

ACADEMIC JOURNAL OF HEALTH SCIENCES

MEDICINA BALEAR

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Hydromyelia regarding a case, should we perform an intrapartum epidural?

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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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CONCESIÓN DE BECAS Y PREMIOS 2023

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 22 de noviembre del presente, acordó la concesión de las siguientes becas y premios:

BECAS DE INNOVACIÓN

Dos becas para estancias en centros sanitarios extranjeros, dotadas cada una con 3.000 euros.

- Lizmar Indira Molina Ochoa, médico general, para realizar una estancia formativa de un mes en el *Sleep Care Clinics* en Leicester, Reino Unido.
- Cristina Merino del Villar, facultativa especialista en Psiquiatría en el Hospital Can Misses, para una estancia de dos meses de duración en el *Douglas Mental Health University Institute* en Montreal, Canadá

Dos becas para estancias en hospitales nacionales, dotadas cada una con 1.500 euros.

1. Cristina Montalvo Ávalos, FEA en Cirugía Pediátrica en el Hospital Universitario Son Espases, para una estancia de un mes en el Servicio de Cirugía Pediátrica y Unidad Plástica del Hospital Universitario "La Paz" en Madrid.
2. Aina Ochogavía Seguí, facultativa especialista en Cirugía General y del Aparato Digestivo en el Hospital Universitario Son Espases, para una estancia de un mes en el Servicio de Cirugía Colorrectal del Hospital Marqués de Valdecilla en Santander.

BECAS FUNDACIÓ BANC SABADELL DE ROTACIÓ EXTERNA PARA MIR

Dos becas para estancias en hospitales internacionales, dotadas cada una con 3.000 euros.

1. Paula Gómez Fernández, residente de la especialidad de Hematología y Hemoterapia en el Hospital Universitario Son Espases, para una estancia de dos meses en el Servicio de Hematología del *St. Michael's Hospital, Unity Health Network-University of Toronto*, Canadá.

* A los pocos días de salir publicado el fallo, nos comunica que, por motivos de organización del Servicio de Hematología del hospital, finalmente no pueden aceptar su estancia, por lo que, en consecuencia, rechaza la beca. A este respecto, el jurado decide adjudicar la misma al siguiente clasificado:

Juan Montes González, residente de la especialidad de Oncología Médica en el Hospital Universitario Son Espases, para una estancia de un mes en el Servicio de Oncología y Cáncer de Mama del *The Royal Marsden, NSH Foundation Trust* de Sutton, Londres.

2. Carla Iglesias i Cels, residente de la especialidad de Neurología en el Hospital Universitario Son Espases, para una estancia de dos meses en el Servicio de Neurología y Unidad de Epilepsia en el *London Health Science Center University (LHSC)-Clinical Neurological Sciences, Western University, London-Ontario*, Canadá.

Dos becas para estancias en hospitales nacionales, dotadas cada una con 1.500 euros.

1. Aitana Bernabeu Follana, residente de la especialidad de Neurología en el Hospital Universitario Son Espases, para una estancia de dos meses en el Servicio de Neurología y Unidad Neuromuscular del Hospital Universitario de Donostia en San Sebastián.
2. María Soledad Parra Carrillo, residente de la especialidad de Medicina Familiar y Comunitaria en el Hospital Can Misses, para una estancia de un mes en el Servicio de Radiodiagnóstico y Urgencias del Hospital General Universitario Morales Meseguer en Murcia.

PREMIOS DE INVESTIGACIÓN

Tres premios de 1.500 euros.

"Premio Mateu Orfila"

Al trabajo científico titulado "Evolución de la parada cardíaca extrahospitalaria en Baleares en la última década", presentado por Laura Asunción Bueno López y María Isabel Ceniceros Rozalén.

"Premio Damià Carbó"

Al trabajo científico titulado "Epidemiología del melanoma cutáneo primario en el sector Migjorn en la isla de Mallorca entre los años 2003-2021", presentado por María Cruz Álvarez-Buylla Puente, Jorge Adsuar Mas, Fernando Terrasa Sagristá, Antoni Nadal Nadal, Cristina Nadal Lladó y Alex Llambrich Mañés.

"Premio Metge Matas"

Al artículo "*Validity and acceptance of self vs conventional sampling for the analysis of human papillomavirus and Pap smear*", cuyas autoras son Maria Josep Gibert Castanyer y María del Carmen Sánchez-Contador Escudero.

PREMIO FUNDACIÓ MUTUAL MÈDICA AL MEJOR PROYECTO DE TESIS DOCTORAL

Un premio dotado con 2.000 euros al proyecto titulado "Método matemático de reconstrucción 3D para la valoración de infiltración tumoral en el cáncer colorrectal", presentado por Sebastián Jerí McFarlane, FEA en Cirugía General y del Aparato Digestivo en el Hospital Universitario Son Espases y en el Hospital Cruz Roja de Palma.

PREMIO CAMILO JOSÉ CELA DE HUMANIDADES MÉDICAS

Un premio dotado con 1.500 euros concedido este año *ex aequo*, con la misma dotación económica, a los trabajos titulados "Conducta sexual y represión inquisitorial", cuyo autor es el Dr. José Tomás Monserrat, Doctor en Medicina, anterior bibliotecario del COMIB y medalla de Oro al Mérito Colegial de la institución; y al trabajo titulado "Las humanidades médicas aplicadas: el paciente como objetivo fundamental", cuyo firmante es el Dr. Juan Manuel Igea Aznar, Doctor en Medicina y especialista en Alergología colegiado en la provincia de Salamanca.

CERTAMEN DE CASOS CLÍNICOS PARA MIR

Tras la exposición de los cinco casos clínicos seleccionados como finalistas, el jurado, reunido el día 27 de noviembre del presente, acordó conceder:

- **El primer premio, dotado de 1.000 euros**, al caso titulado "Ante una bradiarritmia de nueva aparición, ¡máxima precaución!", cuyas autoras son Natalia Mateos Sánchez, María Martín Talavera, Rebeca Sánchez Salmador y Marta López García.
- **El segundo premio, dotado de 500 euros**, al caso titulado "Ataxia cerebelosa como debut de un cáncer diferenciado de tiroides", cuya autora es Camila Soledad Salomón.

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ORIGINAL

Accumulated daily step counts versus physical fitness and sedentary behaviour: A systematic review and meta-analysis

Recuento de pasos diarios acumulados frente a forma física y comportamiento sedentario: Una revisión sistemática y meta-análisis

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Abstract

Background: Physical inactivity and a sedentary lifestyle are major causes of many health issues, including diabetes, obesity, and cardiovascular disorders. Physical activities like walking, which are simple to include into everyday routines, have been pushed as a means of addressing these health issues. Increasing the number of steps taken each day is one such tactic that is frequently suggested to enhance physical health and fitness. The objective of this research was to evaluate the effects of higher daily step counts on various physical fitness metrics while accounting for the diverse results documented in earlier investigations.

Methods: Several databases were combed in accordance with the PRISMA procedure to find pertinent publications. To account for the expected heterogeneity, the meta-analysis generated forest plots showing mean difference (MD) under a random effects (RE) model.

Results: A total of 13 studies were examined. According to certain research, there was little change in heart rate, weight, or body fat. Others demonstrated that some people's cholesterol and body fat decreased. Combined, the data suggested that walking more steps had no effect on VO2 max, a fitness metric (average difference -0.26, 95% confidence interval [-1.27, 0.75], I2 = 79%, p = 0.008). However, increasing step count did appear to reduce body mass index (BMI) (average difference -1.14, 95% confidence interval [-1.92, -0.36], I2 = 32%, p = 0.18). The resting heart rate (RHR) was not significantly affected by an increase in step count (average difference -1.85, 95% confidence interval [-3.82, 0.12], I2 = 0%, p = 0.67).

Conclusion: The review emphasised how different step counts have an influence on health outcomes. Although there were increases in certain fitness metrics, such as BMI, there were no discernible changes in VO2 max and RHR. It is advised to take into account higher step counts as part of a multifaceted strategy to improve general health and well-being, based on the thorough analysis of available data. These results highlight the necessity for tailored advice for physical activity levels depending on particular fitness objectives and health profiles.

Key words: Step counts, Physical fitness, Sedentary behaviour, VO2 max, BMI, Heart rate, Body fat percentage.

Resumen

Antecedentes: La inactividad física y el sedentarismo son causas importantes de muchos problemas de salud, como la diabetes, la obesidad y los trastornos cardiovasculares. Las actividades físicas como caminar, que son fáciles de incluir en las rutinas diarias, se han impulsado como medio para abordar estos problemas de salud. Aumentar el número de pasos que se dan cada día es una de las tácticas que se sugieren con frecuencia para mejorar la salud física y la forma física. El objetivo de esta investigación era evaluar los efectos de un mayor número de pasos diarios en varios parámetros de la forma física, teniendo en cuenta los diversos resultados documentados en investigaciones anteriores.

Métodos: Se examinaron varias bases de datos de acuerdo con el procedimiento PRISMA para encontrar publicaciones pertinentes. Para tener en cuenta la heterogeneidad esperada, el metaanálisis generó diagramas de bosque que mostraban la diferencia de medias (DM) según un modelo de efectos aleatorios (ER).

Resultados: Se examinaron un total de 13 estudios. Según algunas investigaciones, apenas se produjeron cambios en la frecuencia cardíaca, el peso o la grasa corporal. Otros demostraron que el colesterol y la grasa corporal de algunas personas disminuyeron. Combinados, los datos sugerían que caminar más pasos no tenía ningún efecto sobre el VO2 máx, una métrica de la forma física (diferencia media -0,26, intervalo de confianza del 95% [-1,27, 0,75], I2 = 79%, p = 0,008). Sin embargo, el aumento del número de pasos sí pareció reducir el índice de masa corporal (IMC) (diferencia media -1,14, intervalo de confianza del 95% [-1,92, -0,36], I2 = 32%, p = 0,18). La frecuencia cardíaca en reposo (FCR) no se vio afectada significativamente por un aumento del recuento de pasos (diferencia media -1,85, intervalo de confianza del 95% [-3,82, 0,12], I2 = 0%, p = 0,67).

Conclusiones: La revisión enfatizó cómo los diferentes recuentos de pasos influyen en los resultados de salud. Aunque se produjeron aumentos en determinadas métricas de la forma física, como el IMC, no hubo cambios perceptibles en el VO2 máx. y la RHR. Se aconseja tener en cuenta un mayor número de pasos como parte de una estrategia polifacética para mejorar la salud y el bienestar general, basándose en el análisis exhaustivo de los datos disponibles. Estos resultados ponen de relieve la necesidad de un asesoramiento personalizado sobre los niveles de actividad física en función de los objetivos de forma física y los perfiles de salud particulares.

Palabras clave: Recuento de pasos, Condición física, Comportamiento sedentario, VO2 máx, IMC, Frecuencia cardíaca, Porcentaje de grasa corporal.

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Introduction

A number of health issues, including obesity, type 2 diabetes, and cardiovascular diseases, have been related to physical inactivity¹. It is more important than ever to identify effective measures to raise levels of physical activity in today's society, where sedentary lifestyles are common². Walking has been proposed as a useful strategy to improve physical fitness and lessen the negative effects of a sedentary lifestyle. Walking's value as exercise can be readily measured using daily step counts³. Sedentary behaviour is important for the onset and progression of chronic illnesses and is significantly linked to higher chances of death and hospital admissions³. Conversely, increasing physical activity is recognised for its critical health benefits, which include delaying and avoiding the onset of several chronic illnesses.

Given the crucial role that physical exercise plays in the management and prevention of chronic illnesses, it is imperative to promote an active lifestyle⁴. Many therapies, rehabilitation programmes, and physical activity guidelines have been developed to promote an active lifestyle among people worldwide³⁻⁶. In spite of these efforts, new data from the World Health Organisation (WHO) indicates that physical inactivity continues to be a concern for 80% of teenagers and 23% of adults worldwide⁶.

The primary component creating this issue seems to be a very low long-term commitment to appropriate physical activity and a healthy lifestyle. This makes it even more crucial to look at strategies that encourage consistent commitment to a healthy lifestyle and adequate daily activity, especially in populations with chronic conditions⁷. Empirical data substantiates the efficaciousness of structured behaviour modification strategies, encompassing individual education sessions, group talks, telephone counselling, and the distribution of printed educational materials, in elevating physical activity levels⁸. As a result, the progression of chronic diseases may be slowed.

Although most of the evidence for this has come from observational studies and studies on healthy populations, setting goals has also been cited as a potential motivational strategy to improve physical activity⁹. However, these strategies often require a significant time and cost commitment, which may compromise long-term adherence and raise issues with their applicability in conventional clinical settings¹⁰⁻¹². Thus, there is ongoing study and development of workable and durable solutions to encourage physical exercise and healthy lifestyles.

Nevertheless, the relationship between daily step counts and health outcomes is complex, with many moving parts⁴. Quite a number of papers have looked at how more steps each day affect fitness measures like body mass index (BMI), resting heart rate (RHR), and maximal oxygen consumption (VO₂ max). But the results are mixed, so it's hard to say for sure how increasing step

counts affects health⁵. BMI helps tell if a person is a healthy weight. Some studies found that walking more can lower BMI⁶, while others didn't find any link⁷. It's also unclear how step counts relate to RHR, which tells us about heart health. Some studies found that more steps mean lower RHR⁸, but others didn't find this⁹. There's also mixed data about the link between step counts and VO₂ max, which tells us about fitness levels¹⁰.

The mixed results might be because the studies were done differently, looked at different people, or used different ways to measure and increase step counts¹¹⁻¹⁴. Many studies only looked at certain groups of people, like those with chronic diseases or obesity¹²⁻¹⁴. Because of these mixed results, we conducted a systematic review and meta-analysis to get a clearer picture of how more steps each day might affect fitness. This should help us understand better the link between step counts and fitness.

Materials and methods

Review protocol and PECO

This review was carefully guided by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) protocol¹⁵, the schematics of which are represented in **figure 1**. A clear, thorough, and reproducible process was used. Using particular keywords and MeSH phrases, a thorough literature search was first carried out across several databases to find pertinent studies. The search was limited to publications written in the English language, and there was no time limit, thus all relevant material was gathered. After removing duplicates, the relevancy of the titles and abstracts was checked. After that, the full texts of the possibly qualifying studies were obtained and evaluated in light of the pre-established inclusion and exclusion standards. To lessen bias and mistake, the study selection procedure includes two independent reviewers. Any differences of opinion were settled by consensus or by talking to a third reviewer.

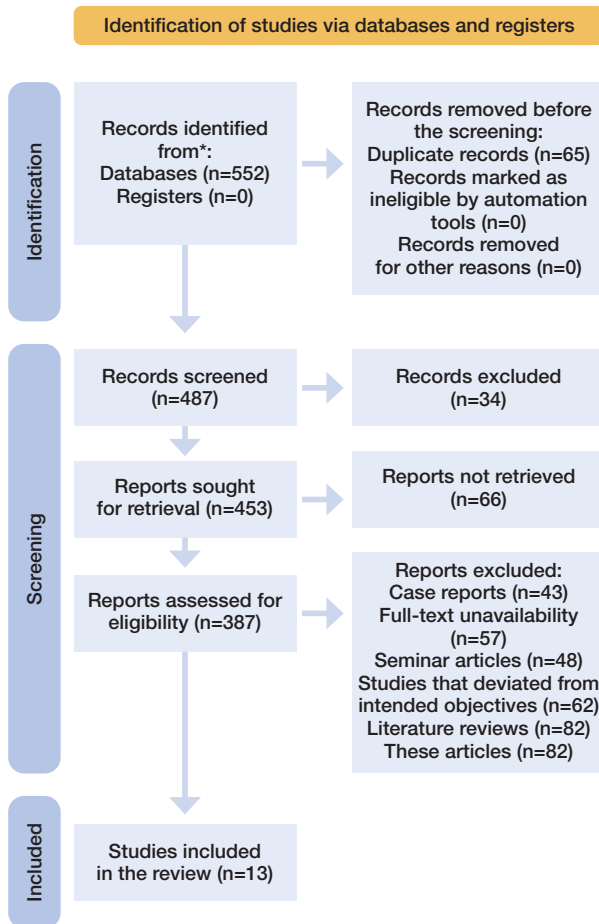
The PECO (Population, Exposure, Comparator, Outcome) protocol used for this review is delineated below-

- **Population:** The studies included individuals of various demographics, including different age groups, genders, and health statuses, from a wide range of geographical regions.
- **Exposure:** The main exposure under consideration was the accumulation of daily step counts. This is typically achieved through walking or other physical activities that can be measured in terms of steps.
- **Comparator:** The comparator was individuals with lower daily step counts or those following their usual lifestyle habits without any specific step-based interventions.
- **Outcome:** The outcomes of interest were indicators of physical fitness and sedentary behaviour.

Database search protocol

The following eight databases were searched: PubMed, EMBASE, Web of Science, Cochrane Library, CINAHL, PsycINFO, Scopus, and Google Scholar. The database search protocol was used. MeSH (Medical Subject Headings) terms and free-text keywords were combined to create a search strategy that ensured comprehensive coverage of the literature. To combine the search phrases, boolean operators AND and OR were employed. The three main concepts that dominated the search phrases were: outcomes (BMI, VO₂ max, resting heart rate), walking or step counts as the exposure, and adults as the population. Each topic was given a list of related keywords and MeSH terms. Next, the Boolean operator AND was used to combine the lists of keywords for the three concepts, as shown in **table 1**.

Figure 1: PRISMA protocol representing the study selection process for the review.



Inclusion and exclusion criterion

Cohort studies, cross-sectional studies, randomised controlled trials, and non-randomized controlled trials were among the study designs covered in the review. This wide range of inclusion allowed for a thorough comprehension of the evidence that was available. On the other hand, because of their poor quality of evidence, editorials, case reports, and case series were not included. Adults who were at least eighteen years old made up the target population. In order to keep the focus on the adult population as a whole, studies including children, adolescents, or certain patient groups (such as individuals with chronic conditions) were eliminated. Any intervention meant to increase step counts by walking or other comparable activities was the intervention of interest. Studies that concentrated on exercise or other types of physical activity were not included. A lower step count, no intervention, or standard care could serve as the comparative. Studies that reported on any of the pre-specified health-related outcomes –weight, body fat, heart rate, BMI, VO₂ max, and RHR– were included in terms of results. Excluded were any studies that did not report on these outcomes. Furthermore, because of the review team's proficiency in the language, studies had to be published in English. Excluded were studies that were published in other languages. Finally, to guarantee the validity of the review findings, studies with a high risk of bias –as indicated by the risk of bias assessment– were also omitted.

Data extraction protocol

A standardized data extraction form was created to capture information relevant to the review question. This form included fields for study characteristics (e.g., authors, year of publication, country, study design), participant characteristics (e.g., age, sex, health status), details about the intervention and comparator, outcome measures, and key findings. Once the form was finalized, two independent reviewers were assigned to extract data from the included studies. Each reviewer was responsible for a set of studies, extracting the data individually. To ensure accuracy and consistency, a pilot test was conducted wherein both reviewers independently extracted data from a subset of included studies and compared their results. Discrepancies were discussed, and the data extraction form was refined as needed. Following the pilot test, the reviewers proceeded with data extraction for their assigned studies. After completing the data extraction, the reviewers cross-checked a random sample of each other's work to verify the accuracy of the data and the consistency of the extraction process.

Table 1: Search strings utilised across the selected databases.

Database	Search string
PubMed	("daily step counts"[All Fields] OR "physical activity"[All Fields]) AND ("physical fitness"[MeSH Terms] OR "sedentary behaviour"[All Fields])
Web of Science	(TS=("daily step*") OR TS=("physical activity*)) AND (TS=("physical fitness") OR TS=("sedentary behavior"))
Scopus	(TITLE-ABS-KEY("daily step counts") OR TITLE-ABS-KEY("physical activity*)) AND (TITLE-ABS-KEY("physical fitness") OR TITLE-ABS-KEY("sedentary behaviour"))
PsycINFO	(AB("daily step counts") OR AB("physical activity*)) AND (AB("physical fitness") OR AB("sedentary behaviour"))
CINAHL	(MH "daily step counts" OR MH "Physical Activity") AND (MH "Physical Fitness" OR MH "Sedentary Behavior")

The interrater reliability test was carried out using Cohen's kappa statistic, which measures the agreement between two raters beyond chance. The kappa values were calculated for the pilot test and the cross-checking stage. The kappa value for the pilot test was 0.82, indicating "almost perfect" agreement according to Landis and Koch's benchmarks. After refining the data extraction form, the kappa value for the cross-checking stage increased to 0.91, further demonstrating the high reliability of the data extraction process. In case of disagreements during data extraction or cross-checking, the reviewers discussed the issue to reach a consensus. If a consensus could not be reached, a third reviewer was consulted.

Bias assessment

The risk of bias in the included studies was assessed using the Cochrane's Risk of Bias 2.0 (RoB 2.0) tool [16]. This tool is specifically designed for assessing the risk of bias in randomized trials, the results of which have represented through **figure 2**.

Meta-analysis protocol

The meta-analysis for this review was carried out using Review Manager 5 (RevMan 5, version 5.4.1). The data extracted from the individual studies were first entered into RevMan 5. For each study, the MDs and standard deviations for the VO2 max, BMI, and RHR between the intervention and control groups were entered. Studies that reported medians and interquartile ranges instead of means and standard deviations were excluded from the meta-analysis due to the different statistical properties of these measures. Following this, a random-effects (RE) meta-analysis was conducted for each outcome. The

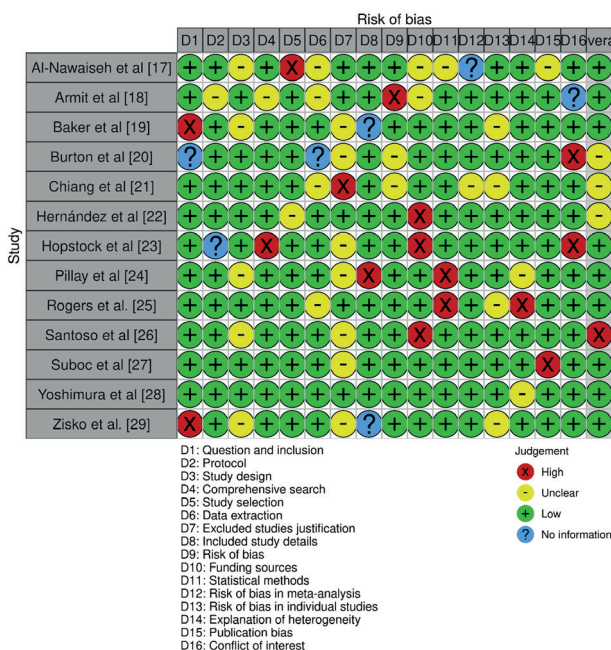
RE model was chosen due to its ability to account for both within-study and between-study variability, which is particularly important when the included studies are heterogeneous in terms of their populations, interventions, or methods. The results of the meta-analyses were presented in forest plots, which provide a visual representation of the individual and pooled effect sizes along with their 95% CIs. The size of the square reflected the weight of the study in the meta-analysis. A diamond was used to represent the pooled MD and its 95% CI. The heterogeneity among the included studies was assessed using the I² statistic.

