients had surgery in Turkey and Saudi Arabia, respectively[19,23]. Fewer surgeries at this center can be due to the lack of debridement and early transplantation, the lack of surgeons, the lack of treatment facilities, and the lack of skin for transplantation. The results of this study can provide relevant information about the status of burn patients to the health care centers and organs of Iran. This study can contribute greatly to the relevant organs in planning, training and treatment of burn patients.

Conclusion

According to the results of this study, it seems that in order to reduce the incidence of burns, more focus should be placed on education, social status and appropriate job of the community. On the other hand, as most burns have occurred at home, it seems to require a public mobilization to educate the public on how to prevent burns at home. The most common cause of burns was flame with oil, gasoline and alcohol. But the main cause of burns in children was boiling water, so parents should pay particular attention to this issue. Today, in developed countries, more efforts are being made to improve the quality of burn survivors and to find new ways to treat hypertrophic scars. In developing countries, including Iran, given the basic requirement, the development of specialized multidisciplinary and focused burn centers alongside public education seems essential.

Conflict of interests

The authors have no conflict of interest.

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ORIGINAL

Determining the relationship between the type of suture used and the incidence and severity of cesarean scar defects (niche) in patients with a history of cesarean: A Double-blind randomized clinical trial

Determinación de la relación entre el tipo de sutura utilizado y la incidencia y gravedad de los defectos de la cicatriz de la cesárea (nicho) en pacientes con antecedentes de cesárea: Un ensayo clínico aleatorio doble ciego

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Abstract

Introduction: One of the complications of cesarean is cesarean section defect (Niche syndrome). One of the etiologies of this disease is incomplete or incorrect closure of the cesarean section, without closing the deep muscle layers due to improper sutures or not allocating enough time for this. The type of suture used to close the cesarean section is an important challenge in predicting this complication. Therefore, our study was performed to determine the relationship between the type of suture used and the incidence and severity of cesarean section defects in patients with a history of cesarean section.

Methods: This study was a prospective clinical trial. 50 patients underwent cesarean section and were randomly divided into two groups of 25 (chromic suture group and vicryl suture group). After 2 months, patients were called to the clinic and underwent vaginal ultrasound by a specialist doctor for cesarean section defects. The information included: the incidence of cesarean section defects, the type of suture used and the amount of cervical dilatation were recorded in a pre-prepared questionnaire. Data was collected by SPSS version 22 and data analysis was performed using frequency distribution tables and statistical tests.

Results: Of the 50 patients studied, 8 (16%) had Niche. Also, 9 patients (18%) had cervical dilatation. The results showed that there was a statistically significant difference between the frequency distribution of Niche according to the type of suture used in the studied patients and the frequency of Niche in patients who used chrome thread was significantly higher ($p = 0.021$). Also, no statistically significant difference was found between the frequency distribution of Niche in terms of cervical dilatation in the studied patients ($p = 0.196$). There was no statistically significant difference between the frequency distribution of cervical dilatation according to the type of suture used in the studied patients ($p = 0.325$).

Conclusion: According to results, can be concluded that the use of chromic thread is associated with more cesarean defects. Therefore, the use of Vicryl thread instead of chromic is recommended to reduce the incidence of cesarean scar defects.

Keywords: Cesarean, niche syndrome, suture.

Resumen

Introducción: Una de las complicaciones de la cesárea es el defecto de cesárea (síndrome de Niche). Una de las etiologías de esta enfermedad es el cierre incompleto o incorrecto de la cesárea, sin cerrar las capas musculares profundas debido a suturas inadecuadas o a no asignar el tiempo suficiente para ello. El tipo de sutura utilizado para cerrar la cesárea es un reto importante para predecir esta complicación. Por lo tanto, nuestro estudio se realizó para determinar la relación entre el tipo de sutura utilizado y la incidencia y gravedad de los defectos de la cesárea en pacientes con antecedentes de cesárea.

Métodos: Este estudio fue un ensayo clínico prospectivo. 50 pacientes se sometieron a una cesárea y se dividieron aleatoriamente en dos grupos de 25 (grupo de sutura crómica y grupo de sutura de vicryl). Al cabo de 2 meses, se citó a las pacientes en la clínica y un médico especialista les hizo una ecografía vaginal para detectar los defectos de la cesárea. En un cuestionario preparado de antemano se registraron los siguientes datos: la incidencia de los defectos de cesárea, el tipo de sutura utilizado y la cantidad de dilatación cervical. Los datos se recogieron con el SPSS versión 22 y el análisis de los datos se realizó mediante tablas de distribución de frecuencias y pruebas estadísticas.

Resultados: De las 50 pacientes estudiadas, 8 (16%) tenían Niche. Además, 9 pacientes (18%) tenían dilatación cervical. Los resultados mostraron que había una diferencia estadísticamente significativa entre la distribución de frecuencias de Niche según el tipo de sutura utilizado en las pacientes estudiadas y la frecuencia de Niche en las pacientes que utilizaron hilo de cromo fue significativamente mayor ($p = 0,021$). Tampoco se encontraron diferencias estadísticamente significativas entre la distribución de frecuencias de Niche en función de la dilatación cervical en las pacientes estudiadas ($p = 0,196$). No hubo diferencias estadísticamente significativas entre la distribución de la frecuencia de la dilatación cervical según el tipo de sutura utilizado en las pacientes estudiadas ($p = 0,325$).

Conclusiones: Según los resultados, se puede concluir que el uso de hilo cromado se asocia a más defectos de cesárea. Por lo tanto, se recomienda el uso de hilo Vicryl en lugar de crómico para reducir la incidencia de defectos de cicatriz de cesárea.

Palabras clave: Cesárea, síndrome del nicho, sutura.

Introduction

Cesarean section is one of the women's most frequent surgeries in the world, which has increased considerably in recent years. According to the World Health Organization, 10-15% of all live births are delivered by cesarean section. Studies conducted in the last two decades have concluded that it is possible that Cesarean section to have many complications that some of which occur during a long period of time. Some of these complications are known such as Placenta Previa and Placenta Accreta. Cesarean section defect or isthmus cell or Niche syndrome are among the complications that have been currently highly considered[1-3].

In fact, the disease is a sac-like myometrial defect in the anterior wall of the isthmus of the uterus (usually) that is caused by a previous cesarean section scar. This defect changes pathologically the wall of the myometrium that cause symptoms in the patient. In this disease, a hypoechoic zone is developed in the myometrium of the uterine isthmus. The size of this defect should be at least 2 mm. Some studies have defined myometrial defect as an echo-free-myometrial thickening higher than 1 mm[4-6].

The actual prevalence rate of this complication is not recognized. The prevalence rate of isthmus cell in women who experienced one or more cesarean section was estimated to be between 24-70% in transvaginal ultrasound examinations and between 56-84% in Sonohysterography examinations in a systematic review study. This value has been higher in patients who have symptoms and has been estimated between 19.4% to 84%[2,7].

No diagnostic criterion is detected to diagnose isthmus. It is possible to use various imaging methods such as ultrasound, Sonohysterography, histography, MRI to observe and examine the anterior abdominal wall and diagnose the disease[8,9].

The type of suture applied to sew different layers of the body is an important challenge in predicting possible complications. Studies have compared different sutures in wound healing of various surgeries. Synthetic sutures such as Vicryl and natural sutures such as chrome are commonly applied in gynecological surgeries. Different studies have examined the results of using these two types of sutures in various sites such as Episiotomy repair, subcutaneous layer repair and fascia, etc., but no comprehensive study has been conducted in order to compare these two types of sutures in myometrial repair has been performed[10].

The rate of cesarean section is increasing and consequently, the possible complications such as defects in the cesarean section scar, which can provide further complications such as uterine rupture or gynecological complications such as non-pregnancy bleeding and infertility, etc. are also increasing, accordingly, it is effective to study possible influencing factors such as the type of suture applied in repair to improve the patients' quality of life[11]. Thus, the present survey was conducted to determining the relationship between the type of suture used and the incidence and severity of cesarean scar defects (niche) in patients with a history of cesarean as a double-blind randomized clinical trial.

Materials and methods

Patient population

The study was conducted in 2020 and was a randomized and prospective clinical trial. We included all women who experienced cesarean section for the first time in the study, and excluded patients with a history of previous cesarean section, diseases such as diabetes, hypertension, pre-eclampsia, and multiple pregnancies.

Ethical consideration

This study was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences, Yazd, Iran and registered with the protocol number "IR.SSU.MEDICINE.REC.1398.141" this trial was also registered in Iranian Clinical Trial Registry (IRCT20210423051055N1) and was conducted in accordance with the Declaration of Helsinki.

Intervention

We included 50 women who experienced cesarean section in this study and classified them in terms of inclusion and exclusion criteria in two groups of 25 people. One group experienced suture with chromium after cesarean section and the other group experienced suture with Vicryl. The study was double-blind and patients and physicians were not informed of the way of grouping them. Patients were asked to refer to the clinic at least 2 months after cesarean section, and specialist physician examined them by vaginal ultrasonography a for cesarean section defects (Niche). Niche diagnosis on ultrasound was based on the observation of a hypoechoic zone as a defect. The considered information included: detection of cesarean section defects (Niche), type of suture used and cervical dilatation rate were recorded in a pre-prepared questionnaire (consort flow diagram).

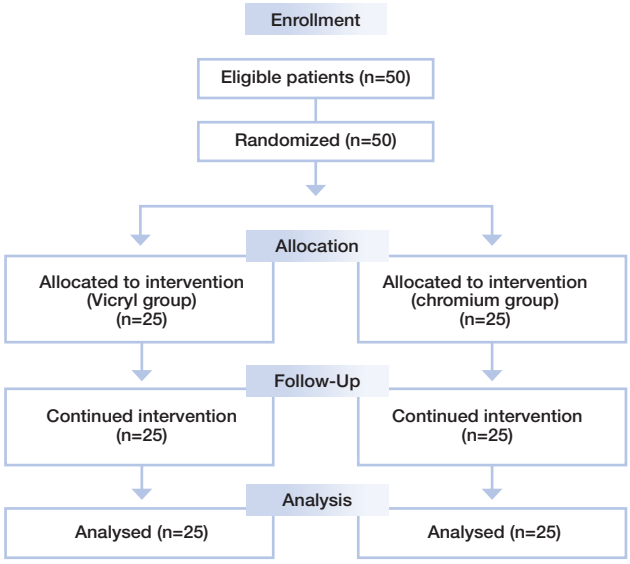
Sampling and blinding

The significant level is 5% and the test power is 80% and the minimum difference is 35% in the previous studies in the two types of sutures, accordingly, 25 people are required in each group (12). We included 50 women who experienced cesarean section in this study in terms of inclusion and exclusion criteria and randomly classified them into two groups of 25 people based on a table of random numbers. **Figure 1** shows the consort flow design of the present study.

Statistical analysis

All registered data were analyzed using SPSS software version 20 for Windows (SPSS, Chicago, IL). For descriptive statistics, the Mean ± SD index was used for quantitative variables with normal distribution. The chi-square test and T-test was used for comparison of data between the two groups. P values of less than 0.05 were considered significant for all analyses.

Figure 1: Consort flow design of the present study.



Results

The results achieved by the study conducted on the frequency distribution of cesarean section defects in the studied patients indicated that among 50 patients 8 (16%) had Niche and 42 patients (84%) had not Niche. The results achieved by the study conducted on the frequency distribution of cervical dilatation in the studied patients indicated that 9 patients had cervical dilatation.

The results achieved by the study conducted on the frequency distribution of niche according to the type of suture applied in the studied patients indicated that 7 (28%) had Niche among 25 people who used chrome for suturing. **Table I** shows other information. Analyzing table using Chi-Square test indicates that a statistically significant difference is observed between the frequency distribution of Niche in terms of the type of suture applied in the patients; so that, the frequency of Niche was significantly higher in patients who used chrome suture.

Table II shows the results achieved by the study conducted on the Niche frequency distribution in terms of cervical dilatation in the studied patients. Analyzing the table using Chi-Square test indicates that no statistically significant difference is observed between the Niche frequency distribution in terms of cervical dilatation in the studied patients.

Table III also shows the results achieved by the study conducted on the frequency distribution of cervical dilatation based on the type of suture in the studied patients. Analyzing Table using Chi-Square test indicated that no statistically significant difference was observed between the rates of cervical dilatation according to the type of suture applied in the studied patients.

Table I: Frequency distribution of niche according to the type of suture applied in the studied patients.

Niche	Type of suture		Total
	Chrome	Vicryl	
Have	7(28%)	1(4%)	8(16%)
Have not	18(72%)	24(96%)	42(84%)
Total	25(100%)	25(100%)	50(100%)
P-value	0.021		

Table II: Frequency distribution of niche according to the cervical dilatation in the studied patients.

Cervical dilatation	Nich e		Total
	Have	Have not	
0-3.9	0(0%)	2(40%)	2(22.2%)
4-7.9	1(25%)	2(40%)	3(33.3%)
8-10	3(75%)	1(20%)	4(44.4%)
Total	4(100%)	5(100%)	9(100%)
P-value	0.196		

Table III: Frequency distribution of cervical dilatation according to the type of suture applied in the studied patients.

Cervical dilatation	Type of suture		Total
	Chrome	Vicryl	
0-3.9	2(40%)	0(0%)	2(22.2%)
4-7.9	1(20%)	2(50%)	3(33.3%)
8-10	2(40%)	2(50%)	4(44.4%)
Total	4(100%)	5(100%)	9(100%)
P-value	0.325		

Discussion

Our study was conducted in order to determine the relationship between the type of suture and the rate and severity of cesarean section defects in patients who experienced cesarean section. Our study that was conducted on 50 patients who experienced cesarean section showed that Niche frequency syndrome was 16% (8 cases). The prevalence rate of isthmus cell in women who experienced one or more cesarean section was estimated to be between 24-70% in transvaginal ultrasound examinations and between 56-84% in Sonohysterography examinations in a systematic review study. This value has been higher in patients who have symptoms and has been estimated from 19.4% to 84%[2].

Various hypotheses have been introduced as the etiology of Niche syndrome. The factors such as the duration of delivery, cervical dilatation, stage of delivery and the site of cesarean section have been considered as effective factors in the detection of isthmus cell in one of these hypotheses[7]. We also examined the relationship between cervical dilatation and the detection of Niche

syndrome in our study. Although, the frequency of Niche cases was higher than 0-3.9 cm dilatation in 8-10 cm cervical dilatation, but this relationship is not statistically significant. It is possible to consider the limited number of samples as a reason for this insignificant relationship. The results achieved by another study conducted in 2018 on 321 women who experienced cesarean section and referred with gynecological complaints such as abnormal bleeding, indicated that previous cesarean section and retroflex uterine incisions are the most significant factors in developing Niche[4].

Another hypothesis introduced in the etiology of Niche syndrome is incorrect surgical technique. Incomplete or incorrect closure of the cesarean section, without suturing the deep muscle layers because of using improper sutures or not spending enough time for this, causes to irregular closure of the myometrium and increases the risk of disease. The results achieved by our study indicates that 7 (28%) had Niche among 25 people who applied chrome for suturing, and a statistically significant difference was observed between the Niche frequency distribution according to the type of suture used in the patients; so that, the Niche frequency was significantly higher in patients who used chrome suture.

Other studies have explained that a relationship between sutures and the detection of Niche syndrome has been confirmed. Basbug et al. conducted a study in Turkey and examined the thickness of the myometrial layer 6-9 months after cesarean section by ultrasound in two groups repaired with monofilament and suture and multifilament. The results explained that applying monofilament suture affects better increasing the thickness of the myometrium layer at the site of cesarean section[12].

The results achieved by a study conducted in Croatia in 2003 also explained that Vicryl group had the best repair and the lowest rupture and catgut group had the highest number of uterine ruptures[13]. Brocklehurst et al. conducted a study in 2002 and compared different techniques in cesarean section. Vicryl was most commonly used suture to repair the uterus[14]. A study conducted in Iran examined the comparison of complications because of using Vicryl suture and Catgut Plain in suturing the subcutaneous layer of the abdomen in cesarean section. The results showed that Vicryl showed less complications in subcutaneous layer repair[15].

Nasrollahi et al. conducted a study on 690 pregnant women in three groups (subcutaneous repair with Plain suture, Vicryl and non-subcutaneous repair), and realized that the rate of wound dehiscence in three groups of subcutaneous repair with Plain suture, subcutaneous repair with Vicryl and no subcutaneous repair were 7%, 2.6% and 0.9%, respectively that there was a statistically significant difference in the rate of wound dehiscence in the three groups. Only two patients showed wound infection and both of them were in the subcutaneous repair group. There was no statistically significant difference in the detection of infection in the three groups[16].

Ziaeeie conducted a study in Gilan on 102 pregnant women in two groups of 51, episiotomy with chromic suture and Vicryl suture repair, and realized that there was no statistically significant difference between two groups in terms of age, gestational age, number of deliveries, length of the second stage of delivery, the interval between delivery and episiotomy repair, the duration of episiotomy repair and the education level. The mean scores of redness at the repair site, edema, ecchymosis and secretion from the wound in the Vicryl group were significantly lower than the Catgut group, but no statistically significant difference was observed between the two groups in the item near the wound edges[17].

Sekhavat et al. conducted a study in Yazd on 100 pregnant women in two groups of 50 people (Vicryl suture and control group) and realized that both groups were same in terms of age, number of deliveries, type of anesthesia and type of incisions. Suppurative infection (positive culture) was observed in 2 cases and 5 patients in control group and dehiscence were observed in 7 cases and 17 people in control group[18]. Similar findings have been reported in previous surveys[19-21].

In general, as the findings of the mentioned studies show, it is possible to state that using Vicryl suture in cesarean section sutures has less complications.

Conclusion

Our According to the results of the study, it can be concluded that there is a relationship between the type of thread used with the incidence of cesarean scar defects (niche), so that the use of chrome thread is associated with more incidence of cesarean scar defects. Therefore, the use of Vicryl thread instead of chrome is recommended to reduce the incidence of cesarean scar defects.

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Conflict of Interest

The authors declare that there is no conflict of interest in the publication of this paper.

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ORIGINAL

Are risk factors and cardiovascular risk scales controlled in hypertensive patients under treatment?

¿Estan controlados los factores de riesgo y las escalas de riesgo cardiovascular en los pacientes hipertensos en tratamiento?

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Summary

Introduction: High blood pressure is considered one of the main cardiovascular risk factors; therefore, it is essential to exercise adequate control over it.
Hypothesis: The blood pressure control in people undergoing treatment is not very accurate and, in addition, the values of the different scales related to cardiovascular risk are high in this group of treated people.
Material and methods: Descriptive cross-sectional study conducted in 34,595 hypertensive patients under treatment for both hypertension and associated comorbidities. We assessed the influence of treatments on the degree of control of arterial hypertension and on the values of different scales related to cardiovascular risk.
Results: 49.31% of our total population exhibited normal values of blood pressure normal (59.25% in women and 44.54% in men). Almost all the scales analyzed (overweight and obesity, atherogenic indices, metabolic syndrome, cardiovascular risk scales and fatty liver scales) presented worse values in the group that was receiving treatment for arterial hypertension, for dyslipidemia and for diabetes simultaneously.
Discussion: Half of the people who were receiving drug treatment for hypertension show high blood pressure levels, so it is necessary discuss about what strategies are necessary to improve this situation.

Keywords: Hypertension, cardiovascular diseases, obesity, dyslipidemia, metabolic syndrome.

Resumen

Introducción: La hipertensión arterial se considera uno de los principales factores de riesgo cardiovascular, por lo que es fundamental ejercer un adecuado control sobre ella.
Hipótesis: El control de la presión arterial en personas en tratamiento es poco preciso y, además, los valores de las diferentes escalas relacionadas con el riesgo cardiovascular son elevados en este grupo de personas tratadas.
Material y métodos: Estudio descriptivo transversal realizado en 34.595 pacientes hipertensos en tratamiento tanto de la hipertensión como de las comorbilidades asociadas. Se evaluó la influencia de los tratamientos en el grado de control de la hipertensión arterial y en los valores de diferentes escalas relacionadas con el riesgo cardiovascular.
Resultados: El 49,31% de nuestra población total presentaba valores normales de presión arterial (59,25% en mujeres y 44,54% en hombres). Casi todas las escalas analizadas (sobrepeso y obesidad, índices aterogénicos, síndrome metabólico, escalas de riesgo cardiovascular y escalas de hígado graso) presentaron peores valores en el grupo que recibía tratamiento para la hipertensión arterial, para la dislipidemia y para la diabetes simultáneamente.
Discusión: La mitad de las personas que estaban recibiendo tratamiento farmacológico para la hipertensión arterial presentan niveles elevados de presión arterial, por lo que es necesario discutir sobre qué estrategias son necesarias para mejorar esta situación.

Palabras clave: Hipertensión, enfermedades cardiovasculares, obesidad, dislipidemia, síndrome metabólico.

Introduction

Systolic blood pressure is the force exerted by the blood on the arteries when the heart contracts, while the diastolic reflects the pressure in the arteries when the heart rests. It is a remarkable feature that arterial hypertension is a disease that can be controlled, which decreases the quality and life expectancy since it increases the risk of cardiovascular diseases. The modification of the lifestyle and the treatment with specific medication allows controlling the arterial hypertension.

Among the main risk factors, we find age (over 50 years), male gender (although women in post-menopause have increased risk of hypertension), family history, obesity, sedentary lifestyle, alcohol, tobacco, stress, high salt consumption and some contraceptives (especially, in smoking women), among others.

Hypertension treatment is based on drugs and lifestyle changes and low salt diet. It is necessary to avoid the consumption of processed foods, sausages, cold meat, hard cheeses; select low-sodium foods and waters; and encourage the consumption of fruits and vegetables as a source of potassium (which helps control blood pressure). In case of overweight, a reduction in body weight is indicated. Quitting smoking is also recommended. Regular physical activity might be patterned according to the age of each patient, but the recommendation is 30 minutes of daily moderate physical activity.

Currently, antihypertensive are classified according to their mechanism of action as:

- Diuretics. Drugs that reduce the cardiovascular morbidity and mortality associated with HT[1]. There are three different subgroups of diuretics: thiazides, loop of Henle diuretics and potassium sparing agents.
- Beta-blockers. Highly effective, both in monotherapy and in association, in the treatment of mild-to-moderate HT, in the prevention of cardiovascular complications[2], in the clear prevention of reinfarction in patients with ischemic heart disease[3] and in increasing survival in patients with heart failure[4].
- Calcium channel blockers are characterized by a very fast onset of action, which can lead to hypotension in vulnerable individuals, especially the elderly[5]. For this reason, these drugs are currently generally prescribed in extended-release presentations.
- Angiotensin-converting enzyme inhibitors not only reduce blood pressure, but also reduce the vascular damage caused by hypertension (renal failure or heart failure[6]).
- Angiotensin II receptor antagonist. Like ACEI, the decrease in BP with these drugs is not accompanied by reflex tachycardia and, unlike those, they do not cause coughing or angioedema.

Study purposes

- To determine the prevalence of cardiovascular risk factors in hypertensive patients receiving pharmacological treatment.
- To determine the values of the cardiovascular risk scales in hypertensive patients receiving pharmacological treatment.
- To determine the prevalence of altered values of cardiovascular risk scales in hypertensive patients receiving pharmacological treatment.

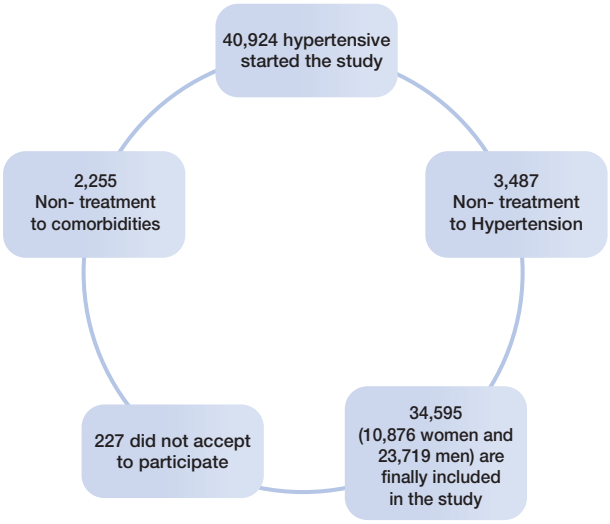
Hypothesis

Hypertensive individuals, with or without associated comorbidity, who are receiving antihypertensive treatment, in addition to treatment for the associated comorbidity, have low control of cardiovascular risk factors and high values on the cardiovascular risk scales.

Material and methods

Descriptive, cross-sectional, and observational study of 40,924 hypertensive patients. Of these, 2,255 were excluded because they were not receiving treatment for comorbidity, 3,847 were not taking their antihypertensive treatment and 227 did not agree to participate in the study. The final number of participants who met all the inclusion criteria was 34,595 (10,876 women and 23,719 men) with mean age of 51.61 years (51.38 years in women and 51.72 years in men). (See flow chart in **figure 1**).

Figure 1: Flowchart of participants.



Inclusion criteria:

- Being diagnosed hypertensive and on active antihypertensive treatment. In case of associated comorbidity, it must also be under active treatment.
- Age between 18 and 70 years.
- Agree to participate in the study.

Parameters related to CVD risk included in the assessment:

Anthropometric and clinical parameters. Anthropometric and clinical measurements and blood sampling to determine the analytical parameters were performed by the health personnel of the occupational health units involved in the study. For the collection of the different anthropometric parameters, international recommendations were followed. All measurements were performed by trained health personnel to minimize interobserver bias.

Weight (in kg) and height (in cm) were determined with a SECA 700 professional measuring scale. Abdominal waist circumference (cm) was calculated with a model 20 SECA Measuring Tape.

Overweight and obesity scales:

Body mass index (BMI) was obtained using the Quetelet index: weight in kilograms divided by the square of the height expressed in meters. Based on the BMI, four categories were established according to the classification of the Spanish Society for the Study of Malnutrition and Obesity (SEEDO)[7]: Underweight: BMI<18.5; Normal weight: BMI 18.5-24.9; Overweight: BMI 25-29.9; Obesity: BMI ≥ 30.

The waist / height ratio (ICALT) was considered high from 0.50.

CUN BAE. -44.988 + (0.503 × age) + (10.689 × sex) + (3.172 × BMI) - (0.026 × BMI2) + (0.181 × BMI × sex) - (0.02 × BMI × age) --- (0.005 × BMI2 × sex) + (0.00021 × BMI2 × age), where men = 0 and women = 1 with respect to sex, measuring age in years[8].

The following classifications were used to stratify into the different categories of overweight and obesity: • Male population: < 20% normal weight, 20-25% overweight, > 25% obesity • Female population: < 30% normal weight, 30-35% overweight, > 35% obesity.

ECORE-BF[9] –97.102 + 0.123 (age) + 11.9 (sex) + 35.959 (LnIMC) where male is equal to 0 and female is equal to 1. The authors propose the same cut-off points as CUN BAE.

Relative fat mass[10].

Women: 76- (20 x (height/w waist))
Men: 64- (20 x (height/w waist))
Suggested cut-off points are 40% in women and 30% in men.

Palafolls formula[11]. Men = ([BMI/BP] *10) + BMI. Women = ([BMI/BP] *10) + BMI + 10. The authors propose the same cut-off points as CUN BAE.

Deuremberg formula[12]. 1.2 x (BMI) + 0.23 x (Age in years) - 10.8 x (sex) - 5.4 where female is equal to 0 and male is equal to 1. It is considered obesity from 25.5% in men and 32% in women.

Body roundness index[13]

$$BRI = 364{,}2 - 365{,}5 \times \sqrt{1 - \left(\frac{(WC/(2\pi))^2}{(0{,}5\ height)^2}\right)}$$

Visceral adiposity index[14]

Females:

$$VAI = \left(\frac{WC}{36{,}58 + (1{,}89 \times BMI)}\right) \times \left(\frac{TG}{0{,}81}\right) \times \left(\frac{1{,}52}{HDL}\right)$$

Males:

$$VAI = \left(\frac{WC}{39{,}68 + (1{,}88 \times BMI)}\right) \times \left(\frac{TG}{1{,}03}\right) \times \left(\frac{1{,}31}{HDL}\right)$$

The waist circumference is expressed in cm and LDL and triglycerides in mmol/L. Obesity cut-off points vary with age.

Normalized weight-adjusted index (NWAI)[15].

NWAI= [(weight/10) – (10 x height) + 10] weight in kg and height in meters

Blood pressure was determined after a resting period of about 10 minutes in the supine position, using a calibrated OMRON M3 automatic sphygmomanometer. Three consecutive readings at one-minute intervals were taken and the mean value of the three measurements was calculated. The measurements were classified according to the ESH/ESC criteria[16]: Normal BP: SBP < 130 mmHg and/or DBP < 85 mmHg; Pre-HT: SBP 130-139 mmHg and/or DBP 85-89 mmHg; HT 1: SBP 140-159 mmHg and/or DBP 90-99 mmHg; HT 2: SBP > 160 mmHg and/or DBP > 100 mmHg.

Analytical parameters. Blood extraction to determine the analytical parameters included in the study was performed by peripheral venipuncture in the same session and at the same place as the anamnesis and physical examination, after a minimum overnight fast of 12 hours. Values were expressed in milligrams/deciliter (mg/dL). The values to define the presence or absence of diabetes were defined based on the 2013 American Diabetes Association recommendations. Fasting plasma glucose: Normal < 100 mg/dl. Altered basal blood glucose: 100-125 mg/dl. Diabetes > 125 mg/dl. The cut-off values for lipids

have been defined based on those included in the 2010 SEMERGEN-SEA Consensus Document for the approach to dyslipemic patients[17].

Atherogenic indices. For the different atherogenic indices, the formulas accepted by the scientific community were used. For each index different cut-off points were defined to establish the atherogenic risk categories according to the existing data in the literature[18].

Metabolic Syndrome.

- NCEP ATP III criteria[19] (Adult Treatment Panel III National Cholesterol Educational Program). At least 3 of the following risk factors are required: Waist circumference >102 cm in men and >88 cm in women. Serum triglycerides ≥ 150 mg/dL or being on specific treatment for this lipid abnormality. Blood pressure ≥ 130/85 mm Hg or being on specific treatment with antihypertensive drugs. cHDL < 40 mg/dL in men and < 50 mg/dL in women or being on specific treatment for this lipid abnormality. Fasting blood glucose > 100 mg/dL or being on specific treatment with antidiabetic drugs.
- International Diabetes Federation (IDF) criteria[20]. Central obesity defined as waist circumference ≥ 94 cm for Caucasian men and ≥ 80 cm and at least two of the 4 factors mentioned above in NCEP-ATPIII are compulsory.
- JIS criteria: presence of at least three of the following factors: abdominal obesity (waist circumference ≥ 94 cm in men and ≥ 80 cm in women); triglycerides ≥ 150 mg/dl or treatment; HDL cholesterol <40 mg/dl in men and <50 mg/dl in women or treatment; blood pressure ≥ 130/85 mmHg or treatment; fasting glucose ≥ 100 mg/dl or treatment[21].

Cardiovascular risk scales

- REGICOR scale (*Registro Gironí del Cor*): Framinghan model calibrated for the Spanish population. The REGICOR tables allow estimation of the risk of suffering a coronary event (angina, symptomatic or silent myocardial infarction and/or death of coronary origin) in the following 10 years. The REGICOR tables are only applicable to subjects aged 35 to 74 years old. Each subject is classified as: < 5%: low risk, 5-9.9% moderate risk, 10 -14.9% high risk and ≥15% very high risk[22].
- DORICA scale[23]. It also indicates the risk of suffering a coronary event within the following 10 years. It is considered low risk < 5, slight risk 5-9, moderate risk 10 -19, high risk 20 -39 and very high risk ≥ 40.
- SCORE (Systematic Coronary Risk Evaluation) scale presents differential tables according to the country's risk level[24]. It estimates the risk of cardiovascular and cerebrovascular death within 10 years. The version for low-risk countries, recommended for Spain[25], was used. It is considered low risk < 3%, moderate risk 4-5% and high risk > 5%[26].
- ERICE scale (Spanish Cardiovascular Risk Equation). Estimates the risk of suffering a fatal or non-fatal cerebrovascular event over a 10-year period. The tables apply to people between 30 and 80 years old. Low risk <5%: low risk, mild risk 5-9%, moderate risk 10-14%, moderate-high risk 15-19%, high risk 20-39% and very high risk over 30%[27].
- Framingham categories[28].
- Framingham vascular age[29]. This tool has its origin in the Framingham cardiovascular risk scale, which can be calculated from the age of 30 years.
- SCORE vascular age[30]. This tool has its origin in the SCORE cardiovascular risk scale. As with the scale from which it derives, it can be calculated in persons between 40 and 65 years.

Nonalcoholic fatty liver scales:

- Fatty liver index[31]

$$FLI = (e^{0.953*\log_e(\text{triglycerides}) + 0.139*BMI + 0.718*\log_e(ggt) + 0.053*\text{waist circumference} - 15.745}) / (1 + e^{0.953*\log_e(\text{triglycerides}) + 0.139*BMI + 0.718*\log_e(ggt) + 0.053*\text{waist circumference} - 15.745}) \times 100$$

A FLI with values over 60 is considered high risk.

- Hepatic steatosis index[32]

HSI = 8 x ALT / AST + BMI (+ 2 if diabetes 2, + 2 if female)
Values over 36 are considered high risk.

- ZJU index[33]

BMI (kg / m 2) + Blood glucose (mmol / L) + TG (mmol / L) + 3 * ALT (IU / L) / AST (IU / L) ratio (+ 2 if female).
Values over 38 are considered high risk.

- Framingham steatosis index[34]

- 7.981 + 0.011 × age(years)–0.146 × sex (female = 1, male = 0) + 0.173 × BMI(kg/m2) + 0.007 × triglycerides(mg/dl) + 0.593 × hypertension(yes = 1, no = 0) + 0.789 × diabetes(yes = 1, no = 0) + 1.1 × ALT/ AST ratio ≥ 1.33(yes = 1, no = 0).

Values over 28 are considered high risk.

- Lipid accumulation product[35].

- In men: (waist circumference (cm) - 65) x (triglyceride concentration (mMol)).
- In women: (waist circumference (cm) - 58) x (triglyceride concentration (mMol))

Other parameters related to cardiovascular risk:

- Triglyceride glucose index triglyceride glucose index-IMC, triglyceride glucose index-p waist TyGindex = LN (TG [mg/dl] × blood glucose [mg/dl]/2). TyGindex-IMC = TyGindex x IMC TyGindex-p waist = TyGindex x p waist[36-39].
- Waist weight index. This indicator is calculated by applying the formula. WWI = waist circumference / √weight
- Cardiometabolic index[40] is calculated by multiplying the waist-height index by the atherogenic triglycerides / HDL-c index.

- Atherogenic dyslipidemia and lipid triad[41]. Atherogenic dyslipidemia is characterized by elevated triglyceride levels (> 150 mg / dl), low HDL (<40 mg / dl in men and <50 mg / dl in women), and normal or mildly elevated LDL. If LDL values are high (> 160 mg / dl) we speak of lipid triad.

Statistical analysis.

The SPSS 27.0 package was used for the statistical study. For the initial descriptive analysis, once the normal distribution had been verified and following the Kolmogorov-Smirnov method, the mean and standard deviation values were used. In subsequent analyses, when the variable was continuous, the comparison of means was performed using Student's t test if the variable followed a normal distribution, or the nonparametric Mann-Whitney U test if it did not meet the normality criterion. When the variable was qualitative, Pearson's chi-squared test was used to compare proportions, with a confidence level of 95%. ROC curves were used to calculate the cut-off points. P values less than 0.05 were considered statistically significant.

Results

The anthropometric, clinical, analytical, and sociodemographic characteristics of the 24,595 people who entered the study are presented in **table II**.

The mean values of the different scales that assess overweight and obesity are presented in **table III**. The results are divided in each sex according to treatment. The highest values appear in almost all cases and in both sexes in the group of people being treated for HT, dyslipidemia, and diabetes.

The values of blood pressure and analytical parameters do not show a homogeneous pattern according to the treatment being received in either sex. The complete data are shown in **table IV**.

Almost all the cardiovascular risk scales studied show higher values in the group of people being treated for the three conditions (HT, dyslipidemia, and diabetes), and this is true for both sexes. The complete data are presented in **table V**.

As shown in **table VI**, the fatty liver scales show higher values in the group receiving the three treatments, in both sexes. The same occurs with the atherogenic indices and with the other metabolic indicators.

When the prevalence of high values of the overweight and obesity scales is evaluated, it is found that in both sexes the highest prevalences are found in the group that receives hypertensive treatment in addition to treatment for dyslipidemia and diabetes. The complete data can be found in **table VII**.

Table II: Anthropometric, clinical, analytical, and sociodemographic characteristics of the population.

	Men n=10,876 Mean (sd)	Women n=23,719 Mean (sd)	Total n=34,595 Mean (sd)	p
Age (years)	51.38 (8.23)	51.72 (7.78)	51.61 (7.93)	<0.0001
Height (cm)	159.61 (6.58)	172.68 (6.97)	168.57 (9.15)	<0.0001
Weight (kg)	73.92 (15.50)	88.86 (15.93)	84.16 (17.25)	<0.0001
Waist (cm)	79.15 (12.02)	90.52 (11.52)	86.95 (12.81)	<0.0001
SBP (mmHg)	132.35 (18.54)	139.04 (18.10)	136.94 (18.50)	<0.0001
DBP (mmHg)	80.90 (11.19)	85.29 (11.16)	83.91 (11.36)	<0.0001
Cholesterol (mg/dl)	207.47 (36.68)	200.20 (38.36)	202.49 (37.99)	<0.0001
HDL (mg/dl)	53.39 (7.96)	46.07 (8.18)	48.37 (8.79)	<0.0001
LDL (mg/dl)	130.77 (35.73)	124.36 (36.81)	126.41 (36.59)	<0.0001
Triglycerides (mg/dl)	117.50 (63.98)	154.14 (99.67)	142.62 (91.58)	<0.0001
Blood glucose (mg/dl)	97.49 (25.06)	105.73 (32.37)	103.14 (30.50)	<0.0001
GPT (U/L)	24.05 (13.84)	33.95 (19.00)	30.86 (18.15)	<0.0001
GOT (U/L)	20.00 (8.68)	25.64 (11.95)	23.77 (11.29)	<0.0001
GGT (U/L)	27.46 (27.26)	48.04 (53.48)	41.63 (47.86)	<0.0001
	%	%	%	p
20-49 years	36.63	34.73	35.33	<0.0001
50-70 years	63.37	65.27	64.67	
Social Class I-II	19.44	19.63	19.57	<0.0001
Social Class III	80.56	80.37	80.43	
Non-smokers	68.46	67.84	68.04	0.476
Smokers	31.54	32.16	31.96	
HT	53.82	43.12	46.48	<0.0001
Diabetes + HT	18.82	22.26	21.18	<0.0001
Dyslipidemia + HT	16.96	18.86	18.27	<0.0001
Diabetes + dyslipidemia + HT	10.40	15.76	14.07	<0.0001

Table III: Mean values of overweight-obesity indicators according to drug consumption by sex.

	Women					Men				
	HT n=5,853 Mean (sd)	HT+Diab n=2,047 Mean (sd)	HT+DLP n=1,845 Mean (sd)	HT+DLP+Diab n=1,131 Mean (sd)	p	HT n=10,228 Mean (sd)	HT+Diab n=5,280 media (sd)	HT+DLP n=4,474 media (sd)	HT+DLP+Diab n=3,737 media (sd)	p
Age	49.47 (8.59)	51.85 (7.70)	54.13 (6.89)	55.91 (5.76)	<0.0001	49.88 (8.28)	52.40 (7.52)	52.75 (7.06)	54.57 (6.13)	<0.0001
BMI	28.81 (5.87)	29.93 (5.91)	28.05 (5.11)	29.85 (5.16)	<0.0001	29.56 (4.80)	30.17 (5.00)	29.19 (4.30)	30.39 (4.63)	<0.0001
Waist/Height	0.49 (0.08)	0.50 (0.07)	0.48 (0.07)	0.50 (0.07)	<0.0001	0.52 (0.06)	0.53 (0.06)	0.52 (0.06)	0.53 (0.06)	<0.0001
CUN BAE	40.85 (6.51)	42.38 (6.29)	40.65 (5.64)	42.88 (5.25)	<0.0001	30.45 (5.84)	31.43 (5.81)	30.35 (5.24)	31.97 (5.33)	<0.0001
ECORE-BF	41.04 (7.13)	42.72 (7.01)	40.78 (6.33)	43.28 (6.01)	<0.0001	30.35 (5.73)	31.39 (5.74)	30.33 (5.24)	31.98 (5.33)	<0.0001
RFM	34.86 (5.90)	35.36 (5.74)	33.83 (5.46)	35.54 (5.11)	<0.0001	25.31 (4.73)	25.43 (4.61)	24.83 (4.56)	25.66 (4.44)	<0.0001
Palafolls	42.43 (6.13)	43.66 (6.18)	41.71 (5.34)	43.60 (5.38)	<0.0001	32.81 (5.00)	33.49 (5.22)	32.48 (4.49)	33.74 (4.83)	<0.0001
IMG	40.56 (7.31)	42.45 (7.26)	40.71 (6.29)	43.28 (6.19)	<0.0001	30.74 (6.02)	32.06 (6.16)	30.96 (5.37)	32.82 (5.60)	<0.0001
NWAI	1.38 (1.52)	1.66 (1.52)	1.20 (1.30)	1.66 (1.31)	<0.0001	1.56 (1.45)	1.74 (1.50)	1.45 (1.28)	1.80 (1.38)	<0.0001
BRI	3.41 (1.52)	3.51 (1.46)	3.12 (1.26)	3.48 (1.28)	<0.0001	3.92 (1.33)	3.94 (1.31)	3.76 (1.19)	3.98 (1.22)	<0.0001
VAI	3.50 (2.06)	3.70 (2.17)	3.94 (2.93)	4.51 (2.62)	<0.0001	9.65 (7.29)	10.27 (8.02)	10.88 (7.87)	12.29 (10.02)	<0.0001

BMI. Body Mass Index. CUN BAE. Body Adiposity Estimator of the Clínica Universitaria de Navarra. ECORE-BF. Cordoba-Body Fat Equation. RFM Relative fat mass. IMG Fat mass index, NWAI Normalized weight adjusted index. BRI Body Roundness Index, VAI Visceral Adiposity Index.

Table IV: Mean values of blood pressure and analytical parameters according to drug consumption by sex.

	Women					Men				
	HT n=5,853 Mean (sd)	HT+Diab n=2,047 Mean (sd)	HT+DLP n=1,845 Mean (sd)	HT+DLP+Diab n=1,131 Mean (sd)	p	HT n=10,228 Mean (sd)	HT+Diab n=5,280 media (sd)	HT+DLP n=4,474 media (sd)	HT+DLP+Diab n=3,737 media (sd)	p
TSBP	131.50 (18.41)	134.60 (18.79)	130.91 (18.65)	135.07 (17.99)	<0.0001	140.31 (18.40)	136.42 (17.10)	139.04 (18.10)	140.51 (17.97)	<0.0001
DBP	81.24 (11.39)	81.67 (11.09)	79.31 (10.75)	80.33 (10.72)	<0.0001	83.80 (10.66)	85.29 (11.16)	83.80 (10.66)	85.76 (11.07)	<0.0001
Cholesterol	208.03 (35.53)	207.42 (35.09)	209.75 (40.10)	200.91 (38.84)	<0.0001	204.04 (36.21)	198.72 (35.50)	199.89 (41.27)	192.17 (42.72)	<0.0001
HDL	54.09 (8.49)	53.02 (7.67)	52.93 (7.21)	51.13 (6.07)	<0.0001	47.13 (8.42)	45.41 (7.98)	45.86 (7.85)	44.37 (7.73)	<0.0001
LDL	131.89 (34.41)	130.88 (33.90)	132.31 (38.99)	122.33 (38.89)	<0.0001	128.79 (34.67)	124.35 (34.85)	122.33 (39.09)	114.44 (4.21)	<0.0001
Triglycerides (mg/dl)	110.93 (55.79)	117.66 (60.69)	125.14 (81.65)	138.76 (70.41)	<0.0001	144.64 (87.45)	149.30 (99.43)	164.74 (103.09)	174.28 (120.90)	<0.0001
Blood glucose (mg/dl)	92.37 (16.12)	104.15 (33.26)	95.33 (17.77)	115.45 (40.42)	<0.0001	97.32 (19.92)	113.63 (40.15)	99.63 (19.93)	124.85 (46.06)	<0.0001
GPT	23.11 (12.73)	23.48 (14.97)	25.34 (13.21)	27.21 (16.42)	<0.0001	32.82 (18.53)	33.15 (18.48)	35.77 (19.27)	35.57 (20.20)	<0.0001
GOT	20.01 (8.49)	19.76 (10.32)	20.09 (6.88)	20.40 (7.94)	<0.0001	24.77 (9.29)	25.20 (11.59)	27.23 (15.31)	26.57 (13.27)	<0.0001
GGT	25.95 (24.34)	26.91 (23.99)	28.16 (22.80)	34.05 (44.67)	<0.0001	45.60 (52.84)	45.27 (49.41)	51.44 (51.51)	53.69 (61.34)	<0.0001

Table V: Mean values of cardiovascular risk scales according to drug use by sex.

	Women					Men				
	HT n=5,853 Mean (sd)	HT+Diab n=2,047 Mean (sd)	HT+DLP n=1,845 Mean (sd)	HT+DLP+Diab n=1,131 Mean (sd)	p	HT n=10,228 Mean (sd)	HT+Diab n=5,280 media (sd)	HT+DLP n=4,474 media (sd)	HT+DLP+Diab n=3,737 media (sd)	p
ALLY EV SCORE	6.69 (5.38)	7.66 (5.60)	7.56 (5.22)	8.42 (5.10)	<0.0001	10.47 (7.26)	11.29 (7.27)	10.39 (7.20)	11.38 (7.16)	<0.0001
SCORE	0.85 (1.28)	1.21 (1.54)	1.32 (1.55)	1.67 (1.60)	<0.0001	2.65 (2.77)	3.18 (3.06)	2.94 (2.83)	3.37 (3.00)	<0.0001
ALLY EV FRAMINGHAM	14.99 (12.92)	29.46 (10.21)	14.89 (12.56)	28.85 (9.46)	<0.0001	16.03 (9.97)	26.53 (8.85)	15.97 (10.17)	26.62 (8.63)	<0.0001
REGICOR	3.30 (2.19)	3.93 (2.19)	3.41 (2.18)	3.81 (2.72)	<0.0001	3.75 (2.44)	4.08 (3.00)	3.65 (2.42)	4.12 (3.06)	<0.0001
ERICE	5.36 (4.62)	9.17 (7.29)	7.65 (4.52)	12.50 (6.67)	<0.0001	10.31 (6.69)	15.73 (9.14)	12.14 (6.94)	17.60 (8.62)	<0.0001
DORICA	4.98 (3.48)	6.51 (4.28)	6.27 (3.76)	8.14 (4.64)	<0.0001	9.14 (5.61)	10.71 (6.42)	9.51 (5.53)	11.46 (7.12)	<0.0001
CVD RISK	9.76 (6.83)	12.11 (8.11)	11.19 (6.94)	14.47 (8.63)	<0.0001	19.22 (10.16)	22.62 (10.54)	20.95 (10.14)	24.93 (10.01)	<0.0001
Framingham categories	6.00 (4.24)	7.80 (5.36)	7.46 (4.45)	10.03 (5.97)	<0.0001	11.61 (7.32)	13.95 (8.75)	12.20 (7.43)	15.05 (9.33)	<0.0001
Framingham categories duro	3.07 (2.97)	4.31 (4.13)	3.94 (3.35)	5.92 (4.92)	<0.0001	8.87 (6.31)	10.87 (7.83)	9.35 (6.38)	11.84 (8.59)	<0.0001

ALLY EV. Lost years of vascular age. CVD RISK. Cardiovascular

Table VI: Mean values of fatty liver scales and atherogenic indices according to drug consumption by sex.

	Women					Men				
	HT n=5,853 Mean (sd)	HT+Diab n=2,047 Mean (sd)	HT+DLP n=1,845 Mean (sd)	HT+DLP+Diab n=1,131 Mean (sd)	p	HT n=10,228 Mean (sd)	HT+Diab n=5,280 media (sd)	HT+DLP n=4,474 media (sd)	HT+DLP+Diab n=3,737 media (sd)	p
Fatty liver index	32.74 (27.64)	37.55 (28.24)	30.99 (25.29)	41.28 (27.85)	<0.0001	54.60 (27.46)	56.43 (26.93)	56.11 (26.09)	61.58 (26.47)	<0.0001
Hepatic steatosis index	40.22 (7.38)	42.67 (7.32)	39.51 (6.59)	43.42 (6.58)	<0.0001	39.54 (6.90)	41.72 (6.90)	39.20 (6.24)	42.28 (6.32)	<0.0001
ZJU index	40.95 (6.65)	42.22 (7.30)	40.28 (5.56)	43.79 (6.66)	<0.0001	40.14 (5.59)	41.16 (6.31)	40.18 (5.46)	42.72 (6.46)	<0.0001
Fatty liver disease index	33.90 (6.44)	34.69 (6.69)	33.12 (5.32)	35.98 (6.14)	<0.0001	34.89 (5.40)	35.49 (5.80)	34.80 (5.10)	36.44 (5.48)	<0.0001
Lipid accumulation product	28.45 (24.86)	30.29 (24.60)	27.66 (25.93)	35.59 (27.66)	<0.0001	44.67 (38.91)	45.27 (40.14)	45.98 (38.59)	53.12 (48.19)	<0.0001
IA cholesterol/HDL	3.94 (0.91)	3.98 (0.85)	4.04 (0.96)	3.98 (0.90)	<0.0001	4.47 (1.15)	4.52 (1.17)	4.48 (1.21)	4.47 (1.31)	<0.0001
IA Triglycerids/HDL	2.13 (1.21)	2.30 (1.33)	2.45 (1.83)	2.80 (1.62)	<0.0001	3.24 (2.26)	3.47 (2.54)	3.77 (2.61)	4.15 (3.19)	<0.0001
IA LDL/HDL	2.51 (0.82)	2.52 (0.76)	2.55 (0.86)	2.43 (0.83)	<0.0001	2.84 (0.98)	2.84 (1.00)	2.75 (1.03)	2.67 (1.11)	<0.0001
IA HDL/LDL+VLDL	0.38 (0.14)	0.37 (0.12)	0.37 (0.12)	0.37 (0.12)	<0.0001	0.33 (0.12)	0.32 (0.13)	0.33 (0.13)	0.34 (0.14)	<0.0001
IA cholesterol-HDL	153.94 (36.64)	154.40 (35.84)	156.83 (40.81)	149.77 (39.56)	<0.0001	156.91 (37.38)	153.32 (36.97)	154.03 (42.05)	147.80 (43.89)	<0.0001
Cardiometabolic index	1.08 (0.69)	1.17 (0.74)	1.20 (0.91)	1.43 (0.89)	<0.0001	1.74 (1.31)	1.86 (1.45)	1.98 (1.42)	2.23 (1.81)	<0.0001
Triglyceride glucose index	8.43 (0.49)	8.59 (0.56)	8.57 (0.50)	8.84 (0.61)	<0.0001	8.71 (0.55)	8.86 (0.64)	8.83 (0.60)	9.09 (0.67)	<0.0001
Waist triglyceride index	101.15 (56.99)	107.40 (59.71)	109.68 (74.25)	126.53 (69.41)	<0.0001	150.91 (98.50)	154.93 (108.39)	166.98 (108.63)	181.13 (131.67)	<0.0001
Waist weight index	9.28 (0.78)	9.20 (0.67)	9.13 (0.70)	9.21 (0.65)	<0.0001	9.67 (0.74)	9.59 (0.68)	9.59 (0.70)	9.60 (0.68)	<0.0001

Table VII: Prevalence of overweight-obesity with different scales according to drug consumption by sex.

	Women					Men				
	HT n=5,853 Mean (sd) %	HT+Diab n=2,047 Mean (sd) %	HT+DLP n=1,845 Mean (sd) %	HT+DLP+Diab n=1,131 Mean (sd) %	p	HT n=10,228 Mean (sd) %	HT+Diab n=5,280 media (sd) %	HT+DLP n=4,474 media (sd) %	HT+DLP+Diab n=3,737 media (sd) %	p
Waist/Height >0,50	40.80	45.43	34.09	47.30	<0.0001	61.61	62.71	59.50	64.97	<0.0001
BMI obesity	37.50	44.70	29.76	42.79	<0.0001	41.13	45.72	38.44	49.69	<0.0001
BMI overweight	34.00	34.49	40.81	41.82		43.56	41.99	46.69	40.49	
CUN BAE obesity	81.12	87.40	85.31	94.08	<0.0001	83.54	87.56	85.49	91.73	<0.0001
CUN BAE overweight	14.37	10.26	11.82	5.31		13.69	10.81	12.43	7.55	
ECORE-BF obesity	79.51	85.69	83.09	93.37	<0.0001	83.52	87.56	85.38	91.30	<0.0001
ECORE-BF overweight	15.27	11.33	12.95	5.13		13.54	10.70	12.41	7.76	
RFM obesity	55.37	59.94	49.92	62.69	<0.0001	71.04	71.82	69.18	73.67	<0.0001

BMI. Body Mass Indez. CUN BAE. Clínica Universitaria de Navarra Body Adiposity Estimator. ECORE-BF. Equation Córdoba-Body Fat. RFM Relative Fat Mass.

Table VIII: Prevalence of altered blood pressure values and analytical parameters according to drug use by sex.

	Women					Men				
	HT n=5,853 Mean (sd) %	HT+Diab n=2,047 Mean (sd) %	HT+DLP n=1,845 Mean (sd) %	HT+DLP+Diab n=1,131 Mean (sd) %	p	HT n=10,228 Mean (sd) %	HT+Diab n=5,280 media (sd) %	HT+DLP n=4,474 media (sd) %	HT+DLP+Diab n=3,737 media (sd) %	p
HT	38.97	44.41	35.34	44.30	<0.0001	56.20	58.24	48.39	59.03	<0.0001
Cholesterol ≥ 200	57.66	57.16	55.72	44.47	<0.0001	53.09	47.27	46.58	37.97	<0.0001
LDL > 130	50.86	49.73	48.08	36.25	<0.0001	47.93	43.81	40.93	32.99	<0.0001
Triglycerides > 150	17.17	20.66	23.96	32.54	<0.0001	34.74	36.63	44.23	46.96	<0.0001
Blood glucosa 100-125	19.78	26.18	27.05	29.44	<0.0001	29.26	32.23	35.83	32.70	<0.0001
Blood glucosa > 125	2.00	12.85	3.36	24.49	<0.0001	4.61	21.33	5.30	32.00	<0.0001

Table IX: Percentage of patients with controlled blood pressure figures according to treatments received.

	Women n=10,876 % HT controlled	Men n=23,719 % HT controlled	Total n=34,595 % HT controlled
HT + Dislypemia + diabetes	55.70	40.97	44.39
HT	61.03	43.80	50.07
HT + diabetes	55.59	41.76	45.63
HT + dislypemia	64.66	51.61	55.42
Mean	59.25	44.54	49.31

Table VIII shows the prevalence of HT and analytical abnormalities in treated patients. **Table IX** shows that women overall have controlled blood pressure in 59.25% of cases, while in men the figure drops to 44.54%.

Table X shows that most of the scales for cardiovascular risk, metabolic syndrome and atherogenic dyslipidemia have higher prevalence of altered values in the group receiving antihypertensive treatment, as opposed to dyslipidemia and diabetes, which is the same in both sexes.

Discussion

No prior study has been found in the literature that assesses the degree of blood pressure control in hypertensive patients with comorbidities (dyslipidemia and diabetes), nor any previous work that focuses on the control of cardiovascular risk parameters or scales in hypertensive patients under treatment; therefore, we cannot compare our results with those of other preceding authors.

For the discussion we will focus on the degree of control of blood pressure in hypertensive patients under treatment.

Remarkably, the overall degree of control of blood pressure in our study was 49.31% (59.25% in women and 44.54% in men).

In a study of 124 patients with an average age of 68 years in ten community pharmacies in different areas of the Valencian Community (Spain), 46.80% of these patients were not under control. Almost half of the patients treated with antihypertensive drugs presented out-of-range blood pressure values according to the 2018 European Guideline for the management of hypertension[42]. Another study in 265 hypertensive individuals on treatment showed control of blood pressure figures in 33% of males versus 49% of females. These studies rank an intermediate-low position compared to other previous studies on Spanish and European populations[43]. Despite this, a significant margin for improvement remains, as shown by the more favorable results presented by studies in Denmark[44], Canada and the United States and other European countries[45] with a control percentage of more than 50% in treated subjects.

An important Spanish study, Di@bet.es, showed that only 26.6% have controlled blood pressure, higher in women (24.90%) than in men (16%)[46]. Di@bet.es is a national study designed to estimate the prevalence of diabetes *mellitus* and other cardiovascular risk factors in

the Spanish adult population. It presents the prevalence of arterial hypertension and the degree to which it is recognized, treated, and controlled. A sample of the Spanish population with 5,048 adults aged ≥ 18 years was included. A clinical interrogation and examination including three resting and sitting blood pressure readings were performed to calculate the mean. Hypertension is defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and/or on antihypertensive drug treatment. The data are lower than those obtained in our study, perhaps because all the people in our study received treatment. The factors associated with poorer control were male sex, overweight or obesity, and an associated diagnosis of diabetes *mellitus*.

Prior to this study, the data on HT control in our country were more encouraging, and even previous registries

Table X: Prevalence of altered values of CVR scales and metabolic scales with different scales according to drug consumption by sex.

	Women					Men				
	HT n=5,853 Mean (sd) %	HT+Diab n=2,047 Mean (sd) %	HT+DLP n=1,845 Mean (sd) %	HT+DLP+Diab n=1,131 Mean (sd) %	p	HT n=10,228 Mean (sd) %	HT+Diab n=5,280 media (sd) %	HT+DLP n=4,474 media (sd) %	HT+DLP+Diab n=3,737 media (sd) %	p
Moderate SCORE	7.56	11.01	11.88	16.09	<0.0001	23.33	25.95	25.57	28.91	<0.0001
High SCORE	2.84	4.74	5.04	5.15		20.43	26.62	24.30	29.13	
Moderate ALLY EV SCORE	14.31	14.38	15.22	18.54	<0.0001	11.79	11.40	12.11	11.67	<0.0001
High ALLY EV SCORE	51.05	40.97	39.05	36.53		55.87	60.88	55.83	62.04	
Moderate REGICOR	20.95	26.00	23.95	25.96	<0.0001	26.67	28.65	26.07	27.90	<0.0001
High-very high REGICOR	1.74	5.31	1.64	3.64		2.94	5.12	2.49	5.23	
Moderate ALLY EV Framingham	18.82	8.25	17.40	5.66	<0.0001	29.18	11.87	26.82	10.34	<0.0001
High ALLY EV Framingham	45.41	86.32	47.30	89.38		42.51	83.94	43.89	85.56	
Moderate-moderately high ERICE	11.63	26.62	23.46	41.15	<0.0001	45.51	48.10	54.88	55.18	<0.0001
High-very high ERICE	0.19	5.93	0.00	12.39		11.38	20.50	16.51	25.05	
Moderate DORICA	12.23	20.89	19.51	31.72	<0.0001	31.73	39.46	34.52	40.69	<0.0001
High-very high DORICA	0.30	1.25	0.67	2.88		6.05	9.16	6.76	11.90	
Sd MTB ATP III	30.33	55.54	50.51	100.00	<0.0001	33.15	56.16	68.10	100.00	<0.0001
Sd MTB ATP IDF	30.31	46.80	35.34	47.39	<0.0001	29.34	38.71	32.32	39.84	<0.0001
Sd MTB ATP JIS	35.01	60.33	58.43	99.12	<0.0001	54.28	82.12	72.42	99.36	<0.0001
Sd MTB ATP SZABO	47.02	94.87	91.33	99.91	<0.0001	56.03	97.14	92.38	99.89	<0.0001
Atherogenic dyslipemia	10.25	13.53	14.58	22.99	<0.0001	14.73	18.64	18.26	25.26	<0.0001
Lipid Triad	2.82	2.88	3.69	3.98	<0.0001	4.01	3.88	4.29	3.98	<0.0001
Hypertriglyceridemic waistline	4.89	4.79	4.28	8.66	<0.0001	15.16	16.34	17.21	22.10	<0.0001

ALLY EV. Lost years of vascular age.

Table XI: Prevalence of altered values of fatty liver scales and metabolic indices according to drug consumption by sex.