Results

Study selection process

The article selection procedure started by identifying possible research from several databases, which produced a total of 552 documents at first. No entries from registries were found. After the identification stage, 487 records remained to be inspected after 65 duplicate records were eliminated. During this screening stage, automated methods were used; however, none of the records were flagged as ineligible by these technologies. Furthermore, at this point, no records were deleted for other reasons. After 34 data were excluded throughout the screening procedure, 453 reports were still sought after for retrieval. 387 of them were then evaluated for eligibility after 66 of the reports could not be obtained. A number of reports were excluded during the eligibility phase examination due to different criteria. Due to their intrinsic limits in offering high-quality evidence and information that can be applied generally, a total of forty-three case reports were eliminated. 48 seminar pieces and 57 reports that could not be found in full text were also eliminated since they frequently lacked peer-reviewed confirmation. Furthermore, 62 papers that did not provide pertinent data for the analysis and diverged from the review's original aims were eliminated. A sizable portion of thesis papers (n = 82) and literature reviews (n = 82) were also disregarded because it was thought that these secondary sources would not offer new information for our meta-analysis. Following this meticulous and methodical procedure of selection, thirteen studies¹⁷⁻²⁹ in all were found to be eligible and included in the final review.

Figure 2: Bias representation across different domains pertaining to the included trials.



Assessed bias in the studies

The majority of studies showed low levels of bias with regard to the question and inclusion criteria, indicating that their research questions and inclusion criteria were well-defined. A few studies, though, were marked as having significant bias or causing some worries, suggesting that there might be problems with their inclusion criteria or study question^{17,19,29}. The majority of the evaluations of the research selection process were low bias, suggesting that the studies used strict and objective procedures to choose their sample. A

few research, meanwhile, raised some questions, and one study showed a significant bias¹⁷. The majority of data extraction evaluations were found to have low bias, demonstrating the adoption of trustworthy data collection techniques in the investigations. A few studies, nevertheless, raised some red flags, and one study's data was unavailable²⁰. The majority of research evaluated the publishing bias to be minimal, while a few were found to have high bias^{20,23}. Although the conflict of interest was rated as minimal overall, a few research raised some red flags, and one study was found to have significant bias²⁶. Most of the studies were judged to have low bias overall, meaning that they were transparently and dependably conducted and reported. A few studies, nevertheless were judged to have somewhat of a noticeable overall bias^{19,29}.

Demographic characteristics

Table II shows the demographic variables assessed across the included papers¹⁷⁻²⁹. All the studies were either RCTs or case-cohort studies. The studies were conducted across USA^{17,20,25,27}, Australia¹⁸, Scotland¹⁹, Taiwan²¹, Spain²², Norway^{23,29}, South Africa²⁴, Indonesia²⁶, and Japan²⁸. The number of participants in each study ranged from as few as 10 to as many as 136. The age range of the participants also varied greatly. Some studies included participants in specific age ranges, such as 18-30 years¹⁷, 50-70 years¹⁸, and 18-65 years¹⁹, while others included participants who were over 18 years of age^{21,22,27}, and some studies provided the mean age of participants^{20,25}. One study did not specify the age range²⁶. The gender ratio of participants in each study was predominantly male, with the number of males ranging from 5 to 71 across the studies. Some studies did not specify the gender ratio^{21,26}. The follow-up period for these studies ranged from as short as 4 days²⁴ to as long as 8 months²⁸, with many studies conducting follow-ups at the 3-month mark^{17,18,19,27}. One study did not specify the follow-up period²⁵.

Inferences assessed

Al-Nawaiseh et al.¹⁷, Armit et al.¹⁸, and Burton et al.²⁰ didn't observe significant changes in weight, body fat, or heart rate as a result of increasing step counts. Chiang et al.²¹ noticed one group had a lower heart rate after a fitness test when their step counts increased. In a similar vein, Hernández et al.²² reported that participants who increased their steps experienced a boost in positive emotions. Hopstock et al.²³ and Pillay et al.²⁴ found that stepping more improved some health outcomes like body fat and cholesterol levels in certain groups, but not in all. Rogers et al.²⁵ discovered that groups that increased their steps lost more weight and had less body fat. Santoso et al.²⁶ reported a decrease in weight and body fat among participants who increased their step counts. Suboc et al.²⁷ discovered similar results, with added observations that higher step counts were linked with better exercise capacity. Yoshimura et al.²⁸ found that groups with higher step counts had improved lipid levels post-exercise, but no changes were seen in other health markers. Zisko et al.²⁹ reported that increasing step counts led to improvements in aerobic fitness. (**Table III**)

Statistical findings pertaining to changes in VO2 max

Figure 3 compares the impact of step count increase on VO2 max changes in different studies. The combined data shows no clear effect on VO2 max, as the mean difference was -0.26 [-1.27, 0.75]. The studies show high variation ($I^2 = 79%$), confirmed by a significant Chi² test ($p=0.008$). In one study²⁴, the VO2 max was notably lower in the step-increase group. Two other studies^{26,29} showed no significant VO2 max difference between groups. This refers to the fact that the combined results did not show a clear improvement. In some studies, VO2 max even decreased slightly in the group that increased their step count. There was also a high level of difference between the results of the studies, suggesting that other factors may be affecting the outcome.

Table II: Demographics variables observed in the selected studies.

Study ID	Region assessed	Protocol	Sample size (n)	Age range (in years)	Gender ratio	Follow-up period (in months)
Al-Nawaiseh et al ¹⁷	USA	RCT	118	18-30	22 males	3
Armit et al ¹⁸	Australia	RCT	136	50-70	54 males	3
Baker et al ¹⁹	Scotland	RCT	79	18-65	16 males	3
Burton et al ²⁰	USA	RCT	10	25.7 ± 1.8 (mean)	7 males	1
Chiang et al ²¹	Taiwan	RCT	64	>18	Unspecified	2
Hernández et al ²²	Spain	RCT	67	>18	23 males	6
Hopstock et al ²³	Norway	RCT	16	55-74	11 males	6
Pillay et al ²⁴	South Africa	Case-cohort	70	21-49	35 males	4 (days)
Rogers et al. ²⁵	USA	RCT	10	30 ± 7 (mean)	5 males	Unspecified
Santoso et al ²⁶	Indonesia	Case-cohort	80	Unspecified	Unspecified	2
Suboc et al ²⁷	USA	RCT	114	≥18	71 males	3
Yoshimura et al ²⁸	Japan	RCT	109	30-60	59 males	8
Zisko et al. ²⁹	Norway	RCT	24	30-50	All males	1.5

Table III: Step counts observed across the included papers and their associated outcomes.

Study ID	Groups assessed	Modality employed for step count	Assessed variables	Inferences pertaining to step counts observed
Al-Nawaiseh et al ¹⁷	Control (58) and Intervention (56)	Not specified	Body weight, body fat percentage, BMI, step count	<ul style="list-style-type: none"> Baseline step count was higher in the control group but not statistically significant ($p=0.056$). Post-intervention, no significant difference in body weight, body fat percentage, and BMI between the two groups.
Armit et al ¹⁸	GP (number not specified), GP+ES (number not specified), GP+ES+P (number not specified)	Pedometer for GP+ES+P group	BMI, resting systolic and diastolic blood pressure, resting heart rate, heart rate after two levels of the Canadian Home Fitness Test	<ul style="list-style-type: none"> No significant change in BMI across all groups from week 1 to week 12 ($p > 0.05$). No significant change in the resting heart rate for any group. Decrease in heart rate after level 1 and 2 of the Canadian Home Fitness Test in the GP group was significant ($p = 0.01$), but not in the other groups.
Baker et al ¹⁹	Intervention group and Control group	Pedometer	Daily step-counts, PANAS score, EQ-5D tariff score, EQ VAS score, Height, Body mass, BMI, Waist and hip circumferences, Waist:hip ratio, Body fat percentage, Systolic and diastolic blood pressure, Heart rate	<ul style="list-style-type: none"> Intervention group had a significant increase in steps per day from 6802 at baseline to 9977 at week 12. Control group showed a minor increase from 6924 to 7078 steps/day. PANAS positive score slightly improved in the intervention group, while it slightly decreased in the control group. No major changes in other health outcomes in both groups.
Burton et al ²⁰	Ten participants across LOW, LIMITED, and NORMAL steps trials	Not specified	Daily step count, Heart rate, RPE, Oxygen consumption, Postprandial plasma triglyceride response	<ul style="list-style-type: none"> No significant differences were noted in the control days' average daily steps. Significant differences were noted in the daily steps on the first two days of the intervention among LOW, LIMITED, and NORMAL trials.
Chiang et al ²¹	Walking Step Goal group (WSG), Walking Exercise group (WEG), Control group (CG)	Smartwatch	Daily step counts, Body composition, Metabolic syndrome variables	<ul style="list-style-type: none"> Average daily steps over 8 weeks did not significantly differ between the WSG and WEG. The WEG exhibited significant improvements in terms of hip circumference, visceral fat area, high-density lipoprotein cholesterol, fasting glucose, and triglycerides. The CG and WSG showed no improvement in body composition.
Hernández et al ²²	Control group and Intervention group	Pedometer app	Daily step counts, Weight, BMI, Body fat percentage, Muscle mass, Body water percentage	<ul style="list-style-type: none"> The intervention group had a significantly greater decrease in weight and BMI than the control group at both 3 and 6 months. The percentage of body fat was significantly lower in the intervention group compared to the control group at both 3 and 6 months. There was no significant difference in muscle mass between the two groups at either 3 or 6 months. The percentage of body water was significantly higher in the intervention group than in the control group at both 3 and 6 months.
Hopstock et al ²³	Single group composed of 11 men and 5 women aged 57-74 years	Physical activity trackers	Adiposity (weight, BMI, body composition, waist circumference), Physical activity, Cardiometabolic risk factors (blood pressure, HbA1c, blood lipids), Diet, Physical capacity	<ul style="list-style-type: none"> Participants' body weight significantly decreased from an average of 106.2 kg at the start of the study to 103.4 kg at the end. BMI also showed a significant reduction. A decrease was observed in the body fat mass. Lean body mass showed an upward trend. There was an increase in weight satisfaction from 0% at baseline to 20% at the end of the intervention. The gap between participants' actual weight and their self-reported ideal weight decreased significantly.
Pillay et al ²⁴	Low group (< 5000 steps/d), High-Low group (≥ 5000 steps/d, no aerobic steps), High-High group (≥ 5000 steps/d, including some aerobic steps)	Pedometer	Estimated maximal oxygen uptake (VO_{2max}), Blood pressure (BP), Body mass index (BMI), Percentage body fat (%BF), and Waist circumference (WC)	<ul style="list-style-type: none"> The higher the physical activity level, the lower the body fat percentage. A higher physical activity level is associated with a lower BMI. Waist circumference decreased with increased physical activity. The maximum volume of oxygen a person can use during intense exercise increased with physical activity level. The number of pedometer steps per day was lowest in the Low group, higher in the High-Low group, and highest in the High-High group.

Study ID	Groups assessed	Modality employed for step count	Assessed variables	Inferences pertaining to step counts observed
Rogers et al. ²⁵	Single group tracked over multiple conditions	Indoor track at a pace of 100 steps/min	Resting energy expenditure (REE), Respiratory exchange ratio (RER), Fat oxidation rate (FATOX), Triglycerides (postprandial lipemia; PPL), Nonesterified fatty acids (NEFAs), Insulin, Glucose	<ul style="list-style-type: none"> • PPL was significantly higher after 2 K versus 10 K. • NEFAs were significantly higher after 15 K versus 2 K. • No differences were found for insulin, glucose, or REE among conditions. RER and FATOX were not significantly different among conditions. • 10 K steps elicited the greatest decrease in PPL, an established cardiovascular disease risk factor. • NEFA levels were highest after the 15 K condition.
Santoso et al. ²⁶	High school students in Palembang, divided into 2 groups: the motivation of physical activity and the control group	Accupedo application	VO2max values measured using the Multistage Fitness Test and the number of daily steps	<ul style="list-style-type: none"> • The pre-test VO2max for the intervention group was 40.5 ± 0.96 (mean ± standard deviation), and this value increased to 42.9 ± 0.93 in the post-test. The difference in averages between the pre-test and post-test was 2.45. This significant increase (p-value < .0001) indicates a marked improvement in VO2max, and thus aerobic fitness, in the intervention group following the intervention. • In the control group, the pre-test VO2max was slightly higher at 41.2 ± 1.08. However, the post-test value of 42.7 ± 1.03 marked a smaller increase than that seen in the intervention group, with an average difference of 1.52. Although this increase was also statistically significant (p-value < .0001), the smaller magnitude of change compared to the intervention group suggests that the intervention had a positive effect on improving VO2max.
Suboc et al. ²⁷	Sedentary older adults aged ≥50, randomized into 3 groups: No intervention (Group 1), Pedometer-only intervention (Group 2), and Pedometer with an interactive website (Group 3)	Pedometer	Endothelial function by brachial flow-mediated dilation (FMD%), vascular stiffness by tonometry, step-count by pedometer, PA intensity/distribution by accelerometer, weight, BMI, waist circumference, glucose, insulin, QUICKI, HOMA-IR, total cholesterol, LDL cholesterol, triglycerides, hsCRP, systolic and diastolic blood pressure, heart rate	<ul style="list-style-type: none"> • Step-count increased in groups 2 and 3 but not in group 1. • Both groups 2 and 3 increased MPA ≥30 min/day. Only group 3 increased MPA in continuous bouts of ≥10 minutes and improved FMD% (P=0.001). • Neither achievement of ≥10 000 steps/day nor ≥30 min/day of MPA resulted in improved FMD%. However, achieving ≥20 min/day in MPA bouts resulted in improved FMD%. • All groups lost some weight over time but the use of a pedometer, whether alone or with a website, did not lead to a significantly different weight loss compared to the control. • The interventions did not significantly affect the change in BMI over time. • There were minor and insignificant changes for glucose, insulin, QUICKI, HOMA-IR, total cholesterol, LDL cholesterol, triglycerides, hsCRP, systolic and diastolic blood pressure, and heart rate
Yoshimura et al. ²⁸	Two groups: one group using a smartphone app, and the control group	Smartphone App	Daily physical activity (step count) measured by accelerometer, body weight	<ul style="list-style-type: none"> • Both groups increased their step count and step counts per wear time over the intervention period. The smartphone app group showed a slightly greater increase. 2. There may be a statistically significant difference in step counts per wear time between the two groups. • No significant difference in weight loss between those using the smartphone app and the control group. • Both groups saw a slight increase in moderate to vigorous physical activity (MVPA) over time.
Zisko et al. ²⁹	Thirty healthy males (39±6 yrs) not exposed to structured exercise training, randomized to either 1x4 min AIT (1-AIT), 4x4 min AIT (4-AIT), or 47 min of MCT at 70% HRmax	Not Specified	Total energy expenditure (TEE), active energy expenditure (AEE), number of steps, active time, sedentary time, VO2max, mitochondrial function in m. vastus lateralis	<ul style="list-style-type: none"> • TEE increased 14% and AEE increased 43% after MCT. • There was no change in TEE or AEE after 1-AIT or 4-AIT. • 1-AIT had significantly lower TEE and step-count compared to MCT post intervention. • VO2max increased 7% after 1-AIT and 9% after 4-AIT, with no change after MCT.

Statistical findings pertaining to changes in BMI

Figure 4 looks at BMI changes due to increased step counts. The combined data shows a significant decrease in BMI (mean difference of -1.14 with a confidence interval of [-1.92, -0.36]). The studies show some variation ($I^2 = 32\%$), but the Chi^2 test was not significant ($p=0.18$), implying consistent findings and suggesting that increasing the step count might have helped to reduce your BMI. However, not all studies agreed on this, with multiple studies^{17,18,19,21,27} showed no significant BMI difference between groups. However, two studies^{22,24} reported significantly lower BMI in the step-increase groups.

Statistical findings pertaining to changes in RHR

Figure 5 elucidates the impact of increased step counts on RHR changes. The combined data from four studies shows no significant effect (mean difference of -1.85 with a confidence interval of [-3.82, 0.12]). The combined data did not show a clear decrease in RHR with increased step count. In some studies, the RHR was the same for both those who increased their steps and those who didn't. However, one study did find a significant decrease in RHR for those who increased their step count. The studies show low variation ($I^2 = 0\%$), supported by a non-significant Chi^2 test ($p=0.67$). Three studies^{18,19,21} showed no significant RHR difference between groups. However, one study²⁷ reported a significantly lower RHR in the step-increase group.

Figure 3: Effect of higher step counts on change in VO2 max.

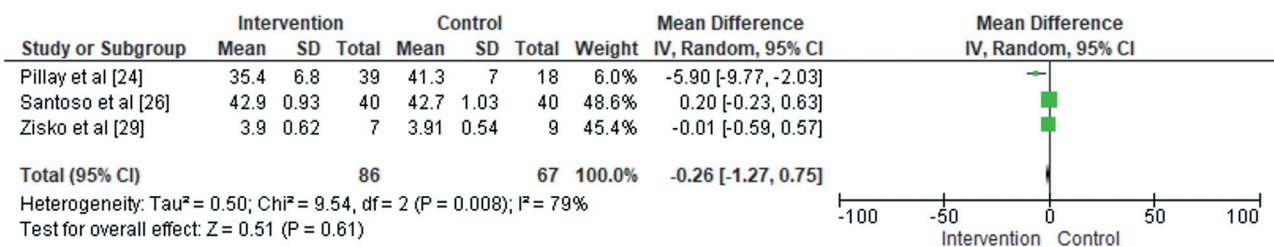


Figure 4: Effect of higher step count on change in BMI.

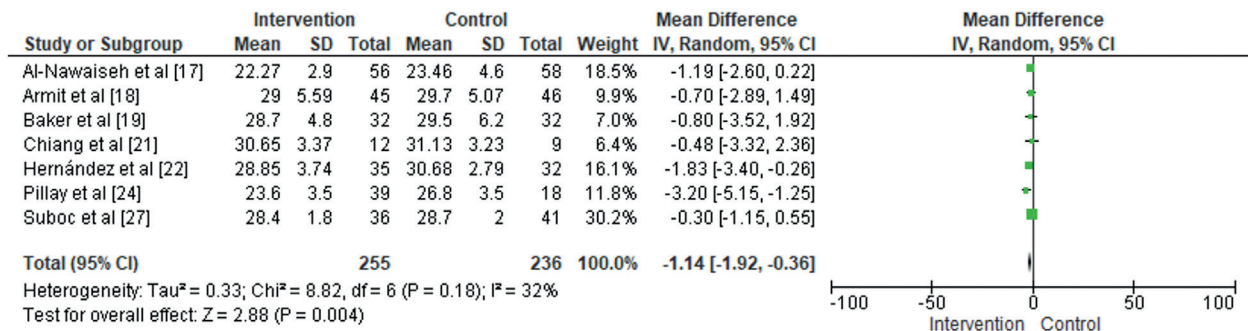
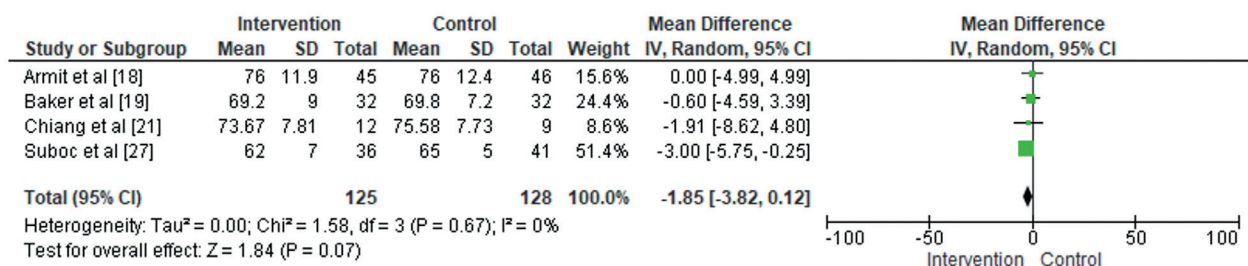


Figure 5: Effect of higher step count on change in RHR.



Discussion

In this analysis, we employed BMI, VO₂ Max, and RHR as surrogate measures of sedentary behaviour because the majority of the selected studies revealed a directly associated measure. When taken together, these three metrics offer a clear picture of a person's degree of fitness and physical activity as well as an implicit indicator of how sedentary their lifestyle is³⁰⁻³¹. The relationship between increasing step counts and declining rates of sedentary behaviour can be inferred thanks to the combination of BMI, VO₂ Max, and RHR, despite the fact that these are indirect markers. It is important to keep in mind that these assessments are subject to a variety of influences and that, although they may indicate patterns in sedentary behaviour, they are not accurate indicators of it³⁰⁻³¹.

When examining the collective results of these investigations comprehensively, it is evident that a multifaceted network of factors interact to shape the association between steps taken, a measure of physical activity, and different health outcomes. Increases in step counts were not significantly correlated with improvements in body weight, body fat percentage, BMI, or resting heart rate, according to several of the included publications¹⁷⁻¹⁸. This brought up the question of whether step counts directly affected these health consequences. However, other research, such that done by Baker et al.¹⁹ and Hernández et al.²², found a link between higher step counts and better health outcomes. Hernández et al.²² found that taking more steps per day was linked to significant decreases in weight and BMI as well as an increase in body water percentage. Baker et al.¹⁹ saw improvements in mood. These results suggest that walking more steps can have a major positive impact on one's health. Chiang et al.²¹ and Hopstock et al.²³ report improvements in health parameters such as visceral fat area, hip circumference, and high-density lipoprotein cholesterol. This suggested that improving health might be influenced by variables other than the quantity of steps completed.

Burton et al.²⁰ and Pillay et al.²⁴ noted significant variations in daily steps during the first two days of the intervention. Furthermore, a relationship was discovered between the degree of physical activity and decreased waist circumference, lower BMI, and body fat percentage, suggesting the possible benefits of higher step counts and activity levels on health outcomes. Research like that conducted by Suboc et al.²⁷ and Rogers et al.²⁵ has shown that varying levels and kinds of physical activity might affect health outcomes. For example, step counts can alter some metabolic indicators, and continuous activity raises FMD%. Santoso et al.²⁶, Zisko et al.²⁹, and Yoshimura et al.²⁸ came to similar conclusions on the effects of organised therapy and various exercise regimens on weight loss and fitness outcomes.