	Women					Men				
	HT n=5,853 Mean (sd) %	HT+Diab n=2,047 Mean (sd) %	HT+DLP n=1,845 Mean (sd) %	HT+DLP+Diab n=1,131 Mean (sd) %	p	HT n=10,228 Mean (sd) %	HT+Diab n=5,280 media (sd) %	HT+DLP n=4,474 media (sd) %	HT+DLP+Diab n=3,737 media (sd) %	p
High Fatty liver index	19.83	24.97	16.07	27.94	<0.0001	45.48	47.49	47.12	55.88	<0.0001
High Hepatic steatosis index	69.25	82.10	71.09	90.08	<0.0001	68.60	81.23	68.51	85.06	<0.0001
High ZJU index	61.32	68.67	66.41	77.10	<0.0001	62.13	66.04	63.20	75.50	<0.0001
High Fatty liver disease index	53.12	50.26	64.58	57.63	<0.0001	60.57	59.19	67.40	52.76	<0.0001
Moderate IA colesterol/HDL	23.71	24.82	26.94	25.73	<0.0001	28.47	30.91	29.28	25.73	<0.0001
High IA colesterol/HDL	0.41	0.39	0.65	0.35		0.15	0.28	0.34	0.35	
High IA triglicéridos/HDL	16.88	19.83	28.30	32.98	<0.0001	40.99	44.77	52.06	56.81	<0.0001
High IA LDL/HDL	25.44	25.11	27.21	22.46	<0.0001	40.02	41.72	38.69	52.59	<0.0001
High IA colesterol-HDL	74.83	75.57	73.66	69.76	<0.0001	76.96	74.28	71.28	64.52	<0.0001

ALLY EV. Lost years of vascular age.

carried out in series, with similar methodologies, such as the PRESCAP[47] 2002, 2006 and 2010 or CARDIOTENS[48] 1999 and 2009 registries, had shown a temporary trend towards a continuous improvement in the degree of control. The PRESCAP studies showed how the percentage of controlled hypertensive patients progressively improved in recent years, from 36% in 2002 to 41.50% in 2006 and 47% in 2010. Similarly, the CARDIOTENS registry showed how the degree of control increased from 40% in 1999 to 55% in 2009, representing a relative increase of 38.50%. In the CARDIOTENS study, lack of blood pressure control was associated with lifestyle and diet-related factors, specifically obesity and smoking, both of which were associated with worse control. The data from our study are more in agreement with those obtained in the Cardiotens study. In a Peruvian study, 53.80% of hypertensive patients showed blood pressure figures within normal values[49].

The fact that the 'poor control' factor is based on a single measurement of blood pressure may have resulted in an overestimation of prevalence and an underestimation of control in some studies[50].

The degree of control in people already being treated is difficult to improve. Despite the existence of treatments that have proven to be very effective and efficient, therapeutic objectives are not met in the 50% of the cases. On the one hand, there is the possibility of influencing on the so-called "therapeutic inertia", and with the change or prescription of combined therapy as soon as necessary, proving that the patient tolerate it. On the other hand, through health education it is necessary to influence greater therapeutic adherence, probably an important pillar for improving the data obtained in this study[51-53].

An Ecuadorian study[54] showed that the prevalence of obesity determined by BMI was 27.70% among hypertensive patients, which coincides with a study carried out in Costa Rica[55] showing a prevalence of 30%. In our study the prevalence of obesity was much higher than that obtained in these studies.

Limitations of the study

The study was carried out in the working and non-working population, aged between 18 and 70 years, and in specific geographical areas, so it cannot be extrapolated to the general population and to the entire national territory.

Strengths of the study

The sample size is very large, one of the largest carried out to date. In addition, it should be noted that the population has been segregated according to possible comorbidities and, in addition, not only blood pressure but also many scales related to cardiovascular risk have been taken into account to assess the usefulness of pharmacological treatments.

Conflict of interests

The authors have no conflict of interest.

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ORIGINAL

Personas sin hogar y salud: vulnerabilidad y riesgos durante la pandemia de COVID-19. Estudio piloto

Homeless people and health: vulnerability and risks during the COVID-19 pandemic. Pilot study

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Resumen

Introducción: El sinhogarismo es un fenómeno complejo que se caracteriza por una extrema vulnerabilidad. El objetivo del presente estudio piloto fue conocer el estado de salud y el uso del sistema sanitario de las personas sin hogar (PSH) en Palma de Mallorca además de describir cómo ha afectado la actual pandemia a las necesidades de esta población.
Sujetos y método: Estudio descriptivo transversal con 31 PSH de Palma de Mallorca. Se administró un cuestionario que contenía: perfil sociodemográfico, apoyo social (SSQ-6) problemas de salud, enfermedades infecciosas, salud mental (PHQ-9), abuso de drogas (DAST-10) y necesidades básicas (higiene, alimentación, seguridad, etc.). Además, se les realizó una serología de SARS-CoV-2, sífilis, hepatitis y VIH, también se revisaron sus historias clínicas informatizadas.
Resultados: La edad media fue de 52±8 años y un 87% (27/31) fueron hombres. Un 48,4% presentaban alguna enfermedad crónica, un 51,6% alguna enfermedad infecciosa y un 42% trastornos del estado de ánimo. El 96,8% de las PSH habían utilizado los servicios de Atención Primaria en 2020 versus el 71% en el año 2019. Las necesidades más afectadas por la pandemia fueron: higiene (41,9%), acceso a los WC públicos (29%) y acceso a alimentos (25,8%).
Conclusiones: Las PSH presentan elevadas tasas de comorbilidad. Nuestros resultados sugieren que el estado de salud de las PSH puede haber empeorado durante la pandemia. Además, se observa que se han visto afectadas necesidades básicas que pueden incrementar su vulnerabilidad.

Palabras clave: personas sin hogar, salud, accesibilidad a los servicios de salud, COVID-19.

Abstract

Background: Homelessness is a complex phenomenon characterized by extreme vulnerability. The objective of the present study was to know the health status and use of the health system by homeless people (HP) in Palma de Mallorca, as well as to describe how the actual pandemic modified the needs of this population.
Subjects and method: Descriptive cross-sectional study with 31 HP from Palma de Mallorca. A questionnaire that included sociodemographic profile, social support (SSQ-6), health problems, infectious diseases, mental health (PHQ-9), drug abuse (DAST-10) and basic needs (hygiene, food, safety, etc.) was administered. In addition, serology test for SARS-CoV-2, syphilis, hepatitis and HIV was performed, also their computerized medical records were reviewed.
Results: The mean age was 52 ± 8 years and 87% (27/31) were men. 48.4% had some chronic disease, 51.6% had some infectious disease and 42% had mood disorders. 96.8% of the HP used Primary Care services in 2020 versus 71% in 2019. The needs most affected by the pandemic were: hygiene (41.9%), access to public toilets (29%) and access to food (25.8%).
Conclusions: HP have high rates of comorbidity. Our results suggest that the health status of HP may have worsened during the pandemic. In addition, vital needs have been affected and their vulnerability could increase.

Keywords: homeless persons, health, health services accessibility, COVID-19.

Introducción

Las personas sin hogar (PSH) se encuentran en una situación de extrema exclusión social y grave vulnerabilidad, determinada por la falta de seguridad física, emocional, social y jurídica[1]. La privación de un hogar constituye además una constante vulneración de los derechos humanos lo que genera un grave problema en la sociedad actual[2]. El sinhogarismo se caracteriza por una interacción continua de factores individuales y estructurales, convirtiéndolo en un fenómeno más complejo que el hecho de no tener un lugar donde dormir[1]. La *European Typology of Homelessness and Housing Exclusion* (ETHOS), define y clasifica a las PSH en las siguientes categorías: personas que no cuentan con ningún tipo de refugio o que duermen en la calle, personas que de forma temporal duermen en una institución o refugio, personas que viven en un hogar inadecuado (en caravanas o campamentos ilegales, lugares hacinados, etc.), y personas que viven en un hogar inseguro (personas en grave riesgo de exclusión residencial como aquellas que han sido desahuciadas o que sufren violencia doméstica)[1]. El último informe publicado por la Federación Europea de Organizaciones Nacionales que trabajan con personas sin hogar (FEANTSA), estima que en Europa durante los últimos 10 años se ha incrementado en un 70% el número de PSH pudiendo alcanzar en la actualidad la cifra de unas 700.000 personas que duermen en la calle o en un refugio temporal[3]. En España habría entre 23.000 y 35.000 PSH, aunque no es posible determinar cifras más concretas debido a dificultades y diferencias metodológicas en los registros[4]. Y, específicamente, en Palma de Mallorca se identificaron 225 PSH en el año 2019[5], lo que supone un incremento del 40% desde el recuento realizado en 2015[4].

El impacto en salud que sufren las PSH es muy amplio y pone de manifiesto la estrecha y compleja relación entre la exclusión residencial y el deterioro de la salud. La esperanza de vida de las PSH es 30 años menor que la de la población general[6], y la mortalidad entre 2 y 5 veces mayor[7]. Algunas de estas diferencias podrían explicarse por una alta exposición a factores de riesgo como el consumo de tabaco, de alcohol, el uso y abuso de drogas ilegales o la presencia de enfermedades mentales[7]. La prevalencia de trastornos mentales, incluyendo drogodependencias con frecuencia en comorbilidad, es elevada[8]. Esto justifica la prevalencia, también elevada respecto a la población general, de ideación e intentos de suicidio[9]. Comúnmente pueden presentar trimorbilidad, que corresponde a la presencia simultánea de problemas de salud mental, de salud física y consumo de sustancias, lo cual aumenta aún más su situación de vulnerabilidad[10]. Aunque algunos estudios muestran que la prevalencia de enfermedades crónicas como la diabetes o la hipertensión es similar a la de la población general, las PSH tendrían más complicaciones y discapacidad asociadas a estas patologías[11]. En cambio, los datos obtenidos sobre enfermedades infecciosas indican que la prevalencia es más elevada, aunque las cifras varían considerablemente entre estudios. Las infecciones más prevalentes son la hepatitis C que varía entre el 3,9% y el 36,2% según los estudios, el VIH entre 0,3% y el 21,1% y la tuberculosis entre 0,2 y el 7,7%[7]. Hasta un 52% de las PSH padecerían alguna enfermedad de transmisión sexual (clamidia, gonorrea, hepatitis C), además, es habitual que presenten más de una de forma simultánea[12]. Las PSH también son objeto de delitos de odio, que se materializan en agresiones verbales, físicas o sexuales. Según un estudio realizado por el observatorio español de delitos de odio contra PSH (observatorio Hatento), al menos 1 de cada 5 personas entrevistadas habría sido víctima de un delito de odio por agresiones físicas[13].

Las PSH tienen necesidades de salud complejas así como dificultades para acceder a los servicios de salud[14]. La atención hospitalaria de las PSH se centra en la atención urgente[15], a pesar de que muchos problemas por los que acuden podrían abordarse de forma más efectiva a través de atención primaria o servicios sociales[6]. Un estudio realizado en la ciudad de Sevilla identifica como los principales motivos de ingreso las patologías mentales (27%), infecciosas (19,6%) y respiratorias (18,4%). Por otro lado, los días de estancia hospitalaria y los reingresos son más elevados que en la población general[15]. Las barreras que encuentra este colectivo para el acceso al sistema sanitario se relacionan con la falta de un seguro de salud, dificultad para acudir a las citas, mala experiencia previa con el sistema de salud o miedo a la discriminación, y prioridades que compiten con la necesidad de comida, descanso o refugio[10]. Estas barreras provocan una mayor probabilidad de acudir de forma repetida a los servicios de urgencias. Por lo tanto, algunos estudios apuntan hacia la necesidad de reforzar la atención primaria y mejorar su acceso[6].

La actual crisis sanitaria por SARS-CoV-2 podría aumentar los riesgos para la salud de las PSH. Las escasas medidas de higiene, la presencia de comorbilidades, patologías de salud mental, o un estado inmunitario comprometido, son algunos de los motivos que harían especialmente vulnerable a este colectivo frente al virus[16]. Experiencias previas similares, como la epidemia de SARS en 2003, identificaron una alta tasa de contagio causada por una coordinación deficiente entre los diferentes organismos involucrados en la gestión. También se destacó un alto nivel de infra diagnóstico y grandes dificultades para encontrar un lugar dónde llevar a cabo un confinamiento seguro[17]. Por tanto, las dificultades añadidas por la pandemia en el acceso al sistema sanitario podrían afectar la atención sanitaria a estos pacientes.

En general, los estudios sobre sinhogarismo se caracterizan por la dificultad en el reclutamiento y el

seguimiento[18], además, la variabilidad en la recogida de datos limita la capacidad de comparar los resultados[8]. Finalmente, la escasez de estudios llevados a cabo en nuestro contexto no permite conocer con exactitud la complejidad del fenómeno.

El progresivo aumento del colectivo de PSH, su elevada morbimortalidad y reducción en la esperanza de vida, sumado a la nueva situación sanitaria, nos plantea la necesidad de conocer el estado de salud de las PSH y cómo la actual crisis sanitaria por SARS-CoV-2 ha afectado a su salud y al uso del sistema sanitario. Además, este estudio piloto pretende determinar la serología de SARS-CoV-2 y otras enfermedades infecciosas en esta población.

Sujetos y métodos

Estudio descriptivo transversal con 31 PSH de Mallorca según criterios de la clasificación ETHOS[1]. La muestra se reclutó entre el 12 de noviembre y el 16 de diciembre de 2020 en las sedes de las dos organizaciones no gubernamentales (ONG) que realizan programas específicos con PSH (Médicos del Mundo y Cruz Roja), dónde se llevaron a cabo las entrevistas y la recogida de muestras sanguíneas.

Se operacionalizó la definición de PSH como aquellas que durante el último año habían vivido en la calle u otro espacio público, o bien un edificio abandonado o lugar que no reuniera las condiciones mínimas de habitabilidad, o personas que pernoctaran en refugios o albergues municipales con una estancia máxima de 3 meses en el momento de la inclusión. Definición similar a la utilizada por otros autores previamente[19,20].

Los criterios de inclusión fueron ser mayor de edad (>18 años), aceptar participar en el estudio y firmar el consentimiento informado. Se excluyeron a las personas que padecían un episodio activo de salud mental grave que imposibilitara la entrevista o que estuvieran bajo los efectos del alcohol o de las drogas en el momento de la captación.

Recogida de datos

Se contó con la colaboración de una técnica de una ONG para contactar con los posibles participantes y la programación de las citas. Un enfermero del equipo previamente entrenado y con experiencia en asistencia a PSH administró la entrevista y realizó la extracción sanguínea a todos los participantes. Finalmente, una enfermera del equipo revisó los diagnósticos de las historias clínicas informatizadas.

El cuestionario utilizado estaba dividido en cuatro bloques y recogía los siguientes aspectos: 1) perfil sociodemográfico que incluía entre otros: edad, sexo, nacionalidad, estudios cursados, tiempo sin hogar, tiempo en un albergue en el último año, situación laboral y si percibían prestación económica; 2) dificultades durante la pandemia por SARS-CoV-2 que incluyó información sobre el período de confinamiento (de marzo hasta junio de 2020); dificultades para encontrar recursos esenciales y cumplimiento de la normativa sanitaria como el uso de mascarilla, lavado higiénico de manos y distancia social; 3) diagnósticos en salud que incluyó enfermedades actuales, tratamientos, riesgo de abuso de substancias (DAST-10)[21], calidad de la dieta (IASE)[22], estado de ánimo (PHQ-9)[23] y 4) necesidades en salud que incluyó un bloque de preguntas adaptadas del modelo de Virginia Henderson[24] para PSH como: alimentación, seguridad, higiene, entre otros. El apoyo social se recogió mediante el cuestionario SSQ-6[25].

Índice de Alimentación Saludable para la población Española (IASE): es una herramienta que se utiliza para determinar la calidad de la dieta. El cuestionario está dividido en diez ítems, nueve de ellos corresponden a diferentes grupos de alimentos y el último ítem corresponde a la variedad de la dieta. La puntuación de cada ítem se basa en la adecuación a la frecuencia de consumo de cada grupo de alimentos. Los ítems se puntúan entre 0 y 10. La suma de las puntuaciones da el valor total del IASE, con un máximo de 100 puntos, y permite categorizar la dieta en tres grupos: dieta saludable (>80 puntos), dieta que necesita cambios (entre 50 y 80 puntos), dieta poco saludable (<50 puntos)[22].

Drug Abuse Screening Test (DAST): es un instrumento que sirve para detectar el abuso de drogas en población adulta y validado para población española en su versión abreviada de diez ítems (DAST-10). Las opciones de respuesta para cada ítem son "sí"/"no". La puntuación máxima es de 10 puntos y el punto de corte para determinar abuso de sustancias es ≥3 puntos[21].

Patient Health Questionnaire (PHQ-9): es una herramienta de ayuda al diagnóstico de depresión que determina también la gravedad del diagnóstico. Es un cuestionario validado para población española adulta[23]. Se compone de 9 ítems con respuesta tipo Likert entre 0 y 3 puntos correspondientes a las últimas dos semanas. De la suma se obtiene una puntuación total entre 0 y 27. Los puntos de corte establecen la gravedad de la depresión: sin depresión (0-4), leve (5-9), moderada (10-14), moderadamente grave (15-19) y grave (20-27). Un segundo criterio de punto de corte (≥10 puntos) establece la presencia de síntomas de trastorno depresivo mayor según un estudio realizado en población sin hogar[26].

Social Support Questionnaire (SSQ-6): es una herramienta que valora el apoyo social percibido. Consta de 6 ítems que representan diferentes situaciones de tensión o necesidad. En cada ítem se recoge el número de personas con las que cada individuo puede contar

en esa situación y el grado de satisfacción en relación al apoyo recibido. Esta herramienta ha sido validada en población española[25].

Tras la encuesta, se realizó una extracción sanguínea para determinar las serologías de SARS-CoV-2, VIH, sífilis y hepatitis B y C y determinar la hemoglobina glicosilada. Las muestras fueron gestionadas según el circuito habitual de Atención Primaria y se analizaron en el hospital de referencia (Hospital Universitario Son Espases). La duración de la entrevista y extracción de muestra fue en total de entre 30 y 40 minutos.

Finalmente se revisaron las historias clínicas informatizadas de los participantes y se recogió el número de visitas a los siguientes servicios sanitarios: Atención Primaria, Servicio de Urgencias de Atención Primaria (SUAP), Unidad de Conductas Adictivas (UCA), Unidad de Salud Mental (USM), Unidad de Salud Bucodental (USBD), consultas externas de hospital, hospitalizaciones y urgencias hospitalarias correspondientes a los dos últimos años y todos los diagnósticos y medicación pautada del último año.

Aspectos éticos

El protocolo del estudio sigue las recomendaciones de la Declaración de Helsinki, la Ley Orgánica 3/2018, del 5 de diciembre, de Protección de Datos Personales y garantía de derechos digitales y fue aprobado por el Comité de Ética de la Investigación de las Illes Balears (CEI-IB), referencia IB4301/20PI el 8 de octubre de 2020. Todos los participantes recibieron información sobre los objetivos del estudio y firmaron consentimiento informado. Los datos se disociaron para preservar el anonimato de los participantes de forma que los investigadores no podían identificar al titular de los mismos en ningún caso.

Análisis de datos

Todas las encuestas se diseñaron en formato escrito mediante el programa Teleform (Autonomy Cardiff, Vista, CA, USA) que permite una entrada automatizada de los datos y su posterior verificación.

Las variables continuas de describieron con la media y desviación estándar, o bien la mediana y rango intercuartílico (en función de la distribución de la variable). Las variables categóricas se describieron con frecuencias absolutas y frecuencias relativas. Para comparar variables categóricas se utilizó el test χ^2 (test de Fisher para observaciones esperadas menores a 5) y para variables continuas el test de Mann-Whitney. Las comparaciones entre uso de servicios sanitarios antes y durante la pandemia se realizaron con el Test de McNemar para muestras apareadas.

Para conocer el número de personas que presentaban trimorbilidad (enfermedad crónica, problema de salud mental y abuso de sustancias), se clasificaron como personas drogodependientes a aquellas que presentaban riesgo de abuso según el DAST-10 o habían realizado al menos una visita a la UCA durante el último año. En el caso de salud mental, se clasificaron como con enfermedad mental a aquellas personas con diagnóstico de salud mental presente en la historia clínica o las que puntuaran ≥10 en el PHQ-9.

Para todos los análisis estadísticos se utilizó el programa informático Statistical Package for Social Science (SPSS) versión 24 (IBM company, NY, Illinois, USA). El nivel de significación estadística se estableció en el valor $p<0,05$.

Resultados

La edad media de la muestra incluida fue de 52,33±8,46 años, mayoritariamente hombres (87,1% de hombres y el 12,9% de mujeres), en situación de desempleo (74,2%), demandantes de empleo (83,9%) y sin ningún tipo de prestación económica (74,2%). Un 25,8% llevaban menos de nueve meses sin hogar, un 29% entre nueve meses y dos años, y el 45,2% más de dos años, y la mayoría (71%) no habían pasado por albergue o refugio municipal durante el último año. La **tabla I** resume las características sociodemográficas de la muestra incluida.

Tabla I: Características sociodemográficas de la muestra incluida.

Característica	N=31 n	%
Edad[a]	52,33±8,46	—
Sexo		
Hombres	27	87,1
Mujeres	4	12,9
Nacionalidad		
Español no nacido en Baleares	10	32,3
Español nacido en Baleares 12	38,7	
Extranjero	9	29
Nivel de estudios máximos cursados		
Sin escolarizar	2	6,5
Estudios primarios	13	41,9
Estudios secundarios	8	25,8
Formación profesional	5	16,1
Estudios universitarios	3	9,7
Situación laboral actual		
Empleado irregular	7	22,6
Desempleado	23	74,2
Jubilado	1	3,2
Demandante de empleo	26	83,9
No recibe prestación económica	23	74,2
Tiene tarjeta sanitaria	28	90,3
Tiempo sin hogar		
Menos de 9 meses	8	25,8
Entre 9 meses y 2 años	9	29
Más de 2 años	14	45,2
Asistencia a albergue en el último año		
No ha estado en albergue	22	71
Ha estado en albergue	9	29

[a] *Media y desviación estándar*

Patologías

La información recogida en las historias clínicas de salud indica que más de la mitad de las PSH (61,3%) presentaba al menos una patología crónica, entre las que destacaba

un 35,5% de hepatopatías. Por otro lado, presentaban un 6,5% de hipertensión y otro 6,5% de diabetes mellitus tipo 2. En el ámbito de la salud mental, destaca que el 41,9% presentaban un trastorno del ánimo y un 6,5% había realizado algún intento autolítico diagnosticado. El PHQ-9 mostró que el 45,2% presentaban síntomas de trastorno depresivo mayor. Según la analítica realizada un 30,8% presenta glucemias alteradas que indicarían un elevado riesgo de padecer diabetes[27]. Respecto a las patologías infecciosas, según la analítica, un 51,6% padecía al menos una patología infecciosa de las siguientes: VIH (7,1%), hepatitis B (11,1%), hepatitis C (42,3%) y sífilis (11,1%).

El 32,3% presentaba al menos una enfermedad crónica, un problema de salud mental y una enfermedad infecciosa. Por otro lado, el 22,6% de las PSH presentaban la trimorbilidad previamente descrita en la literatura, correspondiente a la presencia simultánea de enfermedad crónica, problema de salud mental y abuso de sustancias.

Medicación y consumo de drogas

Según la historia clínica el 74,2% de los participantes del estudio tenía pautado al menos un medicamento, entre ellos destacan los ansiolíticos (38,7%). En cuanto al consumo autodeclarado de drogas, observamos que el 32,3% consume alcohol, el 29% cannabis, el 12,9% cocaína, y otro 12,9% barbitúricos. La mayor parte de las PSH (74,2%) son fumadoras y un 25,8% presentaría abuso de sustancias según el cuestionario DAST-10 (**Tabla II**).

Calidad de la dieta

La calidad de la dieta medida con el cuestionario IASE fue baja, con una media de 57,08±16,28 puntos. Solo el 9,7% de las PSH tendría una dieta saludable, el 61,3% necesita cambios en su dieta, y el 29% tendría una dieta poco saludable. Destaca la baja adherencia mostrada en los siguientes ítems: variedad de alimentos (media de 3,93±2,54) y limitación del consumo de embutidos (media de 4,43±4,17) (**Tabla III**). Los datos sugieren una tendencia a la asociación entre baja calidad de la dieta y el tiempo sin hogar, siendo aquellas que llevan más tiempo sin hogar las que tienen menor puntuación en el IASE (p=0.088).

Uso de servicios sanitarios

Durante el año 2020, la mayoría de las PSH (96,8%) habían utilizado los servicios de Atención Primaria de Salud (AP), tanto consultas de seguimiento (media de 10,5±10,31 visitas) como urgencias de AP (10,26±11,06 visitas). Destaca el uso de UCA, con un total de 10 usuarios (32,3%) y una media de 43,8±47 visitas/usuario. Casi la mitad de las PSH (48,4%) habían utilizado el servicio de consultas externas y de urgencias hospitalarias. Se observa un incremento en la utilización de servicios en el año 2020, comparado con el 2019 (**Figura 1**), que fue estadísticamente significativo en la utilización de los servicios de consultas y urgencias de AP (p=0,008; test de McNemar). Por otro lado, se observa un descenso en la utilización de la UCA y urgencias hospitalarias. En relación al número de visitas, solo ha habido un incremento en las visitas a consulta de AP y de hospital.

Tabla II: Patologías, medicación y consumo de drogas.

Característica	N=31 n	% %
Enfermedades crónicas		
DM II (Hª Clínica)	2	6,5
IAM	1	3,2
HTA	2	6,5
Asma	1	3,2
IRC	1	3,2
Hepatopatía	11	35,5
Otras (neuropatía, hipotiroidismo, IC, etc.)	11	35,5
Al menos una patología crónica	19	61,3
Prediabetes (analítica HbA1c: 5,7) N=26	8	30,8
HbA1c[a]	5,75±0,95	
Enfermedades infecciosas		
VIH	2	7,1
Hepatitis B	3	11,1
Hepatitis C	11	42,3
Sífilis	3	11,1
Al menos una patología infecciosa	16	51,6
COVID-19 (IgG +)	2	7,7
Salud mental (Hª clínica)		
Trastorno de ánimo	13	41,9
Intento autolítico	2	6,5
Síntomas de trastorno depresivo mayor		
(PHQ-9: ≥10 puntos)	14	45,2
Morbilidad y comorbilidad (Hª Clínica)		
Ninguna	7	22,6
1 patología	4	12,9
2 patologías	9	29
≥ 3 patologías	11	35,5
Trimorbilidad:		
Crónica, salud mental e infecciosa	10	32,3
Crónica, salud mental y drogodependencia	7	22,6
Fumador		
Cigarrillos diarios[a]	23 13,61±6,21	74,2
Medicación pautada (Hª Clínica)		
Ansiolíticos	12	38,7
Antidepresivos	4	12,9
Antipsicóticos	3	9,7
Protector gástrico	4	12,9
Analgésicos	4	12,9
Antihipertensivo	3	9,7
Antiagregante	2	6,5
Anticolesterolémico	3	9,7
Broncodilatador	2	6,5
Antidiabético Oral	2	6,5
Insulina	1	3,2
Antirretroviral	2	6,5
Al menos un medicamento pautado	23	74,2
Consumo de drogas		
Alcohol	10	32,3
Cannabis	9	29
Cocaína	4	12,9
Sedantes o ansiolíticos	4	12,9
DAST-10		
Abuso de sustancias (≥3 puntos)	8	25,8

[a] *Media y desviación estándar*

Necesidades vitales

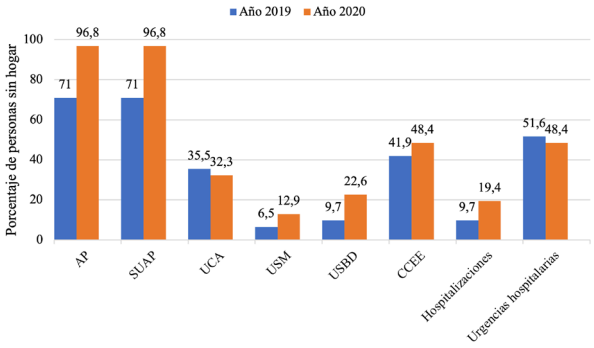
La principal fuente de obtención de alimentos de las PSH fue la compra directa (58,1%), que combinan junto a otras fuentes. El 35,5% refería problemas de masticación o deglución por dolor y la mitad de ellos por problemas relacionados con la dentadura. Una de cada dos personas entrevistadas (48,4%) refería problemas

Tabla III: Necesidades en salud[a].

Característica	N=31 n	%
Alimentación		
IASE[b]: Puntuación total (0-100)	57,08±16,28	
Adecuación por grupo de alimentos (0-10)[b]		
Cereales	7,42±3,38	
Legumbres	5,97±2,93	
Verduras	6,45±3,46	
Frutas	5,64±3,98	
Lácteos	7,02±3,73	
Embutidos	4,43±4,17	
Dulces	5,24±4,25	
Bebidas azucaradas	5,89±4,31	
Carne	5,08±3,44	
Variedad	3,93±2,54	
Adecuación de la dieta según puntuación IASE		
Poco saludable (<50 puntos)	9	29
Necesita cambios (50-80 puntos)	19	61,3
Saludable (>80 puntos)	3	9,7
Dieta pautada:		
Tiene pautada dieta especial	6	19,4
Tiene dificultades para seguir la dieta pautada	2	6,5
Problemas relacionados con la masticación o deglución:		
Dentadura	16	51,6
Dolor	11	35,5
Otros problemas	3	9,7
Principal fuente de obtención de alimentos:		
Compra	18	58,1
Donación	5	16,1
Instituciones	9	29
Zaqueo	12	38,7
Tardor	15	48,4
Otra fuente	13	41,9
Tiene acceso a utensilios de cocina	16	51,6
Tiene dificultad para obtener agua potable	11	35,5
Eliminación		
Tiene dificultad para acceder a baños públicos	14	45,2
Lo hace en la calle	8	25,8
Movilidad y relación con el medio		
Tiene problemas de deambulación:	15	48,4
Discapacidad física	2	6,5
Discapacidad psíquica	1	3,2
Dolor	8	25,8
Cansancio	2	6,5
Otros	1	3,2
Horas que camina al día[b]	3,7±2	
Medio de transporte habitual:		
Vehículo propio	3	9,7
Bicicleta	5	16,1
Transporte público	13	41,9
Ninguno	27	87,1
Dormir y descansar		
Dónde duerme habitualmente		
Calle	3	9,7
Parque	3	9,7
Cajero	2	6,5
Descampado	1	3,2
Otros	25	80,6
Cuantas horas duerme al día[b]	6,5±2,1	
Tiene dificultad para conciliar el sueño	20	64,5
No se siente descansado al levantarse	11	35,5
Ropa		
Dónde consigue la ropa habitualmente:		
Compra	13	41,9
Donaciones	13	41,9
Roperos públicos	5	16,1
Otros	8	25,8
Dificultades para acceder a la ropa	6	19,4
Dificultad para acceder a ropa adecuada a estación	11	35,5
Lava la ropa (sí)	28	90,3
Dónde lava la ropa:		
Tiendas de lavado	13	41,9
Entidades o instituciones	3	9,7
Calle	8	25,8
Baños públicos	2	6,5
Otro lugar	10	32,3
Mantenimiento temperatura corporal		
Problemas para mantener la temperatura (sí)	12	38,7
Calor	2	18,2
Frío	9	81,8
Mantenimiento temperatura corporal		
Recursos para protegerse del clima:		
Fuego	4	12,9
Centros comerciales	1	3,2
Ropa	21	67,7
Otros	8	25,8
Higiene corporal		
No tiene acceso a ducha o aseo completo	20	64,5
Dónde se ducha habitualmente:		
Entorno social	2	6,5
Entidades o instituciones	12	38,7
Calle	5	16,1
Otros	15	48,4
Frecuencia de las duchas:		
Diaria	5	16,1
Casi diaria	13	41,9
Semanal	6	19,4
Quincenal	2	6,5
Mensual	2	6,5
Más tiempo	3	9,7
Agresiones:		
Robo	10	32,3
Físicas	5	16,1
Verbales	3	9,7
Otros	1	3,2
No han denunciado la agresión	8	25,8
Siente miedo o falta de seguridad	11	35,5
Cuando siente miedo o inseguridad:		
Día	2	6,5
Noche	6	19,4
Ambos	1	3,2
Nunca	22	71
Apoyo social (SSQ-6)		
Nadie	3	9,7
Más de una persona	28	90,3

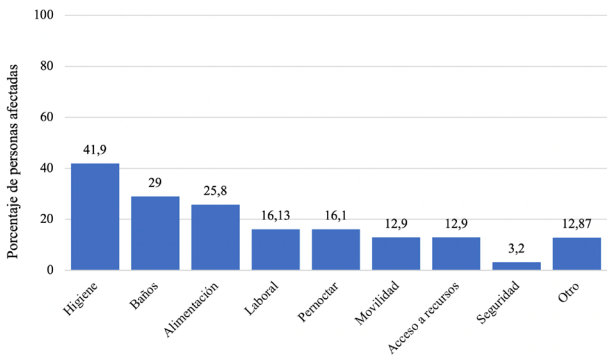
[a]Adaptado de V. Henderson; [b]Media y desviación estándar

Figura 1: Uso de los servicios sanitarios de las PSH en el año 2019 y 2020.



AP: Atención Primaria; SUAP: Servicio de Urgencias de Atención Primaria; UCA: Unidad de Conductas Adictivas; USM: Unidad de Salud Mental; USBD: Unidad de Salud Bucodental; CCEE: Consultas Externas.

Figura 2: Aspectos afectados de las PSH debido a la pandemia por SARS-CoV-2



de deambulación, siendo el dolor el problema más frecuente. Las PSH reportaron caminar una media de 3,7±2 horas al día y en general no utilizar ningún medio transporte para desplazarse. En cuanto al apoyo social percibido (SSQ-6), más de un 90% de los encuestados reportaron que cuentan con el apoyo de al menos una persona si tienen problemas (**Tabla III**).

Las PSH percibían que la satisfacción de sus necesidades vitales se había visto afectada debido a la situación generada por la pandemia de SARS-CoV-2, especialmente la de higiene y alimentación (**Figura 2**). Por otro lado, las personas entrevistadas referían tasas elevadas de cumplimiento con las medidas preventivas de lavado de manos (90,3%), distanciamiento social (96,8%) y uso de mascarilla (100%). Aunque en relación al uso de mascarilla, un 77,4% de los encuestados refería depender de la donación para su uso. El confinamiento durante el estado de alarma se realizó en diferentes ámbitos: la mayoría (35,5%) reportó haber estado en la calle, el 19,4% en un edificio público abandonado, el 12,9% en una casa de forma temporal, el 6,5% con familiares, el 3,2% con amistades, otro 3,2% en un refugio temporal, y el 19,3% restante en otros lugares, como por ejemplo parques, casetas o chabolas.

Discusión

Nuestros resultados sugieren que las PSH presentan una elevada prevalencia de enfermedades crónicas e infecciosas. Un elevado porcentaje presentan trastornos del estado de ánimo y la mayoría de ellos tienen prescritos ansiolíticos. Estas personas utilizan habitualmente los servicios sanitarios públicos, y realizan un uso frecuente de los servicios de urgencias. Las necesidades en salud de las PSH se han visto afectadas por la pandemia por SARS-CoV-2, especialmente en los aspectos de higiene y alimentación.

La edad media de la muestra de nuestro estudio fue de 52 años, similar a la reportada en un reciente estudio realizado en Alemania[8] y algo mayor que la descrita en un estudio similar del año 2017 realizado en Italia con una edad media de 48 años[28]. Algunos estudios indican que la edad media de las PSH estaría incrementando[11] lo que podría tener implicaciones en el manejo de la salud y el acceso al sistema sanitario de estas personas. En una población de PSH más joven las actividades estarían dirigidas a la prevención y a reducir el riesgo de padecer enfermedades y otros eventos adversos, en una población cada vez más mayor, es necesario poner el objetivo en intervenciones dirigidas al manejo de las enfermedades crónicas, la fragilidad y otros problemas relacionados con el final de la vida[7]. De las 31 PSH participantes, la gran mayoría fueron hombres (87,1%), concordando con resultados similares a los reportados por otros estudios[8,15,18]. Estas diferencias podrían ser debidas a que las mujeres que sufren sinhogarismo tienen menos probabilidad de estar en la calle ya que podrían vivir en casas de familiares o conocidos, por lo tanto, el sinhogarismo de las mujeres habitualmente pasa más desapercibido8. Además, es posible que las mujeres, en general, cuenten con una red de apoyo más sólida.

Un 42% de las PSH incluidas en nuestro estudio presenta en su historia clínica un diagnóstico de trastorno del estado de ánimo mientras que la prescripción de ansiolíticos y antidepresivos fue del 38,7% y el 12,9 % de los casos respectivamente. El test PHQ-9 confirmó que el 45,2% de los casos presentaba una sintomatología depresiva de suficiente magnitud como para sugerir el diagnóstico de Depresión Mayor. Estas cifras son similares a las encontradas en otros estudios[29]. Sin embargo, los registros de intentos de suicidio previos en la historia clínica en nuestra muestra (6,5%) fueron claramente inferiores a los encontrados previamente en esta población preguntando específicamente sobre este tema (9,16%-28,8%), lo cual es sin duda más fiable[9]. Es muy llamativa la ausencia de personas con trastorno mental grave o psicosis en nuestra muestra cuando se ha señalado en otros estudios que más de un 20% de las PSH tendrían este diagnóstico[29]. Estos porcentajes incluso aumentan cuando se restringe el estudio a las personas que viven en la calle[30,31]. La explicación a esta discordancia creemos tiene que ver con la selección de nuestra muestra, ya que todos los sujetos están vinculados a programas de ONGs y se excluyeron del estudio a aquellas personas con problemas activos de salud mental que imposibilitara la entrevista o que no aceptaran colaborar firmando el consentimiento informado. Precisamente los pacientes con trastorno mental grave suelen presentar dificultades para la adherencia terapéutica derivados de su habitual falta de conciencia de enfermedad, de su frecuente deterioro volitivo y neurocognitivo y de su probable consumo de sustancias asociado[32]. Por ello es difícil que soliciten ayuda espontáneamente y, tal como los programas actuales basados en el tratamiento asertivo comunitario preconizan, es necesario ir a atender a estos pacientes allá donde se encuentren para ayudarles a mejorar su salud[33].

Uno de los resultados más destacables es la elevada prevalencia de enfermedades infecciosas. Como en estudios previos[7], encontramos que la más común fue la hepatitis C, aunque en nuestro caso en un porcentaje más elevado (42%). En el caso de la sífilis se encontraron 3 personas que dieron positivo y no habían sido previamente diagnosticadas. El VIH, con 2 (7%) casos ya conocidos, tiene una prevalencia similar a la de otros estudios[18,28]. Aunque los factores de riesgo asociados a estas enfermedades son similares a los de la población general (por ejemplo, uso de drogas intravenosas)[7], un sistema inmunitario comprometido

o deficitario, condiciones insalubres o el hacinamiento, podrían contribuir a incrementar el riesgo de contraer dichas enfermedades.

Encontramos que la patología crónica diagnosticada más frecuente es la hepatopatía con un 35,5%, mientras que en el estudio de Calvo et al.[18] fue la hipertensión (15,4%). La prevalencia de enfermedades crónicas más frecuentes (hipertensión, diabetes, EPOC) es menor en nuestra muestra que en otros estudios publicados, no obstante, el porcentaje de PSH con al menos una enfermedad crónica supera el 60%.

Solo el 9% de las personas de nuestro estudio seguiría una dieta saludable, con un consumo más elevado de lo recomendado de embutidos y una variedad escasa en la dieta. Estos datos, junto con las barreras que las PSH suelen reportar sobre la obtención de alimentos, indican que tienen dificultades en el cumplimiento de unos requerimientos nutricionales saludables. En concordancia con nuestros resultados, el estudio realizado por Sprake et al[34], mostró que las PSH tienen un elevado consumo de grasas saturadas y azúcares, mientras que el consumo de fibra, vitamina A, zinc, magnesio y otros micronutrientes es significativamente menor que en la población general. Esta situación podría contribuir a empeorar su estado de salud y/o la evolución de las enfermedades que tienen diagnosticadas.

Según nuestros resultados, las PSH utilizan los servicios sanitarios cuando tienen un problema puntual, donde destaca el uso de urgencias y de hospitalización. Según los datos del ministerio de sanidad español más recientes[35], encontramos que las PSH hacen un mayor uso de servicios sanitarios que la población. Esta mayor demanda asistencial podría indicar un peor manejo de los problemas de salud, pero también una peor percepción de su estado de salud. En el caso de las consultas de medicina en AP las PSH acudieron una media 9,5 veces, mientras que la población general de entre 50 a 54 años acudió 4,6 veces de media en España y concretamente en Baleares 3,8 veces. En las urgencias de AP, la diferencia se ve acentuada, ya que la población general acudió una media de 0,6 veces, mientras que la media de PSH fue de 13,2 veces. Si nos centramos en la estancia hospitalaria también observamos diferencias, dónde la población general pasaba una media de 7,9 días de ingreso, mientras que las PSH pasaban unos 14,3 días de media. Diversos autores coinciden en que muchos de los problemas por los que las PSH acuden a los servicios de urgencias podrían abordarse de forma más eficaz mediante la prevención y el seguimiento desde AP7, pero para ello sería necesario conocer y actuar sobre las dificultades que esta población identifica para acceder a estos servicios sanitarios.

Nuestros resultados muestran que la situación de crisis sanitaria actual por SARS-CoV-2, ha afectado aspectos tan esenciales como la higiene y la alimentación de las PSH lo que posiblemente incrementará los riesgos para la salud de las PSH.

En nuestro estudio destacamos que se ha llevado a cabo en un momento de crisis sanitaria por la pandemia de SARS-CoV-2, por lo que los resultados obtenidos contribuyen a conocer el impacto en salud de las PSH en este momento. Por otro lado, a pesar de tratarse de un estudio piloto, la cantidad de datos recogidos es amplia y diversa, con el objetivo de abarcar todos los aspectos relacionados con la salud de las PSH. Además, hemos recogido datos auto-reportados por las PSH y datos obtenidos de diversas fuentes del sistema sanitario como la historia clínica informatizada.

Una de las principales limitaciones que encontramos es el tamaño muestral reducido, que limita la generalización de los resultados obtenidos. Además, la captación realizada en las sedes de las ONGs ha podido ha podido favorecer que nuestra muestra sea muy homogénea y que algunas características de las PSH se encuentren infrarrepresentadas en nuestro estudio, por ejemplo, en aspectos relacionados con las patologías de salud mental. Las dificultades en la captación de la muestra han sido reportadas también en otros estudios llevados a cabo con PSH[18]. Sobre las patologías de salud mental observamos únicamente un 41,9% de trastornos de ánimo y una nula representación de otras patologías de salud mental, lo que podría indicar que las PSH están infrarrepresentadas en esta esfera en nuestro estudio, ya que como indican otros estudios las enfermedades de salud mental son altamente prevalentes en las PSH[8].

Esta nueva situación sanitaria, y su consecuente repercusión en la esfera social y económica de los países, nos indica que las PSH podrían empeorar su estado de salud y aumentar su vulnerabilidad. Además, es posible que las personas que se encontraban en riesgo de exclusión residencial podrían incrementar el número de PSH como consecuencia de la crisis económica generada por la pandemia.

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Conflicto de interés

Los investigadores declaran no tener conflicto de interés.

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ORIGINAL

Environmental and health strategies for hospital waste management; a case study

Estrategias medioambientales y sanitarias para la gestión de residuos hospitalarios; un estudio de casos

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Summary

Background: Management of hospital and healthcare center wastes is essential to prevent environmental health-related issues and threats The present survey was performed to assess the environmental and health strategies for hospital waste management; a case study.
Materials and methods: This cross-sectional descriptive study was performed to identify the current status of medical waste management in 2 healthcare centers and 2 hospitals in Tehran, Iran. A standard checklist and questionnaire of the Ministry of Health were used, the degree of reliability and validity of which was established. The checklists were completed by highly trained environmental health experts through face-to-face visits, observation and visits under the supervision of environmental health experts of health centers and hospitals. The checklist consisted of two sections, public and private, which did not use general information to evaluate hospital management.
Results: A total of 84.16 kg/d wastes were produced in 2 studied healthcare centers. While, a total of 295.13 kg/d wastes were produced in 2 studied hospitals. Among all studied wastes, the amounts of ordinary, infectious and chemical and pharmaceutical wastes were52.90, 17.50, and 13.76 kg/d, respectively in healthcare units. Among all studied wastes, the amounts of ordinary, infectious and chemical and pharmaceutical wastes were 145.85, 111.11, and 38.17 kg/d, respectively, in hospitals. Studied hospitals had the higher amounts of produced wastes than healthcare units. In about 54% of the studied centers, only one person was assigned to waste collection. None of the studied centers had a temporary storage facility for medical waste.
Conclusion: There were essential need to determine proper strategies to manage the hospital wastes to reduce the risk of infections dissemination in the environment and increase the health conditions.

Keywords: Health strategies, hospital, healthcare, waste management.

Resumen

Antecedentes: La gestión de los residuos de los hospitales y centros de salud es esencial para prevenir problemas y amenazas relacionadas con la salud ambiental El presente estudio se realizó para evaluar las estrategias ambientales y sanitarias para la gestión de los residuos hospitalarios; un estudio de caso.
Materiales y métodos: Este estudio descriptivo transversal se realizó para identificar el estado actual de la gestión de residuos médicos en 2 centros de salud y 2 hospitales de Teherán, Irán. Se utilizaron una lista de comprobación y un cuestionario estándar del Ministerio de Sanidad, cuyo grado de fiabilidad y validez se estableció. Las listas de comprobación fueron completadas por expertos en salud ambiental altamente capacitados mediante visitas presenciales, observación y visitas bajo la supervisión de expertos en salud ambiental de los centros de salud y hospitales. La lista de comprobación constaba de dos secciones, pública y privada, que no utilizaban información general para evaluar la gestión de los hospitales.
Resultados: En 2 centros sanitarios estudiados se produjeron un total de 84,16 kg/d de residuos. Mientras que en 2 hospitales estudiados se produjeron un total de 295,13 kg/d de residuos. Entre todos los residuos estudiados, las cantidades de residuos ordinarios, infecciosos y químicos y farmacéuticos fueron de 52,90, 17,50 y 13,76 kg/d, respectivamente, en las unidades sanitarias. Entre todos los residuos estudiados, las cantidades de residuos ordinarios, infecciosos y químicos y farmacéuticos eran de 145,85, 111,11 y 38,17 kg/d, respectivamente, en los hospitales. Los hospitales estudiados presentaban las mayores cantidades de residuos producidos que las unidades sanitarias. En aproximadamente el 54% de los centros estudiados, sólo había una persona asignada a la recogida de residuos. Ninguno de los centros estudiados disponía de un almacén temporal para los residuos médicos.
Conclusión: Es imprescindible determinar estrategias adecuadas para la gestión de los residuos hospitalarios con el fin de reducir el riesgo de diseminación de infecciones en el entorno y aumentar las condiciones de salud. .

Palabras clave: Estrategias sanitarias, hospital, asistencia sanitaria, gestión de residuos.

Introduction

Expansion of cities, increase in population, and industrial advances caused severe increase in the waste production[1]. In this regard, transporting and disposing of garbage is an important issue. In these cases, a regular system is essential to monitor the transportation of waste and garbage management. This matter is so important for the human, animal, plant and environmental health[2]. Additionally, the increase in the number of healthcare centers, hospitals and laboratories has led to the mass production of hospital wastes. Thus, proper disposal and management of this kinds of waste can prevent the spread of disease and increase the level of public health[3-5].

Medical wastes contain different substances and therefore are considered as a special mixed waste. If these materials are not stored properly, they will be difficult to move. Because infectious wastes contain large amounts of infectious disease-causing agents, contact with susceptible individuals can cause infectious diseases[6]. Annually, 5.2 million persons have been death due to the diseases transmitted through hospital wastes[7]. On the other hand, decontamination of infectious and chemical waste in medical centers requires the use of highly advanced and expensive treatment methods, which will not be practical in low-income countries and even in developing countries[8,9]. Therefore, control and preventive measures to reduce the production and minimize hazardous waste in various health centers is one of the basic strategies of the World Health Organization in developing countries[10].

Many countries have enacted laws and proposals to move and dispose of medical waste from hospitals. All types of solid waste produced by health care centers need to be handled, transported and disposed of in a controlled manner to maintain public health and prevent environmental pollution. This can only be achieved by enforcing mandatory enforcement laws and using guidelines in all aspects of the handling, storage, transportation and disposal of this waste[11,12]. In developed countries, the definition of medical waste and the various methods of collecting, transporting, storing and disposing of this waste are provided in the laws and regulations. Also, the best available technologies have been used to develop methods for proper disposal of medical waste with the least risk to human health and the environment[13,14]. However, no comprehensive efforts have been made to understand how waste generated by hospitals is managed. Waste management is usually left to ordinary workers who do most of the work without proper instructions and inadequate support[15-17]. The present survey was carried out to study and review of hospital waste management process was carried out with the aim of explaining the status of production, collection, separation, temporary storage and storage, disposal and health of personnel working in the collection and disposal of medical waste in health centers and health centers.

Materials and methods

Study type

This cross-sectional descriptive study was performed to identify the current status of medical waste management in 2 healthcare centers and 2 hospitals in Tehran, Iran.

Designing

In this study, a standard checklist and questionnaire of the Ministry of Health were used, the degree of reliability and validity of which was established. The checklists were completed by highly trained environmental health experts through face-to-face visits, observation and visits under the supervision of environmental health experts of health centers and hospitals.

Check lists

The checklist consisted of two sections, public and private, which did not use general information to evaluate hospital management. However, the dedicated section of the checklist, including 5 separate sections of waste generation rate and percentage of infectious waste, segregation, collection and transportation, storage and temporary storage and final disposal of waste was used to evaluate medical waste management.

Data analysis

Qualitative data were analyzed in the form of numerical and descriptive statistics, and quantitative data were analyzed after entering the Excel software, calculating the mean and standard deviation of the values and drawing the relevant tables[18,19].

Results

According to the study, the type of medical waste of health centers and hospitals are divided into three types, which are: 1) ordinary wastes; 2) infectious wastes; and 3) chemical and pharmaceutical wastes. According to this classification of both healthcare centers and hospitals, the amounts of wastes in each group were presented in tables 1 and 2.

Table I shows the amount of waste produced by healthcare centers. A total of 84.16 kg/d wastes were produced in 2 studied healthcare centers. Among all studied wastes, the amounts of ordinary, infectious and chemical and pharmaceutical wastes were 52.90, 17.50, and 13.76 kg/d, respectively. Amounts of produced wastes in healthcare center No 1 were higher than No 2.

Table II shows the amount of waste produced by hospitals. A total of 295.13 kg/d wastes were produced

Table I: The amount of waste produced by healthcare centers.

Healthcare centers	Supported population	Number of employees	Amount of produced wastes (Kg/d)			
			Ordinary wastes	Infectious wastes	Chemical and pharmaceutical wastes	Total
1	6414	12	30.75	10.52	7.23	48.50
2	4289	8	22.15	6.98	6.53	35.66
Total	10703	20	52.90	17.50	13.76	84.16

Table II: The amount of waste produced by hospitals.

Hospitals	Supported population	Number of employees	Amount of produced wastes (Kg/d)			
			Ordinary wastes	Infectious wastes	Chemical and pharmaceutical wastes	Total
1	25123	90	75.22	60.77	20.46	156.45
2	18245	78	70.63	50.34	17.71	138.68
Total	43368	168	145.85	111.11	38.17	295.13

in 2 studied hospitals. Among all studied wastes, the amounts of ordinary, infectious and chemical and pharmaceutical wastes were 145.85, 111.11, and 38.17 kg/d, respectively. Amounts of produced wastes in hospital No 1 were higher than No 2.

There were no strict separation criteria in studied hospitals and healthcare centers. For example, infectious waste of infectious diseases ward s of hospital units is disposed together with the wastes of dental centers. There was no hospital waste management operational plan in any of the health units. Also, the operational plan to reduce the production of hospital waste was not implemented in all studied healthcare units and hospitals. In about 54% of the healthcare centers and hospitals surveyed, only one person was assigned to waste collection. In some cases, the person was responsible for the charge of garbage collection also did other works, such as cleaning. None of the studied centers had a temporary storage facility for medical waste, and basements, warehouses, beds, and courtyards were commonly used for temporary storage. Infectious waste was not stored in any of the centers for a long time. Also, the level of education of a person who were responsible to collect and manage waste were under diploma. The results showed that no training was given to personnel to manage medical waste and collect and dispose of it. None of the disposal wastes were not have significant labels.

Discussion

Despite all advances occurred in medical sciences, several infectious diseases become health-threating in the last century[20-25]. Studies showed that proper management of wastes in hospitals and healthcare centers can diminish the risk of diverse outbreaks of infectious diseases[26,27]. Our findings showed that the low management levels were accompanied for disposal of medical wastes in healthcare units and hospitals studied in the present survey. Regarding the personal hygiene of garbage collectors, it was found that most of them do not have proper work clothes and also did not have regular recruitment and periodic examinations, so it is necessary for the center managers to wear appropriate clothes, gloves and shoes. Prepared for them and introduced to the medical diagnostic laboratory for necessary examinations. The statistics obtained show that the volume of hazardous waste production in the centers and bases is relatively small, shows that with proper planning, waste can be properly separated and separated so that it can be disposed of better.

Given that the bins used in the centers are unlabeled or do not use standard colored containers and bags, it practically means that the separation has not been done properly. Therefore, it is necessary to teach the staff how to label and use different nylons and containers with different colors to identify and separate the types of waste and reduce their risks. There is no special place for washing trash in the centers and if necessary, washing is done in the sanitary facilities.

Comparison of the results of this study with similar studies conducted on hospital waste management in other regions, showed that the amount of hospital waste is somewhat different, which can be due to the type of services provided in each city, cultural and economic situation. and how to manage the hospital.

Bazrafshan et al[28] stated that the he average of total quantity of waste produced in all hospitals was 6096.41 kg/day. Medical waste generation rate for total waste, infectious waste, general waste and sharp waste are 2.76±0.10, 1.36±0.66, 1.37±0.66 and 0.042±0.028 kg/bed-day, respectively, which is comprised of 51.6% (3142.05 kg/day) of infectious waste, 47.2% (2880.25 kg/day) general waste and 1.2% (74.11 kg/day) sharps waste. Soltanian et al[29] reported that total produced waste in any 24 hours duration equal to 61 kg, including 37.8, 22.5 and 0.7 kg of domestic wastes, infectious solid wastes and sharp objects, respectively. The average per annual was 1.9 kg in 24 hours each hospital bed of the study area. Amouei et al[30] reported that the generation

rate of the solid wastes were: total dental wastes: 291.2 kg including general solid wastes: 251.3 kg (86.3%), infectious wastes and sharps: 38 kg (13%) and hazardous chemical waste: 2 kg (0.7%). The total amount of wastes in a year was 69888 kg. The solid wastes are daily produced according to each active dental unit as total, domestic-type, infectious and the hazardous chemical wastes were 3.07 kg, 2.65 kg, 0.4 kg and 0.02 kg, respectively. Gitipour et al[31] mentioned that total active beds in 165 surveyed hospitals were 26444 beds, which produced 91.22 ton/d of medical wastes, and per bed production of wastes was 3.44 kg/d. Of all wastes in hospitals, 38.35% were infected wastes (1.31 kg/day/bed), 57.85% were non- infected wastes (1.99 kg/day/bed) and 3.75% were pharmaceutical and chemical wastes (0.13 kg/day/bed). The treatment efficiency of 81.29 % of hospitals was accepted (TST and Spore test results were negative). Yousefi et al[32] reported that the total amount of hospital waste comprising infectious waste, sharp and pharmaceutical chemicals were related to Imam Khomeini hospital with values of 44 220 012 and 10 kg per day respectively, with 220 kg per day of general waste related to same hospital. Hence, the total weight of waste produced per capita, for infectious waste, general waste, chemical waste, and sharp-machinery were 2.35±0.25, 0.39±0.075, 1.25±0.66, 0.05±0.028, and 0.021±0.015 kg per day per bed respectively. The study of Nemathaga et al[33] in South Africa showed that among the total waste, ordinary waste had an average of 60.74%, medical waste was 30.32% while sharp waste was 8.94%. The average rate of medical waste production was obtained as 0.6 g/patient/d. In other study, the amount of infectious waste, general, sharp and pharmaceutical chemicals were 82.7%, 61.32%, 3.84% and 1.5% of all waste produced, respectively[34].

Study problems regarding hospital waste and lack of proper implementation of laws and principles, and the rules for proper implementation and management of hospital waste need to be revised. This can reduce the quantity and quality of waste in the country to a minimum. Environmental health education is needed for nurses on hospital waste management followed by strict monitoring for compliance[35].

Conclusions

The results indicate that waste management in health centers has serious problems. Therefore, it is necessary to fundamentally review the waste management method, provide regular programs and equip the centers with infectious waste disposal equipment before the final landfill. Also, setting up safety centers or sites to provide services for all existing health care units (public, private) can be one of the necessary solutions to solve this problem.

Conflict of interests

The authors have no conflict of interest.

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ORIGINAL

Identify barriers to efficient drug distribution and provide solutions to improve it

Identificar los obstáculos a la distribución eficiente de medicamentos y aportar soluciones para mejorarla

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Summary

Background: Management of drug distribution is considered the most critical manner in safe and fast drug delivery to pharmacies and healthcare units. This research was carried out to assess the barriers to efficient drug distribution and provide solutions to improve it in a Darupakhsh company, Tehran, Iran as a model.
Methods: Sampling was done using simple sampling method. Customers (pharmacies) were the main subjects of the study. The questionnaire contains a set of indicators to measure the relationship between customer expectations and marketing strategies population of this group. The sample size was estimated to be 108 pharmacies considering the significant level of 95% and the probability of error of 0.09 using the formula No 1. A total of 102 pharmacies were response to the questionnaire.
Results: Because the level of significance was equal to 0.000 and (< 0.05), it was conclude that the study's hypothesis, i.e. the satisfaction of the distribution company's customers, was effective on the drug distribution marketing strategy. Darupakhsh company had high capacity in drug delivery at the expected time and place with acceptable speed, and professional behavior of distributors, deliverers and sellers. However, several items such as provide accurate information about the status of each drug in the future timely referral to follow up claims, flexibility in payment terms, offer trade and cash discounts as expected, and reputation and credibility of the company should revise.
Conclusion: Drug distribution management is one of the most important healthcare related items, especially in diseases outbreaks.

Keywords: Drug delivery, management, darupakhsh company, pharmacies.

Resumen

Antecedentes: La gestión de la distribución de medicamentos se considera la forma más crítica en la entrega segura y rápida de medicamentos a las farmacias y unidades sanitarias. Esta investigación se llevó a cabo para evaluar los obstáculos a la distribución eficiente de medicamentos y aportar soluciones para mejorarla en una empresa de Darupakhsh, Teherán, Irán, como modelo.
Métodos: El muestreo se realizó mediante el método de muestreo simple. Los clientes (farmacias) fueron los sujetos principales del estudio. El cuestionario contiene un conjunto de indicadores para medir la relación entre las expectativas de los clientes y las estrategias de marketing de la población de este grupo. El tamaño de la muestra se estimó en 108 farmacias considerando el nivel de significación del 95% y la probabilidad de error del 0,09 mediante la fórmula nº 1. Un total de 102 farmacias respondieron al cuestionario.
Resultados: Dado que el nivel de significación fue igual a 0,000 y (< 0,05), se concluyó que la hipótesis del estudio, es decir, la satisfacción de los clientes de la empresa de distribución, era efectiva en la estrategia de marketing de la distribución de medicamentos. La empresa Darupakhsh tenía una gran capacidad de entrega de medicamentos en el momento y lugar esperados con una velocidad aceptable, y un comportamiento profesional de los distribuidores, repartidores y vendedores. Sin embargo, varios puntos como proporcionar información precisa sobre el estado de cada medicamento en el futuro remisión oportuna para el seguimiento de las reclamaciones, la flexibilidad en las condiciones de pago, ofrecer descuentos comerciales y en efectivo como se esperaba, y la reputación y la credibilidad de la empresa debe revisar.
Conclusión: La gestión de la distribución de medicamentos es uno de los puntos más importantes relacionados con la asistencia sanitaria, especialmente en los brotes de enfermedades.

Palabras clave: Distribución de medicamentos, gestión, farmacias.

Introduction

Since therapeutic options play a very sensitive role in maintaining the health and treatment of diseases in the community, it is a very important strategic commodity and has always been considered by health care providers[1]. Today, under the rules and regulations of the Iranian Ministry of Health, 92% of therapeutic options are supplied by 77 drug companies, mostly privately owned or covered by non-governmental organizations, and 8% of them are imported[2].

The drug that is thus provided to meet the needs of different segments of society should be in the form of a codified and defined system to enable its supply to different social strata that need to use the drug. This system is called the "drug distribution system"[3].

The drug distribution system directs the production or import of drugs to the level of consumption and supplies the present and demand system. This system must provide a reasonable and appropriate relationship between supply and consumption by providing a suitable access field, in a timely manner and in the shortest possible time. In general, the drug distribution process is affected by 3 categories[4]:

- Capacity and power of drug manufacturers and importers and their joining the drug distribution company
- Policies of the Department of Medicine, Food and Narcotics of the Ministry of Health
- Customer satisfaction (pharmacies and medical centers)

At present, what is called drug distribution in Iran is responsible for receiving drugs from importers or manufacturers and delivering them to pharmacies by 22 companies. Darupakhsh Company is one of the largest drug distribution companies in Iran and in terms of turnover is the first among them. The company faces a variety of challenges, and market management practices to identify the shortcomings and challenges and analyze the factors affecting marketing in order to achieve the desired results along with strong competitors in the company is essential and is very important.

The present survey was carried out to identify barriers to efficient drug distribution and provide solutions to improve it in A Darupakhsh company.

Material and methods

Study area

The survey was conducted on data abstained from years 2008-2009. This research is based on correlation research method. The statistical population in this study is all experts in drug distribution. But given that each of the factors influencing drug marketing strategies was related to a group of distribution company audiences, the statistical population of each questionnaire was determined separately and independently.

Sampling procedure

Sampling was done using simple sampling method. Customers (pharmacies) were the main subjects of the study. The questionnaire contains a set of indicators to measure the relationship between customer expectations and marketing strategies and in fact looks at the set of real and practical customer expectations that are widely available in the country's pharmacies.

Since it was not possible to count and distribute the questionnaire among all pharmacies, Tehran pharmacies, which had purchased more than 550 million Rials in 2007 were consider. A total of 541 pharmacies were selected as the statistical population of this group. The sample size was estimated to be 108 pharmacies considering the significant level of 95% and the probability of error of 0.09 using the formula No 1. A total of 102 pharmacies were response to the questionnaire.