A meta-analysis of 19 RCTs by Ashur et al.³² revealed a substantial increase in VO₂max and daily step

count in CR participants who used accelerometers or pedometers. These findings are in contrast to ours, where we found that there was significant heterogeneity in the data and no discernible influence on VO₂max. The disparity between our results and those of Ashur et al.³², who concentrated exclusively on cardiac rehabilitation patients, may be the result of variations in the research populations. Furthermore, there were variations in the quantity of RCTs incorporated into the meta-analysis, which might have affected the accuracy and dependability of the findings. The effectiveness of wearable-based interventions in increasing physical activity and cardiometabolic health in people with chronic conditions was thoroughly assessed by Franssen et al.³³. Significant reductions in low-density lipoprotein cholesterol content, waist circumference, and systolic blood pressure were observed, along with improvements in physical activity levels. These results only agree with our review in part. While there was no discernible change in heart rate, we did see a considerable drop in BMI. Once more, the differences in study populations and the particular outcomes assessed in each review may be the cause of the diversity in results.

Step count and death rate were found to have a strong negative connection by Paluch et al.³⁴, with lower all-cause mortality hazard rates being associated with quartiles having higher daily step counts. While our review indicated a more moderate link, these findings were partly consistent with our findings, which also found an unfavourable correlation between step count and mortality. Paluch's study³⁴, which had a longer median follow-up of 7.1 years and a larger sample size of 47,471 people, may have contributed to the variations in participant diversity. In response to the widespread belief that 10,000 steps a day is the ideal, Sheng et al.³⁵ discovered evidence of a nonlinear dose-response association between step count and the risk of cardiovascular disease or all-cause death. This was consistent with our findings, which showed a nonlinear relationship as well. Sheng et al.³⁵ did point out that in contrast to the first quartile, the third quartile had a noticeably decreased risk of cardiovascular events and all-cause death. Our research, which discovered a more gradual decline in risk with greater step count, did not find this precise cut-off point.

Activity trackers have been shown to effectively enhance physical activity, body composition, and fitness across many age groups and both clinical and non-clinical populations, according to Ferguson et al.'s comprehensive review³⁶. They reported losing about 1 kg of body weight and taking about 1800 more steps a day on average. On the other hand, their impacts on psychosocial (pain and quality of life) and physiological (blood pressure, cholesterol, and glycosylated haemoglobin) outcomes were generally modest and frequently non-significant. Similar to what we discovered in our research, activity trackers are useful for promoting physical activity.

However, while we did see a significant drop in BMI, we were unable to identify a meaningful impact on heart rate. The variations in the physiological and psychosocial results may result from the different parameters that were assessed in each study. Step counts increased by 1126 steps per day at ≤ 4 months, decreased to 464 steps per day at one year, and then decreased to 434 steps per day at 3-4 years, as demonstrated by Chaudhry et al.³⁷ using multivariate meta-analysis. They discovered that smartphone apps and body-worn trackers performed worse than pedometers. The results of our review, which shown a considerable increase in daily step count with the usage of activity trackers, were partly compatible with these findings. Some of the difference in results, however, may be explained by the fact that our review did not examine the effect over time or differentiate between different types of activity trackers.

Over the last twenty years, step counters have been a standard component of behavioural techniques used in outpatient settings to increase physical activity among individuals who are not active^{11, 38-39}. There is a substantial body of research that condenses this element^{11, 38-39}. Bravata et al.'s study¹¹ examined studies that employed pedometers –devices that track your steps– to motivate people to move more. In randomised controlled trials, which are studies in which participants are assigned to different groups at random, the researchers discovered that pedometer-using groups boosted their daily step count by an average of 2491 more than the group that did not use pedometers. Pedometer users raised their daily steps by an average of 2183 from what they were performing previously in studies that were not controlled in this manner. Setting a step goal and maintaining an activity log were useful tactics. Upon analysing all the studies together, they discovered that using a pedometer was associated with a minor drop in both systolic blood pressure (the pressure in your arteries during a heartbeat) and body mass index (a measurement of body fat based on height and weight).

Richardson et al.³⁸ identified nine studies that satisfied their requirements; the studies' average duration was 16 weeks, but they ranged from 4 to 52 weeks. They discovered that participants in the research they included dropped 1.29 kg, or roughly 2.8 pounds, on average. Participants lost almost 0.05 kg every week on average. They came to the conclusion that longer programmes resulted in greater weight loss and that pedometer-based programmes only little reduced weight. In a study by Kang et al.³⁹, they examined earlier research that promoted regular physical activity with pedometers. They specifically searched for research that recorded the number of steps taken before and after an intervention, and that employed pedometers to encourage participants to move more. Additionally, only studies with an intervention lasting at least four weeks were included. Nevertheless, not all of them

offered sufficient information to determine the impact size—a metric used to measure how successful a specific intervention is. The average impact size for the 32 studies that were conducted was 0.62, meaning that the group who used pedometers increased their daily step count on average by 2000 steps. They discovered that when a daily target of 10,000 steps was set, the pedometers had a bigger impact on the female participants.

Limitations

The present investigation had certain inherent weaknesses that should be addressed as they may have had an impact on the outcome. Their conclusions showed a substantial lot of heterogeneity, which the meta-analysis occasionally corroborated with significant Chi2 tests. This suggests that other factors that the research did not account for could be influencing the outcomes. Moreover, although several research papers associated greater step counts with positive health outcomes, these findings were not consistent across all studies or health indicators. While some research produced contradictory results, other studies found no appreciable changes in RHR, weight, or body fat. The aforementioned disparity highlights the necessity for additional investigation to completely grasp the complex correlation between physical activity and health consequences. It could be the result of differences in the methods used for assessment, demographics, or study design.

Recommendations for everyday practice

It is advised to take into account higher step counts as part of a multifaceted strategy to improve general health and well-being, based on the thorough analysis of available data. This can be attributed to the documented advantages concerning particular health metrics, including a reduction in BMI. It is imperative to acknowledge that the impact of elevated step counts on health outcomes may not be uniformly relevant and may differ among distinct demographic subgroups. Walking and related activities may still be beneficial, even though there was no conclusive evidence of a substantial increase in VO2 max or RHR with higher step counts. Step counts are correlated with total physical activity, which is known to have a wide range of positive health effects, including the avoidance of chronic diseases and improvements in mental health.

The literature in this regard continuously emphasises how important it is to approach health promotion with a context-specific and tailored strategy. Given the variances observed between various geographic regions and demographic groupings, interventions must to be customised to take individual traits, cultural norms, and environmental factors into account. Furthermore, a holistic approach to health should take into account not just the promotion of physical activity but also other lifestyle factors like dietary habits, sleep patterns, and stress management.

Conclusion

We have found out that there is a relationship exists between the degree of physical activity and decreased waist circumference, lower BMI, and body fat percentage, suggesting the possible benefits of higher step counts and activity levels on health outcomes. Also, literatures suggests that accumulating steps counts over 8000 steps/day or more has reduced the risks that leads to cardiovascular mortality. We may not have taken into account other characteristics such as age, gender, lifestyle, and environment, which could explain the inconsistent results. Despite the wide range of results, they do point to the possibility that exercise can enhance wellbeing and health. However, further study is required to fully comprehend this. A challenge facing our study was the diversity of the research we examined, each with a unique set of participants. Future studies should aim to determine the significance of additional variables and

how they interact with physical activity to influence health. Better, more individualised guidance on how to increase wellbeing and health through exercise may result from this. We ought to strive towards providing individuals with more comprehensive guidance on physical activity, considering the intricate correlation between various health consequences and physical exercise. Ultimately, Walking is a low-impact, affordable, and easily accessible type of physical activity that is suitable for a variety of people, regardless of their financial situation or degree of fitness. Therefore, encouraging higher step counts can still improve public health and noticeable changes in particular health markers.

Conflicts of Interest

The authors declare no conflict of interest.

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ORIGINAL

Exploring the Knowledge and Practices of Health Professionals Regarding Oxygen Therapy: A Hospital-Based Study

Exploración del conocimiento y las prácticas de los profesionales de la salud con respecto a la oxigenoterapia: un estudio hospitalario

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Introduction: Oxygen therapy is a double-edged tool. On one hand, oxygen is vital for human survival. On the other hand, its administration can be toxic if the doses or methods used are not appropriate.

Methods: In this context, a study was conducted to assess the knowledge and practices of nurses regarding the appropriate administration of oxygen therapy at the Provincial Hospital Center in Ouarzazate. The study included 54 nurses, and data were collected through a questionnaire evaluating nurses' practices and knowledge.

Results: The results of the study showed that the majority of nurses had a good level of knowledge. However, there were knowledge gaps in areas such as indications, methods of assessing saturation, and symptoms of hyperoxia. Additionally, obstacles like the unavailability of therapeutic protocols and workload were mentioned by nurses, hindering the appropriate administration of oxygen therapy.

Conclusions: This study provides valuable insights to enhance the practice of oxygen therapy at the Provincial Hospital Center in Ouarzazate. By strengthening nurses' knowledge, establishing clear protocols, and addressing identified obstacles, it is possible to improve the quality of care and optimize outcomes for patients benefiting from this essential therapy.

Key words: Oxygen therapy, knowledge and practices, administration of oxygen, nursing, nurses.

Resumen

Introducción: La terapia de oxígeno es una herramienta de doble filo. Por un lado, el oxígeno es vital para la supervivencia humana. Por otro lado, su administración puede ser tóxica si las dosis o los métodos utilizados no son apropiados.

Metodología: En este contexto, se realizó un estudio para evaluar el conocimiento y las prácticas de las enfermeras con respecto a la administración adecuada de la terapia de oxígeno en el Centro Hospitalario Provincial de Ouarzazate. El estudio incluyó a 54 enfermeras y se recopiló datos a través de un cuestionario que evaluaba las prácticas y el conocimiento de las enfermeras.

Resultados: Los resultados del estudio mostraron que la mayoría de las enfermeras tenían un buen nivel de conocimiento. Sin embargo, hubo lagunas en áreas como las indicaciones, los métodos para evaluar la saturación y los síntomas de hiperoxia. Además, las enfermeras mencionaron obstáculos como la falta de protocolos terapéuticos y la carga de trabajo, lo que dificulta la administración adecuada de la terapia de oxígeno.

Conclusiones: Este estudio proporciona valiosas ideas para mejorar la práctica de la terapia de oxígeno en el Centro Hospitalario Provincial de Ouarzazate. Al fortalecer el conocimiento de las enfermeras, establecer protocolos claros y abordar los obstáculos identificados, es posible mejorar la calidad de la atención y optimizar los resultados para los pacientes que se benefician de esta terapia esencial.

Palabras clave: Terapia de oxígeno, conocimientos y prácticas, administración de oxígeno, enfermería, enfermeras.

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Introduction

Oxygen therapy is one of the most common prescriptions in emergency settings and is considered a medical treatment primarily prescribed for hypoxic patients. A well-targeted therapeutic goal allows for balancing the benefits and risks, as well as better managing hospital expenses due to excessive oxygen consumption, especially in resource-limited countries¹.

Oxygen therapy is a life-saving treatment. However, it is important to recognize that it can be misused, either by being administered at inadequate doses or by being inappropriately prescribed in situations where it is no longer necessary. To ensure its effectiveness, oxygen therapy must be properly applied regardless of the administration method used. Furthermore, its prescription in emergency cases must be prompt and tailored to the underlying cause of the medical problem and its identified etiology².

A study conducted by Nam Kamran analyzed data on oxygen prescription and administration practices at Royal Perth Hospital (RPH) in Western Australia. A total of 65 patients received oxygen supplementation, and among them, 36 patients (55.4%) received oxygen saturation prescriptions established by physicians. However, 25% of the prescribed goals were deemed inappropriate. Overall, 49 patients (75.4%) were exposed to a potential risk related to oxygen therapy due to prescription and/or administration errors. A real risk was identified in 19 patients (29.2%) as they received oxygen at levels outside their medically indicated target range³. Hence, it is crucial for every nurse to be aware of the potential side effects and significant costs associated with oxygen therapy, just like any other treatment when administered incorrectly⁴.

Studies conducted in various countries have generally shown a significant knowledge deficit among nurses regarding the correct use of oxygen. For example, studies conducted in Ethiopia have shown that only one-third of nurses had the necessary practical knowledge to use oxygen. Furthermore, nurses who had good practical knowledge of administering supplemental oxygen were 12 times more likely (AOR = 12.25, 95% CI = 6.48-32.93) to have good practice in administering supplemental oxygen than those with poor knowledge⁵. Another study conducted in Saudi Arabia also showed a lack of adequate knowledge among nurses regarding the therapeutic use of oxygen, particularly regarding indications for oxygen therapy. According to their findings, high workload and lack of local guidelines were the main causes⁶.

Conducting a study to assess nurses' knowledge of oxygen therapy has several significant advantages. This type of study helps identify existing gaps in nurses' knowledge of oxygen therapy. It raises awareness of specific areas where improvements are needed and focuses training efforts on these key aspects. By identifying areas that require additional training, the study

facilitates the design of tailored training programs. These programs can target the specific gaps highlighted by the study, providing nurses with the knowledge and skills needed to improve their practice. The training programs developed as a result of the study can contribute to enhancing nursing practice in oxygen therapy. By providing nurses with the necessary information and tools, they can strengthen their understanding and ability to properly administer oxygen therapy, thus reducing errors and risks to patients.

In this context, this study aims to evaluate the knowledge of nurses working at the Provincial Hospital Center of Ouarzazate regarding normobaric oxygen therapy, as well as the factors associated with it.

Material and methods

Study design, participants and sampling method

This is a cross sectional, study aiming to assess the knowledge of nurses regarding oxygen therapy. The target population for this study comprised nurses working at the Provincial Hospital Center in Ouarzazate, focusing on specific departments, including (a) the emergency department, (b) the intensive care unit, (c) the surgery department, (d) the medicine department, (e) the pediatrics and pediatric surgery department, (f) the maternity department, (g) the postpartum unit, and (h) the operating room. These departments were chosen due to their frequent use of oxygen therapy compared to other departments. A total of 54 nurses were included in this study through an exhaustive sampling method.

Data Collection Instrument

Data for this study were collected using a questionnaire that was developed based on an extensive review of the existing literature. The instrument consisted of a set of questions to gather participants' socio-demographic data, theoretical knowledge related to oxygen therapy, and practices of nurses during its administration. A score was calculated for each component by awarding one point for each correct answer. Then, an overall score was obtained by summing up the scores of theoretical and practical knowledge. Data collection was carried out from April 15, 2023, to May 23, 2023. Once the questionnaire was tested and validated, it was distributed to nurses and collected on the same day to avoid information exchange between participants.

Data Analysis

The collected data were analyzed using the "SPSS 21.0" software. A p-value of 0.5 was considered. Quantitative variables were expressed as mean \pm standard deviation, while qualitative variables were presented in tables as frequencies. The t-test and ANOVA were used to study the associations between variables.

Ethical considerations

The researchers adhered to ethical guidelines by seeking permission from the administration to conduct the study, providing a clear explanation of the study's purpose to participating nurses, ensuring the participants' anonymity, obtaining their consent, and maintaining strict confidentiality of the collected data.

Results

The study examined the results of a questionnaire that was distributed to 98 nurses from various hospital departments. Out of the 98 distributed surveys, a total of 54 responses were obtained, yielding a response rate of 55.1%.

1. Description of Demographic Characteristics of Nurses Participating in the Study

The distribution of the sample by gender demonstrates the predominance of females, accounting for 70.4% compared to 29.6% males. Furthermore, the distribution of the sample by age reveals that the age group between 20 and 25 years is the most dominant (38.9%), followed by the age group between 26 and 35 years (25.9%), while the age group of 46 years and older constitutes only 11.1%.

Regarding the distribution of the sample by specialty, generalist nurses represent the majority with a percentage of 53.7%, followed by midwives with a percentage of

24.1%, while nurses specializing in anesthesia and intensive care account for 16.7% and emergency and critical care nurses make up 5.6% of the sample. Nurses with a seniority of 0-5 years constitute 46.3% of the sample, followed by nurses with a seniority of 11-15 years (16.7%), and those with a seniority of 6-10 years and 21 years and above participate with percentages of 14.8% and 11.1%, respectively.

According to the table, the majority of nurses have a basic training background (74.1%), 1.9% have received continuing education, while 24.1% have not received any training on oxygen therapy. **Table I.**

2. Theoretical knowledge according to nurses' characteristics

The results reveal that younger nurses with less than 10 years of experience have, on average, a higher level of knowledge compared to their colleagues with over 10 years of experience. However, this correlation did not reach statistical significance. Additionally, no statistically significant relationship was found between the level of theoretical knowledge of the studied sample and factors such as sex, age, specialization, department of practice, and receiving training on oxygen therapy. These results indicate that these factors do not appear to have a direct impact on the nurses' theoretical knowledge level. **Table II.**

Table I: Socio-demographic characteristics of the nurses targeted by the study.

	N = 54
Sex	
Male	16 (29.6%)
Female	38 (70.4%)
Age (Years Old)	
20 - 25	21 (38.9%)
26 - 35	14 (25.9%)
36 - 45	13 (24.1%)
> 46	6 (11.1%)
Specialty	
Generalist nurse	29 (53.7%)
Nurse in anesthesia and intensive care	9 (16.7%)
Nurse in emergency and intensive care	3 (5.6%)
Midwife	13 (24.1%)
Seniority (Years)	
<10	35 (41.7%)
>10	19 (22.6%)
Department	
Emergency department	7 (13.0%)
Intensive Care Unit	7 (13.0%)
Internal medicine	6 (11.1%)
Pediatric surgery	5 (9.3%)
General surgery department	5 (9.3%)
Pediatrics	6 (11.1%)
Maternity unit	6 (11.1%)
Postpartum unit	5 (9.3%)
Operating room	7 (13.0%)
Oxygen administration Training	
Basic training	40 (74.1%)
Continuing training	1 (1.9%)
No training	13 (24.1%)

Table II: Presentation of Theoretical Knowledge Results Based on Nurse Characteristics.

	Mean	SD	T-test	Sig
Sex				
Male	9.23	1.16	1.34	0.18
Female	8.51	1.74		
Protocol availability				
Yes	8.78	1.66	0.58	0.56
No	8.64	1.54		
	Mean	SD	F	Sig
Age (Years Old)				
20 - 25	8.56	1.45	2.00	0.13
26 - 35	9.50	1.95		
36 - 45	8.00	1.41		
> 46	9.40	1.14		
Specialty				
Generalist nurse	8.90	1.26	0.50	0.68
Nurse in anesthesia and intensive care	9.00	2.58		
Nurse in emergency and intensive care	9.00	0.00		
Midwife	8.25	1.65		
Seniority (Years)				
<10	8.92	1.69	0.95	0.34
>10	8.43	1.45		
Department				
Emergency department	8.71	0.95	0.55	0.80
Intensive Care Unit	8.20	1.30		
Internal medicine	9.75	1.50		
Pediatric surgery	7.50	0.70		
General surgery department	9.25	0.95		
Pediatrics	9.25	1.25		
Maternity unit	8.33	1.63		
Postpartum unit	8.40	1.94		
Operating room	9.00	3.08		
Oxygen administration Training				
Basic training	9.00	1.70	1.61	0.21
Continuing training	8.00	0.04		
No training	8.00	1.05		

The vast majority of individuals who participated in the study had good knowledge of oxygen therapy, particularly in areas related to hypoxemia, hypoxia, and respiratory pathologies. An intriguing observation to highlight is that 90.7% of nurses fully agree that excessive oxygen supply can cause toxicity, yet only 27.8% know the signs and symptoms of this toxicity. Similarly, most nurses (81.5%) answered incorrectly regarding the indications for oxygenation, with only 27.8% correctly identifying hypoxemia as an indication, and only 18.5% were able to mark all the indications correctly. Furthermore, the results also reveal a gap in the participants' knowledge regarding methods of oxygen saturation assessment, with only 20.4% knowing all the methods, and the majority of participants selecting the answer "pulse oximeter".

Table III.

3. Practical knowledge according to the characteristics of nurses

Concerning the nurses' practices based on their characteristics, no significant variance was observed between the nurses' practice level and their years of experience, specialization, training, and age. However, a statistically significant relationship was found between the practice level and the department of practice (P value = 0.007).

Table IV.

The majority of participants in the study demonstrated good practices during the administration of oxygen therapy. The practical questions specifically focused on the best practices to be followed before, during, and after administering oxygen therapy. It is interesting

Table III: Theoretical Knowledge of Oxygen Therapy Among Nurses.

Questions	Correct response	Incorrect response
Indications for oxygen therapy	18.5%	81.5%
Methods of assessing blood oxygen saturation	20.4%	79.6%
Monitoring pulse oximetry	5.6%	92.6%
Complications of excessive oxygen delivery	90.7%	9.3%
Symptoms of oxygen toxicity	27.8%	63.0%
Side effects of oxygenation	90.7%	9.3%
Recommendations for oxygen concentrations in children with pneumothorax	83.3%	5.6%
Shortness of breath is not always a sign of hypoxemia	88.9%	11.1%
In severe anemia, heart failure, and brain injuries, providing oxygen to patients with an SpO ₂ <94% is more appropriate	63.0%	35.2%
Prescription of oxygen should be based on a target SpO ₂ range rather than a fixed dose	81.5%	16.7%
Hypoxia can be clinically detected	83.3%	16.7%
Blood gas analysis is useful to confirm hypoxemia	79.6%	18.5%
The administration of concentrated oxygen leads to the creation of surfactant on the surface of the lungs	42.6%	50.0%
The target level of SpO ₂ in patients with COPD is generally set between 88% and 92%.	70.4%	24.1%

to note that 61.1% of participants strongly agreed that sterilizing the equipment with an antiseptic solution is sufficient, while in reality, the equipment used should be disposable. Furthermore, 53.7% of participants indicated that they do not place gauze pads under the tubing, even when necessary. This preventive measure seems to be neglected by the majority of nurses.

Table V.

Table IV: Practical knowledge according to the characteristics of nurses.