Formula No 1

P = 0.05 Z = 1.96 d = 0.09

$$n = \frac{NZ_{a/2}^2 S^2 (1 - S^2)}{N\theta^2 + Z_{a/2}^2 S^2 (1 - S^2)}$$

$$n = \frac{Z_{a/2}^2 P(1-P)}{d^2}$$

Data analysis

The data obtained from the questionnaire were stratified and descriptive analysis was used to test partial and general hypotheses. Cronbach's alpha test was used to assess the validity of the questionnaire. To calculate the Cronbach's alpha coefficient, the variance of the scores of each subset of the questionnaire (or subtest) questions and the total variance were calculated. Then, the value of alpha coefficient was calculated using formula number 2.

Formula No 2

$$r_a = \frac{J}{J-1}\left(1 - \frac{\sum S_j^2}{S^2}\right)$$

Whereas:
J = Number of question or test question subsets
S_j^2 = Variance following j test
S^2 = Total test variance

In this research, in relation to the use of secondary data, an attempt has been made to use reliable data

and information that is approved by the organization's monitoring system, so the information is reliable and seems to be far from biases and distortions.

Results

Evaluation of the validity of the questions in questionnaire

For the questionnaire questions, Alpha = 0.81010 was obtained. Considering that the alpha value is greater than 0.7, it was concluded that the questionnaire was reliable.

Chi-square test to investigate the effect of distribution company customer satisfaction on drug distribution strategies

Table I shows the designed questionnaire. Because the level of significance was equal to 0.000 and was lesser than the error value of 0.05, so with 95% confidence, we conclude the study's hypothesis, i.e. the satisfaction of the distribution company's customers, was effective on the drug distribution marketing strategy.

Discussion

In recent years, many diseases have caused health problems, except among the people[5-11]. However, proper management of drug distribution can prevent severe epidemics. Distribution is an important activity in the integrated supply-chain management of pharmaceutical products.

The drug distribution network is one of the most important pillars of the Iranian pharmaceutical system which plays a vital role in rapid and easy access to drugs. The purpose of this study is to "explain the effective characteristics in attracting and gaining the trust of drug manufacturers, customer satisfaction by observing the criteria of the Ministry of Health, Treatment and Medical Education and identifying the shortcomings of Darupakhsh company in the field of human drug distribution and strategies to achieve a "Distribution has been profitable and correct." Findings showed that the Darupakhsh company had the highest scores for the drug delivery at the expected time, drug delivery at the expected place, drug delivery speed as expected, and professional behavior of distributors, deliverers and sellers. While, the scores for the provide accurate information about the status of each drug in the future and predict the future timely referral to follow up claims, flexibility in payment terms, offer trade and cash discounts as expected, and reputation and credibility of the company were low. Sepahi et al[12] stated that, 11 complications were identified for the drug distribution network in Iran. Drug unavailability or shortage, supply of near-expiration drugs, supply of counterfeit drugs, improper sale of over-the-counter drugs, black market activity and drug trafficking, sharp price fluctuations, insufficient interaction with consumption pharmacist, high distribution costs, low distribution network performance in emergency deliveries, long time to search and find drugs (in case of certain drugs) and low quality of response and consumer complaints seem to be some of the complications identified in this study[12]. Also, Mojaradi and Mozaffari[13] in a research aimed at existing management in the drug supply chain using system dynamics simulation approach, assess the drug supply chain of Plavix drug on 2 levels of pharmacies and hospitals. Some research also only identifies some distribution network problems. In this regard, Ekhtiari et al[14] conducted a study entitled

Table I: Designed questionnaire in the present study.

No questions	Questions	Responses (%)			
		Very low	Low	Medium	High
1	Drug delivery at the expected time (during daily activities)	-	-	7 (6.86)	95 (93.13)
2	Drug delivery at the expected place	-	2 (1.96)	8 (7.84)	92 (90.19)
3	Drug delivery speed as expected (time interval from order announcement to drug receipt)	5 (4.90)	3 (2.94)	10 (9.80)	84 (82.35)
4	Professional behavior of distributors, deliverers and sellers (having job qualifications)	4 (3/92)	2 (1.96)	15 (14.70)	81 (79.41)
5	Pay attention to the opinions and reflect them to the officials and provide timely answers	7 (6.86)	5 (4.90)	25 (24.50)	65 (63.72)
6	Politeness in the behavior of distributors, deliverers and sellers	2 (1.96)	4 (3/92)	20 (19.60)	76 (74.50)
7	Present scientific and pharmacological information, especially regarding new drugs to physicians before drug distribution	9 (8.82)	8 (7.84)	31 (30.39)	54 (52.94)
8	Safely drug delivery	4 (3/92)	6 (5.88)	55 (53.92)	37 (36.27)
9	Provide accurate information about the status of each drug in the future and predict the future	10 (9.80)	51 (50.00)	34 (33.33)	7 (6.86)
10	Submit invoices at the expected time and in a timely manner	20 (19.60)	17 (16.66)	33 (32.35)	32 (31.37)
11	Provide drug brochures and pharmaceutical scientific information	2 (1.96)	7 (6.86)	11 (10.78)	82 (80.39)
12	Timely referral to follow up claims	12 (11.76)	18 (17.64)	48 (47.05)	20 (19.60)
13	Flexibility in payment terms	8 (7.84)	42 (41.17)	31 (30.39)	21 (20.58)
14	Offer trade and cash discounts as expected	15 (14.70)	35 (34.31)	35 (34.31)	17 (16.66)
15	Reputation and credibility of the company	22 (21.56)	29 (28.43)	26 (25.49)	25 (24.50)

"Assessing the status of supply, distribution and Prescribing medicine in pharmacies of Kermanshah according to Food and Drug Administration standards.

Dzierba et al[15] reported that drug delivery well management was the most important factor affected the well control of the corona virus diseases 2019 (COVID-19) in New York city, USA. Grujic et al[16] identified 78 risk factors in the distribution channels of drugs and pharmaceutical services in Serbia. The results of the research combined separate evaluations for risk factors in all categories for easier data analysis. After data were obtained, results were arranged to show which risk factors had the biggest influence upon the distribution of drugs and to determine the negative effects they can produce. The research of risks was done primarily to help the representatives of distribution channels gain better insight into drug distribution[16]. Kumar and Jha[17] stated that there are cases of unresolved customer complaints and batch failures originated due to inadequacies during distribution of pharmaceutical products. In absence of established quality risk management system during product shipment, there is no effective preventive plan related to risk factors. A corollary of manufacturing quality risk management has been drawn to the distribution of pharmaceutical products through this study. The quality risk management during pharmaceutical distribution may be useful to avoid market complaints, drug recalls, and regulatory actions[17].

Investments on measuring patients' needs correctly, supporting drug retailing competitive brands development, improving drug distribution system information comprehensive system throughout the country within needs measurement loops, network inventory, production and importation, improving the utilization of modern tools and technologies such as internet-based sales, seller-free shops, establishing electronic files for patients and similar ones, utilizing direct sale methods and fostering the roles of potentialities such as insurance in planning, decision making and monitoring drug distribution system countrywide are some of the solutions obtained from this research that are used to improve the drug distribution system in the country.

Conclusions

This survey showed that the Darupakhsh company had a high capacity in drug distribution among different customers, particularly pharmacies and healthcare centers. It seems that the company had high capacity in drug delivery at the expected time and place with acceptable speed, and professional behavior of distributors, deliverers and sellers. However, several items such as provide accurate information about the status of each drug in the future timely referral to follow up claims, flexibility in payment terms, offer trade and cash discounts as expected, and reputation and credibility of the company should revise. Finally, the important role of drug distribution system was studied in this survey. The present study was preliminary survey in this field. Thus, several multifactorial studies should perform to identify barriers in the drug delivery system.

Conflict of interests

The authors have no conflict of interest.

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ORIGINAL

Cancer, vellesa i SARS-CoV-2

Cancer, old age and SARS-CoV-2

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Resum

Es presenten i discuteixen les circumstàncies epidemiològiques - incidència, mortalitat, relació amb l'edat - dels quatre càncers més incidents a Espanya i Illes Balears i l'impacte que en elles ha tingut i tindrà la pandèmia per SARS-CoV-2. Els missatges clau son que l'edat alta es en si mateix un factor de risc per desenvolupa un càncer, especialment el poblacionalment mes incident, colon, també els dos mes incidents per gènere, mama femenina a dones i pròstata a homes, i el que presenta una de les taxes de mortalitat mes altes, pulmó. A mes, la pandèmia per COVID19 ha dificultat enormement els procediments preventius i, en conseqüència, es esperable un repunt de la incidència del càncer per el proper any.

Palabras clave: Càncer, envelliment, SARS-cov 2.

Summary

The epidemiological circumstances - incidence, mortality, relationship with age - of the four most common cancers in Spain and the Balearic Islands and the impact that the SARS-CoV-2 pandemic has had and will have on them are presented and discussed. The key messages are that old age is in itself a risk factor for developing cancer, especially the population most incident, colon, also the two most incidental by gender, female breast in women and prostate in men, and what has one of the highest mortality rates, lung. In addition, the SARS-CoV-2 pandemic has made preventive procedures extremely difficult and, as a result, a rise in the incidence of cancer is expected for next year.

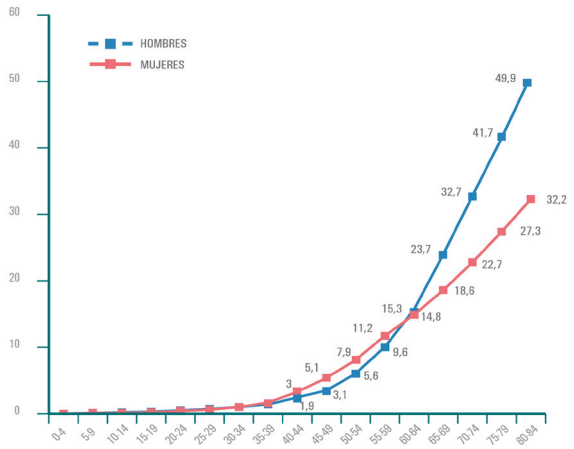
Keywords: Cancer, aging, SARS-cov 2

Introducció

Les últimes dades publicades per la Societat Espanyola d'Oncologia Mèdica deixen molt clar que el risc de patir un càncer s'incrementa amb l'edat: a la **figura 1** es pot veure que a partir dels 50 anys es dispara cap amunt la possibilitat, en homes i dones, de ser diagnosticats de càncer. Assolir la vellesa és, en conseqüència, causa principal de ser diagnosticat d'un càncer, tot i que en molts casos aquesta circumstància –ser una persona d'edat– es pot associar amb un millor pronòstic de la malaltia, cas dels dos tumors més incidents tant en homes –pròstata– com en dones –mama–, però també amb la alta freqüència de la vida en soledat que pateixen els nostres avis, tal com els serveis socials de la Associació Espanyola contra el Càncer (AECC) viuen cada dia.

La **taula I** recull la incidència en 2012 i 2020 dels càncers més freqüents en Illes Balears, poblacionalment i per gènere, detallant el nombre de casos.

Figura 1.



Font: Las Cifras del Cáncer en España 2020. Sociedad Española de Oncología Médica. https://seom.org/seomcms/images/stories/recursos/Cifras_del_cancer_2020.pdf Accés 24.03.2021

La **taula II** recull els tipus de càncer que van causar més mortalitat en 2012 i 2020 a Illes Balears, poblacionalment i per gènere, detallant el nombre de casos.

Taula I

	2012	2020
Poblacional	Colo-rectal: 710	Colo-rectal: 806
Dones	Mama: 676	Mama: 754
Homes	Pròstata: 643	Pròstata: 730

Font: Observatorio del Cáncer. Asociación Española contra el Cáncer. http://observatorio.aecc.es/ Accés 23.03.2021

Taula II

	2012	2020
Poblacional	Pulmó: 491	Pulmó: 533
Dones	Mama: 133	Mama: 146
Homes	Pulmó: 378	Pulmó: 408

Font: Observatorio del Cáncer. Asociación Española contra el Cáncer. http://observatorio.aecc.es/ Accés 23.03.2021

En funció d'aquestes dades, quatre càncers haurien de focalitzar la nostra preocupació a la feina oncològica, els de còlon-recte, pulmó, mama femenina i pròstata.

A continuació valorarem cada un dels casos en particular i a partir de la idea bàsica de que res hi ha més eficaç –en termes de salut personal– i eficient (cost-benefici) –en termes de salut pública– que la prevenció primària –evitar la o les causes– i / o la secundària, el diagnòstic precoç, discutirem quina és la situació preventiva de cada un d'ells en la nostra Comunitat Autònoma i l'impacte que en la seva implantació i cobertura ha tingut la pandèmia per la infecció pel virus SARS-CoV-2, acrònim anglès de *Severe Acute Respiratory Syndrome – Corona Virus*, amb el 2 final per ser el segon coronavirus identificat, i la seva malaltia derivada, la COVID19, acrònim del nom en anglès de la malaltia, *COronaVIrusDesease* sumat a l'any –2019– de la seva descripció.

Càncer de pulmó

La majoria de les persones diagnosticades amb càncer de pulmó té 65 anys o més; un nombre molt petit de persones diagnosticades tenen menys de 45 anys. L'edat mitjana de les persones en el moment de la diagnosi és aproximadament 70 anys[1]. Un càncer de gent gran, està clar.

Nou de cada deu càncers de pulmó estan relacionats causalment amb el consum directe de tabac, però també amb el consum secundari, el del fumador passiu, que veu incrementat en un 35% la seva probabilitat de patir un càncer de pulmó[2] en comparació amb el del no fumador. El tabac, la gran droga additiva de venda i ús regularitzats i socialment acceptada. Des de l'AECC a nivell Nacional i també a Illes Balears estem treballant en cursos de desintoxicació tabàquica, amb un cert èxit: el 60% dels que els atenen ha deixat de fumar als 6 mesos.

Encara que en els mesos pandèmics s'ha registrat al voltant d'un 6% de disminució en el consum de tabac[4], d'acord amb el descens en els homes anotat en els últims 25 anys –d'un 45% a un 26% de fumadors–, però no amb la situació del tabaquisme en dones, estable a la mateixa fracció de temps sobre el 25%[5]. La pitjor de les notícies és que curem no més d'un 15% de càncers de pulmó: 609 diagnosticats a Illes Balears el 2020, 533 morts, un 88%. Per tant treballar en la prevenció primària –evitar el tabac– és prioritari, perquè la prevenció secundària –diagnòstic precoç– està en període d'assaig clínic: l'aplicació de la tomografia axial computeritzada de baixa intensitat a grans fumadors (més de 20 cigarrets / dia durant més de 20 anys) sembla que pot facilità l'accés al diagnòstic de càncers de pulmó inicials asimptomàtics no detectables per radiologia convencional, amb molt altes possibilitats de curació[6].

Càncer de mama femenina

La precisió de gènere no és ociosa: només un de cada cent càncers de mama apareix en un home, generalment d'edat avançada. A l'home, les causes i la seva prevenció no han estat establertes[7].

I en la dona? Sabem moltes coses del càncer més incident en la dona[8]. Hi ha una fracció de càncer de mama, de l'ordre del 10-15% de casos, que es diagnostiquen en el primer terç de la vida i que està vinculada a alteracions genètic-hereditàries, l'expressió dels gens BRCA 1 i 2. Sabem que el càncer de mama és més freqüent en dones que han tingut la primera regla abans dels 12 anys –menarquia precoç– i l'última després dels 55 –menopausa tardana–, que no han tingut fills, en les que els han tingut més enllà dels 30 anys, amb risc incrementat si a més no han lactat. Sabem també que els tractaments hormonals substitutius de la menopausa de llarga durada augmenten el risc, igual que l'obesitat. I l'edat? L'edat mitjana de diagnòstic d'un càncer de mama està sobre els 62 anys, un altre càncer majoritàriament de gent gran. L'increment de diagnòstic s'accentua a partir dels 50 anys, raó per la qual els programes de prevenció secundària, buscant l'eficiència, s'inicien a aquesta edat. La **taula III** recull els percentatges de diagnòstics per talls d'edat, fent paleses les dades que estem comentant.

Taula III

Edat	% de casos
30 – 39	7.41
40 – 49	14.81
50 – 59	24.44
60 – 69	22.96
70 – 79	16.30
> 80	14.07

Font: https://www.elsevier.es/es-revista-medicina-integral-63-articulo-el-riesgo-cancer-mama-conceptos-13024489 Accés 26.03.2021

L'increment de casos diagnosticats que s'observa a la **taula I** es pot explicar per l'acumulació epidemiològica dels factors de risc: els índexs de natalitat a Espanya i en Illes Balears s'han ensorrat des d'un 3 en els anys 60 a un 1,3 el 2017, segons dades del Banc Mundial[9]; l'edat mitjana del primer fill a Espanya ara és 31 anys, amb el 30% a partir dels 35[10], i l'obesitat té nivells pandèmics al primer món econòmic[11]. Són factors corregibles, abordables en accions de prevenció primària, per exemple que la dona no hagi d'esperar a tenir 30 anys complerts per poder oferir al seu fill una certa estabilitat laboral i econòmica i que l'alimentació sana, lluny del *fast-food* i els precuinats, sigui assequible.

La millor notícia és la gran eficàcia –en termes de diagnòstics de càncers de mama inicials– i la bona eficiència –en termes de cost / benefici per a la salut pública– que tenen els programes de cribratge, de diagnòstic precoç, és a dir, de prevenció secundària. En Illes Balears el programa està en funcionament des de fa anys, amb resultats que no han estat comunicats en els últims temps. Potser es pugui estimar l'efectivitat del programa analitzant la **taula IV**, que reflecteix les tendències d'incidència i mortalitat per càncer de mama femenina a Illes Balears:

Taula IV

	Anys			
	2020	2019	2013	2012
Incidència	754	735	678	676
Mortalitat	149	141	131	135

Font: Observatorio del Cáncer. Asociación Española contra el Cáncer. http://observatorio.aecc.es/ Accés 26.03.2021

En els anys 20/19 la mortalitat ha estat del 19,5%; en els anys 13/12 va ser del 19.6%. És a dir, mortalitat estable. No sembla, per aquestes dades, que el programa tal qual està sent aplicat en Illes Balears hagi aconseguit baixar la mortalitat, conseqüència esperada principal en un programa de cribratge que ha de facilitar l'accés a diagnòstics més inicials del càncer i, per tant, més curables. Res agradaria més a l'autor d'aquestes consideracions que les xifres oficials, quan es coneguin, corregeixin per bé aquestes dades.

Càncer de pròstata

Com ha estat detallat a la **taula I**, és el més incident en homes, però en l'estadística de mortalitat apareix en cinquè lloc. La raó pot raure en:

- La millora de les estratègies de diagnòstic precoç[12], sense que estigui consolidada encara l'evidència de l'eficàcia i eficiència dels programes de cribratge poblacional[13]. El cribratge amb antigen prostàtic específic, PSA, acrònim de les inicials angleses. *Prostatic Specific Antigen*, pot reduir la mortalitat per càncer de pròstata però està associat a resultats positius falsos. A més, comparat amb conductes conservadores, els tractaments actius dels casos detectats en el cribratge produeixen resultats incerts sobre la supervivència i estan associats a dificultats sexuals i urinàries. El diagnòstic precoç en activitat clínica assistencial ha d'estar basat en la valoració del nivell en sang de PSA més una exploració clínica adequada, amb suport de tècniques d'imatge, bàsicament l'ecografia. Aquest control assistencial és recomanable que sigui aplicat a tots els homes a partir dels 50 anys i més si presenten algun símptoma com micció imperiosa o incontinència urinària[14].
- La consolidació de noves variables de tractament[15], que inclouen la immunoteràpia i el seguiment sense teràpia amb vigilància activa d'alguns casos, especialment en homes d'edat avançada, dada important perquè la majoria dels càncers de pròstata es diagnostiquen més enllà dels 60 anys: tens mes d'aquesta edat? Si? Cuida la teva pròstata.

L'evolució de la mortalitat a Illes Balears mostra una certa estabilització, amb un lleuger descens comparant xifres de 2012 amb les de 2020, tal com es pot comprovar a la **taula V**.

Taula V

	Incidència/N de casos	Mortalitat
Any 2012	693	117 (17%)
2020	730	110 (15%)

Font: Observatorio del Cáncer. Asociación Española contra el Cáncer. http://observatorio.aecc.es/ Accés 26.03.2021

A partir d'aquestes dades, i amb l'objectiu d'intentar millorar-los, la conclusió hauria de ser estar molt atents als beneficis que pugui aportar una bona política de cribratge poblacional, probablement iniciada als 50 anys i basada en les evidències que es vagin consolidant i, mentre això arriba, aplicar a l'assistència preventiva i als tractaments els nous protocols.

Càncer de còlon

Recordem el apuntat: el càncer de còlon és el més incident en Illes Balears, 806 casos diagnosticats l'any 2020, 710 el 2012; en els mateixos anys, 320 i 301 defuncions, respectivament. Són aquestes xifres acceptables? No ho son: el càncer de còlon és, amb diferència, aquell en el qual els protocols de prevenció secundària –cribratge poblacional– poden i han de ser aplicats amb més alta eficàcia i eficiència. Aquesta acció reduiria dràsticament no probablement el nombre de casos però si el moment clínic del seu diagnòstic, mes inicial, facilitant el tractament i la seva eficàcia, al temps que es diagnosticarien lesions pre-canceroses silents, ambdues coses en nombre molt important. Els resultats

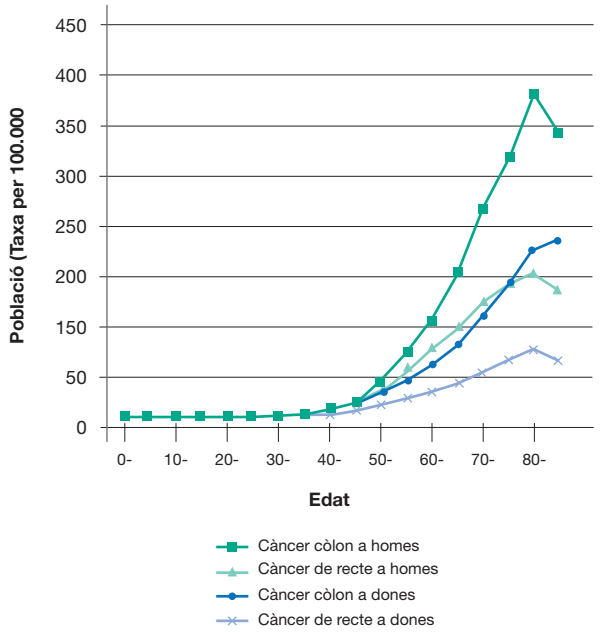
obtinguts en el programa pilot dut a terme a la zona del Raiguer de Mallorca[16] així ho demostren: en persones asimptomàtiques, 57 càncers diagnosticats, 46 d'ells en fases I i II del seu desenvolupament, i 246 adenomes avançats. Pràcticament tots aquests casos han sigut o seran perfectament curables amb mesures poc agressives. Fer créixer la implantació d'aquest programa per arribar a tota la comunitat autònoma sembla un objectiu inajornable: en aquesta línia, la bona nova es que el 23 d'agost 2021 s'ha fet públic el compromís de la Conselleria de Salut del Govern Balear de implantar de forma immediata el programa a tots els Hospitals Públics de la Comunitat Autònoma, decisió que es complementa de forma altament positiva en la aprovació de l'adquisició de torres de endoscòpia d'última generació[17].

A quina edat iniciar el programa? A la **figura 2** es pot veure la corba etària de diagnòstic de càncer de còlon, amb un molt evident increment a partir dels 50 anys, edat que en conseqüència serà la d'inici de l'aplicació del programa.

Prevenció primària, modificació de factors de risc? Bàsicament, alimentació: poc greix, pocs aliments processats, poca carn vermella, molta verdura, fruita, llegum. Res de tabac –una altra vegada– i molt limitat consum d'alcohol, millor res.

Amb bona cultura de salut orientada a la prevenció primària i l'aplicació poblacional no demorada del cribratge, podrem aconseguir limitar a molt escasses la incidència i la mortalitat de càncer de còlon. Aplicar-se a això és una prioritat sanitària.

Figura 1:.



Càncer i impacte pandèmia SARS-CoV-2

A una publicació molt recent[18] del *National Cancer Institute* de Estats Units (EEUU) es prediu que l'any 2022 es pràcticament doblaran las morts per càncer de colon i de mama femenina als EEUU. També a l'AECC hem treballat en un informe, "*Impacto de la pandemia COVID19 en las persones con cáncer en España*", fet públic en febrer 2021[19]. L'informe recull els resultats d'un estudi realitzat al desembre 2020 a nivell nacional, mesurant les diferències en algunes activitats que s'havien produït entre març / juny 2019 i març / juny 2020. Es va realitzar en col·laboració amb les Societats Espanyoles d'Anatomia Patològica, Infermeria Oncològica, Hematologia i Hemoteràpia, Oncologia Mèdica i Oncologia Radioteràpica. Els resultats globals són coincidents amb els obtinguts en Illes Balears. Aquestes són algunes de les principals conclusions de l'estudi:

- Impacte en els procediments diagnòstics: 30% menys de citologies i 24% menys de biòpsies practicades.
- Problemes d'accés al sistema sanitari, encara que el pacient ja inclòs no ha patit en general retards en el seu procés diagnòstic o terapèutic.
- El 41% dels pacients oncològics ha vist afectada la seva estabilitat psicològica.
- El 19% de malalts oncològics ha patit un deteriorament important de la seva situació econòmica que els ha col·locat en risc d'exclusió social, més acusat en les dones, 40%.
- Retrocés en l'ordenament del consum públic de tabac.
- Aturada en l'acció sobre els tres programes de cribratge, amb necessitats diferenciades:
  - Càncer de Mama femenina: Actualització de situació i resultats.
  - Càncer de Coll d'Úter: Redisseny integral del programa.
  - Càncer de Còlon: Ampliació a poblacional de la seva aplicació.

Comentaris en relació a aquestes dades:

- De moment aquesta disminució en citologies i biòpsies no ha tingut repercussió en la taxa d'incidència del càncer a Illes Balears, tal com es pot comprovar en la **taula VI**:

Taula VI

	N de casos	
Cancer	**2019**	**2020**
Colon	782	806
Mama femenina	735	754
Pròstata	707	730

Font: Observatorio del Cáncer. Asociación Española contra el Cáncer. http://observatorio.aecc.es/ Accés 26.03.2021

No obstant això és molt recomanable fer cas a las estimacions publicades sobre un augment de casos a registrar a partir de 2022 i que a més seran diagnosticats molt probablement en estadis clínics més avançats, situació que podríem previndre i afrontar adequant convenientment a la nova situació les estructures preventives i diagnostiques.

- Només un 20% dels malalts de càncer reben suport psicològic per part del Sistema Nacional de Salut[19]. A més, no existeix un programa específic públic d'assessoria laboral per a malalts de càncer que pateixen una situació de risc de pèrdua d'ocupació, més gran en pacients de més de 50 anys. Les dues accions, suport psicològic i ajuda econòmica i laboral, són prioritàries per a la AECC, que a nivell de Illes Balears ha duplicat en temps de pandèmia SARS-CoV-2 la seva inversió en aquestes àrees. A més, les dones han de rebre suport prioritari, perquè estan empleades en sectors més afectats per la caiguda de la demanda i per ser objecte d'una elevada presència dins de l'ocupació a temps parcial o temporal.

- El camí en l'ordenació del consum públic de tabac ha de ser el contrari del recorregut darrerament, més permissiu, ha de ser necessàriament restrictiu: més espais sense fum, des de platges a parcs, passant per cotxes amb nens al seu interior o espais esportius. En paral·lel, treball educatiu en l'adolescència per evitar l'inici en el consum, està clar que és molt més fàcil no començar que deixar-ho.

- Ja s'han fet en els epígrafs respectives previs els comentaris en quant a la situació dels programes de cribratge de mama femenina i còlon, però potser el que estructural i metodològicament està pitjor és el de coll d'úter, de cèrvix. Estructura oportunista que només revisa a les dones que consulten –un 30% no ho fa, en dades publicades en 2008 20 que no han sigut corregides– i un mètode de revisió bàsicament citològic, que es una bona alternativa al que ha de ser prioritari basat en la determinació per mètode validat del virus del papil·loma humà[21], causa necessària del càncer de cèrvix[22], dues situacions – estructura i mètode – en aplicació a casa nostre que contradiuen les recomanacions de les Societats Científiques[23], de el Ministeri de Sanitat[24] i de la Organització Mundial de la Salut[25], que ha declarat al càncer de cèrvix com el primer càncer erradicable del nostre entorn.

A manera de conclusions

1. La pandèmia per SARS-CoV-2 ha desestabilitzat al Sistema Nacional de Salut, generant retards en l'actualització i l'aplicació dels procediments preventius oncològics. Cal un prioritari esforç, planificador i pressupostari, per corregir aquesta situació sobrevinguda i poder afrontar amb garanties futurs problemes.

2. La incidència del càncer és molt probable que presenti un repunt en 2022. Hem d'estar preparats per afrontar-la, ja que no hauria de desbordar la capacitat diagnostica i terapèutica que estigui disponible.

3. Treballar en reduir obesitat i consum de tabac és imprescindible, bàsicament des de la millora de l'accessibilitat a l'alimentació sana i de l'educació per evitar l'inici al tabaquisme.

4. Concentrar el treball de suport psicològic i social sobre els pacients oncològics que més han patit els efectes de la pandèmia és importantíssim. Atenció preferent a alleujar la soledat dels nostres avis i la situació laboral de las dones.

Com va deixar escrit Albert Einstein "la crisi és la millor benedicció que pot succeir-li a les persones i els països, perquè la crisi porta progressos" i "és en la crisi on neixen la inventiva, els descobriments i les grans estratègies". Aprenguem d'ell i sortim d'aquesta crisi des de la solidaritat millorada i la innovació, creant un espai sanitari equitatiu i molt actualitzat en tot el concernent al món oncològic, que és el que aquí i ara ens concerneix.

Conflicto de interés

Los investigadores declaran no tener conflicto de interés.

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ORIGINAL

Effect of zinc on SIRT1 and PGC-1 alpha gene expression among ulcerative colitis patients

Efecto del zinc en la expresión de los genes SIRT1 y PGC-1 alfa en pacientes con colitis ulcerosa

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Summary

Zinc has so many beneficial effects as a supplement, particularly for the treatment of diseases and prevention of the occurrence of several disorders through inflammatory reactions, especially in gastrointestinal cases. The present study was done to assess the Zn effect on Silent Information Regulator 1 (SIRT1) and Peroxisome proliferator activated receptor γ coactivator-1α (PGC-1α) gene expression among ulcerative colitis (UC) patients. Fifty patients with mild-to-moderate active UC were included and divided into two groups of treatment (25 patients received Zn (35 mg Zn gluconate/day for 40 days) and control (25 patients received placebo similar to the Zn capsules in shape and color for 40 days). The expression rates of SIRT1 and PGC-1α were examined in the patients using the Real-Time PCR. The mean age of included patients was 37.2±10.6 years. The male to female ratio was 23/27. Totally, the distribution of smoking and alcohol among patients were 55% and 31%, respectively. Pan UC (40%) and lift-sided (40%) had the higher distribution. The mean expression of the PGC1-α gene was increased amongst the UC patients treated with Zn supplement (P <0.05). The mean expression of the SIRT1 gene was increased amongst the UC patients treated with Zn supplement (P <0.05). However, in the control group, no any changes have been recorded for both genes. It seems that Zn caused significant decrease in the inflammatory response of the colon by significant increase in the expression of the SIRT1 and PGC1-α genes.