	Mean	SD	T-test	Sig
Sex				
Male	8.71	1.81	-0.38	0.70
Female	8.91	1.67		
Protocol availability				
Yes	9.18	1.16	0.70	0.48
No	8.77	1.81		
	Mean	SD	F	Sig
Age (Years Old)				
20 - 25	9.00	1.55	1.16	0.33
26 - 35	9.23	1.58		
36 - 45	8.08	2.10		
> 46	9.16	1.32		
Specialty				
Generalist nurse	8.67	1.96	1.07	0.37
Nurse in anesthesia and intensive care	9.77	0.97		
Nurse in emergency and intensive care	8.50	2.12		
Midwife	8.66	1.30		
Seniority (Years)				
<10	9.09	1.54		1.19
>10	8.44	1.96		
Department				
Emergency department	7.33	1.86	3.14	0.007
Intensive Care Unit	10.33	0.51		
Internal medicine	8.00	1.67		
Pediatric surgery	9.20	1.30		
General surgery department	9.80	1.09		
Pediatrics	7.83	2.40		
Maternity unit	8.16	1.32		
Postpartum unit	9.75	0.50		
Operating room	9.71	1.11		
Training				
Basic training	8.75	1.68	0.39	0.67
Continuing training	10.00			
No training	9.07	1.80		

Table V: Practical Knowledge of Oxygen Therapy Among Nurses.

Questions	Correct response	Incorrect response
The disinfection of the equipment with an antiseptic solution is sufficient	61.1%	38.9%
Explain the procedure to the patient	94.4%	5.6%
Disinfect your hands	68.5%	31.5%
Wear disposable gloves	61.1%	38.9%
Evaluate the patient's oxygen saturation	100%	0.0%
Assess the patient's respiratory status	96.3%	3.7%
Fill the humidifier with distilled water	94.4%	5.6%
Place gauze pads under the tubing, if necessary	42.6%	53.7%
Dispose of used oxygen mask and tubing	74.1%	5.6%
Document the date and time of oxygen therapy administration	94.4%	5.6%
Evaluate the patient's condition before and after the intervention to assess any improvement	96.3%	3.7%

4. Obstacles to the appropriate use of oxygen therapy reported by nurses

The studied nurses mentioned certain obstacles to the appropriate use of oxygen therapy. Indeed, 66.7% of the studied sample identified the unavailability of a standardized protocol for oxygen therapy as a major obstacle. Additionally, 61.1% of the nurses highlighted that workload and time constraints impact the administration of oxygen therapy to their patients.

Table VI.

Table VI: Obstacles to the proper use of oxygen therapy.

Obstacles	N = 54
Limited availability of oxygen in sufficient and regular quantity	
Yes	14 (25.9%)
No	40 (74.1%)
Insufficient training and education for medical and nursing staff	
Yes	21 (38.9%)
No	33 (61.1%)
Lack of understanding of the effects, role, and dangers of oxygen therapy	
Yes	23 (42.6%)
No	31 (57.4%)
Lack of equipment, supplies, and monitoring devices	
Yes	24 (44.4%)
No	30 (55.6%)
Lack of familiarity with the use of different oxygen therapy devices	
Yes	19 (35.2%)
No	35 (64.8%)
Workload and time constraints	
Yes	33 (61.1%)
No	21 (38.9%)
Lack of staff motivation	
Yes	24 (44.4%)
No	30 (55.6%)
Unclear and incomplete oral/written prescription for oxygen therapy	
Yes	21 (38.9%)
No	33 (61.1%)
Difficulties in changing long-established behavior	
Yes	16 (29.6%)
No	38 (70.4%)
Patients transferred from other services or departments with existing oxygen therapy in place	
Yes	8 (14.8%)
No	46 (85.2%)
Unavailability of a protocol for oxygen therapy	
Yes	36 (66.7%)
No	18 (33.3%)

Discussion

Excessive oxygen consumption can result from improper patient assessment or inappropriate administration, potentially leading to health deterioration, respiratory complications, or other adverse effects. Conversely, insufficient access to oxygen or inadequate equipment may limit treatment efficacy and compromise the well-being of patients in need. Therefore, it is essential for healthcare professionals to be well-informed about appropriate oxygen therapy protocols and accurately

assess each patient's individual needs. In this regard, the objective of this study was to evaluate the level of knowledge of nursing staff regarding oxygen therapy.

The present study indicated that slightly over half of the studied sample (60.45%) demonstrated a good level of theoretical knowledge concerning oxygen therapy administration. This finding is comparable to research conducted in Ethiopia at Debre Tabor General Hospital, where 52% of participants reported having good knowledge, while 48% of nurses had poor knowledge of oxygen therapy⁵. Similarly, in Egypt, at one of Cairo's university hospitals in 2018, the majority of the studied sample had a satisfactory level of knowledge regarding the purpose of oxygen therapy administration (54%), different methods used to assess blood oxygen saturation (58%), precautions to take during oxygen therapy administration (80%), and nursing interventions related to oxygen therapy administration (50%)⁷. In contrast to our results, previous studies conducted in Turkey and Nigeria demonstrated that nurses had poor knowledge of oxygen therapy⁸. However, the results of this study indicate that the majority of nurses had a low level of knowledge concerning the indications for oxygen therapy. Only 18.5% of nurses answered correctly, which is similar to a study conducted by Amairah Fahad Aloushan in Riyadh in 2017, where only 12.4% of nurses accurately knew the indications⁶.

Furthermore, this study reported that most participants (92.6%) had inadequate knowledge regarding pulse oximetry monitoring, and (79.6%) responded incorrectly to questions about methods of saturation assessment. These results could be attributed to a lack of training and unawareness of the seriousness of oxygen therapy. Such knowledge gaps among nurses may have detrimental consequences on patients' health, especially in critical situations where oxygen therapy is crucial. Improper administration or incorrect usage of oxygen therapy can lead to severe complications and compromise patient safety. In line with this finding some authors^{9,10}. In their studies emphasized that to ensure safe and effective oxygen therapy administration, nurses must possess appropriate knowledge and understanding of the subject. The relevance of continuous training is crucial in this context. A recent study conducted by Ait Ali et al. in 2022 in Morocco demonstrated that a significant majority of nurses (57%) do not participate in continuous training sessions, attributing this behavior, among other reasons, to the themes not being applicable to their daily practice¹¹.

Another result of this study is that most nurses are aware of the side effects of oxygenation, and (90.7%) know that excessive oxygen supply can cause toxicity; however, only (27.8%) are aware of the signs and symptoms of this toxicity. In this context, it is interesting to note that the observed knowledge gaps among nurses concerning oxygen toxicity could be attributed to a lack of awareness of its status as a medication. It is essential to emphasize

that oxygen therapy should be considered as a full-fledged medication, requiring precise administration and appropriate dosages to ensure patient safety and optimize therapeutic benefits.

The results of this study also provide valuable insights into the relationships between theoretical knowledge and the seniority within the studied sample. Traditionally, experience is considered a fundamental pillar for gaining solid knowledge and proficiency. However, this research highlights a different observation: there is a slight difference in favor of younger nurses with less than 10 years of experience, but this experience/knowledge level relationship is not statistically significant ($p=0.34$). Furthermore, the results demonstrated that there was no statistically significant correlation between participants' knowledge level and other socio-demographic characteristics.

Regarding nurses' practice level, our study indicates that the majority of nurses had good practice (78.27%). However, research conducted in different contexts reported lower percentages of good practices among nurses. In the study conducted at Debre Tabor Hospital⁵, only 33% of nurses had good practice. Similarly, in hospitals in Addis Ababa, 43.4% had a good level of practice⁵, and 47.5 % in Eritrean hospitals¹².

The questions evaluating nurses' practices specifically focused on best practices before, during, and after oxygen therapy administration. The results of practical knowledge before oxygenation administration in this study are higher than those of the Egyptian hospital study, where only 18.7% of the studied sample performed all nursing interventions before oxygen therapy administration⁷.

Despite 77.8% of participants reporting the unavailability of standardized oxygen therapy protocols, this study confirmed that nurses had sufficient practical knowledge. It was found that participants' practice had a statistically significant relationship with their working department ($p=0.007$). Regarding other demographic characteristics studied, such as gender, tenure, and specialty, no statistically significant correlation was observed with participants' practice level.

The results of this study provide valuable insights into specific knowledge and practice gaps identified among nurses regarding oxygen therapy. These findings can serve as a valuable tool for planning and implementing

targeted continuous training programs. However, this study has some limitations to consider. Firstly, the study was conducted using a limited sample size. Additionally, it was a single-center study, and the research results are limited to the hospital where it was conducted, making it necessary to exercise caution when generalizing the results to other hospitals. Furthermore, the subjectivity of participants' responses to the study (in the case of the questionnaire) means that the results were measured by self-reporting and may be biased. Lastly, it is important to acknowledge that the level of nurses' knowledge evaluated in this study is limited to their responses to the questions provided in the questionnaire, which may not comprehensively reflect their actual knowledge or clinical practice. Thus, it is crucial to consider these limitations when interpreting the study's results.

Conclusion

Oxygen therapy is a vital medical treatment to ensure adequate oxygenation in various medical or surgical conditions. The health of patients can be greatly influenced by their oxygen supply, whether it is excessive, insufficient, or absent, which largely depends on the level of competence and attitude of healthcare professionals towards oxygen therapy.

The results of this study evaluating the knowledge of nurses regarding oxygen therapy at the Provincial Hospital Center in Ouarzazate demonstrated that most nurses have a good level of theoretical and practical knowledge. However, when addressing obstacles that could affect the safe administration of oxygen therapy, the majority of nurses reported the lack of clear protocols to follow. Additionally, they emphasized that workload was the most serious obstacle they faced.

Given the vital importance of oxygen therapy, it is imperative to promote research in this field to address knowledge gaps and explore new approaches or technologies that could enhance both the effectiveness and safety of this essential treatment.

Conflict of interest

The authors affirm that they have no conflicts of interest to disclose.

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Retinal Diseases among Patients Attending to the Department of Ophthalmology in a Tertiary Care Center of Central Nepal

Enfermedades de la retina en pacientes que acuden al Departamento de Oftalmología de un centro de atención terciaria: Un estudio descriptivo transversal

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Abstract

Introduction: Retinal diseases are emerging causes of visual impairment and blindness in the developing world. The prevalence of retinal diseases is on the rise due to the increasing prevalence of non-communicable diseases like hypertension, diabetes mellitus, and refractive error, particularly myopia. This study aimed to find out the prevalence and types of retinal diseases among patients attending the outpatient Department of Ophthalmology in a tertiary care hospital.

Methods: A descriptive cross-sectional study was conducted among patients attending the Department of Ophthalmology after receiving ethical approval from the Institutional Review Committee (Reference number: CMC-IRC/079/80-054). The study was conducted from 15 September 2022 to 25 March 2023. Basic demographic data, risk factors, clinical characteristics, and diagnosis of retinal diseases were entered into a specified proforma for the study. Convenience sampling was done. Data analysis was done using Statistical Package for the Social Sciences version 26, point estimate at a 95% Confidence Interval (CI) was calculated along with frequency and proportion for binary data.

Results: Among 1256 participants, retinal disease was found in 224 (17.83%) (15.82-20.05, 95% Confidence Interval) participants in at least one eye. Diabetic retinopathy 110 (49.10%) was the most common retinal morbidity followed by hypertensive retinopathy 47 (20.98%). Posterior vitreous detachment 12 (5.57%), lattice degeneration 10 (4.46%), and myopic degeneration 09 (4.01%) were the other commoner retinal diseases in the study subjects.

Conclusions: The prevalence of retinal diseases in the current study was lower than the national estimates. The alarming rise of diabetes and hypertension in Nepal was reflected by the higher prevalence of diabetic, and hypertensive retinopathies.

Key words: Age-related macular degeneration; diabetic retinopathy; hypertensive retinopathy; myopia; retinal detachment.

Resumen

Introducción: Las enfermedades de la retina son causas emergentes de discapacidad visual y ceguera en el mundo en desarrollo. La prevalencia de las enfermedades de la retina va en aumento debido a la creciente prevalencia de enfermedades no transmisibles como la hipertensión, la diabetes mellitus y los defectos de refracción, en particular la miopía. El objetivo de este estudio era averiguar la prevalencia y los tipos de enfermedades de la retina entre los pacientes que acuden al Departamento de Oftalmología de un hospital de atención terciaria.

Métodos: Se realizó un estudio descriptivo transversal entre los pacientes que acudían al Departamento de Oftalmología tras recibir la aprobación ética del Comité de Revisión Institucional (Número de referencia: CMC-IRC/079/80-054). El estudio se llevó a cabo del 15 de septiembre de 2022 al 25 de marzo de 2023. Los datos demográficos básicos, los factores de riesgo, las características clínicas y el diagnóstico de las enfermedades de la retina se introdujeron en un formulario específico para el estudio. Se realizó un muestreo de conveniencia. El análisis de los datos se realizó con el paquete estadístico Statistical Package for the Social Sciences versión 26. Se calculó la estimación puntual con un intervalo de confianza (IC) del 95%, junto con la frecuencia y la proporción de los datos binarios.

Resultados: Entre los 1056 participantes, se encontró enfermedad retiniana en 224 (21,21%) (18,85-23,78, intervalo de confianza del 95%) participantes en al menos un ojo. La retinopatía diabética 110 (49,10%) fue la morbilidad retiniana más frecuente, seguida de la retinopatía hipertensiva 47 (20,98%). El desprendimiento vítreo posterior 12 (5,57%), la degeneración reticular 10 (4,46%) y la degeneración miópica 09 (4,01%) fueron las otras enfermedades retinianas más frecuentes en los sujetos del estudio.

Conclusiones: La prevalencia de las enfermedades de la retina en el presente estudio fue inferior a las estimaciones nacionales. El alarmante aumento de la diabetes y la hipertensión en Nepal se reflejó en la mayor prevalencia de retinopatías diabéticas e hipertensivas.

Palabras clave: Degeneración macular asociada a la edad; retinopatía diabética; retinopatía hipertensiva; miopía; desprendimiento de retina.

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Introduction

Retinal diseases are an important cause of ocular morbidity, and visual impairment globally. The prevalence of retinal diseases is on the rise lately due to various factors¹.

The reported prevalence of various population-based studies on retinal diseases varies. Increased life expectancy, changing lifestyles, and chronic systemic illnesses like diabetes mellitus, and hypertension are the leading contributing factors to develop retinal diseases in the modern world^{2,3}. In various population and hospital-based studies, age-related macular degeneration (AMD), hypertensive retinopathy, diabetic retinopathy, and retina vascular occlusions have been reported to be more common vitreoretinal disorders⁴⁻⁶. In Nepal, retinal diseases were the third most common leading cause of blindness in the 1981 survey¹.

There is a paucity of data on the prevalence of retinal diseases in Nepal, this study aimed to find out the prevalence, and types of retinal diseases among patients attending a tertiary care hospital in central Nepal.

Methods

A descriptive cross-sectional study was conducted on the patients visiting the outpatient Department (OPD) of Ophthalmology at Chitwan Medical College (CMC), Bharatpur, Nepal after obtaining ethical clearance from the Institutional Review Committee (Reference number: CMC-IRC/079/80-054). The study was conducted from 15 September 2022 to 25 March 2023 over seven and a half months. All patients visiting the outpatient Department of Ophthalmology were included in the study. Critically ill patients, patients from the emergency department, patients below 20 years of age, and more than 90 years of age, glaucoma suspects, patients with glaucomatous disc damage, patients with hazy media due to anterior segment pathologies, and patients not willing to provide consent for the study were excluded from the study. A convenience sampling technique was used. The sample size was calculated using the formula:

$$n = \frac{Z^2 \times (p \times q)}{e^2}$$

$$= 1.96^2 \times \frac{(0.52 \times 0.48)}{(0.05)^2} = 383$$

Where,

n= minimum required sample size

Z= 1.96 at 95% Confidence interval (CI)

p= prevalence of any retinal pathology reported by a similar study, 52.37%¹

q= 1-p

e= margin of error, 5%

The minimum sample size calculated was 383, considering the non-respondent rate of 10%, the total sample size becomes 421. However, we took 1256 participants in the study.

After explaining the purpose of the study and the confidentiality of data collection, informed consent was obtained from each participant. The study participants were evaluated in detail in the following sequence: visual acuity measurement of each eye separately (unaided and with a pinhole), extra-ocular movement assessment, cover test, cover-uncover test, refraction using a Heine Beta 200 retinoscope, anterior segment examination with a slit lamp, and detailed fundus examination. Evaluation of the fundus was done by a retina specialist and consultant Ophthalmologist of the Department of Ophthalmology. Fundus evaluation was done using direct Ophthalmoscope and indirect Ophthalmoscopy using +20 Diopter (D), +78D, and +90D lenses. Tropicamide 1% and or tropicamide 0.8% + phenylephrine 5% eye drops were used to dilate the pupils for fundus evaluation. All four quadrants of the retina superior, inferior, nasal, and temporal were examined in detail. The macular and foveal region was given special attention during the fundus evaluation. The significant findings from the fundus were documented and a picture of the fundus was drawn for the record.

Modified Airlie House classification and early treatment and diabetic retinopathy study (ETDRS) were used for the evaluation of different stages of diabetic retinopathy and macular edema in the study subjects⁵. Keith Wagner and Baker classification was used for the classification of hypertensive retinopathy in known hypertensive study participants⁶. Baseline socio-demographic characteristics, awareness about diabetic retinopathy in diabetic patients, data regarding associated factors like family history of diabetes mellitus (DM) and hypertension (HTN), duration of DM in years, type of DM, smoking habit, alcohol consumption, body mass index, other co-morbid conditions like myopia, trauma were entered in a specifically made proforma for the study. In addition, investigations like blood sugar levels, serum total cholesterol levels, and glycated hemoglobin levels (HbA1c) were done in study participants when indicated.

Patients with suspected retinal morbidities needing further investigations like Optical coherence tomography (OCT), Fundus photography, and fundus fluorescein angiography (FFA) were suggested and advised to undertake the investigations and follow up with reports. In patients with suspected cardiac problems investigations like Electrocardiogram (ECG) and Serum lipids were advised and referred to the internists for management and control of the systemic problems. Accurate diagnosis was made using clinical findings, investigation reports, and interobserver agreement.

Data were entered and analyzed using IBM SPSS Statistics version 26.0. Point estimate and 95% CI were calculated.

Results

Among 1256 participants, retinal disease was found in 224 (17.83%) (15.82-20.05, 95% Confidence Interval) participants in at least one eye. Diabetic retinopathy 110 (49.10%) was the most common retinal morbidity followed by hypertensive retinopathy 47 (20.98%). Posterior vitreous detachment 12 (5.57%), lattice degeneration 10 (4.46%), and myopic degeneration 09 (4.01%) were the other commoner retinal diseases in the study subjects (**Table I**).

Of 224 participants with retinal pathologies, 79 (35.26%) were obese or overweight, 177 (79.01%) were diagnosed as diabetics, 118 (52.67%) were hypertensives, 139 (62.05%) were aware of retinal consequences due to chronic diseases, 138 (61.60%) gave a prior history of cataract surgery, and 28 (12.50%) study participants had electrocardiogram changes as summarized (**Table II**).

The mean age of presentation of the study participants was 60.15±15.00 years. Males 118 (57.62%) just outnumbered the females. The majority of the study participants were above the age of 50 years 187 (83.49%). Geographic distribution wise 192 (85.72%) belonged to the urban areas, and literacy wise 178 (79.46%) study participants were literate. Agriculture 84 (37.50%) was the most common occupation of the study participants as summarized (**Table III**).

Table I: Types of retinal diseases among the study subjects (n = 224).

Variables	n (%)
Diabetic retinopathy	110 (49.10)
Grade I HTN retinopathy	31 (13.84)
Grade II HTN retinopathy	4 (1.78)
Grade III HTN retinopathy	3 (1.33)
Grade IV HTN retinopathy	9 (4.01)
Myopic degeneration/Tigroid fundus	9 (4.01)
Retinal detachment	5 (2.23)
Age-related macular degeneration (ARMD)	4 (1.78)
Hereditary drusen	4 (1.78)
Retinal detachment	1 (0.44)
Macular hole/retinal holes	4 (1.78)
Lattice degeneration	10 (4.46)
Chorioretinal scar	2 (0.89)
Chorioretinal coloboma	1 (0.44)
Epiretinal membrane	3 (1.33)
Macular scar	2 (0.89)
Posterior Vitreous Detachment (PVD)	12 (5.35)
Central Retinal Vein Occlusion (CRVO)	1 (0.44)
Central Retinal Artery Occlusion (CRAO)	1 (0.44)
Branch Retinal Vein Occlusion (BRVO)	1 (0.44)
Optic atrophy	2 (0.89)
Retinitis pigmentosa	1 (0.44)
Central serous chorioretinopathy (CSCR)	1 (0.44)
Asteroid hyalosis/Synchisis scintillans	2 (0.89)
Others	1 (0.44)
Total	224 (100)

Discussion

In the present study, Among 1256 participants, retinal disease was found in 224 (17.83%) (15.82-20.05, 95% Confidence Interval) participants in at least one eye. Diabetic retinopathy 110 (49.10%) was the most common retinal morbidity followed by hypertensive retinopathy 47 (20.98%). Posterior vitreous detachment 12 (5.57%), lattice degeneration 10 (4.46%), and myopic degeneration 09 (4.01%) were the other commoner retinal diseases in the study subjects. In a study done in Nepal¹, the overall prevalence of vitreoretinal diseases was found to be 52.37%, this did not compare well with the current study as in the current study the prevalence of retinal disease was much lower at 21.21%. However, in another study from Nepal⁴ from a similar setting the prevalence of vitreoretinal disease was found to be 5.35% which was lower than the current study findings. In a study done in rural Southern India, the prevalence of vitreoretinal disease was found to be 10.40% which was lower than our study findings and did not correlate with our study findings². This difference in the prevalence

Table II: Clinical characteristics of the study participants with retinal pathologies (n=224).

Variables	n (%)
Body Mass Index (BMI)	
Overweight	67 (29.91)
Obese	12 (5.35)
Alcohol Consumption	
Social alcohol consumption	74 (33.03)
Regular alcohol consumption	11 (4.91)
Alcohol addiction	2 (.89)
Current smokers	63 (28.15)
History of ocular trauma	21 (9.37)
Participants with Diabetes Mellitus	177 (79.01)
Participants aware of retinal diseases	139 (62.05)
Participants diagnosed as Hypertensives	118 (52.67)
Visual impairment in the participants due to refractive error	20 (89.28)
Prior history of cataract surgery	138 (61.60)
Abnormal electrocardiogram (ECG) findings in the participants	28 (12.50)
Total	224 (100.00)

Table III: Demographic profile of the study participants (n= 224).

Variables	n (%)
Gender distribution	
Male	118 (57.62)
Female	106 (42.38)
The age group of the study participants	
More than 50 years of age	187 (83.49)
Below 50 years of age	37 (16.51)
Geographical distribution of the study participants	
Rural areas	32 (14.28)
Urban areas	192 (85.72)
Occupation of the study participants	
Agriculture	84 (37.50)
Retired	58 (25.90)
Other	82 (36.90)
Educational background of the study participants	
Literate	178 (79.46)
Illiterate	46 (20.53)
Total	224 (100.00)

rate of vitreoretinal study could be attributed to various factors but we believe the sample size, the study age group, and study site, and risks associated were important contributing factors, needless the mention the current study being a hospital-based study and the aforementioned studies being population based surveys.

Age-related macular degeneration (ARMD) has been described as the most common vitreoretinal pathology in studies from other parts of Nepal with prevalence being 35.43% and 1.50% respectively^{1,4}. In the current study, diabetic retinopathy was the commonest vitreoretinal pathology 49.10% encountered followed by hypertensive retinopathy 20.98%, these were followed by posterior vitreous detachment in 5.35%, myopic degeneration in 4.01% and lattice degeneration in 4.68%, in the current study ARMD was seen only in 1.78% study subjects. The prevalence of ARMD at 1.78% in the current study did compare with the findings from a study from Nepal⁴ where the prevalence of ARMD was 1.50%. The higher prevalence of diabetic retinopathy and hypertensive retinopathy in the current study is attributed to the study site and study population, in the current hospital-based study the study participants with chronic diseases like diabetes and hypertension were very high 79.01%, and 52.67% respectively. A very low prevalence of ARMD when compared to other studies from Nepal^{1,4} could be attributed again to the study population and the risks associated, our study had participants below 50 years of age accounting for 16.51% of total study participants, and age is one of the most important risks to develop ARMD as per existing literature ARMD is believed to occur in people above 50 years of age with the risk advancing high with each passing year^{7,8}. Findings of other vitreoretinal pathologies like retinitis pigmentosa, macular hole, retinal detachment, lattice degeneration, CSCR, Chorioretinal scars, Chorioretinal coloboma, epiretinal membrane (ERM) in the current study were consistent and comparable to findings of other studies from Nepal and abroad^{1-4,10}. Only a case of CRAO in the present study could be attributed to the rarity of the disease and presentation of the patient mostly to the Department of Emergency and Critical Care before the Ophthalmology Department.

In the current study advancing age, smoking, alcohol intake, overweight and obesity, electrocardiogram changes, hypertension, diabetes prior history of cataract surgery, and history of ocular trauma have been identified as the potential risks in developing vitreoretinal diseases these findings of the study correlated and compared very well with study findings from studies done in Nepal

and abroad^{1-6,8-14}. Importantly retinal problems can remain largely asymptomatic until advanced stages in many cases, so timely precautions, early detection, screening, and prompt treatment are some measures necessary to prevent irreversible blindness in these high-risk populations.

In the current study 62.05% of the study subjects were aware of the vitreoretinal disease this figure could have been attributed to factors like literacy, 79.46% of the study subjects were literate, 85.52% of the study subjects represented urban areas with easy access to tertiary care hospitals and eye care centers, and presence of chronic systemic diseases like diabetes mellitus and hypertension 79.01%, 52.67% respectively, requiring regular follow up to the hospital besides periodic retinal evaluation and health education to the patients. The current study included patients below the age of 50 years which was one of the important reasons for a lower prevalence of ARMD when compared to other studies from Nepal^{1,4}. Other demographic features of the study participants were consistent with a similar study from Nepal¹.

Conclusions

The prevalence of retinal diseases in the current study was lower than the national estimates. The alarming rise of diabetes and hypertension in Nepal was reflected by the higher prevalence of diabetic, and hypertensive retinopathies. Health promotion and education, periodic screening, and provision of early treatment in identified patients with risks and or vitreoretinal disease prevent vision-threatening consequences. An Ophthalmic evaluation referral system should be in place in all the hospitals for patients with diabetes mellitus, hypertension, and other metabolic diseases for periodic fundus evaluation by the Ophthalmologists.

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ORIGINAL

An Investigation of the Attempts by Anesthesia Intensive Care Nurses to Increase Lung Capacity After Extubation of the Patient

Una investigación sobre los intentos de las enfermeras de cuidados intensivos de anestesia para aumentar la capacidad pulmonar tras la extubación del paciente

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Abstract

Objective: This study aimed to examine the efforts made by Anesthesiology Intensive Care nurses to increase patient lung capacity after extubation.

Materials and Methods: The research is descriptive and cross-sectional in design. The sample comprised 120 volunteer nurses working in the 3rd step Anesthesia Intensive Care Unit in İzmir. Data were collected online using a 41-item questionnaire created by the researchers. Research data were analyzed using SPSS (for Windows 25.0). Descriptive statistics (number, percentage, min-max values, mean, and standard deviation) were employed for data evaluation.

Results: 67.5% of nurses are women and 32.5% are men. It was determined that 30% of the nurses received training on Lung Capacity Increasing Interventions, but only 13.3% used evidence-based guidelines. It was determined that 87.5% of the nurses applied interventions to increase the patient's lung capacity after extubation. Usually (frequently) 37.9% postural drainage, 27.6% deep breathing-coughing exercise, 25% triflow exercise, 4.3% positioning (dik-fowler's), 2.6% Noninvasive Ventilation (NI), 2% It was determined that they applied 6 nebulate treatments. While implementing all these, nurses stated that their workload was high, the team's knowledge level was insufficient, some patients rejected the interventions, and the lack of materials (such as triflow) were obstacles.

Conclusion: Nurses were found to have knowledge and training in Interventions to Increase Lung Capacity. Nevertheless, their training in this area was insufficient, and the use of evidence-based guidelines in practice was limited.

Key words: Anesthesia Intensive Care, Nursing Interventions, Lung Capacity Increasing Interventions.

Resumen

Objetivo: Este estudio tuvo como objetivo examinar los esfuerzos realizados por las enfermeras de Cuidados Intensivos de Anestesiología para aumentar la capacidad pulmonar del paciente después de la extubación.

Materiales y métodos: La investigación tiene un diseño descriptivo y transversal. La muestra estuvo compuesta por 120 enfermeras voluntarias que trabajaban en la Unidad de Cuidados Intensivos de Anestesia de 3^{er} escalón en İzmir. Los datos se recogieron en línea mediante un cuestionario de 41 preguntas creado por los investigadores. Los datos de la investigación se analizaron con el programa SPSS (para Windows 25.0). Para la evaluación de los datos se emplearon estadísticas descriptivas (número, porcentaje, valores mínimo-máximo, media y desviación estándar).

Resultados: El 67,5% de los enfermeros son mujeres y el 32,5% son hombres. Se determinó que el 30% de las enfermeras recibió formación sobre Intervenciones para Aumentar la Capacidad Pulmonar, pero sólo el 13,3% utilizó directrices basadas en la evidencia. Se determinó que el 87,5% de las enfermeras aplicaron intervenciones para aumentar la capacidad pulmonar del paciente tras la extubación. Habitualmente (frecuentemente) 37,9% drenaje postural, 27,6% ejercicio de respiración profundatos, 25% ejercicio triflow, 4,3% posicionamiento (dik-fowler's), 2,6% Ventilación No Invasiva (VNI), 2% Se determinó que aplicaron 6 tratamientos con nebulizaciones. Durante la aplicación de todos ellos, las enfermeras manifestaron que su carga de trabajo era elevada, el nivel de conocimientos del equipo era insuficiente, algunos pacientes rechazaban las intervenciones y la falta de material (como el triflow) eran obstáculos.

Conclusiones: Se observó que el personal de enfermería tenía conocimientos y formación sobre las intervenciones para aumentar la capacidad pulmonar. Sin embargo, su formación en esta área fue insuficiente y el uso de guías basadas en la evidencia en la práctica fue limitado.

Palabras clave: Cuidados Intensivos de Anestesia, Intervenciones de Enfermería, Intervenciones para Aumentar la Capacidad Pulmonar.

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Introduction

Nowadays, mechanical ventilator (MV) devices are used in patients who cannot or are inadequate to maintain their breathing on their own¹. After the condition requiring mechanical ventilation disappears, the patient should be extubated as soon as possible². Extubation involves discontinuing respiratory support and gradually weaning from MV once the patient can breathe independently¹. If the appropriate timing for extubation (considering factors such as blood gas parameters, the patient's tolerance of P/S mode while on MV support, and consciousness) and method are not selected correctly, this process can be prolonged. Additionally, it can lead to potential complications, including pneumothorax, lung injury, alveolar damage, and VAP (Ventilator-Associated Pneumonia)^{1,3}. Patients who are on mechanical ventilator support for a long time have lung diseases that cause decreased mucociliary activities, prolongation of hospital stay, limited mobility of the patient or being immobile, presence of problems such as dehydration and shortness of breath; It causes secretions to accumulate in the lungs and not be excreted adequately⁴. However, laryngeal damage in patients who are mechanically ventilated reduces the excretion of secretion by preventing the patient from coughing⁵. Considering all these problems, many studies have highlighted that unnecessarily prolonged mechanical ventilation is a significant cause of mortality and morbidity^{6,7}.

The majority of these patients are followed up in anesthesia intensive care units defined as the third level of the Ministry of Health⁸. In this context, nurses working in these units play an active role in preventing prolonged MV-related mortality and morbidity by implementing a number of interventions to increase the patient's lung capacity after extubation. It is important to implement lung capacity-increasing interventions such as postural drainage, use of spirometer (triflow), deep breathing and coughing exercises in order to reduce the risk of complications that may occur in patients, correct impaired respiratory activity, ensure secretion in the bronchi, strengthen respiratory muscles and reduce the need for oxygen in the body^{9,10,11,12,13}. These practices, referred to as chest physiotherapy (CP) in many literatures, are performed by physiotherapists in intensive care units in today's conditions. However, due to the lack of sufficient number of physiotherapists (the number of patients per physiotherapist is high), all practices are carried out with the support of nurses²².

Intensive care units necessitate a multidisciplinary approach. While physiotherapists often claim responsibility for these tasks, their limited numbers prevent them from actively participating in rehabilitation efforts. As a result, nurses, who provide comprehensive holistic care in the intensive care unit, effectively perform chest physiotherapy rehabilitation procedures within the bounds of the legal framework^{8,16}. For this reason, it is

very important that intensive care nurses are trained on the subject and have sufficient knowledge¹⁴.

When the literature is examined, studies have been conducted to assess the knowledge levels and attitudes of intensive care nurses towards lung capacity-increasing interventions (LCI-I). However, there is a gap in the literature regarding specific examinations of interventions aimed at increasing lung capacity performed by anesthesia intensive care nurses. Therefore, this study was planned to examine the attempts of anesthesia intensive care nurses to increase the lung capacity of the patient after extubation.

Materials and methods

Study Design and Aim

This research is descriptive-cross-sectional in nature. This study was planned to examine the attempts of anesthesia intensive care nurses to increase the lung capacity of the patient after extubation.

Sample and Context (Sample size calculation)

The sample consisted of 120 volunteer nurses working in the 3rd step Anesthesia Intensive Care Unit in İzmir. Since it was sent to nurses online, no sample calculation was made. Nurses working in the Anesthesia Intensive Care Unit in İzmir (private, state and university hospitals) were reached via whatsapp groups. The Question Form has been sent as a link.

Data collection and instruments

Data was collected online with a questionnaire created by the researchers. The questionnaire includes information about the nurses' sociodemographic characteristics, clinical experience and post-extubation interventions (such as knowing the methods that increase lung capacity, their educational status, using these methods in intensive care, their obstacles in practice, etc.), and also includes open-ended questions to allow nurses to make additional comments. It consisted of 29 questions in total. Answers to open-ended questions; The answers reflecting the nurses' opinions were grouped in their own words, and the answers regarding the concepts were grouped based on literature knowledge.

Data analysis

The data obtained in the study were analyzed using the SPSS (Statistical Package for Social Sciences) for Windows 25.0 program. Descriptive statistics (number, percentage, min-max values, mean and standard deviation) were used when evaluating the data.

Ethical issues

Ethical permission for the study was obtained from the Non-Interventional Ethics Committee of İzmir Katip Çelebi

University (Ethics Committee Approval Date: 04.03.2021 Decision No: 0130). In addition, the participants were assured that they could leave the study whenever they wanted. In this context, online consent was obtained from each individual with an informed consent form.

Results

Information about the sociodemographic and working status of the nurses participating in the study is given in **table I**.

The criteria for nurses to decide on extubation before extubation, attempts at the preparation stage, first attempts after extubation, and Lung Capacity Increasing Interventions (LCI-I) at all these stages were examined.

When the criteria used as a team to decide on extubation for the patient are examined; 32.5% of nurses stated that blood gas parameters should be sufficient for extubation, 5.7% stated that the patient's saturation should be over 95%, 24.2% stated that the patient should tolerate P/S (spontaneous) mode on the mechanical ventilator, 17.9% stated that the FIO₂ value (which is the amount of oxygen given to the patient on mechanical ventilator support) should be below 30%, 7.7% stated that extubation was a physician's decision, and 12% stated that the patient should be conscious and hemodynamically stable.

In order to accelerate the extubation of the patient in the intensive care unit, 28.3% of the nurses said that they applied interventions to increase lung capacity (postural drainage, active passive ROM exercises, etc.), 24.8% said that they turned off sedation support to encourage the patient to spontaneously breathe, and 9% said that 7 of them stated that they put the patient in P/S mode on the ventilator and monitor their tolerance and blood gas values, 3.5% stated that the patient should be protected from Ventilator Associated Pneumonia (VAP), 4.4% stated that they applied bronchodilator treatment and 0.9% stated that the orientation of the patient to the intensive care unit should be ensured.

When the first interventions they applied to the patient immediately after extubation were examined; 70.5% of nurses stated that oxygen mask should be worn and oxygen support should be started, 4.9% stated that intraoral secretions should be aspirated, 4.9% stated that postural drainage should be applied to the patient at frequent intervals to facilitate secretion excretion, 4.1% bronchodilator treatment should be started to prevent bronchospasm, 3.3% the patient should be followed in the upright-fowler's position, 6.6% stated that coughing exercises should be applied, 4.9% stated that saturation should be followed, 0.8% stated that the patient should be encouraged to breathe.

Table I: Sociodemographic characteristics.

Sociodemographics	n	%
Age mean±SD: 26,03±3,59 (min:21- max:47)		
Gender		
Female	81	67,5
Man	39	32,5
Education Level		
High School	15	12,5
University/Graduate	90	75
Master's Degree	13	10,8
PhD Graduate	2	1,7
Hospital		
Public Hospital	68	56,7
University Hospital	49	40,8
Private Hospital	3	2,5
Previous experience working in intensive care		
Yes	52	43,3
No	68	56,7
Do you have knowledge about lung capacity-increasing interventions (LCI-I)?		
Yes	61	50,8
No	59	49,2
Status of receiving training on LCI-I		
Yes	36	30,0
No	84	70,0
Status of implementing LCI-I		
Yes	105	87,5
No	15	12,5
Status of using evidence-based guidelines when applying LCI-I		
Yes	16	13,3
No	104	86,7
Total	120	100,0

Mean: Arithmetic Mean, SD: Standard deviation, Min: Smallest value, Max: Largest value

Nurses stated that some changes in the patient should be taken into account to decide on LCI-I. These changes were listed by the nurses as follows: The patient had respiratory distress and difficulty breathing (39% of the nurses), the patient started to breathe in the abdomen (6.8%), blood gas parameters deteriorated (3.4%), saturation It drops below 90 (29.7%) and the patient begins to become confused (6.8%).

After extubation, nurses usually perform 37.9% postural drainage, 27.6% deep breathing-coughing exercise, 25% trifold exercise, 4.3% positioning (dik-fowler's), 2.6% Noninvasive Ventilation (NIV). 2.6% stated that they applied nebulizer treatment.

When the nurses' knowledge regarding all these issues (LCI-I) was questioned, 50.8% stated that they knew these initiatives, while 30% were found to have received training on LCI-I. 87.5% of the nurses stated that they applied LCI-I to the patient after extubation. However, only 13.3% of them said that they used evidence-based guidelines when implementing these interventions (Table II).

Of the Anesthesia Intensive Care nurses participating in the study, 97.3% stated that they performed postural drainage every two hours, 39.8% performed deep breathing and coughing exercises every two hours, 77.9% performed suctioning every two hours and 41.2% performed the trifold exercise four times at two hour intervals. They stated that all these applications facilitated spontaneous breathing (60.8%) (Table II). 96.7% of the nurses stated that a chest x-ray was taken to measure the effect of their practices on the patient's lung capacity.

The problems experienced by nurses while performing LCI-I were examined. The problems experienced by nurses in this regard were grouped into 5 main themes (individual, team, patient, environment and equipment-related obstacles) and sub-themes (Table III).

Nurses commonly identified staff shortages and excessive workloads as obstacles they encountered in implementing LCI-I. The majority of nurses (n: 82) mentioned that their individual performance declined due to heavy workloads and insufficient staffing, viewing this as an individual challenge. Furthermore, some nurses cited occupational health issues and a lack of education as individual barriers. Similarly, an excess workload and a shortage of personnel were prominent themes in the perceived obstacles for the team. Nurses mentioned that this situation hindered coordinated teamwork. In response to this issue, one nurse reported that the crowded team environment led to breakdowns in communication. Additionally, insufficient knowledge among the team was identified as one of the reported obstacles.

The majority of obstacles experienced by patients were due to their refusal of intervention due to pain (n:99). Additionally, nurses reported that caring for obese patients posed obstacles for both the patient, the team, and the individual.

More than half of the nurses (n:70) stated that they perceived the noise caused by the devices in the intensive care unit as an environmental obstacle. Regarding equipment-related obstacles, almost all nurses (n:103) reported that a lack of equipment (such as trifold) made it difficult to apply LCI-I.

Table II: Questions asked to nurses regarding LCI-I.

Questions-Nurse Answers	n	%
Nurses' opinions about the benefits of AKA-Gs to patients*		
It increases lung capacity.	22	18,3
It helps reduce the length of stay in intensive care.	4	3,3
It facilitates the patient's spontaneous breathing.	73	60,8
The development of atelectasis is prevented.	9	7,5
It facilitates the patient's secretion excretion.	4	3,3
Reintubation of the patient is prevented.	8	6,7
Lung X-ray Status		
Yes	116	96,7
No	4	3,3
How often do you perform postural drainage on patients?*		
1 time per hour	2	1,8
1 time in 2 hours	108	97,3
1 time per day	1	0,9
How often do you have patients do deep breathing and coughing exercises?*		
1-2 times per hour	44	37,3
3-4 times per hour	27	22,9
Once every 2 hours	47	39,8
How often do you have patients do spirometry?*		
3 times at 1 hour intervals	42	36,8
4 times at 2 hour intervals	47	41,2
1 time per hour	25	21,9
How often do you aspirate patients?*		
1-2 times per hour	23	20,4
3-4 times per hour	2	1,8
Once every 2 hours	88	77,9

Table III: Themes and subthemes regarding nurses' perceived barriers to LCI-I implementation.

Main Themes	Subthemes
Individual Barriers	Time Pressure Providing Care to Obese Patients Excess Workload Due to Personnel Lack Lack of Equipment Occupational Diseases Lack of Education
Team-Related Barriers	Staff Shortage Workload Excess Lack of Information of People in the Team Providing Care to Obese Patients Lack of Equipment Crowded Team (Lack of Communication)
Patient-Related Barriers	Staff Shortage Providing Care to Obese Patients Refusal of Treatment/Intervention Due to Pain Lack of Equipment
Environmental Barriers	Staff Shortage Lack of Equipment High Patient Change Noisy Time Pressure Intensity
Equipment Related Barriers	Lack of Equipment (Especially Like Triflow) Staff Shortage

Discussion

In healthy individuals, airway cleaning is typically accomplished through mucociliary activity and coughing. However, in intensive care patients receiving mechanical ventilation support, factors like impaired oxygenation, dehydration, limited mobility, reduced use of intercostal muscles in breathing, and ineffective coughing can lead to the accumulation of thick and dark secretions¹⁵. Intensive care nurses are responsible for planning, implementing, and evaluating interventions to address respiratory issues in patients unable to effectively clear their airways¹⁶.

It was determined that almost half of the nurses participating in the study did not know LCI-I (49.2%) and only 30% had received training on the subject. Additionally, it was determined that only 13.3% of nurses used evidence-based guidelines when implementing these initiatives. Although 87.5% of the nurses stated that they used LCI-I in intensive care, when other results are evaluated, it can be thought that these nurses lack evidence-based and up-to-date knowledge. It suggested that these deficiencies were a limiting factor in the effective and regular implementation of these patient-specific interventions. It is very important for nurses to know these methods in order to be aware of the needs of the patients and to plan the appropriate intervention for the patient in cooperation with the team.

There are various LGI-Is that positively affect physiological and metabolic processes in patients in intensive care^{17,18}. According to study data, nurses frequently apply postural drainage (37.9%), deep breathing and coughing exercises (27.6%) and triflow exercises (25%)

for this purpose. In a similar study, nurses applied Chest Physiotherapy (CP) techniques at the following rates: 93% for deep breathing exercises, 62% for percussion, 62% for postural drainage, and 55% for vibration¹⁴. As nurses' CP technique, Karaali et al. stated that they used positioning, postural drainage, percussion and vibration¹⁹. In another study, it was stated that aspiration and percussion were the most frequently used CP techniques⁶. When studies on the subject are examined, it is seen that nurses implement similar initiatives.

A healthy person produces about 100 ml of secretion daily. In intensive care, patients with compromised respiratory function, mechanical ventilation, and weakened or lost cough and swallowing reflexes require aspiration to remove secretions due to inadequate ciliary movement and alveolar ventilation¹⁸. In this study, nurses mentioned that patient saturation decreased due to secretions, leading 77.9% of them to perform secretion aspiration as part of their LCI-I every two hours.

In this study, 60.8% of the nurses said that LCI-I facilitated spontaneous breathing, while 6.7% mentioned that it reduced the re-intubation rate. A similar result was found in a study by Flenady and Gray²⁰, which showed that LCI-Is, especially when applied after extubation, reduced the re-intubation rate.

Nurses encounter various obstacles, including individual, patient-related, team-related, and environmental factors, while performing their nursing practices. In this study, nurses stated that their workload was high (56.9%), the team's knowledge level was insufficient (42.9%), and

some patients refused interventions (67.5%) and lack of materials (such as trifold) (59.3%) as obstacles. Similarly, in their study by Kira et al., during GF practices, nurses paid attention to the patient being overweight (29.33%), lack of personnel (27.8%), excessive workload (24%) and having a musculoskeletal disorder (%18.8) was found to be an obstacle²¹. Intensive care nurses complain about excess workload not only in LCI-I practices, but also in all stages of patient care. This can be attributed to the fact that intensive care nurses unfortunately care for more patients than the calculated workload (number of bed-patients-nurses). The low number of nurses and staff working in these units causes short-term injuries to this group of caregivers during care and permanent musculoskeletal disorders in the long term. In this context, these problems are not sufficient to provide the desired level of quality of care in patient care.