Keywords: Ulcerative colitis, PGC1-α, SIRT1, Gene expression, Zinc supplement.

Resumen

El zinc tiene muchos efectos beneficiosos como suplemento, en particular para el tratamiento de enfermedades y la prevención de la aparición de varios trastornos por reacciones inflamatorias, especialmente en casos gastrointestinales. El presente estudio se llevó a cabo para evaluar el efecto del Zn sobre el regulador silencioso de la información 1 (SIRT1) y el receptor activado por el proliferador de peroxisomas γ coactivador-1α (PGC-1α) en pacientes con colitis ulcerosa (CU). Se incluyeron 50 pacientes con CU activa de leve a moderada y se dividieron en dos grupos de tratamiento (25 pacientes recibieron Zn (35 mg de gluconato de Zn/día durante 40 días) y control (25 pacientes recibieron placebo similar a las cápsulas de Zn en forma y color durante 40 días). Se examinaron los índices de expresión de SIRT1 y PGC-1α en los pacientes utilizando la PCR en tiempo real. La edad media de los pacientes incluidos fue de 37,2±10,6 años. La proporción entre hombres y mujeres fue de 23/27. En total, la distribución del tabaquismo y el alcohol entre los pacientes fue del 55% y el 31%, respectivamente. La distribución más alta fue la de la CU de tipo pan (40%) y la de tipo lifting (40%). La expresión media del gen PGC1-α aumentó entre los pacientes con CU tratados con suplementos de Zn (P <0,05). La expresión media del gen SIRT1 aumentó entre los pacientes con CU tratados con suplemento de Zn (P <0,05). Sin embargo, en el grupo de control no se registraron cambios en ambos genes. Parece que el Zn provocó una disminución significativa de la respuesta inflamatoria del colon mediante un aumento significativo de la expresión de los genes SIRT1 y PGC1-α.

Palabras clave: Colitis ulcerosa, PGC1-α, SIRT1, expresión génica, suplemento de Zinc.

Introduction

Ulcerative colitis (UC) is a disease mainly characterized by chronic inflammation and an increased production of pro inflammatory cytokines and reactive oxygen species, particularly in the intestine. UC is consider chronic inflammatory bowel disease (IBD) with higher incidence rate amongst 30-40 years old people[1]. It has a high annual distribution globally, particularly 24.3 per 100,000 cases in Europe and 6.3 per 100,000 cases in Asia[2]. The main clinical signs of the UC are diarrhea, abdominal pain, bowel movements, local inflammation, and rectal bleeding[3]. Epidemiological surveys revealed that many factors play important roles in the UC pathogenesis[4].

Previous report showed that the UC occurrence is frequently associated with zinc (Zn) deficiency[5]. Zn supplementation can be beneficial to UC treatment, owing to its anti-inflammatory and antioxidant properties[6]. Zn deficiency is common in patients with IBD, throughout both active and remission phases, with a prevalence ranging from 15% to 40%[7]. Studies on animal models and translational studies proved that decreased serum Zn concentrations may improve inflammation through numerous pathophysiological mechanism, including disruption of epithelial barrier, altered mucosal immunity, and increased proinflammatory cytokines[8].

Silent Information Regulator 1 (SIRT1) is NAD(+)-dependent histone deacetylases involved in the antioxidant defense regulation, cell apoptosis and inflammation[9]. SIRT1 activation will cause several developments in the UC and IBD[10-13]. SIRT1 is an important factor in the activation of Peroxisome proliferator activated receptor γ coactivator-1α (PGC-1α)[14]. PGC-1α controls numerous biological activities, such as oxidation, mitochondrial biogenesis and inflammation[15]. PGC-1α activation caused several decreased in the occurrence of UC among models[16,17]. In IBD models, increase in the PGC-1α expression caused significant decrease in the occurrence of IBD through antioxidant activities[16,17].

However, the main roles of the Zn supplement on the regulation of and SIRT1 and PGC-1α genes is not determined yet. Thus, this survey was aimed to assess the effects of Zn supplement on SIRT1 and PGC-1αgenes expression in patients with UC.

Materials and methods

Inclusion and exclusion criteria

The current study was conducted on 50 patients with mild-to-moderate active UC who were referred to medical clinics. Patients ≥20 years of age with a confirmed histological and endoscopic diagnosis of UC, body mass index (BMI) 20-30 kg/m^2 were selected. In the survey active mild to moderate UC was determined by a Simple Clinical Colitis Activity Index (SCCAI) score of ≥5 and <12.

Exclusion criteria were use of anti–tumor necrosis factor agents and omega-3, use of non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, use of multivitamin-mineral, polyphenolic and antioxidant supplements and also changing the type or dose of medication over the past month. In addition patients with other diseases (cancer, renal, liver or cardiovascular disease and diabetes mellitus), as well as pregnancy or lactation women were excluded. Additionally, patients with the signs of the Corona Virus Diseases 2019 (COVID-19) were excluded from the study.

Interferences

Patients were randomly divided into two groups according to permuted block randomization design generated via www.Randomization.com website. Patients were given Zn (35 mg Zn gluconate/day for 40 days) or placebo for 40 days (25 patients in each group). Placebo capsules contained rice flour in size and color similar to Zn capsules, also packaged like to Zn boxes. The randomization list and numbered packing of intervention were performed by a person not involved in the study. The intervention packs were placed in the laboratory and given to the patients by the secretary according to the code numbers. Patients and all study personnel, were blinded to treatment assignment throughout the study.

RNA extraction and cDNA synthesis

Buffy coat samples of blood white cells were separated by centrifugation (Shimadzu, Japan). RNA was extracted using RNX-plus Sinacolon Kit (Cinnagen Co, Iran) according to the protocol of the producing company. The RNA concentrations were determined by Nanodrop device (NanoDrop, Wilmington, USA). All RNA samples had a 260:280 absorbance ratio between 1.9 and 2.1. Then, cDNA was synthesized using SinaClon first strand cDNA synthesis kit (Cinnagen Co, Iran) according to the protocol of the producing company. Extracted cDNA samples were subjected to quantification by NanoDrop device (NanoDrop, Thermo Scientific, Waltham, USA), qualification (2% agarose gel) and purity checking (A260/A280). The cDNA was stored at -80°C until subsequent analysis.

Gene expression

Real-Time Polymerase Chain Reaction (Real-Time PCR) was carried out to determine the levels of SIRT1 and PGC-1α genes expression in extracted cDNA samples. **Table I** describes list of primers used in the real-time PCR reaction.

Table I: Primers used in the real-time PCR reaction[18].

Target gene	Oligonucleotide primers (5'-3')
PGC-1α	F: GTCAACATTCAAAGCAGCAGAGAG R: GACACATAATCATTACCTACTGGAAGC
SIRT1	F: TAGTAGGCGGCTTGATGGTAATC R: GGTTCTTCTAAACTTGGACTCTGG

Real-Time PCR thermocycler (Rotorgene 6000, Corbett research, Mortlake, London, UK) was used to assess the expression rates of the SIRT1 and PGC-1α genes in examined groups using SYBR Green PCR master mix (Applied Biosystems), according to the manufacturer's instructions. The real-time PCR reaction were performed by 5 µL of SinaSYBR Blue HS-qPCR Mix (2x) (Sinaclone. Iran), 1 µL of extracted cDNA, 0.25 µL of each 10 µM forward and reverse primers, and 3.5 µL sterile distilled water, making a total volume of 10 µL. Forty cycles of 95ºC for 15 sec, 60ºC for 30 sec, and 72ºC for 20 sec were run after the denaturation of DNA at 95ºC for 5 min. The melting curve analysis was conducted from 55ºC to 99ºC with 0.2 sec interval. The data were analyzed according to the delta–delta Ct (ΔΔCT) method and were normalized to SIRT1 and PGC-1α expression in each sample.

Statistical analysis

Data were analyzed using the SPSS statistical software. Chi-square and fisher exact two tailed tests. Quantitative data were analyzed using the ANOVA test. *P*-value was considered to be statistically significant when 0.05.

Results

Study population

Table II shows the demographic characters of an included population. According to data, the mean age of included patients was 37.2±10.6 years. The male to female ratio was 23/27. Totally, the distribution of smoking and alcohol among patients were 55% and 31%, respectively. Pan UC (40%) and lift-sided (40%) had the higher distribution.

Table II: Demographic characters of an included population.

Characters	Frequency (%)
Mean age (SD)	37.2 (10.6)
sex (M/F)	23/27
Mean Weight (SD)	70.7 (13.4)
Smoking (%)	55
Alcohol (%)	31
Extension of disease Pan UC (%)	40
Left-sided (%)	40
Extensive (%)	5
Rectosigmoid (%)	15

Gene expression

Figures 1 and **2** show the PGC1-α and SIRT1 gene expression amongst the patients of the present survey. The mean expression of the PGC1-α gene was increased amongst the UC patients treated with Zn supplement (*P* <0.05). However, in the control group, no any changes have been recorded for this gene.

The mean expression of the SIRT1 gene was increased amongst the UC patients treated with Zn supplement (P <0.05). However, in the control group, no any changes have been recorded for this gene.

Figure 1: Effect of Zn on PGC1-α gene expression.

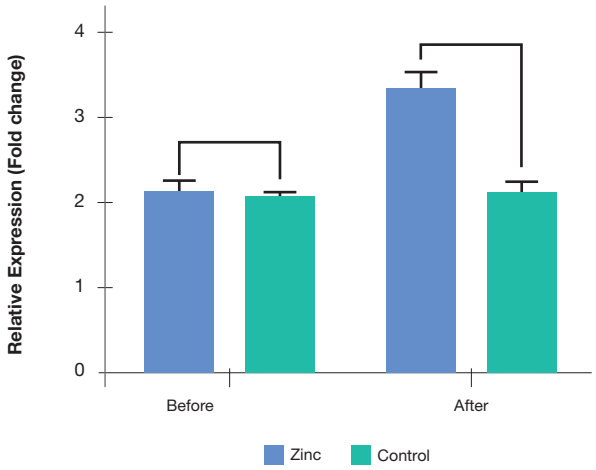
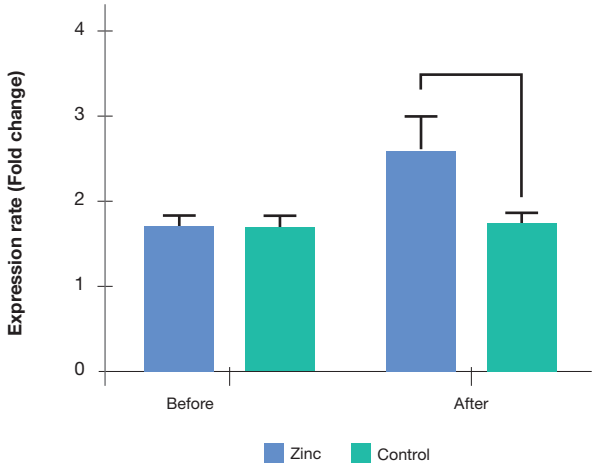


Figure 2: Effect of Zn on SIRT1 gene expression.



Discussion

Diet plays a role in the pathogenesis of gastrointestinal diseases, particularly UC and IBD. Dietary Zn may influence risk of disease through effects on autophagy, innate and adaptive immune response and maintenance of the intestinal barrier[19]. In cell culture experiments and colitis animal models, Zn administration improves intestinal barrier function and reduces expression of pro-inflammatory cytokines[20,21].

According to our knowledge, this is the first clinical trial that investigated the effects of Zn supplementation on expression of genes involved in the inflammatory response in UC patients. The study findings revealed that the expression of both SIRT1 and PGC1-α genes were significantly increased after Zn supplementation. However, in the control group no significant changes was occurred in the expression of examined genes. This finding may show the Zn therapeutic effect in UC patients through the up-regulate expression of SIRT1 and PGC1-α genes.

Zn deficiency is associated with more severe colitis and a larger inflammatory burden[22]. In human researches, Zn administration reduces intestinal permeability in Crohn's disease[23] and is effective in numerous diarrheal diseases treatment. Zn also is a co-factor for numerous enzymes involved in maintenance of intestinal integrity and regulates autophagy and bacterial clearance in macrophages[24].

In a similar survey, Khazdouz et al. (2020)[25] reported that Selenium supplement caused some changes in the SIRT1 and PGC1-α genes in UC patients. They reported that the SIRT1 gene expression in the Se group was significantly increased compared to the placebo ($p < 0.001$). An increase in the expression of the PGC-1α gene in the Se group was not statistically significant. It seems that Se supplementation caused a significant decrease in the inflammatory response of the colon by a significant increase in the expression of the SIRT1 gene. Researches established that SIRT1 can regulation of intestinal inflammation and tissue homeostasis in UC model[26-28]. Since, down-regulation the expression of SIRT1 upraise the pro-inflammatory cytokines concentrations, that are involved in UC pathogenesis, whereas, activation of SIRT1 caused significant reduction in the symptoms of the disease in IBD[29].

Conclusion

This is the first report of the effect of Zn supplements on the SIRT1 and PGC-1α gene expression in UC patients. It seems that the Zn caused significant decrease in the inflammatory response from the over expression of the SIRT1 and PGC-1α genes. However, further surveys are required to found the exact role of the Se in the controlling of UC through expression of the SIRT1 and PGC-1α genes.

Conflict of interests

The authors have no conflict of interest.

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SPECIAL ARTICLE

A review on the role of the anterolateral ligament (ALL) in the knee joint stability

Una revisión sobre el papel del ligamento anterolateral (LLA) en la estabilidad de la articulación de la rodilla

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Summary

Background: It has been demonstrated that the anterolateral ligament (ALL) plays an important role in the Knee joint stability. However, because of the paucity of current literature on the native biomechanics of the ALL of the knee, this review, will summarizes the present literature related to various aspects of the ALL, especially the biomechanical ALL function with attention to its role in the knee joint stability.
Methods: An online search was performed for human literatures that reported role of the ALL in the stability of the knee joint. The electronic databases PUBMED, MEDLINE, and EMBASE were searched up to September 2020. Inclusion criteria included English language, human corpse study, and biomechanical or biomechanical studies of ALL knee function.
Results: The ALL was first described by French surgeon Paul Segond, in 1879. This "some years later" described structure was called the "anterolateral ligament" in 2007, by Vieira et al. Several studies suggest that the ALL passively, is important for stability of the knee. Briefly, the ALL is a capsular ligament located in the anterior part of the knee, in the deepest layer of lateral structures. Biomechanical reports have indicated that the ALL contributes to the overall rotational stability of the knee. Overall, biomechanical data are required in several aspects of anterior reconstruction, including insertion, fixed angle, and initial graft tension. It has been demonstrated that ALL mainly acts as an additional rotational stabilizer of the knee. In other words, it mainly controls internal tibial rotation, so is involved in the pivot shift phenomenon mechanism.
Conclusion: This fact that Segond fractures are linked to ACL tears is an indication of a knee-stabilizing performance of ALL. Biomechanical researchers suggest that ALL reconstruction may plays an important role in knee stability; thus it is essential for surgeons to understand the structure and function of this ligament.

Keywords: Anterolateral ligament, Knee joint, Stability.

Resumen

Antecedentes: Se ha demostrado que el ligamento anterolateral (LLA) desempeña un papel importante en la estabilidad de la articulación de la rodilla. Sin embargo, debido a la escasez de literatura actual sobre la biomecánica nativa del LLA de la rodilla, esta revisión, resumirá la literatura actual relacionada con varios aspectos del LLA, especialmente la función biomecánica del LLA con atención a su papel en la estabilidad de la articulación de la rodilla.
Métodos: Se realizó una búsqueda en línea de literatura humana que informara sobre el papel del LLA en la estabilidad de la articulación de la rodilla. Se realizaron búsquedas en las bases de datos electrónicas PUBMED, MEDLINE y EMBASE hasta septiembre de 2020. Los criterios de inclusión incluyeron el idioma inglés, el estudio de cadáveres humanos y los estudios biomecánicos o de la función de la rodilla del LLA.
Resultados: La LLA fue descrita por primera vez por el cirujano francés Paul Segond, en 1879. Esta estructura descrita "algunos años más tarde" fue denominada "ligamento anterolateral" en 2007, por Vieira et al. Varios estudios sugieren que el LLA, de forma pasiva, es importante para la estabilidad de la rodilla. Brevemente, el LLA es un ligamento capsular situado en la parte anterior de la rodilla, en la capa más profunda de las estructuras laterales. Los informes biomecánicos han indicado que el LLA contribuye a la estabilidad rotacional general de la rodilla. En general, se necesitan datos biomecánicos en varios aspectos de la reconstrucción anterior, como la inserción, el ángulo fijo y la tensión inicial del injerto. Se ha demostrado que la LLA actúa principalmente como un estabilizador rotacional adicional de la rodilla. En otras palabras, controla principalmente la rotación interna de la tibia, por lo que participa en el mecanismo del fenómeno de desplazamiento del pivote.
Conclusión: El hecho de que las fracturas de Segond estén vinculadas a las roturas del LCA es un indicio de la actuación estabilizadora de la rodilla de la LLA. Los investigadores biomecánicos sugieren que la reconstrucción del LLA puede desempeñar un papel importante en la estabilidad de la rodilla; por lo tanto, es esencial que los cirujanos comprendan la estructura y la función de este ligamento.

Palabras clave: Ligamento anterolateral, Articulación de la rodilla, Estabilidad.

Introduction

Knee joint stability is warranted by a several factors such as interaction of ligaments and muscles[1]. Anterior cruciate ligament, posterior cruciate ligament, medial and lateral collateral ligaments play the main role as passive stabilizers. Studies report that the anterolateral ligament (ALL) also passively, is important for stability of knee. The ALL was first described by French surgeon Paul Segond, in 1879[2], but, this forgotten again, and its role was recognized only some years ago. However, Segond described it as "a resistant, pearly, fibrous band, which, in an exaggeration of internal rotational movement, is always subjected to an extreme degree of tension" as well as a remarkably constant avulsion fracture pattern at anterolateral proximal tibial plateau that now called and referred to "Segond's fracture"[2,3]. Segond's fracture defined as an ALL avulsion those results in a bone fragment of the lateral proximal tibial plateau. This "some years later" described structure was called the "anterolateral ligament" in 2007, by Vieira et al.[4]. This topic has been the subject of many recent studies although it is still highly disputed with each other in the it's anatomic[5,6]. Claes et al.[5] published their descriptive anatomical results with reference to this structure as an important stabilizer of knee rotation, followed by various other studies on the detailed anatomy, epidemiology, biomechanics and clinical relevance of ALL[7-10]. Nowadays, it has been reported that the ALL is an anterior knee joint stabilizer that works to prevent anterolateral subluxation and anterior subluxation at certain flexion angles in the knee[11].

In spite recent improvements in surgical techniques and understanding of ACL anatomy, however, it has been proposed that the knee normal rotational stability is not fully restored by methods of reconstructive for ACL tears[12,13]. Because of the fact that there is a pathognomonic radiological sign for ACL injuries, on the other hand according to Mohtadi et al.[14] who, suggested an incidence of pivot shifts after reconstruction of ACL with either hamstring (single- and double-bundle) or patellar tendon graft, this high incidence of postoperative rotational instabilities was considered to investigate. Therefore, due to mentioned abnormal biomechanics, in the past few years, surgeons have more focus on anterolateral structures, so that the ALL of the knee has been investigated with regard to its anatomy and biomechanics[5,15,16]. Although several studies have been reported that the ALL is an important anterolateral stabilizer of the knee joint which prevents anterolateral and anterior subluxation at certain flexion angles in the knee, however, some concepts regarding the biomechanical function of the ALL are controversial, which is due to the variability in anatomic descriptions and methodology in biomechanical testing[15,17,18]. Considering the paucity of current literature on the native biomechanics of the ALL of the knee, this review, with this hypothesis that the ALL contributes to the stability of the knee and it can be clearly identified by anatomic dissection, will summarizes the present literature related to history of the ALL, its anatomic variances, imaging modalities, arthroscopic aspects and techniques for a possible anterolateral stabilization of the knee joint, and it tries to provide a review of the biomechanical ALL function with attention to relevant diagnostic and therapeutic strategies, especially its role in the knee joint stability.

Literature search

We conducted a comprehensive review of the English-language literature involved the role of the ALL in the knee joint stability. The electronic databases PUBMED, MEDLINE, and EMBASE were searched up to September 2020. Reference lists of published papers were then also hand-searched in an attempt to identify further studies. The following search protocol was used: anterolateral ligament, anterior lateral ligament, ALL, Segond fracture, biomechanical study, biomechanical function, history of ALL, imaging modalities, ALL reconstruction and knee joint stabilization. The search terms were then entered onto Google Scholar, to ensure that articles were not missed. Inclusion criteria included English, human corpse study, and biomechanical or biomechanical studies of ALL knee function. Papers were excluded if they were case reports or had a patient cohort, were not written in English, lacked documentation, non-human studies, narrative reviews, studies without clinical outcomes data, systematic reviews that did not pool data or perform a meta-analysis, and technique articles without outcomes. We then obtained full manuscripts for those studies that met the inclusion criteria.

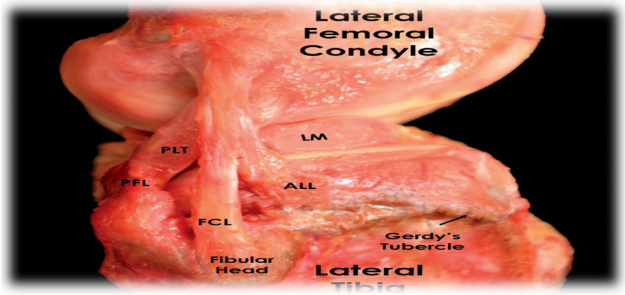
Anatomy of the ALL and historical aspects

The ALL was mentioned as a "pearly, resistant, fibrous band" for First time by Segond in 1879[2]. Then, Last in 1948[19] named this structure as short lateral ligament (SLL). Since the 1970s, the anatomic structure known as the ALL nowadays has been described various times in anatomic dissection studies[1]. Although, Johnson coined the term lateral capsular ligament[20], however, the term mid-third lateral capsular ligament, was first introduced by Hughston in 1976[21]. Fulkerson and Gosling, in 1980 while trying to describe the structures of the lateral retinaculum of the knee, noted an anterior slip of the lateral capsular ligament[22]. In 1986, Terry et al.[23] recognized the structure as being a capsulo-osseous layer of the iliotibial tract, which called it 'some sort of anterolateral ligament' meaning a combination of superficial and deep part of the iliotibial tract. The structure anterior oblique band named by Irvine et al.[24], in 1987 and it as well as correlated Segond's fracture to it. Then, Vieira et al.[4], in 2007 used the term "anterolateral ligament" (ALL) of

the knee and described the structure as being part of the iliotibial tract. Vincent et al.[25], in 2012, performed complete knee arthroplasty, citing ALL as a compatible structure attached to the lateral condyle of the femur, lateral meniscus, and lateral tibia. Claes et al.[5], in 2013, presented more detailed anatomical description[5,26].

There are several reports on investigating the extraarticular ligamentous structures in and around the knee. Although the ALL has been studied in a numerous researches, however, consensus regarding the exact structure of this ligament remains unclear[5,27,28]. It has characteristic ligament pattern of dense and well-organized collagen fibers and peripheral nerve structure with mechanoreceptors[7,25,29]. As can be seen in **figure 1** the proximal origin is close to the lateral epicondyle of the femur[27,30,31]. Tibial attachment is approximately 24.7 mm posterior to the center of Gerdy's tubercle and about 26.1 mm anterior to the fibula head[32]. The exact femoral origin is controversial, already reported as anterior-distal or posterior-proximal to the lateral collateral ligament, with blending fibers between these ligaments[5,7]. The current finding based on recent cadaveric dissection study is that the origin is located posterior and proximal to the lateral collateral ligament[10].

Figure 1: Anatomy of the anterolateral ligament adapted from Kraeutler et al.[32].



Fibular collateral ligament (FCL); Lateral meniscus (LM); Popliteo-fibular ligament (PFL); Popliteus tendon (PLT)

Imaging

Several studies reported that magnetic resonance imaging (MRI) and ultrasound were able to identify the structure of ALL[33,34]. Previous studies have demonstrated the identification of the ALL with ultrasound as a hyperechogenic and fibrillar structure, with a 97 to 100% detection rate[35-37]. The structure can be identified in MRI as a thin, linear, regular and low-signal band[38,39]. Meniscal and tibial insertions are the most clearly identified parts, and the femoral attachment, due to partial volume effect near the lateral epicondyle, is related to most MRI variations[7,33,40]. Although MRI evaluation of the ALL is already well described, however, the imaging findings of surgical techniques for the anterolateral complex of the knee have not been described in details by literatures[41-43]. Sonographic visualization of the ALL was first introduced by Cianca et al.[35] and Cavaignac et al.[36] using a GE P6 musculoskeletal ultrasound machine, which used ultrasonography, obtaining an ALL visualization rate of 100%. Recent studies reported that most of the ALL segments could be identified, making ultrasonography a useful examination for diagnosing the injuries of ALL[37]. Also it has been shown an ALL visualization rate of 75%, then observed that ultrasonography was unable to reliably identify the femoral and tibial origins[44]. An arthroscopic technique was described by Zein[45] also by Sonnery-Cottet et al.[46] that identifies the ALL and showed that the meniscotibial insertion of the ALL could be seen and touched with a probe on the lateral meniscus. Rezansoff et al.[47], using fluoroscopy, described the ALL femoral origin as overlying the posterior femoral cortical line, between the Blumensaat line and a line from the posterior condylar articular edge parallel to the Blumensaat line. These methods may be used more to control ALL regeneration during surgery[10,26].

Surgical considerations

Anterolateral extra-articular fixation techniques are much older than our current finding of ALL and its biomechanical function[1]. The finding behind extra-articular anterolateral reconstructions resides on the ALL biomechanics, resisting pivotshift phenomenon in the ACL-deficient knee[48,49]. It is suggested that reconstructions of extra-articular anterolateral performed in a context of ACL reconstruction augmentation procedure improves postoperative clinical result regarding residual pivot-shifting and anterolateral instability[50]. Drews et al.[51] hypothesized that ALL reconstruction resulted in a reduction of internal rotational laxity and to a load sharing with the ACL graft. They also reported that ALL reconstruction leads to an increase in ACL graft tension during continuous passive motion and with additional internal rotation moment. Combined ACL with ALL reconstructions have indicated good results, as measured by objective and subjective scores[52,53]. The results of laboratory study by investigated the effects of combined ACL with ALL reconstruction on rotatory instability of cadaveric knees have demonstrated that the combined procedures improved internal tibial rotation at low flexion angles (0-30°)[54]. Since reconstructions of ALL are majorly conducted combined with ACL reconstruction; therefore, it is suggested to achieve understanding with post-surgical ACL imaging, as it will be, in many cases, analyzed with the extra-articular procedure simultaneously[50]. As a result in those cases an anterolateral rotational stabilization or reconstruction of the ALL in combination with a reconstruction of the ACL should be noted to avoid treatment failures in terms of post-operative rotational stability[1]. There are many known techniques for anterolateral stabilization, which is a stabilizer of the internal tibial rotation or rotational stabilization of the knee joint, that some of them are presented in **table I**.

Table I: Some of the known procedures for anterolateral stabilization of the knee joint (adapted from[1,55]).

Author (s)	Year	Technique	Ref.
Ibrahim et al.	2017	Single bundle- Gracilis	(56)
Mogos et al.	2017	Double bundle-Gracilis	(57)
Sonnery-Cottet et al.	2015	Double bundle-Gracilis	(53)
Claes et al.	2013	Minimally invasive tenodesis with a gracilis graft with anatomical anchor fixation over the lateral femoral epicondyle and the anterolateral proximal tibial plateau.	(5)
Marcacci et al.	2009	Single bundle- semitendinosus tendon and Gracilis	(58)
Zaffagnini et al.	2006	Single bundle- semitendinosus tendon and Gracilis	(59)
Patella et al.	2002	"One-loop plasty": Iliotibial band (ITB) graft looped below the capsule through a femoral tunnel and proximally fixed with a staple and distally in a tibial cortico-cancellous groove.	(60)
Andrews and Sanders	1983	ITB is split into two isometric bundles distally, sutured up against the distal femur and tied medially creating a "neo" Ligament.	(61)
Ellison	1979	Distal ITB transfer	(62)
Losee et al.	1978	"Sling and reef" procedure	(63)
Galway et al.	1972	ITB graft with anchor fixation to the proximal tibia	(64)
Slocum and Larson	1968	Distal flap of the pes anserine conjoined tendons	(65)
Lemaire	1967	ITB is prepared femoral with preservation of the tibial insertion and then shuttled under the FCL and pulled through a lateral femoral tunnel	(66)

Table II: Characteristics of biomechanical, imaging, mixed cadaveric and clinical studies of ALL (adapted from[11,27,73])

Author (s)	Year	Conclusion	Ref.
		Biomechanical	
Drews et al.	2017	ALL does not function under passive motion and with no influence on tibial rotation.	(74)
Inderhaug et al.	2017	Significant increase in anterior tibial translation and internal tibial rotation with additional section of ALL to ACL.	(17)
Bonanzinga et al.	2016	No further increase in anterior tibial translation was found after ALL section. Significant increase of internal tibial rotation at 30° and 90° flexion only after additional ALL sectioning. ACL- and ALL-sectioned knees have significantly more acceleration of pivot shift than that in intact knees.	(15)
Spencer et al.	2015	ALL section had no significant impact on anterior tibial translation in ACL-deficient knees. ALL section had significant impact only on early pivot shift in ACL-deficient knees.	(75)
Parsons et al.	2015	ALL is important stabilizer of internal rotation at flexion angles greater than 35°. The ACL is the primary resister during anterior draw at all flexion angles and during internal rotation at flexion angles less than 35°.	(70)
Monaco et al.	2012	5.5° increase of internal tibial rotation at 30° flexion after additional ALL sectioning. No significant increase of anterior tibial translation after additional ALL sectioning.	(76)
		Imaging	
Gaunder et al.	2018	Patients with ACL injury on MRI do not have a tear of the ALL. The interobserver reliability of surgeons and radiologists is fair. musculoskeletal radiologists have higher intraobserver reliability when looking for an ALL tear.	(77)
Marwan et al	2018	ALL injury is highly prevalent among dislocated knees. Most of the injuries are of a high grade and involve the proximal, suprameniscal fibers of the ligament.	(78)
McDonald et al.	2017	Knees with ALL injuries may be in the "resting pivoted position" in almost 30% of cases, possibly requiring surgical treatment. This, however, needs further assessment because an ALL injury is not an independent predictor of anterior tibial subluxation.	(79)
Hartigan et al.	2016	ALL tears are currently unable to be reliably identified as torn or intact on standard 1.5-T MRI sequences. Proper imaging sequences are of crucial importance to reliably follow these tears to determine their clinical significance.	(80)
		Cadaveric	
Dodds et al.	2014	The ALL may control pivot shift and contribute to rotatory stability and associated with Segond fracture	(8)
Helito et al.	2013	The ALL attaches anteriorly and distally to the LCL. It has 2 distal attachments, one at the lateral meniscus and another between the Gerdy tubercle and the fibular head.	(9)
Vieira et al.	2007	The ALL is a well-defined functional and anatomic structure.	(4)
		Clinical	
Campos et al.	2001	The fibers of the anterior oblique band contribute to the pathogenesis of the Segond fracture and therefore have a stabilizing effect on the knee.	(81)
Irvine et al.	1987	The Segond fracture may occur by avulsion of the anterior oblique band.	(24)
Hughston et al.	1976	Anterolateral rotatory instability is primarily the result of a midthird lateral capsular ligament tear and can be accentuated by an associated ACL tear.	(21)

Stability of the knee joint

Biomechanical researchers suggest that ALL reconstruction may plays an important role in knee stability; thus it is essential for surgeons to understand the structure and function of this ligament. Biomechanical reports have indicated that the ALL contributes to the overall rotational stability of the knee. Overall, biomechanical data are required in several aspects of anterior reconstruction, including insertion, fixed angle, and initial graft tension[53]. It has been demonstrated that ALL mainly acts as an additional rotational stabilizer of the knee. In other words, it mainly controls internal tibial rotation, so is involved in the pivot shift phenomenon mechanism[1]. Primary biomechanical trials found a behavior near to isometricity between 0o to 60o flexion with a tightening of the ALL in internal rotation and relaxation in external rotation of the tibia[8]. Since the ALL length increases with internal tibial rotation, so the ALL is non-isometric, assuming an mean length of 35-40 mm and a thickness of 1-3 mm, and it is under tension during internal tibial rotation at 30° of flexion[10,30]. Dodds et al.[8] noted this stabilizing effect could not be seen in extension though, therefore, speculations about the influence of the ALL on the pivot shift were undertaken, due to its

rotational control. Also, a systematic review indicated a high correlation between clinical results and pivot shift grades[67]. Because of its connecting fibers to the lateral meniscus it was also stated that there may be a stabilizing effect of this structure, which preventing it from posterior dislocation[9,25]. In a biomechanical trial reported that doing an isolated ACL reconstruction could not restore anterior translation stability under a simulated pivot shift in comparison with the intact knee[68]. Additional ALL reconstruction with fixation at 75° and 88 N could decrease anterior tibial translation at all flexion angles[8,26,69-72]. Characteristics of biomechanical, reconstruction, imaging identification, cadaveric, structural and clinical studies of Anterolateral Ligament are summarized in **Table II**.