In addition, in anesthesia intensive care units, which are multidisciplinary working areas, CP is undertaken by physiotherapists. In this study, it is seen that nurses apply CP in the intensive care unit, either in line with their wishes or obligations. Moreover, they expressed the excessive workload as an obstacle as a reason for not being able to implement it. Although it is the primary duty of another professional group, nurses apply LCI-I diligently in line with their duty awareness due to staff shortage (increasing the quality and comfort of the patient's care is also included in their job responsibilities).

In this study, trifold, which is the simplest applicable method in LCI-I, was reported by nurses as a missing material in intensive care units (59.3%). It seems that the lack of this material, which has a wide range of applications, limits LCI-I applications.

Evidence-based guidelines are important at every step of care. Utilizing evidence-based guidelines and up-to-date information in LCI-I practices increases the quality of care. In the LCI-I applied in this study, it was determined that only 13.3% of the nurses benefited from evidence-based guidelines. It is a pity that the nurses who take care to apply LCI-I (87.5%) while caring for so many patients in practice have not consulted evidence-based guidelines. Similarly, in Karagözoğlu's study, only 2.1% of the nurses stated that there was a standard guide regarding LCI-I in the department where they worked¹⁵. This is an indication that although nurses know the practices they perform, they cannot spare enough time to follow current information due to the excessive workload in the clinic and difficulties in patient care processes. It is important for nurses to have up-to-date and accurate information about LCI-I in order to plan and implement these practices accurately and effectively in intensive care.

Strengths and limitations

Due to the limited number of participants in the study, there were difficulties in collecting sufficient data through survey responses, necessitating a time extension.

Conclusions and recommendations

In conclusion, nurses in the study exhibited knowledge and training in Interventions to Increase Lung Capacity. Nevertheless, the training they received was found to be insufficient, and the utilization of evidence-based guidelines in practice was limited. It is crucial to offer in-service training for nurses to ensure the regular updating of their knowledge in this area. Additionally, it is advisable to develop a standardized guide for intensive care units to enhance the effectiveness and accuracy of these interventions. It is necessary to ensure that healthcare professionals (nurses, physicians and physiotherapists) receive training that supports each other. Thanks to the guides to be created, teamwork can be strengthened by ensuring unity of language and application in common applications. In light of the study's findings and the researchers' current roles in education, it is recommended that undergraduate nursing programs consider extending the duration of intensive care clinical rotations and further integrating this topic into the curriculum.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Evaluation of EDARADD (rs79233817) Gene Polymorphism in Children with Dental Caries Compared to Caries-Free Controls

Evaluación del polimorfismo del gen EDARADD (rs79233817) en niños con caries dental comparados con controles libres de caries

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Abstract

Objective: Dental caries is a complex condition that results from a combination of genetic and environmental factors. The EDARADD gene has been found to play a role in the teeth development and has been associated with various dental traits. In this study, our objective was to examine the potential correlation between the EDARADD gene polymorphism (rs79233817) and susceptibility to dental carie.

Methods: The study included a total of 400 participants, comprising 200 individuals with dental caries and 200 caries-free controls. The genotyping of the EDARADD gene polymorphism was performed using the tetra-primer amplification refractory mutation system PCR metho.

Results: Individuals with dental caries were found to have a meaningfully higher frequency of the A allele (minor allele) for rs79233817 compared to controls. The odds ratio (95% confidence interval) was determined to be 0.745 (0.624-0.751), with a p-value of 0.002. The specific SNP (rs79233817) was associated with an elevated risk of dental caries (DC) in both the co-dominant and dominant genetic models. The odds ratios were calculated as 0.45 (0.27-0.75) and 0.41 (0.26-0.72) for the respective models, with corresponding p-values of 0.012 and 0.02.

Conclusions: It can be inferred that the EDARADD gene polymorphism (rs79233817) potentially plays a role in the genetic susceptibility to dental caries. To validate and delve deeper into these findings, it is necessary to conduct additional studies with larger sample sizes in diverse populations. This will help to establish the robustness of the results and further investigate the underlying mechanisms involved.

Key words: Dental caries, EDARADD gene, Genetics, Diagnosis and treatment planning.

Resumen

Objetivo: La caries dental es una enfermedad compleja que resulta de una combinación de factores genéticos y ambientales. Se ha descubierto que el gen EDARADD desempeña un papel en el desarrollo de los dientes y se ha asociado a diversos rasgos dentales. En este estudio, nuestro objetivo fue examinar la posible correlación entre el polimorfismo del gen EDARADD (rs79233817) y la susceptibilidad a la caries dental.

Métodos: El estudio incluyó un total de 400 participantes, de los cuales 200 eran individuos con caries dental y 200 controles libres de caries. El genotipado del polimorfismo del gen EDARADD se realizó mediante el método PCR del sistema de mutación refractaria por amplificación de tetraprimer.

Resultados: Se observó que los individuos con caries dental presentaban una frecuencia significativamente mayor del alelo A (alelo menor) para rs79233817 en comparación con los controles. Se determinó que la odds ratio (intervalo de confianza del 95%) era de 0,745 (0,624-0,751), con un valor p de 0,002. El SNP específico (rs79233817) se asoció con un riesgo elevado de caries dental (DC) tanto en el modelo genético codominante como en el dominante. Las odds ratio se calcularon en 0,45 (0,27-0,75) y 0,41 (0,26-0,72) para los respectivos modelos, con valores p correspondientes de 0,012 y 0,02.

Conclusiones: Se puede inferir que el polimorfismo del gen EDARADD (rs79233817) desempeña potencialmente un papel en la susceptibilidad genética a la caries dental. Para validar y profundizar en estos hallazgos, es necesario realizar estudios adicionales con muestras de mayor tamaño en poblaciones diversas. Esto ayudará a establecer la solidez de los resultados y a investigar más a fondo los mecanismos subyacentes implicados.

Palabras clave: Caries dental, Gen EDARADD, Genética, Diagnóstico y planificación del tratamiento.

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Introduction

Ensuring proper oral health is vital for the overall well-being and development of children¹. Tooth decay, also known as dental caries, is a chronic condition that affects the tooth enamel² and is prevalent worldwide^{2,3}. Among children, dental caries (DC) is widely recognized as the most prevalent chronic condition^{4,5}, with around 500 million cases reported in children aged 0-14 years, specifically affecting their deciduous teeth⁶. DC is a widespread and multifactorial disease, despite the various preventive methods employed⁷. The development of caries is strongly influenced by a combination of genetic and environmental factors, with their interplay affecting the disease's progression. Identifying these factors and understanding their mechanisms is crucial to fully comprehend the nature of caries^{8,9}. Several environmental factors can contribute to DC in children, including oral bacteria^{10,11}, dietary habits such as high sugar intake¹², oral health behavior like using fluoridated toothpaste and regular brushing¹³, feeding practices including breastfeeding and night bottle-feeding^{13,14}, geographic location¹⁵, and socioeconomic status such as income, education, and social class. Additionally, in the past century, scientists have investigated the impact of hereditary factors on caries risk through various studies. The advancement of molecular biology techniques, including DNA sequence analysis techniques has enabled more sophisticated and well-conducted and trustworthy studies, which have confirmed the importance of genetic traits in DC^{16,17}. Furthermore, the human genome project has facilitated the identification of specific genes located on chromosomes that contribute to an increased susceptibility to caries^{18,19}. Recent meta-analyses²⁰⁻²² have additionally demonstrated an association between polymorphisms and an elevated susceptibility to DC.

EDARADD is a protein made up of 208 amino acids. The N-terminus of the protein contains a Tnf receptor-associated factor (Traf)-binding consensus sequence, while the C-terminus features a death domain (DD). The Traf-binding consensus sequence serves as a docking site for Traf1, Traf2, and Traf3, which then recruit Traf members and activate NF- κ B²³. On the other hand, the DD helps EDARADD self-associate and interact with EDAR^{23,24}. Therefore, EDARADD plays a critical role in Edar signaling, where the N-terminal region is responsible for signal transduction, and the C-terminal death domain (DD) is necessary for receptor engagement.

The current evidence on the association between SNPs within EDARADD gene and DC susceptibility is limited. Additional studies are necessary to explore and investigate the functional effects of EDARADD gene on tooth development and to replicate the association between polymorphisms and DC in diverse populations²⁵. Such studies can help uncover the molecular and genetic mechanisms underlying DC and inform the development of targeted prevention and treatment strategies for this widespread oral disease. The objective of this study is to explore the possible association between rs79233817 and the susceptibility to DC in a population-based sample. The findings from our study have the potential to provide insights into the genetic basis of DC. In addition, these findings may contribute to the development of personalized prevention strategies for DC and treatment approaches for this prevalent oral condition.

Material and methods

Patients

To determine the sample size, the researchers used the formula $n = Z^2 p(1-p)/e^2$, where Z was set to 1.96 and the prevalence was assumed to be 60%. According to the parameters, the sample size was determined to be 300 patients. The study included a control group consisting of age-matched individuals who did not have DC. Non-consenting individuals were not included in the study and were excluded from the analysis. A total of 400 individuals, including 200 individuals with a definite clinical diagnosis of DC and 200 healthy controls with similar demographic characteristics, were included in the study. The study was conducted following the guidelines set forth in the Declaration of Helsinki, and it received approval from the relevant ethics committee. Written informed consent was obtained from all participants, and 5 ml of peripheral blood was collected in EDTA-containing tubes.

DNA Genotyping

The standard salting-out method was employed to extract genomic DNA from the blood samples collected in EDTA anti-coagulated tubes. SNP rs79233817 genotyping, with primers designed using the Primer 1 online tool (<http://primer1.soton.ac.uk/primer1.html>), was performed using Tetra-ARMS-PCR method. **Table I** displays the primer sequences used in this study. Negative control samples lacking genomic DNA and positive controls with

Table I: The primer sequences and Product size.

Primers	Sequence	Product size
Forward inner primer (G allele)	CAGAGAATTAAGAAGCCAAACTCAACAGCG	For G allele: 156
Reverse inner primer (A allele)	CTGTTTAGTCGTCTGAGGCCATTGT	For A allele: 207
Forward outer primer (5' - 3')	AAATTTCCCTTCTATCCGAAGGCAGAC	Two outer primers: 306
Reverse outer primer (5' - 3')	AGCAACCTCTGGCTAAAAACTCAGCTCTG	

known genotypes were included to ensure genotyping accuracy. These control samples were subsequently compared to the sequencing results. The amplification temperature protocol included an initial denaturation step at 95°C for 5 minutes, followed by 30 cycles of 95°C for 30 seconds, 63°C for 30 seconds, and 72°C for 2 minutes, and a final extension at 72°C for 5 minutes. Additionally, for each PCR reaction, 1.5µl of each inner primer (10 PM) and 1.5µl of each outer primer (5PM), 2µl of Mastermix (amplicon® Mastermix containing MgCl₂, Taq PCR buffer, Taq DNA polymerase, and dNTPs), and 3µl of DNA (50ng/ul) adjusted to 20 µl with ddH₂O were used.

Statistical Analysis

The selected SNP underwent a test for Hardy-Weinberg equilibrium (HWE). Using SNPStats (<https://www.snpstats.net/start.htm>), associations between rs79233817 and DC were examined under various models, including co-dominant, dominant, recessive, and over dominant. The odds ratio (OR) and its corresponding 95% confidence interval were used to determine the effect size of each variant. A significance level of 0.05 or lower was considered statistically significant.

Results

The study involved 200 patients with DC and 200 healthy controls, with the former having a mean age of 15 years and the latter of 17 years. The case group included 53 males (26.5%) and 147 females (73.5%), while the control group comprised 65 males (32.5%) and 135

females (67.5%). The severity of DC was evaluated using the DMFT score, which tallies the number of decayed, missing, and filled teeth in each participant. Our findings, presented in **table II**, demonstrate a correlation between the rs79233817 SNP in the EDARADD gene and DMFT score in DC cases (p=0.015).

Accordance with Hardy-Weinberg equilibrium

The distribution of genotypes for the tested SNP was found to be consistent with Hardy-Weinberg equilibrium (p > 0.05). In cases and controls, the exact test for rs79233817 yielded P-values of 0.13 and 0.10, respectively (**Table III**).

Concordance with sequencing results

To verify the precision of T-ARMS genotyping, we selected a few samples that were previously genotyped and subjected them to genetic sequencing analysis. As depicted in **figure 1**, the Gel electrophoresis of the Tetra-ARMS PCR products from of EDARADD (rs79233817) gene on 2.5% agarose has been shown.

Case-control study

The frequency of the A allele (minor allele) for rs79233817 was observed to be significantly higher in DC patients compared to controls. The odds ratio (95% confidence interval) for this association was calculated as 0.745 (0.624-0.751) and a p-value of 0.002 (refer to Table 4). In both co-dominant and dominant genetic models, this specific SNP (rs79233817) was found to be associated with an elevated risk of DC. The odds ratios (95% confidence intervals) were determined as 0.45 (0.27-0.75) and 0.41 (0.26-0.72) for the respective models, with corresponding p-values of 0.012 and 0.02.

Table II: The correlation between the EDARADD (rs79233817) genotype and the decayed missing filled teeth (DMFT) score in DC cases.

Genotype in DMFT Score n=200	Decayed Missing Filled Teeth Score (DMFT score)							p-value
	1 DMFT 130 (65%)	2 DMFT 40(20%)	3 DMFT 15 (7.5%)	4 DMFT 8(4%)	5 DMFT 4(2%)	6 DMFT 2(1%)	7 DMFT 1(0.5%)	
AA	89	25	9	6	3	2	-	<0.05
AG	30	11	4	-	-	-	-	
GG	11	4	2	2	1	-	1	

Table III: Exact test for Hardy-Weinberg equilibrium.

SNP	rs79233817			P-value
	A/A	A/G	G/G	
Patients	134	45	21	>0.05
Healthy controls	111	54	35	>0.05

Table IV: The frequencies of allele and genotype distributions of SNPs in both patients and healthy controls.

SNP	Model		DC patients Number (%)	Controls Number (%)	OR (95% CI)	P-value
rs79233817	Allele	A vs. G	313(78.25%) 87(21.75%)	276(69%) 124(31%)	0.745 (0.624-0.751)	0.002
	Co-dominant	A/A	134 (67%)	111 (55.5%)	1.00	0.012
		A/G	45 (22.5%)	54 (27%)	0.45 (0.27-0.75)	
		G/G	21 (10.5%)	35 (17.5%)	1.00	
	Dominant	A/A	134 (67%)	111 (55.5%)	0.48 (0.26-1.25)	0.02
A/G-G/G	66 (33%)	89 (44.5%)	0.41 (0.26-0.72)			
Recessive	A/A-A/G	179 (89.5%)	165 (82.5%)	0.53 (0.45-1.15)	0.16	
G/G	21 (10.5%)	35 (17.5%)	0.42 (0.25-1.06)			
Overdominant	A/A-G/G	155 (77.5%)	146 (73%)	1.00	0.059	
	A/G	45 (22.5%)	54 (27%)	0.49 (0.55-1.03)		

Figure 1: Gel electrophoresis of the T-ARMS PCR products from of EDARADD (rs79233817) gene on 2.5% agarose gel electrophoresis. Lane A: AG genotype (306, 207 and 156 bp); Lanes B, C and D: AA genotype (306 and 207 bp).



Discussion

Advancements in the field of molecular biology and DNA sequencing techniques have enabled researchers to determine the significance of hereditary factors in DC²⁶. Indeed, our current understanding of the precise contribution of genetic factors to the risk of DC remains limited²¹. Previous research investigating the role of genetic factors in DC has predominantly concentrated on four main categories of genes. These include genes associated with enamel development, saliva formation and composition, immune response, and carbohydrate metabolism. These genetic factors have been explored due to their potential influence on the susceptibility to DC²⁷. However, recent studies have shown that other genes, which were not previously thought to have an impact on this disease, may also play a role. EDARADD (located on 1q42–q43; MIM# 606603) is the gene responsible for encoding the protein EDAR-associated death domain (EDARADD) and has been reported to associated with DC in a GWAS study²⁶. Current study aimed to investigate the association of a SNP (rs79233817) within this EDARADD with DC in Iranian population. The findings of this study have expanded our understanding of the genetic factors involved in the development and progression of DC, including gene-environment interactions. These insights could potentially pave the way for improved early detection, risk assessment, dental treatment, and more effective public health interventions.

Our results have shown that rs79233817 is meaningfully higher in cases compared to controls (P-value: 0.002). Our data is consistent with another study performed by Shaffer et al.,²⁶ and they have found that SNPs within EDARADD are associated with DC in US children aged 3 to 12 yrs. Our study is important from the point of view that association studies of SNPs with complex diseases should be based on ethnic and population²⁸, and the present study in the Iranian population confirms the role of EDARADD gene in susceptibility to DC among US patients.

In 2001, Headon and colleagues²⁹ discovered that the EDARADD and EDAR genes are co-expressed in epithelial cells during the development of hair follicles and teeth. They also found that EDARADD has a self-associating

property, which is typical of many death domain proteins. Overexpression of EDARADD in HEK293T cells led to the activation of an NF-kappa-B reporter gene, with activation levels correlated to the dose. The researchers also determined that the activation of EDAR is triggered by EDA, and that EDARADD serves as an adaptor to create an intracellular signal-transducing complex. This linear pathway is responsible for the similar phenotypes observed in Tabby, downless, and crinkled mutant mice, as well as the genetic heterogeneity of hypohidrotic ectodermal dysplasia in humans²⁹.

The study did not take into account environmental risk factors such as the duration and frequency of tooth brushing, frequency of sugar intake, use of fluoridated toothpaste, and dental flossing. Additionally, other single nucleotide polymorphisms of EDARADD should be assessed to confirm the important role of this gene in susceptibility of DC.

Conclusion

Our study presents evidence that supports an association between the polymorphism (rs79233817) in the EDARADD gene and susceptibility to DC. In our study, we identified a statistically significant difference in the frequency of the minor allele (A allele) between individuals with DC and caries-free controls, with a higher frequency observed in the DC group. The observed association between this specific genetic variant and a higher frequency of DC suggests that this variant may indeed contribute to an increased risk of developing DC. Furthermore, our findings indicate that the rs79233817 polymorphism is associated with DC susceptibility in both co-dominant and dominant genetic models. These results strengthen the significance of this genetic variant in influencing the development of dental caries. Nevertheless, it is important to acknowledge that our findings require further validation and replication through additional research. Larger sample sizes and studies involving diverse populations would help to confirm the association between the EDARADD gene polymorphism and DC susceptibility. Additionally, investigating the underlying mechanisms by which this genetic variant influences DC risk would provide valuable insights into the pathogenesis of the disease. The identification of genetic risk factors, such as the EDARADD gene polymorphism, holds promise for the development of personalized preventive strategies for DC. By understanding the genetic predisposition to DC, healthcare professionals can tailor preventive interventions and treatment approaches to individuals based on their genetic profiles. This approach may lead to more effective and targeted strategies in the prevention and management of DC.

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Conflict of interest

All authors have no conflict of interest to report.




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ORIGINAL

Knowledge, attitudes and practices towards HPV infections, complications of HPV infections and the HPV vaccine among students of Medical Science in North Macedonia

Conocimientos, actitudes y prácticas respecto a las infecciones por VPH, las complicaciones de las infecciones por VPH y la vacuna contra el VPH entre los estudiantes de Ciencias Médicas de Macedonia del Norte

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Abstract

Introduction: Human papillomavirus (HPV) is one of the most common causes of sexually transmitted diseases. The HPV vaccine is crucial in the primary prevention of HPV infection and associated diseases and complications. This objective of the study was to determine the knowledge, attitude and practices of the Medical students in North Macedonia towards HPV infections, complications of HPV infections and the HPV vaccine.

Materials and methods: In the period of November 2022 – December 2022 a study using a semi - structured questionnaire was conducted in Medical Faculties in North Macedonia, covering 728 people over 18 years old that are medical students. Standard descriptive statistics were used to summarize the demographic characteristics.

Results: A total of 728 participants took part in the survey, predominantly female (n=601, 82.5%). Around one third of all respondents (36.4%) have received the HPV vaccine. We established a statistically significant difference between the vaccinated and non-vaccinated respondents in terms of gender ($\chi^2=22.231$, $p<0.001$) and this proved to be the strongest predictor for vaccination in the logistic regression analysis. The main driver for hesitation regarding the HPV vaccine was the fear of possible side effects and there was an association between the fear of possible side effects and the probability for vaccination (15.1% (n=40) vaccinated vs. 41.2% (n=191) non-vaccinated students, $\chi^2=73.020$, $p<0.001$). The students who didn't agree with the statement that recommending the HPV vaccine to teenagers will send a message that it is okay to become sexually active at an early age were 1.89 times more likely to have been vaccinated.

Conclusions: The current study demonstrated that medical students in North Macedonia had a suboptimal uptake of the HPV vaccine. To increase the coverage, it is essential that people get the right information. Having doubts about the vaccine's safety and effectiveness is the main cause of vaccination hesitancy.

Key words: HPV, vaccine, knowledge, attitudes, practices.

Resumen

Introducción: El virus del papiloma humano (VPH) es una de las causas más frecuentes de enfermedades de transmisión sexual. La vacuna contra el VPH es crucial en la prevención primaria de la infección por VPH y de las enfermedades y complicaciones asociadas. El objetivo del estudio era determinar los conocimientos, la actitud y las prácticas de los estudiantes de Medicina de Macedonia del Norte en relación con las infecciones por VPH, las complicaciones de las infecciones por VPH y la vacuna contra el VPH.

Materiales y métodos: Entre noviembre de 2022 y diciembre de 2022 se llevó a cabo un estudio con un cuestionario semiestructurado en las facultades de medicina de Macedonia del Norte, que abarcó a 728 personas mayores de 18 años estudiantes de medicina. Se utilizaron estadísticas descriptivas estándar para resumir las características demográficas.