Conclusion

Several studies show that the ALL passively, is important for knee stability. Briefly, ALL is a capsular ligament located in the anterior part of the knee, in the deepest layer of lateral structures. Biomechanical reports have indicated that the ALL contributes to the overall rotational stability of the knee. Overall, biomechanical data are required in several aspects of anterior reconstruction, including insertion, fixed angle, and initial graft tension. It has been demonstrated that ALL mainly acts as an additional rotational stabilizer of the knee. In other words, it mainly controls internal tibial rotation, so is involved in the pivot shift phenomenon mechanism. Biomechanical researchers suggest that ALL reconstruction may plays an important role in stability of the knee; thus it is necessary for surgeons to understand the structure and function of this ligament.

Conflict of interests

The authors have no conflict of interest.

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ARTÍCULO ESPECIAL

Leyendas y documentos sobre la vía del contagio en la epidemia de peste del levante mallorquín en 1820

Legends and documents on the way of the contagion in the epidemic of plague of the majorcan east in 1820

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Resumen

En 1820 se produjo una epidemia de peste en la zona del Levante mallorquín, que causó una destacada mortalidad y un destacado impacto en la demografía de la zona. El modo como se introdujo la enfermedad y la vía del contagio fueron objeto de una especial atención por parte de los médicos que la enfrentaron y de los que le dedicaron posteriormente su atención. Esta cuestión fue objeto asimismo de una descripción literaria imaginativa y alejada de la realidad, que paradójicamente fue la que conoció mejor fortuna y dio lugar a la leyenda que actualmente viene siendo admitida como veraz. La recuperación de un oficio de la Junta Superior de Sanidad local, que explica un posible camino por el cual pudo producirse la transmisión de la enfermedad, permite contrastar la presumible realidad con las hipotéticas opciones mencionadas. La información contenida en dicho escrito ha sido desconocida por los autores que abordaron el estudio de dicha epidemia y por la historiografía posterior, aunque ese camino ha sido señalado como una vía previsible por algunos autores. El artículo recupera esa información e intenta poner de manifiesto cual parece haber sido la verdadera vía de la transmisión de la enfermedad en la epidemia de peste mencionada.

Palabras clave: Peste, contagio, contrabando, Mallorca, 1820, Levante, Artà, Son Servera, Capdepera, Sant Llorenç.

Summary

In 1820, a plague epidemic broke out in the East of the island of Majorca, and caused great mortality and impact on the demography of the area. The way the disease entered the island and the way of contagion were studied intensely by the physicians who had to face it, and also by those who studied it later. This issue was also the object of imaginative literary description far from reality, and gave rise to the legend that, paradoxically, is very much accepted as a true story nowadays. The finding of an official document by the local *Junta Superior de Sanidad* explaining how the way for the contagion really came to be, allows us to compare the already mentioned hypothetic alternatives. The contents of that document have been unknown by the authors who dealt with the study of the epidemic, as well as by the later historiography, although this way has been mentioned as forseeable by some authors. This paper revives that information, and tries to reveal which could have been the true transmission path of the disease.

Keywords: Plague, contagion, smuggling, Majorca, 1820, East, Artà, Son Servera, Capdepera, Sant Llorenç.

El impacto en 1820 de la llamada Peste del Levante sobre la estructura social de Mallorca resultó decididamente importante, a pesar de que sus devastadores efectos directos consiguieron limitarse a nuestra comarca levantina. La vía de introducción de la enfermedad, como en tantas otras ocasiones en que las enfermedades de tipo epidémico causaron graves mortalidades, fue una de las cuestiones a las que más atención se prestó. Establecerla con certeza era imprescindible para poder adoptar medidas preventivas y coercitivas, a fin de evitar que en un futuro se produjera de nuevo un contagio similar. A pesar de ello, la memoria colectiva de esta cuestión derivó más en leyenda que del verdadero recuerdo de lo que ocurrió.

Intentaremos establecer los comienzos de esa confusión y las posibilidades de su certeza, contrastándola con lo aportado por la documentación coetánea y posterior.

La leyenda

Actualmente la leyenda que relata el hecho se centra en atribuir la penetración y difusión de la epidemia a través de un joven pastor, de nombre desconocido o ignorado. Este personaje sospechosamente anónimo, habría recogido un capote abandonado sobre una tumba donde habría sido sepultado el cadáver de un sujeto fallecido a causa de la peste, sin conocimiento ni autorización de las autoridades locales. Este supuesto apestado, hipotético punto de partida de la epidemia, habría sido desembarcado de un barco sin nombre identificado, al que se atribuye proceder de Tánger. La nave estaría supuestamente en tránsito y se habría detenido, sin otra causa que la del hipotético entierro, en las proximidades de la costa de Son Servera, concretamente en las proximidades de la *caseta d'en Bastó*. El desembarco y sepultura, para lo

cual la nave en cuestión debería haberse detenido a una distancia y durante un tiempo suficientes como para ser advertido desde la costa sin dificultad, habrían pasado desapercibidos para todo el mundo. Excepto para el pastor mencionado, casual y oportunamente oculto. Una vez finalizada la tarea fúnebre se habría apropiado del capote que había envuelto al cadáver, dejado por los enterradores sobre la tumba. Esta prenda sería la transmisora de la enfermedad, cuyo contagio se habría extendido a cuantos tuvo ocasión de contactar.

La hipotética narración parece tener un objetivo indudable: exculpar a todo el mundo. Desde la población local a las autoridades de todo nivel, por permitir, o por lo menos no impedir con suficiente eficacia, la introducción de la epidemia y su difusión. El análisis de la misma, aunque sea excluyendo las pruebas históricas y solo desde un punto de vista meramente lógico y razonable, no le asigna crédito alguno. En primer lugar extraña el anonimato del personaje o cualquier circunstancia que proporcione algún indicio sobre el mismo, a pesar del impacto atribuido a su acción. Otro aspecto del mismo orden es el desembarco para su entierro de un tripulante o viajero de un barco, navegando casual o intencionadamente por las proximidades de la costa. Es bien sabido que por entonces los fallecidos a bordo de cualquier navío recibían su inmediata sepultura en el mar. Un tercero es el abandono de un capote de presumible calidad sobre la tumba, tras haber servido supuestamente de mortaja o para transportar el cadáver apestado. Tanto si era su mortaja, como si había servido de cobertura mortuoria temporal, lo normal y lógico es que el fallecido hubiera sido enterrado envuelto o cubierto con él y no dejado o abandonado sobre la fosa.

Contrastando con estas noticias, conocemos diversas informaciones que proporcionan una perspectiva claramente distinta, que revisamos seguidamente.

Informaciones en la documentación de la época

La abundante documentación coetánea sobre el suceso no aporta indicación alguna, ni atisbos de confirmación del relato. No se da cuenta alguna, ni se menciona la existencia de la ubicación de la tumba del supuesto fallecido y enterrado en la costa serverina. Tampoco aparece en el listado de fallecidos ningún sujeto de características atribuibles al pastor entre las primeras defunciones. Éste extremo sería discutible, si no fuera porque conocemos puntualmente los nombres y domicilio de los dos primeros fallecidos en Son Servera, si bien ignoramos sus profesiones respectivas[1]. Se sabe también el de la presumible primera fallecida a causa de la peste en Artà y la probable procedencia de su contagio en Son Servera, así como la transmisión a un segundo fallecido[2].

Los escritos coetáneos e inmediatamente posteriores sobre la epidemia proporcionan, en cambio, una visión con muchos más visos de certeza de la vía por la cual penetró la enfermedad. Permiten, además, situar la creación y el comienzo de esa leyenda que hizo fortuna en el imaginario colectivo y consiguió explicar y simbolizar la creencia de un comienzo poco menos que casual, pero fruto de la ignorancia y la codicia.

Buen número de los que relatan detalles de ese comienzo con más o menos coherencia son médicos. Su interés se centra en intentar fijar el individuo que inicia la epidemia, el enfermo 0 que diríamos actualmente, en las descripciones epidemiológicas que redactan sobre ella. Es una información básica para identificar la puerta de entrada de la enfermedad, con vistas a controlarla mejor y más eficazmente en un futuro.

El médico Juan Lliteras, que afrontó la epidemia desde el primer momento y cuya opinión desde sus comienzos fue que se trataba de la peste, evita deliberadamente fijar cuando y donde se produce el contagio inicial[3]. Uno de los primeros que empieza a forjar el relato es el médico Mariano Morey[4], que algo más de veinte años después (1843) describe la posible vía de entrada en un escrito de carácter académico. Dice textualmente:

> No admite duda de que a principios de mayo de 1820 ancló en la Playa del pueblo de Son Servera de esta isla un buque procedente de Tánger; que su tripulación introdujo clandestinamente varios géneros susceptibles de anidar el germen contagioso que entre ellos, según noticias positivas que pude indagar durante mi mandato en aquel punto, se verificó éste desgraciado hecho en la casa de Juan Servera y Francisca Brunet, consortes y moradores en la calle Nueva de dicho pueblo en la que desde el 9 de mayo hasta el 15 del mismo mes perecieron estos, su único hijo y un vecino que unido con dicho Servera pasaron a bordo de aquel buque donde compraron un capote superior de lana[5]…

Este autor fija ya la procedencia tangerina del buque que transportó la peste, la transmisión de la misma a través de objetos desembarcados de contrabando y el fallecimiento de los primeros contagiados de los que proporciona nombres y domicilio. En este escrito es donde aparece por primera vez *un capote superior de lana* como elemento fundamental de la transmisión. Mucho más escueto es el también médico Fernado Weyler y Laviña que treinta y cuatro años más tarde se limita a señalar su importación por vía marítima, sin aportar más detalles ni información[6].

El médico Jaime Escalas y Adrover, en su preceptivo «Discurso» anual ante la Real Academia de Medicina y Cirugía de Mallorca, pronunciado en 1880, recogía las

noticias existentes hasta el momento. Se basa, sobre todo, en lo dicho por su colega Mariano Morey, ampliando sus explicaciones sobre la expansión de la enfermedad y sus observaciones médicas:

> A principios de mayo de 1820 fondeó en la playa de Son Servera, procedente de Tánjer, un buque apestado; allí se echaron a tierra ocultamente efectos que anidaban el pestilente germen y muy pronto se declaró el contajio en la calle nueva del referido pueblo en casa de los consortes Juan Servera y Francisca Brunet, quedando dicha mujer invadida el cinco del citado mes y falleciendo el siete del mismo. Desde este día al quince murieron su esposo, su hijo y un vecino que con el desgraciado Servera pasó a bordo de aquella embarcación a comprar un capote de lana. El roce continuo que tuvieron con los enfermos sus parientes y amigos, y el acompañamiento de los cadáveres hasta haberles dado sepultura, dio lugar a que la enfermedad se propagara con pasmosa rapidez, en términos que el veinte y uno se llamaron algunos facultativos de Artà quienes en unión de los del pueblo, calificaron las dolencias de malignas sin carácter peligroso de contajio[7].

El principal autor de lo que llegará a ser la leyenda sobre la penetración del contagio es Pere d'Alcàntara Penya i Nicolau (1803-1906). Este polígrafo describió el comienzo de la peste de 1820, al publicar un listado de las distintas epidemias que habían afectado Mallorca. Su relación, hecha a modo de un artículo divulgativo, se publicó en un semanario de la prensa local (1885) firmado con su seudónimo de Pep d'Aubenya. La mención de lo ocurrido en 1820 es hecha en estos términos:

> L'any 1820 un pastó de Son Servera, per aprofitá un capot de grego qu´una barca que passava havia deixat en terra, escampà per dins aquella comarca sa Pèste de bubó, essent ell mateix sa primera víctima. Aquesta epidèmia que no sortí de Son Servera y Artá va fé en pochs mesos multitud de morts[8]...

Aquí aparece convenientemente adornada la historia del capote abandonado, fómite esencial para la transmisión de la enfermedad.

Otro de los autores que dan crédito a esta historia del suceso, es el médico Pedro Servera Nebot, autor de un estudio sobre esa epidemia (1932). Explica el episodio del capote que envolvía un cadáver, supuestamente fallecido de peste y enterrado en la playa, sobre cuya tumba fue abandonado y recogido por el joven porquerizo. Repite que el fallecido habría sido desembarcado de un barco procedente de Tànger y fondeado frente a Son Servera. Compara esta versión con la más probable de haberse producido el contagio a través de un desembarco clandestino de trigo, en el cual habrían intervenido como obreros de descarga Juan Servera, marido de Francisca Brunet, primera víctima identificada de la peste y Pedro Morey, los cuales *adquirieron u obtuvieron en pago un capote del barco fondeado*[9].

Esta última versión parece la más creíble y coherente, pero la realidad habría sido otra notablemente distinta aunque con ciertos paralelismos. Una notificación remitida a la Junta Superior de Sanidad el 18 setiembre de 1820 por el *Dr. en medicina D. Buenaventura Casals, inspector del expurgo de la villa de Arta*, hace saber que

> El Sr. D. Pascual Saco[10] ha descubierto y sorprendido un contrabando de ropas que a primeros de mayo el hermano del molinero de Amunt había comprado de un barco, que también trajo sal, y la vendió en estas costas. Dicho paisano y su hija murieron con el bubón a principios de junio, y el molinero tuvo uno [bubón] en el sobaco en aquella época. Las ropas serán quemadas esta tarde en el campamento de las Paisas [Ses Païsses] a presencia de una diputación del Ayuntamiento y Junta de Sanidad, del Sr. Comandante auxiliar de la fuerza armada de este punto, y mía.

El autor de la comunicación referida es Bonaventura Casals i d'Echauz (Barcelona, 1791-1864) miembro de una larga y antigua familia de médicos. Era nieto del médico de la Barceloneta Bonaventura Casals Oriol, hijo y sobrino, respectivamente, del *cirurgià* de Barcelona Bonaventura Casals Anglí[11] y del cirurgià militar de Infantería Manuel Casals i Anglí, con los cuales no debe ser confundido. Realizó sus estudios en Barcelona, graduándose como bachiller en Medicina en 1808, pero no los finalizó hasta 1816. En 1814, cursaba estudios en la Escola de Física Experimental de Barcelona y en 1817 era socio residente de la Acadèmia Mèdico Pràctica de Barcelona, institución de la cual su padre había sido uno de sus fundadores. En 1819 ganó por oposición la plaza de *metge de casa* del Hospital de la Santa Creu de Barcelona[12]. El año siguiente fue nombrado vocal de la *Junta de Sanitat del Principat de Catalunya i de les Illes Balears*[13]. A raíz de este último cargo, cuando se produjo la epidemia en Mallorca, se ofreció para acudir a prestar sus servicios en Mallorca voluntariamente[14].

El oficio hace notar que *Esta es la única noticia oficial que hasta ahora ha tenido la Junta Superior de Sanidad sobre introducción de contrabando en el país contagiado*. Es también la que cuenta con más visos de certeza. Primero por proceder de uno de los encargados de vigilar el cumplimiento de la normativa de seguridad del recinto acordonado durante la fase álgida de la epidemia. Además es refrendada por el Inspector del expurgo de Artà. Aparte del fallecimiento del contraventor y su hija, el indicio que proporciona acerca de un bubón en el sobaco del molinero, resulta un detalle significativo. Los

ganglios linfáticos de la axila son uno de los lugares más frecuentes y típicos de presentación de estas lesiones. Las picaduras más corrientes de las pulgas transmisoras de la peste eran frecuentes en manos y brazos de los contagiados, los cuales tenían su filtro linfático principal en la zona subaxilar.

La noticia fue oportunamente publicada en el *Diario Constitucional*, al cual la remitió el secretario de la Junta Superior de Sanidad isleña. En apariencia fue deliberadamente omitida o acaso ignorada, por la historiografía al uso. Sería, en cambio, recogida y reproducida por el benemérito José Llabrés, destacado recopilador de noticias sobre el siglo XIX mallorquín de quién procede la información expuesta más arriba[15].

A pesar de ser una versión oficializada del acontecimiento y con más visos de certeza que las restantes, Mascaró Pasarius (1962) la relegó también al comentar la epidemia que nos ocupa. Su descripción de Son Servera en el *Corpus de Toponimia de Mallorca*, aporta el detalle de que el barco procedente de Tànger de donde desembarcaron al fallecido había anclado cerca de cierta caseta llamada *d'es Bastó*. Cuenta una vez más la historia del enterramiento de un supuesto apestado y el abandono de una manta portadora de la enfermedad y su recogida por el consabido guardián de ganado. Valora como alternativa más probable la del desembarco de un alijo de trigo de contrabando y que sus autores fueran los primeros fallecidos. No obstante señala que el primer fallecimiento causado por la peste fue el del hipotético y anónimo pastor, que curiosamente residía en la calle Nueva de Son Servera. Esto permitiría aventurar que el desconocido y anónimo pastor o porquero podría ser el mismo que Juan Servera, marido de Francisca Brunet a quién suele atribuirse haber sido la primera víctima fallecida en esta epidemia, aunque en su momento se desconociese la causa de su muerte[16]. Tal vez fuera también la misma persona que hemos visto citada como el hermano del molinero de Amunt, contrabandista de ropas y fallecido a causa de la peste junto con su hija.

Conclusiones

El conjunto de textos sobre la llegada de la peste, coincide en determinar su llegada a través de un buque contagiado, de procedencia supuesta e hipotéticamente tangerina. Este origen es recogido y repetido desde el primer momento, contando con la aquiescencia de todos los autores. Desde ese navío se habrían introducido de contrabando, o de alguna otra manera fraudulenta, ropas, trigo u otros bienes que serían los vehiculadores de los vectores de la peste. La documentación de la época confirma esta opción, apuntada ya por Picazo Muntaner (1990 y 1991) y más recientemente por Salas-Vives y Pujadas-Mora (2020)[17]. A partir de aquí derivan dos posibles opciones. Una es más que dudosa e imaginaria, sin fundamento documental alguno, mientras que la otra resulta más plausible y viene acreditada por la documentación oficial coetánea.

La primera narra el desembarco de un cadáver apestado para enterrarlo en la playa, sobre cuya fosa se abandona u olvida una manta o un capote. Este objeto, bien sea olvidado o abandonado sobre la playa, obsequiado, adquirido directamente o parte del salario por descargar mercancías de contrabando, es siempre identificado como el indudable transmisor del contagio. La infección transmitida principalmente mediante prendas o tejidos, era una de las vías entonces admitidas para justificar una transmisión loimológica. Desde tiempos medievales tanto ropas como telas eran consideradas eficaces y temidas transportadoras de la peste[18]. La atribución era razonablemente verídica, aunque por razones entonces ignoradas. En realidad los tejidos y telas permitían una cómoda y duradera instalación de las pulgas, transmisoras necesarias de la peste, aunque entonces se desconociese su papel en ese proceso.

La segunda opción es que de forma simultánea, paralela o alternativa, hubiese desembarcos ilegales de ropas, trigo o sal, no sometidos al supuestamente necesario control y rigor cuarentenario. En sus descargas e introducción en la isla, habrían intervenido bien dos hombres de la localidad serverina o según parece el hermano del molinero del aún existente *Molí d'Amunt*. Cualquiera que fuese el contagiado, o todos ellos, podrían haber contraído la peste sin duda en el curso de dicha tarea o con posterioridad por el contacto con las pulgas vehiculadas por el producto introducido.

En ambos casos transmitieron la infección al resto de miembros de su familia y probablemente luego a otra gente. La documentación coetánea confirma que en el primer caso uno de los dos hombres que intervinieron en la descarga de las mercancías, la transmitió a su hijo y esposa. La muerte de ésta, inicialmente atribuida a causa no identificada, viene siendo considerada la primera de la epidemia. La seguirían su marido, el hijo de ambos y el otro colaborador en la descarga de cualquiera que fuese el género introducido de manera ilegal[19]. A este punto de partida de la epidemia hay que añadir la vía identificada por la documentación coetánea, que señala una trayectoria y motivación similar. Se habría contagiado el introductor de las ropas y su hija, falleciendo ambos, no sin transmitir la enfermedad antes a su hermano, del cual sabemos que padeció, con certeza, la peste, de la cual pudo ser un eficiente transmisor.

El contagio procedería, como siempre ocurre en una isla donde no es un endemismo, del exterior. En éste caso, llegado por vía marítima e importado por personas más o menos conscientes de la contagiosidad y elevado riesgo de morbimortalidad de la patología que arriesgaban transmitir. El contacto entre esas personas y los primeros infectados

por la enfermedad estuvo, como suele estarlo habitualmente en otros casos similares, determinado por intercambios comerciales. A menudo estos suelen llevarse a término de manera fraudulenta en buena parte de los casos de transmisión de enfermedades. El motivo de la introducción suele responder a la búsqueda de beneficio a través de los bienes que intercambian con los ocasionales visitantes.

Conflicto de interés

Los investigadores declaran no tener conflicto de interés.

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2. Andreu Ferrer (1920) «Peste llevantina. De com vengué a Artà», *Llevant*, Artà, 15 de maig, Any IV, nº 91 pág. 5: «una dona ja vella el dia 26 de Maig del dit any vengué d'aquell poble [Son Servera] perque se sentia malalta. Arribà a l'horabaixa i morí aquell mateix vespre. La tradició confirma tal noticia i diu que era sa *Mestra Bidigus*, dona d'edat natural d'Artà que s'ocupava en l'ensenyansa de nines de Son Servcra i que tenguent la casa pairal an el carre del Castellet d'Artà, vengué aquí essent la primera víctima de la pesta... El primer que d'ella la prengué fou el cabo dels milicians d'Artà en Miquel Ferrer que morí l'ondemà en el carre de la Puresa».

3. Juan Lliteras (1821) pág. 5: «no entraré en examen alguno sobre la naturaleza del mal, ni de su causa…»

4. Mariano Morey Roselló era natural de Palma e hijo del cirujano Cristóbal Morey. Realizó su formación como médico en la Facultad de Medicina de Mallorca entre 1810 y 1812. En ese último año se alistó en el ejército, completando su año de «Práctica» en 1813. Participó en la Guerra de Catalunya encuadrado en la División mallorquina de Wittingham. Se examinó en el Colegio de Cirugía de Barcelona para seguir la profesión de su padre, titulándose cirujano (1814) y en la Facultad de Medicina de la Universidad de Zaragoza como Bachiller en Medicina (1815). Se doctoró en ambas disciplinas en Palma (1817), apadrinado en el de Medicina por el Dr. Miquel Pascual. Además de atender enfermos en la peste de 1820, hizo otro tanto con los de la epidemia de fiebre amarilla (1821), así como en 1834 con los internados en el Lazareto de Cabrera a causa del cólera morbo que se declaró en Mahón. Falleció en Palma, el 24 de junio de 1853, a los 60 años. Entre sus escritos cabe destacar: *Observaciones médico-sanitarias en contestación al no contagio de la peste bubónica que pretende introducir el Dr. Aubert, profesor de Medicina en París*, Imprenta de Pedro José Umbert, Palma, 1843, donde aporta interesantes datos sobre ésta epidemia.

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10. Pascual Saco, junto a Antonio Canela, fueron dos oficiales del ejército que se presentaron voluntarios para acudir a la zona de la epidemia con un contingente de diez presidiarios bajo su mando respectivo. Se responsabilizaron de mantener el orden público *manu militari* en el interior de la comarca infectada. Los presidiarios seleccionados para redimir sus condenas con este cometido, también realizaron otras tareas necesarias para controlar la epidemia que la gente de la zona rechazaba realizar. Por ejemplo la de sepultar a los fallecidos, por el riesgo de contagio que esa actividad u otras parecidas conllevaban a quienes debían acometerlas. Los cuatro primeros sepultureros contratados en Artà fallecieron a los pocos días y de todos los que se dedicaron a esta tarea solo dos sobrevivieron.

11. Bonaventura Casals i Anglí (n. Llers, Baix Empordà) era hijo y nieto de médicos de l'Empordà, con ejercicios en Figueres i Llers. Formado como médico en Huesca, obtuvo los grados de Bachiller en 1765, licenciado en 1767 i doctor en 1769. Fue uno de los fundadores de la Acadèmia Mèdico Pràctica de Barcelona (02-06-1770) de la cual fue Tresorer en 1804 y Vice-President desde el 17.11.1806 hasta 1809.

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18. La Morberia, institución sanitaria de Mallorca encargada de controlar la sanidad exterior desde la Edad Media, incluía en su legislación un largo apartado expresamente dedicado a controlar este material. En el *Capitol* XVI de su reglamento de 1475, se hace constar que *segons la experientia les robes e molts altres utensilis sien medi de molta contagio de peste. Per ço, per squivar de tot perill, es statuit, provehit e ordinat circa les vendicions e distractions de robas en aquesta forma, ço es que qualsevol corredor o altre qualsevol persone si es vol sia venadora de la sua propia roba o si es vol sia migana persona no gos ni presumesca, publicament o amagada, vendre, donar o en altre manera de hun a altre transportar qualsevol specia de robes axi de lit com de vestir*. Antonio Contreras Mas (1977) «Legislación frente a la peste en Mallorca Bajomedieval» *Medicina & historia*, núm. 74 págs. 7-25.

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SPECIAL ARTICLE

WHO's call to eradicate cervical cancer: are we doing what we must?

El llamamiento de la OMS para erradicar el cáncer de cuello de útero: ¿estamos haciendo lo que debemos?

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Abstract

Based on the call made by the World Health Organization to achieve the global eradication of cervical cancer, its primary and secondary preventive conditions in application in the Balearic Islands are described and discussed.

Keywords: Cancer, cervix, papilloma, vaccine, screening.

Resumen

A partir del llamamiento realizado por la Organización Mundial de la Salud para conseguir la erradicación mundial del cáncer de cuello de útero, se describen y discuten sus condiciones preventivas primarias y secundarias de aplicación en las Islas Baleares.

Palabras clave: Cáncer, cervix, papiloma, vacuna, *screening*.

In May 2018, the Director General of the World Health Organization (WHO), Tedros A. Ghebreyesus, in an executive agency meeting[1], declared cervical cancer (CC) as the first and only eradicable cancer in our world. He verbatim expressed his desire to assume and fulfil a challenge focused on ensuring that all girls around the world are vaccinated against HPV and that all women over 30 years of age are duly screened for precancerous lesions and, where appropriate, treated.

The deep knowledge of the natural history of CC acquired in recent years, with human papillomavirus infection as the necessary cause of its development[2], associated with the extremely high efficacy and safety of primary preventive procedures –vaccination against HPV[3]–, secondary –population screening with the determination of HPV by a validated technique as an initial test[4]– and tertiary –comfortable, feasible and very effective treatment of pre-cancerous lesions, fully identified[4]– they make it possible. In no other cancer do these three circumstances occur, neither in female breast or colorectal cancer, the other two with preventive population application recommended in Public Health policies, two cancers with highly effective and efficient possibilities of secondary prevention[5,6].

Are we in this line of preventive work in the Balearic Islands? The answer to this question is not as satisfactory as we would like it to be.

In vaccination against HPV, the active recommendation of the Ministry of Health (MH) of the Government of Spain is to "vaccinate girls aged 12-13 years with two doses of the vaccine, with a separation between doses of 5-6 months, depending on the vaccine used; if vaccination is started from the age of 14 or 15, 3 doses will be administered with a schedule of 0, 1-2, 6 months, depending on the vaccine used"[7]. Disregarding the recommendation of the European Center for Diseases Prevention and Control, collected and assumed by the Spanish Pediatric Association[8], the MH does not recommend vaccinating children, as similar Ministries in Austria, Croatia, the Czech Republic, Liechtenstein, Belgium, Germany, United Kingdom, France, Italy and Switzerland have already done. It is to be hoped that Spain will soon join this list of countries in our closest environment, recommending from the MH the vaccination of boys against HPV. The objective is to protect them from other causal HPV cancers –oropharyngeal[9], anal[10]–, drastically correct the high prevalence of HPV in men, which is between 50 and 70%[11] –more or less double than in women[12]– and also cut off the main source of female contagion, given the long-known nature of a sexually transmitted infection of HPV[13].