Resultados: Un total de 728 participantes tomaron parte en la encuesta, predominantemente mujeres (n=601, 82,5%). Alrededor de un tercio de todos los encuestados (36,4%) han recibido la vacuna contra el VPH. Establecimos una diferencia estadísticamente significativa entre los encuestados vacunados y los no vacunados en términos de género ($\chi^2=22,231$, $p<0,001$) y esto demostró ser el predictor más fuerte para la vacunación en el análisis de regresión logística. El principal impulsor de la indecisión respecto a la vacuna contra el VPH fue el miedo a los posibles efectos secundarios y hubo una asociación entre el miedo a los posibles efectos secundarios y la probabilidad de vacunación (15,1% (n=40) estudiantes vacunados frente a 41,2% (n=191) no vacunados, $\chi^2=73,020$, $p<0,001$). Los estudiantes que no estaban de acuerdo con la afirmación de que recomendar la vacuna contra el VPH a los adolescentes enviará el mensaje de que está bien ser sexualmente activo a una edad temprana tenían 1,89 veces más probabilidades de haberse vacunado.

Conclusiones: El presente estudio demostró que los estudiantes de medicina de Macedonia del Norte tuvieron una aceptación subóptima de la vacuna contra el VPH. Para aumentar la cobertura, es esencial que las personas reciban la información adecuada. Tener dudas sobre la seguridad y eficacia de la vacuna es la principal causa de indecisión en la vacunación.

Palabras clave: VPH, vacuna, conocimientos, actitudes, prácticas.

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Introduction

One of the most common causes of sexually transmitted viruses is the human papillomavirus (HPV). HPV consists of a family of small, double-stranded DNA viruses with more than 200 distinct types. Research shows that more than 90% of all sexually active men and women will acquire at least one type of HPV in their lifetime¹. HPV is an unavoidable part of life for the majority of people. Condyloma is the consequence of low-risk HPV types, while malignancies of the genital areas, head and neck are the result of high-risk HPV types.

Up to 14 million people get a new HPV infection each year, and 45,300 of them could develop malignancies as a result of the infection^{2,3}. Cervical cancer is the most common cause of cancer death among African women⁴. In North Macedonia the incidence of cervical cancer for 2020 is estimated at 10.9 per 100 000 women⁵. In Spain a 14% rise in the overall number of cancers, specifically resulting in a notable increase in cases of cervical and oropharyngeal cancer caused by HPV infection is reported⁶. The cumulative number of deaths due to cervical cancer for 2019 for North Macedonia is 68 of overall 12 100 deaths registered among women⁷. Regarding the therapeutic options for reducing the risk of an infection with the HPV virus to progress to cervical cancer there have been several options: cryosurgery, laser surgical removal, loop electrosurgical excision procedure and cold knife conization. A novel non-invasive approach that enhances the elimination of the HPV virus and promotes the healing of the cervix's epithelium involves the application of a gel containing *Coriolus versicolor*, a fungus rich in polysaccharidopeptides⁸. This approach has been studied in an observational non-comparative open-label prospective pilot study (EPICERVIX). The researchers reported that the application of the gel for 21 consecutive days had a favourable effect on cervix epithelization and vaginal microbiota which could prevent the clinical course of HPV-related lesions⁹.

The HPV vaccine is crucial in the primary prevention of HPV infection and associated diseases and complications. Three vaccine types –2-valent, 4-valent, and 9-valent– have been shown to be safe and effective against HPV and it has been discovered that the HPV vaccine alone reduces HPV infection by 70% and cervical cancer by 48%¹. HPV vaccine is recommended for routine vaccination for both girls and boys at age 11 or 12 years and can be started at age 9.⁷ The Advisory Committee on Immunization Practices (ACIP) also recommends vaccination for everyone through age 26 years if not adequately vaccinated when younger and vaccination is not recommended for everyone older than age 26 years¹⁰. Some adults ages 27 through 45 years might decide to get the HPV vaccine based on discussion with their clinician, if they did not get vaccinated when they were younger and HPV vaccination of people in this age range provides less benefit, for several reasons, including

that more people in this age range have already been exposed to HPV¹⁰.

To increase the awareness regarding HPV infection and HPV vaccine the public should have good knowledge about the risk factors, prevention methods, early diagnosis, screening, and treatment. Even though the HPV vaccine has been shown to reduce the frequency of infections and malignancies that may be associated with the virus, only 47.0% of adults between the ages of 18 and 26 had received at least one dose in 2019 in USA (811). In North Macedonia a national program for HPV vaccination was introduced in 2009. In 2020 every 3 in 10 girls turning 15 years old have received their final vaccination dose in 2020. The overall coverage with an HPV vaccine among women in 2020 was estimated to be 30 %⁷.

The present study aimed to determine the knowledge, attitude and practices of the students of Medical Science in North Macedonia towards HPV infections, complications of HPV infections and the HPV vaccine.

Materials and methods

Study design and participants

In the period of November 2022 - December 2022 a cross-sectional study using a semi - structured questionnaire was conducted in North Macedonia. The questionnaire was sent among three Medical universities in North Macedonia- Ss. Cyril and Methodius University (UKIM), Skopje, University of Tetova, University "Goce Delcev".

For recruiting the participants, we used a random convenience sampling method using social media to distribute the questionnaire. The sample size was calculated using G* Power version 3.1.9.7. The margin of error (the maximum difference between the sample results and the total population) and the confidence interval (the probability that the sample accurately reflects the attitudes of the targeted population) were set at 5% and 95%, respectively. The number of participants needed for our study was estimated to be 602. The total sample size during our study was 728 respondents over 18 years of age.

The questionnaire included 40 questions, 1 of which with more than one possible answer. The questions were divided in 5 sections: demographic information - 7 questions, assessment of the knowledge about cervical cancer - 8 questions, assessment of the knowledge about HPV infection - 11 questions, assessment of the knowledge about HPV vaccine - 6 questions, the attitudes for HPV immunization - 7 questions. An anonymous survey was generated through the web - based platform provided by Google Forms. The questionnaire was distributed in Macedonian since it is the native language of the country.

Data analysis

The SPSS programme, version 25.0 (IBM Corp, Armonk, NY, USA), was used to enter and analyse the data. The respondents' demographics were analyzed using descriptive statistics. Numbers/totals and percentages (n, %) are used to represent qualitative factors in data. P-values lower than 0.05 were regarded as statistically significant. The distribution of the sampled participants was determined using the Kolmogorov-Smirnov test. Any discrepancies between the observed and hypothesized distributions were checked using the chi-square test for independence. The z-test was used to test for differences between proportions. To examine the impact of the various variables on the likelihood of immunization, a logistic regression was utilized.

Results

Demographic

A total of 728 students took part in the study, predominantly female (n=601, 82.5%). The median age of the respondents was 22 years. Approximately 94,9% (n = 691) were students at Ss. Cyril and Methodius University in Skopje and 92,2% (n = 671) were students of the Medical Faculty. A minority were smokers (20,9%, n = 152). (Table I).

When asked whether they have received the HPV vaccine 36.4% (n=265) participants gave a positive answer. As the programme for immunization with the HPV vaccine in North Macedonia targets girls above the age of 12 years expectedly the uptake with the vaccine was higher in females (40.3% for females vs. 18.1% for males). We established a statistically significant difference between

the vaccinated and non-vaccinated respondents in terms of gender ($\chi^2=22.231$, $p<0.001$). Regarding the other demographic variables, no statistically significant differences were observed between the two groups (Table I).

Knowledge

The respondents showed an overall good knowledge of the characteristics of the HPV virus in terms of contagiousness, risk groups and complications due to the HPV infection (Table II). Six hundred and sixty-two (90,9%) correctly identified that there are specific types of HPV that can cause cervical cancer and 97,3% (n = 708) were aware that HPV is a sexually transmitted virus. Only 26,9% (n = 196) were not familiar with the fact that more than 50% of sexually active men and women become infected with HPV at some point in their lives. Most of the students were aware that HPV is associated with oropharyngeal cancer, genital warts and lung carcinoma and 81,3% (n = 592) answered correctly that you can be infected with HPV for many years without having any symptoms and 87,1% (n = 634) responded that HPV can affect both men and women. Only 9,8% (n = 71) were not aware that condoms are effective in protecting against HPV infection.

Just 50,5% (n = 368) of the participants answered that HPV vaccine is in the calendar for regular immunization and there was statistically significant difference between the vaccinated and non-vaccinated students in regards to this question (69.8% for vaccinated vs. 39.5% for non-vaccinated $\chi^2=61.845$, $p<0.001$). Further when asked what is the preferred age for administration of the HPV vaccine we estimated statistically significant difference among the vaccinated and non-vaccinated respondents ($\chi^2=29.915$, $p<0.001$).

Table I: Demographics of the respondents (n=728).

Variables	All respondents (n=728)	Vaccinated (n=265)	Non-vaccinated (n=463)	p-value
Age	22 y.o (21 y.o.; 23 y.o.)			
Gender				
Male	127 (17.5)	23 (8.7)	104 (22.5)	0.000
Female	601 (82.5)	242 (91.3)	359 (77.5)	
University				
Ss. Cyril and Methodius University in Skopje	691 (94.9)	258 (97.3)	433 (93.5)	0.054
University of Tetovo	33 (4.5)	7 (2.7)	26 (5.6)	
Goce Delcev University	4 (0.6)	0 (0)	4 (0.9)	
Faculty				
Medicine	671 (92.2)	242 (91.3)	429 (92.6)	0.600
Dentistry	19 (2.6)	9 (3.4)	10 (2.1)	
Pharmacy	38 (5.2)	14 (5.3)	24 (5.3)	
Year of study				
1 st year	86 (11.8)	24 (9.0)	62 (13.4)	0.368
2 nd year	94 (12.9)	34 (12.8)	60 (12.9)	
3 rd year	218 (29.9)	89 (33.6)	129 (27.9)	
4 th year	141 (19.4)	54 (20.4)	87 (18.8)	
5 th year	104 (14.3)	34 (12.8)	70 (15.1)	
6 th year	85 (11.7)	30 (11.4)	55 (11.9)	
Smoking				
Yes	152 (20.9)	53 (20)	99 (21.4)	0.659

Table II: Knowledge of the respondents regarding the characteristics of the HPV virus and the HPV infection.

Variables	All respondents (n=728)	Vaccinated (n=265)	Non-vaccinated (n=463)	p-value
HPV is a sexually transmitted infection. Correct	708 (97.2)	255 (96.2)	453 (97.8)	0.200
There are specific types of the HPV virus that cause cervical cancer. Correct	662 (90.9)	245 (92.4)	417 (90.1)	0.280
More than 50% of sexually active men and women become infected with HPV after starting sexual activities. Correct	532 (73.1)	194 (80.2)	338 (73.0)	0.952
HPV can cause oropharyngeal cancer. Correct	520 (71.4)	190 (71.7)	345 (74.5)	0.360
HPV is associated with genital warts. Correct	562 (77.2)	201 (75.8)	361 (77.9)	0.512
HPV can cause lung cancer. Correct	207 (28.4)	71 (26.8)	136 (29.3)	0.458
You can be infected with HPV for many years without having symptoms. Correct	592 (81.3)	217 (81.9)	375 (81.0)	0.766
HPV can infect both women and men. Correct	634 (87.1)	227 (85.7)	407 (87.9)	0.385
Condoms are effective in protecting against HPV infection Correct	657 (90.2)	236 (89.0)	421 (90.9)	0.413
For whom is the HPV vaccine recommended? Men Women Men and women	5 (0.7) 359 (49.3) 364 (50.0)	0 (0) 135 (50.9) 130 (49.1)	5 (1.1) 224 (48.4) 234 (50.5)	0.206
At what age should the HPV vaccine be administered? 9-14 y.o. 15-17 y.o. 18-26 y.o. Regardless of age	226 (48.8) 84 (18.1) 68 (14.8) 85 (18.3)	153 (57.7) 69 (26.0) 23 (8.7) 20 (7.6)	73 (37.2) 15 (7.7) 43 (21.9) 65 (33.2)	0.000
Is the HPV part of the immunization calendar of North Macedonia? Yes	368 (50.5)	185 (69.8)	183 (39.5)	0.000

As in North Macedonia the HPV vaccine is administered free of charge to females since 2009 we wanted to assess the knowledge and the practices of our female respondents regarding the HPV virus and the HPV vaccine.

Variables	Vaccinated female respondents (n=242)	Non-vaccinated female respondents (n=359)	p-value
Cervical cancer is a common oncological disease in women Correct	236 (97.5)	343 (95.5)	0.205
Cervical cancer is most commonly diagnosed in women aged between: 25-35 y.o. 35-45 y.o. 45-55 y.o.	50 (20.7) 138 (57.0) 54 (22.3)	64 (17.8) 220 (61.3) 75 (20.9)	0.552
What is the most common method used for screening for cervical cancer? Pap test Vaginal smear Colposcopy	220 (90.9) 12 (5.0) 10 (4.1)	325 (90.5) 14 (3.9) 20 (5.6)	0.614
Have you ever been screened for cervical cancer? Yes	89 (36.8)	113 (31.5)	0.177
Which are the risk factors for cervical cancer? HPV infection Multiple sexual partners Smoking Low socio-economic status Early sexual activity	240 (99.2) 218 (90.1) 206 (85.1) 186 (76.8) 187 (77.2)	347 (96.6) 333 (92.7) 284 (79.1) 242 (67.4) 271 (75.5)	0.182 0.184 0.070 0.013 0.611

Attitudes

The respondents in our study showed an overall positive attitude towards the HPV vaccine. Statistically significantly higher is the share of vaccinated respondents who believe the vaccine is effective in preventing cervical cancer (80.4% (n=213) vaccinated vs. 59.1% (n=275) non-vaccinated students, $\chi^2=34.180$, $p<0.001$) and who are on the opinion that the vaccine should be recommended to all

teenagers (85.7% (n=227) vaccinated vs. 57.9% (n=268) non-vaccinated students, $\chi^2=82.339$, $p<0.001$). The main driver for hesitation regarding the HPV vaccine was the fear of possible side effects and there was an association between the fear of possible side effects and the probability for vaccination (15.1% (n=40) vaccinated vs. 41.2% (n=191) non-vaccinated students, $\chi^2=73.020$, $p<0.001$).

Variables	All respondents (n=728)	Vaccinated (n=265)	Non-vaccinated (n=463)	p-value
The HPV vaccine is effective in preventing cervical cancer. Completely agree/Agree	488 (67.0)	213 (80.4)	275 (59.1)	0.000
Getting the HPV vaccine can protect you from HPV infection. Completely agree/Agree	497 (68.3)	194 (73.2)	303 (65.2)	0.027
I am worried about the side effects of the HPV vaccine. Completely agree/Agree	231 (31.7)	40 (15.1)	191 (41.2)	0.000
I believe that HPV vaccine should be recommended to all teenagers. Completely agree/Agree	495 (68.0)	227 (85.7)	268 (57.9)	0.000
Getting the HPV vaccine will send a message to the teenagers that it is okay to have unprotected sex. Completely agree/Agree	135 (18.5)	50 (18.9)	85 (18.3)	0.599
I would recommend the HPV vaccine to family and friends. Completely agree/Agree	436 (59.9)	214 (80.7)	222 (47.7)	0.000

Model	Unstandardized Coefficients		Wald	df	Sig.	Exp (B)	95% Confidence Interval for B	
	B	Std. Error					Lower Bound	Upper Bound
(Constant)								
Faculty								
Faculty of Medicine (baseline)								
Faculty of Dental Medicine	1.063	0.559	3.615	1	0.057	2.896	0.968	8.669
Faculty of Pharmacy	0.162	0.420	0.149	1	0.700	1.176	0.516	2.679
Year of study								
1 st year of study (baseline)								
2 nd year of study	0.172	0.403	0.181	1	0.670	1.187	0.538	2.618
3 rd year of study	0.086	0.348	0.061	1	0.804	1.090	0.551	2.156
4 th year of study	-0.099	0.371	0.072	1	0.789	0.905	0.437	1.875
5 th year of study	-0.771	0.400	3.707	1	0.054	0.463	0.211	1.014
6 th year of study	-0.954	0.413	5.333	1	0.021	0.385	0.171	0.866
Gender								
89Male gender (baseline)								
Female gender	1.627	0.298	29.768	1	0.000	5.087	2.836	9.125
Worried about possible side effects of the HPV vaccine								
Strongly disagree (baseline)								
Disagree	-0.605	0.367	2.717	1	0.099	0.546	0.266	1.121
Neither agree nor disagree	-0.808	0.361	5.021	1	0.025	0.446	0.220	0.904
Agree	-1.575	0.404	15.193	1	0.000	0.207	0.094	0.457
Completely agree	-2.479	0.631	15.445	1	0.000	0.084	0.024	0.289
Believe the HPV vaccine should be recommended to all teenagers								
Strongly disagree (baseline)								
Disagree	-1.808	1.108	2.663	1	0.103	0.164	0.019	1.438
Neither agree nor disagree	-1.662	0.869	3.659	1	0.056	0.190	0.035	1.042
Agree	-1.161	0.856	1.841	1	0.175	0.313	0.059	1.676
Completely agree	-0.106	0.867	0.015	1	0.903	0.900	0.165	4.920
Getting the HPV vaccine can effectively protect you								
Strongly disagree (baseline)								
Disagree	0.686	0.994	0.476	1	0.490	1.985	0.283	13.929
Neither agree nor disagree	0.068	0.942	0.005	1	0.943	1.070	0.169	6.781
Agree	-0.144	0.930	0.024	1	0.877	0.866	0.140	5.357
Completely agree	-0.663	0.951	0.486	1	0.486	0.516	0.080	3.321
Getting the HPV vaccine will send a message to teens that it is okay to become sexually active from an early age								
Strongly disagree (baseline)								
Disagree	0.641	0.295	4.718	1	0.030	1.889	1.065	3.387
Neither agree nor disagree	0.427	0.283	2.275	1	0.131	1.532	0.880	2.667
Agree	0.355	0.344	1.066	1	0.302	1.426	0.727	2.796
Completely agree	0.326	0.482	0.457	1	0.499	1.386	0.538	3.565
I would recommend the HPV vaccine to family and friends								
Strongly disagree (baseline)								
Disagree	-0.147	1.344	0.012	1	0.913	0.863	0.062	12.013
Neither agree nor disagree	0.187	1.288	0.021	1	0.885	1.205	0.097	15.051
Agree	1.019	1.303	0.611	1	0.434	2.769	0.215	35.606
Completely agree	0.816	1.337	0.373	1	0.541	2.262	0.165	31.065

We performed a logistic regression to determine the effects on the likelihood of receiving the HPV vaccine. The logistic regression model was statistically significant ($\chi^2 = 247.558$, $p < 0.001$). The model correctly classified 39.5% of the cases. In terms of demographic characteristics respondents who were in the 6th year of their study were 0.385 less likely to have received the HPV vaccine whereas the female students were 5.1 times more likely to have been vaccinated. Regarding the attitudes of the respondents who were afraid of possible adverse events following the administration of the HPV vaccine were less likely to have received the vaccine. On the contrary the students who didn't agree with the statement that recommending the HPV vaccine to teenagers will send a message that it is okay to become sexually active at an early age were 1.89 times more likely to have been vaccinated.

Discussion

To the best of our knowledge this is the first study to assess the knowledge, practices and attitudes towards the HPV vaccine among students in medical universities in North Macedonia. As future healthcare providers it is critical that students are thoroughly educated about the HPV virus and the vaccines available for and the recommendations for vaccination.

North Macedonia has a population of 2,065 million, 890,171 of them women aged 15 years or older. Current estimates suggest that every year 113 women are diagnosed with cervical cancer and among them 62 die from the disease and for 2023 the incidence from cervical cancer is 10.9⁵. North Macedonia has introduced a national screening program for cervical cancer since 2021 which is covering women 24 through 60 years of age and it is reported that 6 in 10 women have been screened for cervical cancer in the last 5 years⁷.

HPV vaccination is the primary and the most effective way to prevent HPV and its potentially serious complications and malignancy. Currently, three HPV vaccines are available and shown to be effective worldwide¹. The quadrivalent HPV vaccine has been found to be successful in preventing genital warts and external genital lesions in males. Additionally, both the quadrivalent and ninevalent HPV vaccines have been shown to provide comparable levels of protection against precancerous lesions and cancer in the cervix, vagina, and vulva in young women¹².

Our students demonstrated good knowledge about some aspects of the HPV virus and the risk of cervical cancer, but there were substantial gaps in their knowledge regarding other HPV-related oncological diseases. This supports the necessity of advocating for educational initiatives targeting young individuals and implementing modifications to the existing curriculum of university

students enrolled in health sciences schools. These measures aim to enhance the knowledge and awareness of future healthcare professionals regarding HPV. In comparison, a study in Serbia also proved that students involved in medical studies or those that attended medical high school had the highest knowledge about cervical cancer¹³. The level of knowledge about cervical cancer (CC) and human papillomavirus HPV virus is generally inadequate in other Balkan countries. A study conducted in Romania revealed that although most women were familiar with HPV, their understanding of the risk factors for infection was limited¹⁴. In Greece, adolescents were also found to have insufficient knowledge about the risk factors and methods of protection against cervical cancer¹⁵. Similarly, Hungary and Slovenia also reported a similar situation with regards to cervical cancer and HPV knowledge^{16,17}.

The HPV vaccine uptake in our study was 36.4% (40.3% for females vs. 18.1% for males). We established a statistically significant difference between the vaccinated and non-vaccinated respondents in terms of gender ($\chi^2 = 22.231$, $p < 0.001$) and in the binary logistic regression analysis being female was the strongest variable associated with the probability to have received the HPV vaccine. The vaccine development and implementation approach has been primarily targeted towards women with the goal of avoiding cervical cancer, which has led to the phenomenon of vaccination feminization¹⁸. Similarly, the HPV vaccine was introduced in 2009 in North Macedonia and the immunization program targets females above 12 years of age. The latest global guidelines for HPV vaccination now encompass a wider range of age groups. In addition to adolescents of both genders aged 11-12 years, females aged 13-26 years who have not received prior vaccination or completed the vaccine series are also recommended to be vaccinated. Furthermore, males aged 13-21 years and 22-26 years, who either have specific medical conditions or want to protect themselves against the disease, are also advised to receive the vaccine¹⁹. For 2021 the coverage with HPV vaccine among females has been estimated to be 32%⁵. In our study the uptake among females is higher-40.3% which can be explained that our respondents are students in medical universities and they have better knowledge regarding the HPV virus and are more motivated to receive the vaccine.

Our results for the vaccine uptake among our respondents (36.4%) are higher than the results of studies from India (6.8% uptake), Turkey (4.3% uptake) and similar to studies from Brazil (21% uptake), and USA (32.1% uptake)²⁰⁻²³. The variations in the adoption of the HPV vaccine across different countries can be attributed to barriers that impede the uptake of the vaccine. These barriers include insufficient understanding of HPV infection and its associated illnesses, concerns about the safety of the vaccine, the high cost of the HPV vaccine, logistical challenges in organising vaccine campaigns, and

difficulties in ensuring that both recipients and providers adhere to the recommended vaccine schedule.