The latest official Spanish information on HPV vaccination reports that the average coverage for Spain is 79% in the second dose[14], with a range that ranges from 91% reached in La Rioja to 75% in Madrid, an average rate that should

be considered as satisfactory[15], but there is no detail on the coverage obtained in the Balearic Islands, neither in Asturias, the Canary Islands or Catalonia. A recent instruction –November 16, 2020– from the Department of Public Health of the Balearic Government (DPH.BG)[16], introduces vaccination with Gardasil9® to all women over 12 years of age and under 27 who have not been vaccinated at the age marked by the official calendar. This document calls for a recruitment / recommendation effort since the coverage of HPV vaccination is detailed as being significantly lower than that of the rest of vaccines administered at the same ages, a very striking fact given the very consistent evidence regarding the high safety, efficacy, effectiveness and efficiency of this vaccine[17].

How is CC screening being applied in the Balearic Islands? On the Balearic Government website[18] there is an update on the secondary prevention programs for female breast and colorectal cancers, but nothing related to CC, which as of the day of writing this article is still opportunistic and cytological based. In the AFRODITA study[19] it was shown that over 30% of Spanish women do not regularly access secondary prevention of CC –Extremadura, Castilla La Mancha, Cantabria and Andalusia present clearly lower figures and the Balearic Islands are in the average–, which also there is a clear neglect of women over 50 years of age, of low socioeconomic status and living in rural areas, and there is a general tendency to over-control women who consult the National Health System. On the other hand, 60% of incident CC are diagnosed in women with a deficient historical schedule of revisions[20]. These data should definitely invalidate the proposition of opportunistic structures for the screening of CC.

The authors of this work are aware of the work that the Balearic Government is carrying out to adapt the program now in application in the Balearic Islands, opportunistic and based on cytology, to the most current evidence, which on the other hand and is also collected in the decision of recommendations adopted at the meeting of the Interterritorial Health Council dated November 18, 2018[21], in which an executive call is made for secondary CC preventive programs to be redirected to the population base with the determination of HPV practiced using a validated technique[22] as the main and initial screening test. The reason for this change in the review procedure lies in the unequivocal demonstration that regarding the detection of intraepithelial lesions of the cervix, the objective of the screening programs, the negative and positive predictive values of HPV determination are clearly better than those of cytology[23,24], consequently implementing the efficacy, effectiveness and also the efficiency of the program thus executed. Cytology remains an acceptable resource if HPV determination by validated technique is not available.

In short, only with high vaccination coverage against HPV and with the population application of a CC screening program redesigned and well adapted to the most current recommendations, will we be able to attend and be faithful to the call of the WHO and achieve that the next generation of women of our Community are free from the threat of CC. This is our challenge.

Conflict of Interest

JC has received travel and / or research grants and / or conference and / or consulting fees from Genomics, GSK, Merck, Procare Health, Qiagen, Roche, and SPMSD.

AF has received travel and / or research grants and / or conference and / or consultancy fees from Roche.

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ESTUDIO DE CASOS

Síndrome de Cushing secundario a un carcinoma suprarrenal metastásico como causa de hipertensión resistente

Cushing's syndrome secondary to metastatic suprarrenal carcinoma as cause of resistant hypertension

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Resumen

Mujer de 67 años con antecedentes de hipertensión arterial y diabetes mellitus, ingresada en Traumatología por una infección protésica precoz. Se solicitó valoración por Medicina Interna debido a mal control tensional y glucémico asociado a alteración conductual. En la analítica destacaban una alcalosis metabólica, hemoglobina de 10.1 mg/dl con VCM de 101 fl, función renal preservada con hipocaliemia y perfil lipídico sin alteraciones. Se realizó un estudio de hipertensión secundaria, detectando un cortisol urinario elevado (2396.8 ug/24h), con ACTH en plasma normal. Por la sospecha de síndrome de Cushing, se solicitó una TC toraco-abdominal que reveló una gran masa suprarrenal heterogénea sugestiva de neoformación junto con micronódulos pulmonares (sospechosos de M1). La anatomía patológica reveló un carcinoma adrenocortical tipo oncocítico de alto grado. El TC de control a los 3 meses reveló progresión local y metastásica. Finalmente la paciente fue éxitus durante el seguimiento.

Palabras clave: Hipertensión, síndrome de Cushing, neoplasia adrenal.

Abstract

A 67 years old woman with a medical history of hypertension and diabetes mellitus was admitted to the Traumatology ward to treat early prosthetic infection. A consult to Internal Medicine was done due to poor blood pressure and glycaemic control as well as behavioural swings. The blood tests showed metabolic alkalosis, haemoglobin of 10.1 mg/dl with MCV of 101 fl, preserved renal function with hypokalaemia and lipid profile without alterations. Secondary hypertension was screened for, detecting high urinary cortisol (2396.8 ug/24h) with normal serum ACTH. A thoracoabdominal CT scan was asked for, suspecting Cushing syndrome. The CT scan revealed a big heterogenic adrenal mass as well as pulmonary micronodules, that seemed to be compatible with neoplastic origin with metastasis. The anatopathological report disclosed a high nuclear grade oncocytic adrenocortical carcinoma. Control CT scan revealed local and metastatic progression. Finally the patient passed away during the follow-up.

Keywords: Hypertension, Cushing syndrome, adrenal neoplasm.

Caso clínico

Una mujer de 67 años se encontraba ingresada en la planta de traumatología por una infección protésica precoz de una prótesis de fémur. Como antecedentes personales, la paciente era natural de Alemania, vivía sola sin apoyo familiar y negaba consumo de tóxicos. Como antecedentes patológicos presentaba una hipertensión arterial en tratamiento con ramipril, diabetes mellitus tipo II en tratamiento con insulina y una fractura subcapital de cadera derecha en fase de convalecencia que había sido intervenida el mes previo. La paciente no había acudido al centro de salud en los 7 años previos ni a la consulta de control tras la intervención quirúrgica.

Se solicitó valoración por Medicina Interna debido a mal control tensional a pesar de tratamiento con 5 fármacos (enalapril, espironolactona, carvedilol, amlodipino y furosemida) y mal control glucémico. En la exploración inicial se objetivó anasarca, equimosis cutánea y alteración conductual. En la analítica destacaban alcalosis metabólica, hipocaliemia e hipoalbuminemia severa. Ante dichos hallazgos se amplió el estudio con orina de 24 horas incluyendo cortisol y actividad de la renina y aldosterona en plasma para descartar un posible origen secundario de la hipertensión. El cociente aldosterona/renina fue 0.05 (normal hasta 1.2)

Se detectó un cortisol urinario elevado a 2396.8 ug/24h (límite de la normalidad 176 ug/24h), con hormona adrenocorticotropa (ACTH) en plasma normal (19,4 ug/dl). Por la sospecha de síndrome de Cushing, se solicitó una TC toraco-abdominal que reveló una gran masa suprarrenal heterogénea sugestiva de neoformación junto con micronódulos pulmonares (sospechosos de M1). Para completar el estudio se realizó una PET-TC que detectó una M1 hepática. Se solicitaron hormonas sexuales, que mostraron hiperandrogenismo. El caso se orientó como síndrome de Cushing e hiperandrogenismo por probable carcinoma suprarrenal.

Tras los resultados de las pruebas de imagen se inició ketoconazol, con mejoría de la tensión arterial. Se presentó el caso en sesión médico-quirúrgica y se decidió realizar cirugía citorreductora. Se realizó una extracción completa de la masa. El estudio macroscópico objetivó un tumor de 15x14x13.5 cm con extensas áreas de necrosis y hemorragia. El análisis microscópico reveló que se trataba de un carcinoma adrenocortical tipo oncocítico de alto grado que sobrepasaba la cortical glandular, sin invasión linfática, vascular ni perineural.

Tras la intervención, se inició mitotano debido a que se trataba de una neoplasia avanzada y se pautó hidrocortisona como sustitución adrenal. Se solicitó una TC de control a los 3 meses de la cirugía, que reveló incontables nódulos pulmonares bilaterales y múltiples lesiones hepáticas que habían aumentado en tamaño y en número, así como una lesión de aspecto quístico con masas sólidas lobuladas en el lecho quirúrgico en relación con recidiva tumoral. También se solicitaron varios controles de hormonas androgénicas, que persistieron elevadas. Por lo tanto, la paciente presentó una progresión tumoral tanto a nivel radiológico como hormonal. Finalmente, la paciente fue dada de alta a un centro sociosanitario y fue éxitus.

Discusión

La hipertensión resistente se define como aquella superior a 140/90 mmHg a pesar de 3 fármacos (siendo 1 de ellos un diurético). Inicialmente hay que descartar mal cumplimiento terapéutico, una medición incorrecta de la tensión arterial y el efecto de bata blanca[1]. El segundo paso es descartar una hipertensión arterial secundaria, cuyas causas más frecuentes son: apnea obstructiva del sueño, enfermedad renal, estenosis de la arteria renal, hiperaldosteronismo primario, enfermedad tiroidea, síndrome de Cushing, feocromocitoma y coartación de aorta[2].

Debe realizarse una exploración física completa a todos los pacientes, prestando atención a los pulsos y a soplos. Además, es imprescindible un ECG, una radiografía de tórax, una analítica con función renal, ionograma, perfil lipídico, ácido úrico y hormonas tiroideas, un sedimento de orina, el cociente albúmina/creatinina en orina, una ecografía renal y un ecocardiograma. Según los resultados de las pruebas de primera línea y según la sospecha diagnóstica, se realizaran otras pruebas más dirigidas (aldosterona y renina séricas, cortisol en orina, metanefrinas en orina, angioRM renal, estudio del sueño o TC toraco-abdominal)[3].

En nuestro caso la exploración cardiopulmonar y abdominal fueron anodinas y los pulsos estaban presentes y eran simétricos. La paciente pesaba 85 kg y medía 174 cm (IMC 28 kg/m^2). En la analítica destacaban una alcalosis metabólica, hemoglobina de 10.1 mg/dl con volumen corpuscular medio (VCM) de 101 fl, hiperglucemia, función renal preservada con hipocaliemia y perfil lipídico sin alteraciones (TG 76 mg/dl, colesterol total 108 mg/dl, LDL 61 mg/dl, HDL 32 mg/dl). El ECG mostró un bloqueo de rama derecha. No hubo hallazgos significativos en la radiografía de tórax ni en la ecografía renal. En el ecocardiograma se objetivó una función de eyección preservada, disfunción diastólica grado I, hipertrofia concéntrica ligera del ventrículo izquierdo y ausencia de alteraciones en aorta ascendente.

En nuestra paciente se llegó a sospechar una enfermedad renal debido a la anasarca y la hipoalbuminemia, pero la paciente no presentó alteración de la función renal. Se solicitó orina de 24h, que descartó proteinuria en rango nefrótico. La paciente no presentó hematuria ni alteración de la función renal durante el ingreso. En la ecografía renal no se visualizaron alteraciones del parénquima renal.

Dadas la alcalosis metabólica y la hipocaliemia, se sospechó un posible hiperaldosteronismo; sin embargo, los niveles de renina, aldosterona y el cociente entre ambas fueron normales.

La masa suprarrenal también podría orientarse como un feocromocitoma, aunque la paciente no presentaba la clínica típica de crisis paroxísticas de hipertensión arterial, cefalea, palpitaciones, palidez y sudoración. Se solicitaron metanefrinas en orina, que fueron negativas.

La estenosis de la arteria renal se sospecha habitualmente por empeoramiento agudo de la función renal al iniciar IECA, cosa que no sucedió con nuestra paciente. En la TC realizada no se visualizó esta alteración vascular. Otros diagnósticos posibles que se descartaron con las exploraciones complementarias fueron la alteración de las hormonas tiroideas y la coartación de aorta.

El síndrome de apnea obstructiva del sueño es una causa frecuente de hipertensión resistente, pero nuestra paciente no presentaba la clínica típica de ronquidos, apneas, somnolencia diurna y cefalea, por lo que no se solicitó una polisomnografía en el estudio inicial.

En nuestro caso de llegó al diagnóstico de síndrome de Cushing por los niveles elevados de cortisol en orina. El siguiente paso es localizar el origen de la producción de cortisol. La primera causa es la aportación exógena, que quedó excluida porque la paciente se encontraba ingresada. Un adenoma hipofisario productor de ACTH o la producción ectópica de ACTH secundaria a un tumor neuroendocrino se descartaron porque los niveles de ACTH eran normales. Se solicitó una TC toracoabdominal buscando una etiología suprarrenal (adenoma adrenal, carcinoma suprarrenal o hiperplasia suprarrenal bilateral)[5]. La TC mostró la masa suprarrenal sugestiva de neoformación que posteriormente se confirmó con la anatomía patológica de la muestra.

El síndrome de Cushing es una causa infrecuente de hipertensión arterial secundaria, con una prevalencia de 0.5% en pacientes hipertensos. Se sospecha por hábito pícnico, plétora facial, hirsutismo y estrías violáceas. A su vez, el carcinoma suprarrenal también es raro. Según las guías Europeas de carcinoma suprarrenal de 2018, la incidencia de este tipo de tumor es entre 0.7-2 por millón de personas por año. Pueden aparecer a cualquier edad, pero hay un pico de incidencia entre los 40 y 60 años y es más frecuente en mujeres. Habitualmente son esporádicos en adultos, pero también pueden formar parte de síndromes hereditarios (como el síndrome de Lynch). Los carcinomas se pueden presentar como exceso hormonal (50-60%) como en nuestra paciente, por síntomas inespecíficos de masa abdominal (30-40%) o como hallazgo incidental (10-15%). La mediana de supervivencia es de entre 3 y 4 años[5,6].

Conflicto de interés

Los investigadores declaran no tener conflicto de interés.

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ESTUDIO DE CASOS

Tumores carcinoides pulmonares múltiples como primera manifestación de una neoplasia endocrina múltiple tipo 1

Multiple pulmonary carcinoid tumours as the first manifestation of multiple endocrine neoplasia type 1

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Resumen

En las neoplasias endocrinas múltiples (MEN) encontramos tumores que afectan al menos a dos glándulas endocrinas. En este caso clínico se presenta a una mujer caucásica de 38 años con tumores carcinoides de pulmón como primera manifestación clínica de una MEN.

Palabras clave: Neoplasia endocrina multiple, tumor carcinoide, síndrome de Wermer.

Abstract

Multiple endocrine neoplasms (MEN) include tumours affecting at least two endocrine glands. This case report presents a 38-year-old Caucasian woman with carcinoid tumours of the lung as the first clinical manifestation of MEN.

Keywords: Multiple endocrine neoplasia, carcinoid tumor, Wermer syndrome

Introducción

Los síndromes de neoplasias endocrinas múltiples (MEN) se caracterizan por la aparición de tumores que involucran a dos o más glándulas endocrinas en un mismo paciente[1]. La MEN 1 también se conoce como síndrome de Wermer, es un síndrome hereditario autosómico dominante causado por la mutación de un gen supresor situado en el cromosoma 11q13[1-5].

Los tumores carcinoides en el síndrome de MEN1 se localizan fundamentalmente en el tracto gastrointestinal siendo muy poco frecuentes en el timo y el pulmón3. Se considera que la prevalencia aproximada de los tumores carcinoides bronquiales es del 5% aproximadamente[2,4-6].

Se describe un caso clínico de una mujer con tumores carcinoides pulmonares múltiples como manifestación inicial de una MEN 1.

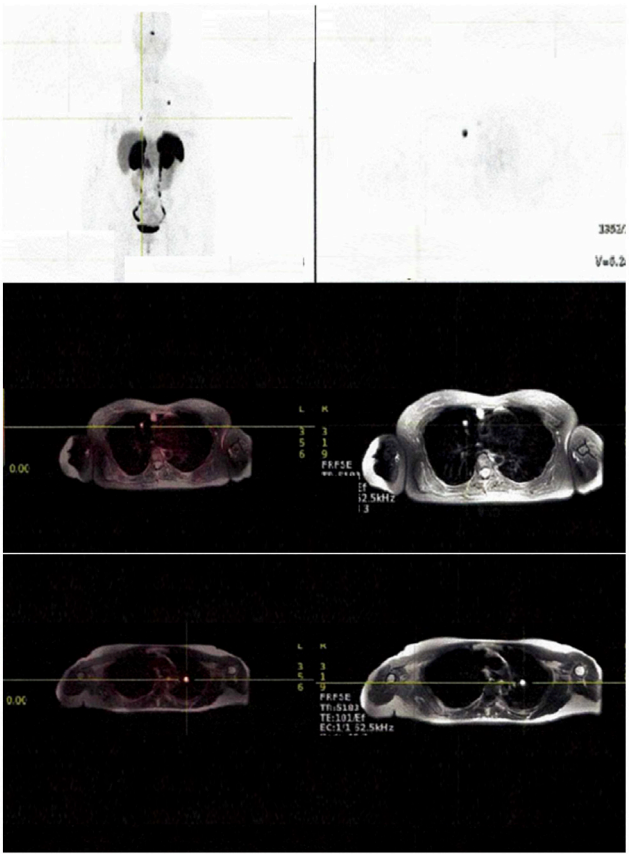
Presentación del caso clínico

Presentamos a continuación el caso clínico de una mujer caucásica de 38 años, con antecedentes de asma extrínseco desde los 12 años. Como antecedentes familiares relevantes, su padre (74 años) presentaba hiperparatiroidismo primario intervenido, con diagnóstico dudoso entre adenoma paratiroideo e hiperplasia. Sus dos hermanas (43 y 45 años) padecían asma extrínseco y su madre (68 años) enfermedad tiroidea autoinmune. Tiene dos hijos sanos de 14 y 10 años.

En 2017 consultó por tos irritativa persistente de un año de evolución y disnea de medianos esfuerzos. Se solicitó radiografía y TC de tórax donde se constataron varios nódulos pulmonares milimétricos distribuidos bilateralmente en todos los lóbulos pulmonares. Se realizó una fibrobroncoscopia que descartó lesiones endobronquiales y una biopsia pulmonar, en la que se

apreciaban múltiples nidos sólidos de células poligonales de tamaño intermedio con núcleos redondeados con cromatina irregular y sin mitosis, compatibles con hiperplasia de células neurorendocrinas y tumor carcinoide G1, Ki67 < 5%, típico. Se realizó una TC de tórax con contraste y un estudio PET/RM tras la administración de 68Ga-DOTA (**Figura 1**) que mostró sobreexpresión de receptores de somatostatina de los nódulos pulmonares bilaterales, apoyando el diagnóstico de tumor carcinoide múltiple asociado a hiperplasia difusa idiopática de células neuroendocrinas de pulmón (DIPNECH). Se inició tratamiento con Lareotida 60mg cada 28 días por vía subcutánea obteniéndose una mejoría de los síntomas.

Figure 1: PET/RM tras la administración de 68Ga-DOTA que muestra hipercaptación del trazador de los nódulos a nivel de ambos pulmones.



La analítica inicial resultó anodina; en una analítica de control en 2020 se constató hipercalcemia, con calcio sérico corregido de 11,6 mg/dl (8,4-10,2), confirmándose en una nueva determinación. Además, destacaba un fosfato de 2,10 mg/dl (2,3-4,7) y una parathormona intacta de 447,50 pg/ml (15-68). El resto de parámetros bioquímicos fue normal.

Se solicitaron informes médicos del padre intervenido por hiperparatiroidismo primario (HPP) con diagnostico dudoso entre adenoma/hiperplasia de paratiroides (2017). Su calcio corregido era de 10,70 mg/dl (2020). En un estudio por sospecha de EPOC, se constataron en TC torácico, múltiples nódulos pulmonares sin diagnostico histológico claro. Las citologías por BAS fueron negativas para malignidad.

Se planteó el diagnóstico de una neoplasia endocrina múltiple tipo 1 y menos probable una MEN tipo 4 por lo que se solicitó estudio genético secuencial con el siguiente orden: MEN 1, CDKN1B (MEN4).

Se confirmó la presencia de la variante c.145_146delinsTT (p.Ala49Phe) positiva, detectada en el gen MEN1, la cual predice la sustitución del aminoácido alanina por fenilalanina.

Una vez confirmado por estudio genético la mutación para MEN 1, se solicitó el estudio genético a familiares de primer grado que está pendiente de resultados.

A su vez se solicitaron otras pruebas complementarias:

A) TC toraco-abdominal (**Figura 2**) donde se describe:

1. Nódulo infratiroideo derecho (1.7x0.5cm) posiblemente paratiroideo.
2. Nódulos pulmonares múltiples bilaterales (<2cm) ya conocidos: tumores +/- hiperplasias neuroendocrinas pulmonares múltiples.
3. Resto tímico (nódulo mediastínico anterior 1.3cm).
4. Tumores focales sólidos (no grasos) en tejido conectivo graso abdominal anterior (1cm cada uno) compatibles con colagenomas.
5. Pequeños tumores grasos (lipomas/variantes) en páncreas (<1 cm) y gástrico (1-2mm, en curvadura menor).
6. Hiperplasia grasa predominio periférico y abdomen/cintura pélvica.
7. Microlitiasis renales bilaterales.

B) RM hipofisaria (**Figura 3**) que muestra un pequeño nódulo intraselar de 7mm sugerente de microadenoma de hipófisis.

Figure 2: TC Abdominal. A. Nódulos subcentimétricos en páncreas B. Resto tímico. C/D. Nódulos en tejido subcutáneo.

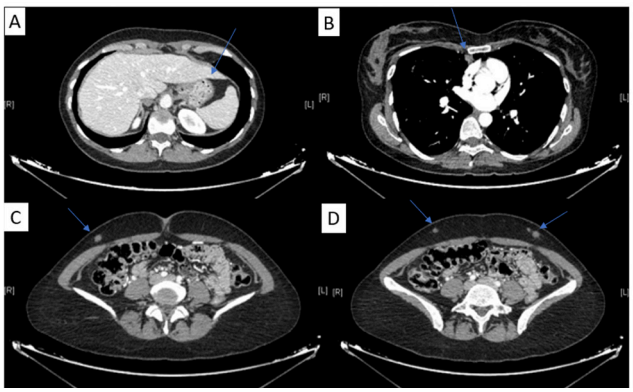
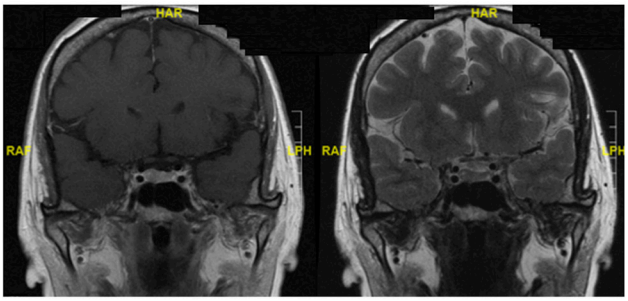
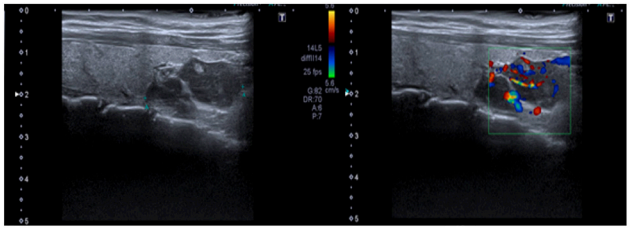


Figure 3: Microadenoma de hipófisis. En el margen derecho de la adenohipófisis se identifica una pequeña imagen nodular de aprox. 0.7cm ligeramente heterogénea en imágenes potenciadas en T2 y que es hipocaptante en las imágenes postcontraste con respecto al resto de la glándula.



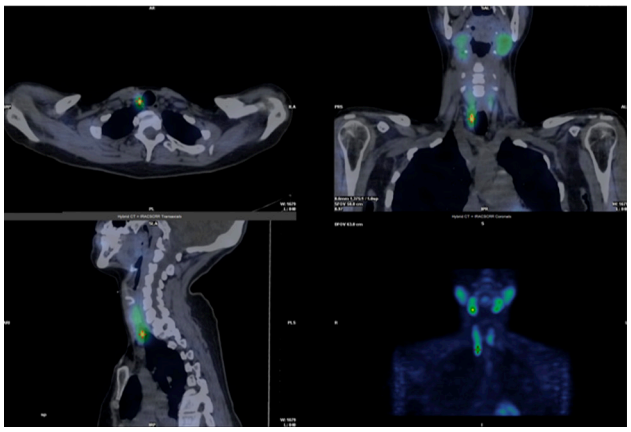
C) Ecografía cervical (**Figura 4**) que describe un nódulo posteroinferior al lóbulo tiroideo derecho que sugiere adenoma de paratiroides; sin adenopatías significativas.

Figure 4: Posterior al polo inferior del lóbulo tiroideo derecho se observa una lesión nodular hipoecogénica de contorno lobulado, hipervascular, que mide aprox. 2.8x1.2x0.7cm compatible con adenoma de paratiroides.



D) SPEC-CT de paratiroides (99mTc-MIBI) (**Figura 5**) que mostró un posible adenoma paratiroideo inferior derecho en situación paratraqueal a nivel de D1.

Figure 5: SPEC-CT (99mTc-MIBI) de paratiroides compatible con adenoma paratiroideo inferior derecho. La imagen tardía muestra un lavado incompleto con retención focal anómala en la porción inferior de LTD. Las imágenes tomográficas muestran que dicha retención se localiza en una estructura de gran tamaño situada caudal al polo inferior del LTD de localización paratraqueal a nivel de D1.



Se solicitó valoración por dermatología, constatándose en la exploración física múltiples pápulas firmes malares y nasales, sugestivas de angiofibromas, confirmadas en el estudio anatomopatológico. Estas lesiones se consideran características de MEN1.

Se realizó una gastroscopia para descartar tumores neuroendocrinos (TNE) que resultó normal, se tomaron biopsias que describieron una gastritis crónica antral y corporal leve. Además, una ecoendoscopia mostró una glándula pancreática con morfología normal y una ecogenicidad homogénea en toda su extensión con la presencia de tres lesiones milimétricas hipoecoicas bien delimitadas de 7 mm, 4 mm y 3 mm, respectivamente. El informe anatomopatológico de la PAAF de la lesión de mayor tamaño no fue concluyente.

Discusión

La MEN1 es un trastorno autosómico dominante que se debe a mutaciones en el gen supresor de tumores MEN1, que se encuentra en el cromosoma 11q13 y codifica una proteína de 610 aminoácidos: la menina[1-6].

El hallazgo de MEN 1, tiene una gran relevancia para los miembros de una familia, ya que los familiares de primer grado tienen un riesgo del 50% de desarrollar la enfermedad y, a menudo, pueden identificarse mediante análisis mutacional de MEN1[6]. A su vez, el diagnóstico precoz de los pacientes con MEN1 podría mejorar la detección de tumores presintomáticos y la realización de un tratamiento específico de los mismos[3,4,7].

La clínica está en relación con la localización de los tumores y en función de si son o no secretores[7].

Los tumores paratiroideos, que dan como resultado hiperparatiroidismo primario (HPP), son la característica más común de la MEN1 y ocurren en aproximadamente el 95% de los pacientes con MEN1. En estos pacientes, el diagnóstico de MEN1 es muy importante puesto que el manejo quirúrgico, a diferencia del hiperparatiroidismo primario esporádico, requerirá una paratiroidectomia subtotal con la exéresis de tres glándulas y media. En caso contrario, la hipercalcemia persistirá o se producirá una recidiva en la mayoría de los casos, precisándose una segunda cirugía.

Los TNE pancreáticos ocurren en el 40% de pacientes con MEN1 y los tumores de la hipófisis anterior, que consisten en prolactinomas, somatotroinomas, corticotrofinomas y adenomas no funcionantes, ocurren en aproximadamente el 30% de los pacientes[6]. Menos frecuentemente, presentan tumores carcinoides, feocromocitomas, lipomas viscerales o subcutáneos, angiofibromas y colagenomas dérmicos[1,5,7].

Los tumores carcinoides se presentan en un 3-5% de los pacientes con síndrome de MEN 1. Pueden estar localizados en bronquios, páncreas, tracto gastrointestinal o timo [2-5,8].

Los tumores neuroendocrinos broncopulmonares representan el 20% de las neoplasias de pulmón, y surgen de las células neuroendocrinas del epitelio broncopulmonar[5]. La Organización Mundial de la Salud los clasifica en 4 subgrupos: tumor carcinoide típico (bajo grado de malignidad), tumor carcinoide atípico (de grado intermedio de malignidad), y 2 neoplasias de alto grado: carcinoma neuroendocrino de células grandes y carcinoma neuroendocrino de células pequeñas. Los 2 primeros subtipos se engloban conjuntamente como tumores carcinoides[5,9].

Los tumores carcinoides pulmonares (TCP) ocurren en el 5% aproximadamente de los pacientes con mutaciones en la línea germinal MEN16. Son más frecuentes en mujeres (4:1) y suelen presentarse a edades más tempranas que los TCP esporádicos[2,5,8].

La presentación clínica del MEN 1 como TCP múltiple es muy infrecuente; existen pocos casos descritos en la literatura. Se diagnostican por las pruebas de imagen en la mayoría de los casos, sin presentar expresión clínica.

A diferencia del tumor carcinoide tímico, que tiene un curso clínico agresivo y un pronóstico precario, el carcinoide broncopulmonar que se presenta en la mayoría de los pacientes con MEN 1 tiene un curso indolente, aunque con el potencial efecto de masa local, metástasis y recurrencia después de la resección lo que podría relacionarse con la morbilidad y mortalidad de los pacientes con MEN1[4,5,9].

Los síntomas relacionados con la liberación de serotonina (síndrome carcinoide) son raros en estos tumores[5,10]. Un rasgo hormonal diferencial del carcinoide asociado a síndrome de MEN1 es que no se ha descrito secreción de serotonina por el tumor por lo que el diagnóstico en la mayoría de los casos se realiza mediante estudios de imagen: TC o RMN de tórax, recomendándose su realización cada 1-2 años aunque con discrepancias entre autores, debido posiblemente a la escasa evidencia disponible, por la baja prevalencia de esta entidad[4-7,10].

En cuanto al tratamiento del tumor carcinoide, es de elección la cirugía. Sin embargo, en nuestro caso, al ser múltiple, no se considera tributario. En estos pacientes, especialmente en aquellos que expresan receptores para la somatostatina demostrados en el PET con 68Ga-DOTA, es razonable un intento de tratamiento a largo plazo con análogos de la somatostatina como lanreotido u octreotido de liberación prolongada. En este sentido, algunas observaciones sugieren que podría estabilizarse el crecimiento de los carcinoides y mejorar la sintomatología respiratoria asociada al DIPNECH[11,12].

En resumen, presentamos el caso de una mujer con MEN1 cuya forma de presentación ha sido la presencia de múltiples carcinoides pulmonares. El correcto diagnóstico del MEN1 facilitará el tratamiento adecuado del hiperparatiroidismo y el seguimiento adecuado de las otras neoplasias asociadas. También, permitirá el diagnóstico genético de los familiares afectados.

Conclusión

El tumor carcinoide pulmonar múltiple en el contexto de una hiperplasia difusa de células neuroendocrinas de pulmón puede ser la forma de presentación de una neoplasia endocrina múltiple tipo 1. El diagnóstico precoz de MEN 1 y su manejo individualizado pueden influir en la morbimortalidad de los pacientes y de los familiares portadores de la mutación.

Conflicto de interés

Los investigadores declaran no tener conflicto de interés.

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