When exploring the attitudes of the students regarding the HPV vaccine we found that there was a substantial part of respondents that were having doubts about the effectiveness (67 % of all respondents agree/completely agree with the statement that the HPV vaccine is effective in preventing cervical cancer), and safety of the vaccine (31.7% of respondents were concerned about possible side effects after HPV vaccination). The findings of this survey align with a previous study conducted in Spain, which reported that 66.5% and 65.4% of students agree or strongly agree that HPV can prevent cervical cancer and that the associated side effects are acceptable, respectively²⁴. Furthermore, the fear of possible side effects after HPV vaccination proved to be negatively associated with the probability of vaccination.

The findings of our study continuously emphasise the necessity for further educational interventions to enhance understanding and consciousness regarding the prevention of cervical cancer. It is important to increase awareness of cervical cancer and screening programmes using various communication channels. These programs can take various forms, such as seminars, group discussions, and interactive sessions, and can involve both pharmaceutical companies and government initiatives. In addition, the media can play a significant role in increasing awareness about HPV and cervical cancer. This was confirmed by a Serbian study, which found that the media was the primary source

of information for participants²⁵. Similarly, an American study involving young women also demonstrated the media's influence on public opinion. Overall, promoting accurate information about HPV and its prevention is crucial to increasing vaccination rates and preventing cervical cancer²⁶.

Conclusion

The medical students in the present study demonstrated an overall good knowledge of the HPV virus, cervical cancer, and vaccination, although exhibited deficiencies in their knowledge pertaining to HPV-related illnesses. The present investigation revealed that medical students in North Macedonia had suboptimal uptake of the HPV vaccine. To enhance the acceptance of the HPV vaccine, it is crucial for individuals to acquire accurate information, possess awareness of its existence, and obtain it from trustworthy sources. The primary factor contributing to vaccination hesitation is scepticism regarding the safety and efficacy of the vaccine. It is recommended to utilise diverse audio-visual platforms for carrying out educational programmes aimed at promoting vaccination within the community. These programmes should aim to enhance positive attitudes about HPV vaccines, raise information about vaccine availability, and bolster public trust in the safety of vaccines.

Conflict of Interest

None.

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ORIGINAL

¿Puede la manometría clasificar las disfunciones del suelo pélvico? Propuesta y efectividad de un algoritmo terapéutico

*Can manometry classify pelvic floor dysfunctions?
Proposal and effectiveness of a therapeutic algorithm*

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Resumen

Objetivo: a) establecer valores para clasificar las disfunciones suelo pélvico (DSP) en hipotónicas (incontinencia urinaria esfuerzo [IUE] y urgencia [IUU], prolapso órganos pélvicos [POP]) o hipertónicas (dolor pélvico crónico [DPC]); b) establecer diferencias etarias; y c) evaluar el tratamiento rehabilitador multimodal (biofeedback [BFB] + neuromodulación tibial posterior [NMTP] + radiofrecuencia [RF]) en DSP.

Material y métodos: Estudio observacional retrospectivo, 190 pacientes (DPC=43, POP=52, IUE=40, IUU=55). Tratamiento: BFB + NMTP + RF. Variables resultado: EVA, fuerza manométrica vaginal máxima y media, frecuencia urinaria diurna (FUD) y nocturna (FUN), y grado POP.

Resultados: Existen diferencias etarias y manométricas significativas ($p < 0.05$) entre DPC e IUE, IUU y POP. Las pacientes con DPC (46.34 años) son más jóvenes que IUE (54.4 años), IUU (56.36 años) y POP (55.4 años). Las pacientes con DPC (45.49 mm Hg) presentan mayor fuerza que en IUE (23.75 mm Hg), IUU (27.52 mm Hg) y POP (21.17 mm Hg). En general, los pacientes con DPC, presentan una fuerza > 45 mm Hg; los pacientes con IUE, IUU y POP una fuerza < 30 mm Hg.

Conclusiones: Existen diferencias etarias y manométricas entre las DSP hipertónicas (DPC) e hipotónicas (IUE, IUU y POP). Los puntos de corte > 45 y < 30 mm Hg podrían clasificarlas. El tratamiento multimodal (BFB [+], RF y NMTP) mejora la fuerza y disminuye el dolor en DPC. El BFB (-) con RF y NMTP mejora la fuerza, disminuye la FUD y FUN y el grado de prolapso en IUE, IUU y POP.

Palabras clave: Disfunción suelo pélvico, manometría vaginal, biofeedback, radiofrecuencia, neuromodulación del tibial posterior.

Abstract

Objective: a) to establish values to classify pelvic floor dysfunctions (PFD) as hypotonic (stress urinary incontinence [SUI] and urgency [UUI], pelvic organ prolapse [POP]) or hypertonic (chronic pelvic pain [CPP]); b) to establish age differences; and c) to evaluate multimodal rehabilitation treatment (biofeedback [BFB] + posterior tibial neuromodulation [PTNM] + radiofrequency [RF]) in PFD.

Material and methods: Retrospective observational study, 190 patients (CPP=43, POP=52, IUE=40, IUU=55). Treatment: BFB + PTNM + RF. Outcome variables: VAS, maximum and mean vaginal manometric force, daytime urinary frequency (DUF) and nighttime urinary frequency (NUF), and POP grade.

Results: There are significant age and manometric differences ($p < 0.05$) between CPP and SUI, UUI and POP. Patients with CPP (46.34 years) are younger than SUI (54.4 years), UUI (56.36 years) and POP (55.4 years). Patients with CPP (45.49 mm Hg) have higher strength than SUI (23.75 mm Hg), UUI (27.52 mm Hg) and POP (21.17 mm Hg). In general, patients with CPP, present a force > 45 mm Hg; patients with SUI, UUI and POP a force < 30 mm Hg.

Conclusions: There are age and manometric differences between hypertonic (CPP) and hypotonic (SUI, UUI and POP) PFDs. Cut-off points > 45 and < 30 mm Hg could classify them. Multimodal treatment (BFB [+], RF and PTNM) improves strength and decreases pain in CPP. BFB (-) with RF and PTNM improves strength, decreases DUF and NUF and the degree of prolapse in SUI, UUI and POP.

Key words: Pelvic floor dysfunction, vaginal manometry, biofeedback, radiofrequency, posterior tibial neuromodulation.

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Introducción

Las disfunciones del Suelo Pélvico (DSP) son comunes en mujeres. Las DSP causadas por un suelo pélvico (SP) hipotónico incluyen la incontinencia urinaria (IU) y el prolapso de órganos pélvicos (POP). Los síntomas de SP hipertónico incluyen el síndrome miofascial del SP, los síntomas por dificultad de vaciado, al estreñimiento crónico, la dispareunia y el dolor pélvico crónico (DPC)¹.

El SP está formado por huesos, músculos y fascias tendinosas que soportan los órganos pélvicos y asisten en la función urinaria, defecatoria y sexual. Una alteración en la relajación o una contracción paradójica podría resultar en disfunción sexual, de vaciado y dolor¹.

La hipertonidad del SP es difícil de evaluar y cuantificar. No hay un punto de corte para determinar esa condición. La hipertonidad esta relacionada con vejiga dolorosa, estreñimiento, vulvodinia, vestibulodinia y DPC. Se han sugerido como métodos de valoración la manometría, la dinamometría y el EMG de superficie (EMGs)².

Los músculos del SP están conformados por fibras tipo I (65%) y II (35%). Las fibras tipo I (lentas) son responsables del tono y del soporte de órganos pélvicos; las tipo II (rápidas) son responsables de la contracción voluntaria de los esfínteres ante un aumento súbito de la presión abdominal³. Kegel en 1948 relacionó la debilidad del SP con la IU y propuso que los ejercicios mejorarían la incontinencia y los prolapsos (Biofeedback positivo o BFB [+])³.

En el Biofeedback negativo (BFB [-]), la teoría de contracción/relajación descrita por Jacobson (1938) establece que el tono elevado se normalizaría y por ello relajaría la musculatura del SP y sería útil en hipertonia [2,3] porque después de una contracción voluntaria se produce una reducción de la excitabilidad, lo que permitiría a las fibras musculares estirarse⁴. Bo y Naess demostraron que la contracción voluntaria del SP podría disminuir la hipertonia².

La neuromodulación del tibial posterior (NMTP) es útil en el manejo de la urgencia urinaria (DSP hipotónica) y del DPC (DSP hipertónica)⁵. La Radiofrecuencia capacitiva resistiva (RF) puede modular la formación de colágeno actuar sobre los POP (DSP hipotónica) y sobre el dolor^{6,7}. Ambas pueden utilizarse en DSP.

No existe un método estandar para evaluar la función del SP¹. El objetivo del estudio es establecer valores de referencia mediante medición vaginal manométrica y clasificar las DSP hipotónicas (IUE, IU urgencia [IUU], POP) e hipertónicas (DPC, dispareunia, vaginismo, vulvodinia); establecer diferencias etarias y evaluar la efectividad del tratamiento de rehabilitación multimodal (BFB + NMTP + RF) sobre las DSP.

Material y métodos

Estudio observacional retrospectivo a 190 pacientes con DSP (DPC=43 pacientes, POP=52, IUE=40, IUU=55) que acudieron a nuestro Hospital (Octubre-2021 a Junio-2022). El estudio ha sido aprobado por el Comité de Ética para la Investigación Médica (CEIm) del Hospital Universitario de Salamanca (Código Referencia PI 2022-07-1134). Los pacientes firmaron consentimiento informado.

Criterios inclusión: 1) mujeres mayores de 18 años; 2) DSP hipotónica (POP, IUE, IUU) o hipertónica (DPC, dispareunia, vulvodinia, vaginismo) con 6 o más meses evolución; 3) evaluación manométrica vaginal.

Criterios exclusión: 1) nula comprensión y/o colaboración, 2) ictus, demencia o lesión medular que impiden producir contracciones voluntarias, 3) neoplasia, infección activa, embarazo, trombosis venosa profunda, hipoestesia, piel dañada, marcapasos o neuroestimulador lumbosacro.

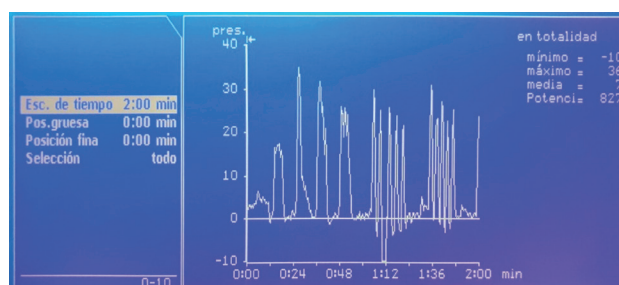
En la evaluación inicial y final se registró la edad, el dolor medido por una escala visual analógica (EVA 0-10), la frecuencia urinaria diurna (FUD, normal < 8/día) y nocturna (FUN, normal < 2/noche). Se realizó valoración manual según escala de Laycock modificada (**Tabla I**), valoración manométrica vaginal y del grado de POP⁸.

Tabla I: Relación entre la evaluación digital o manual (Laycock modificado) y la valoración manométrica con sonda vaginal⁸.

Evaluación Manual (Laycock modificado)	Presión manométrica en mm Hg
0/5	0 - 9
1/5	10 - 19
2/5	20 - 29
3/5	30 - 39
4/5	40 - 49
5/5	> 50

La valoración de la fuerza de la musculatura de SP se realizó mediante manometría vaginal (equipo Biofeedback Myomed 932), realizando contracciones tónicas (5 segundos/trabajo y 5 segundos/reposo por 1 minuto) y fásicas (5 contracciones rápidas seguidas de 10 segundos reposo) por 1 minuto, para objetivar la fuerza máxima y media⁹. **Figura 1.**

Figura 1: Contracciones tónicas (1 minuto) y fásicas (1 minuto). En la valoración inicial, la presión máxima (fuerza) de la musculatura suelo pélvico obtenida en una paciente fue de 36 mm Hg y la presión o fuerza media fue de 7 mm Hg, como se observa en el equipo Myomed © 932.



El prolapso se valoró a través de una escala de 4 grados, según la relación del órgano prolapsado/introito vaginal. El Grado I, el órgano se sitúa a nivel de las espinas ciáticas (Normal); el Grado II, entre las espinas ciáticas y el himen; el Grado III si desciende fuera del himen; y el Grado IV si está totalmente prolapsado³.

La neuromodulación del tibial posterior (NMTP) usó 2 electrodos de superficie, uno a 5 cm proximal al maléolo medial (trayecto del nervio tibial posterior), el otro sobre el calcáneo ipsilateral. Se utilizó el equipo TENStem eco basic (Wetzlar, Germany). Se aplicó una corriente rectangular bifásica simétrica (0 a 9 mA-20Hz-200µs-30 min)⁹.

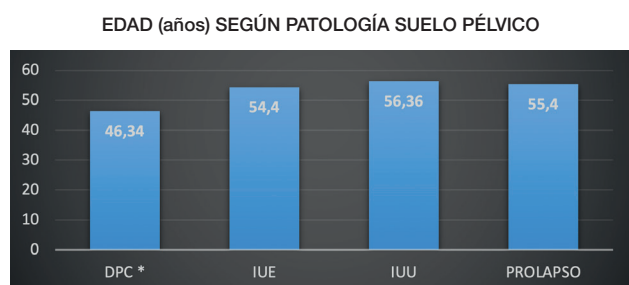
La RF capacitiva-resistiva utilizó el equipo INDIBA® activ ProRecovery HCR902 (Barcelona, España), que emite calor profundo a 448 kHz. El electrodo capacitivo se aplicó sobre la región suprapúbica/periné. El electrodo resistivo cubierto en gel conductor se colocó en la vagina, y el electrodo pasivo se colocó sobre la región lumbosacra, para transmitir el calor a la región pélvica. El tratamiento consistió en 5 min de periodo capacitivo y 10 minutos de periodo resistivo, 2 veces por semana (8 sesiones)⁶.

El análisis estadístico se llevó a cabo con el programa SPSS® v.20 (IBM, NY, Estados Unidos). Para valorar la distribución de la normalidad se utilizó el Test de Kruskal-Wallis. Para variables cuantitativas se utilizó la prueba T de Student tanto para muestras independientes (inter-grupo) como para muestras apareadas (pre-test y post-test). Se valoraron las medias y la desviación estándar considerando un intervalo de confianza del 95%. Se consideró el valor $p < 0.05$ como grado de significación estadística.

Resultados

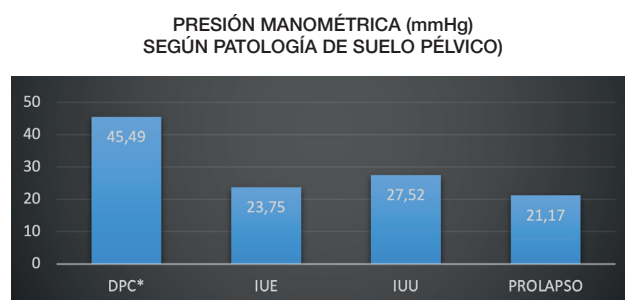
La edad media en DPC era 46.34 ± 13.25 años; en POP 55.4 ± 11.3 años, en IUE 54.4 ± 13.21 y en IUU 56.36 ± 11.94 años. Existían diferencias significativas entre la edad en DPC e IUE (46.34 vs 54.4 , $p=0.0030$), DPC e IUU (46.34 vs 56.36 , $p= 0.0003$), y DPC y POP (46.34 vs 55.4 , $p= 0.0036$). **Figura 2.**

Figura 2: Edad según diferentes disfunciones del suelo pélvico: Dolor pélvico crónico (DPC), Incontinencia Urinaria de Esfuerzo (IUE), Incontinencia Urinaria de Urgencia (IUU) y prolapso de órganos pélvicos (POP). * $p < 0.05$.



La fuerza manométrica máxima en DPC era 45.49 ± 17.28 mm Hg, en IUE 23.75 ± 13.12 mm Hg, en IUU 27.52 ± 14.21 mm Hg y en POP 21.17 ± 13.10 mm Hg. Existían diferencias significativas entre DPC e IUE (45.49 vs 23.75 , $p=0.0001$), DPC e IUU (45.49 vs 27.52 mm Hg, $p=0.0001$) y DPC y POP (45.49 vs 21.17 mm Hg, $p= 0.0001$). Por el contrario, no existían diferencias significativas entre la fuerza en IUE e IUU (23.75 vs 27.52 mm Hg, $p= 0.1438$), IUE con POP (23.75 vs 21.17 mm Hg, $p= 0.5939$) ni IUU con POP (27.52 vs 21.17 mm Hg, $p= 0.0789$). **Figura 3.**

Figura 3: Presión manométrica según diferentes disfunciones del suelo pélvico: Dolor pélvico crónico (DPC), Incontinencia Urinaria de Esfuerzo (IUE), Incontinencia Urinaria de Urgencia (IUU) y prolapso de órganos pélvicos (POP). * $p < 0.05$.



En DPC ($n=43$), el protocolo rehabilitador (BFB + RF + NMTP) ha disminuido el dolor (EVA) de 8 ± 1.57 a 4.97 ± 2.43 ($p= 0.0001$) y mejorado la fuerza máxima de 45.49 ± 17.28 a 51.83 ± 22.31 mm Hg ($p= 0.0045$) y la fuerza media de 9.18 ± 3.91 a 10.7 ± 5.13 mm Hg ($p= 0.0075$). **Tabla II.**

En IUE ($n=40$), el protocolo multimodal ha mejorado la fuerza máxima de 23.75 ± 13.12 a 28.42 ± 14.32 mm Hg ($p= 0.0001$), la fuerza media de 4.3 ± 2.68 a 6 ± 3.39 mm Hg ($p= 0.0001$), además ha disminuido la FUD de 8.52 ± 3.72 a 6.32 ± 1.49 episodios/día ($p= 0.0003$) y la FUN de 2.17 ± 1.41 a 0.72 ± 1.06 episodios/noche ($p= 0.0001$). **Tabla II.**

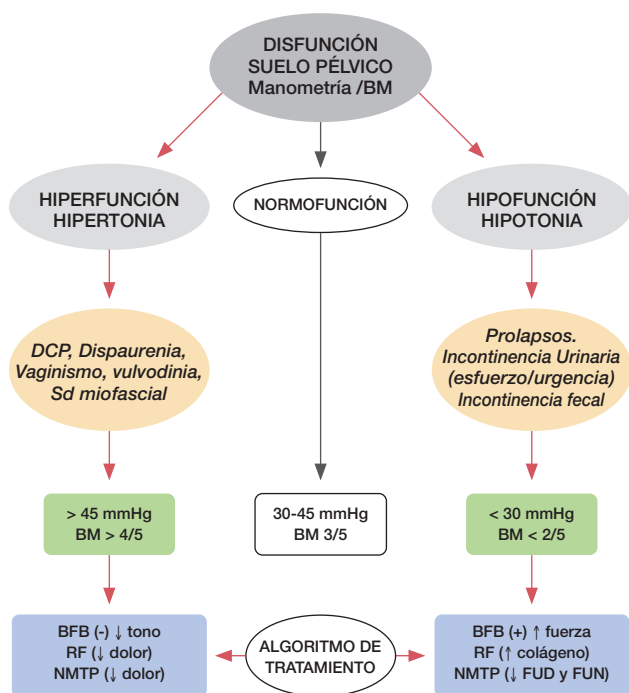
En IUU ($n=55$), el BFB + RF + NMTP ha mejorado la fuerza máxima de 27.52 ± 14.21 a 30.85 ± 15.56 mm Hg ($p= 0.0060$), la fuerza media de 5.18 ± 3.17 a 6.52 ± 3.67 mm Hg ($p= 0.0011$), además ha disminuido la FUD de 10.45 ± 4.20 a 6.8 ± 2.39 episodios/día ($p= 0.0001$) y la FUN de 2.85 ± 1.6 a 0.78 ± 0.89 episodios/noche ($p= 0.0001$). **Tabla II.**

En POP ($n=52$), el protocolo rehabilitador multimodal ha mejorado la fuerza máxima de 21.17 ± 13.10 a 24.01 ± 12.06 mm Hg ($p= 0.0069$), la fuerza media de 4.30 ± 3.23 a 5.17 ± 3.04 mm Hg ($p= 0.0007$), además ha disminuido el grado de POP de 2.21 ± 0.63 a 2.03 ± 0.76 puntos ($p= 0.0019$). **Tabla II.**

Los pacientes con DPC, vulvodinia o vaginismo presentan una fuerza manométrica máxima > 45 mm Hg; los pacientes con IUE, IUU y POP presentan una

fuerza < 30 mm Hg. Los pacientes con fuerza normal estarían en el rango 30-45 mm Hg (Figura 4). Según algoritmo de tratamiento, el BFB (+) mejoraría la fuerza y el BFB (-) normalizaría el tono; la RF disminuiría el dolor o favorecería la formación de colágeno; y la NMTP disminuiría el dolor y la FUD y FUN. El algoritmo mejoró las variables de resultado (p<0.05). Figura 4 y tabla II.

Figura 4: Clasificación de las diferentes disfunciones del suelo pélvico según manometría vaginal en hipertónicas (dolor pélvico crónico [DPC]), o hipotónicas (incontinencia urinaria de esfuerzo, incontinencia urinaria de urgencia y prolapso de órganos pélvicos) y una propuesta de algoritmo de tratamiento. BM, balance muscular. BFB, biofeedback, (+), positivo, (-), negativo. RF, radiofrecuencia. NMTP, neuromodulación del tibial posterior. FUD, frecuencia urinaria diurna. FUN, frecuencia urinaria nocturna.



Discusión

Existen pocos estudios que valoren la fuerza en las DSP y que las clasifiquen en hipo/hipertonía³. Por primera vez se ha utilizado la manometría vaginal para clasificar las DSP en hipertónicas (DPC, dispareunia, vulvodinia, vaginismo) teniendo en cuenta el valor de referencia > 45 mm Hg; o hipotónicas (POP, IUE, IUU) teniendo en cuenta el valor < 30 mm Hg. Esto nos ha permitido postular un algoritmo de tratamiento multimodal, el cual ha sido efectivo al mejorar las distintas variables de resultado en POP, IUE, IUU y DPC.

Los músculos hipoactivos se relacionan con la incontinencia y el prolapso; los hiperactivos con el espasmo muscular, mialgia, dolor e hipertonicidad¹⁰. Las mujeres con menor fuerza presentan IU y fecal, las mujeres con mayor fuerza presentan disfunción sexual¹¹. Evidencia creciente indica que las DSP hipertónicas incluyen DPC, dispareunia, vulvodinia, vaginismo y dolor miofascial¹²; existe controversia en saber si las mujeres hipertónicas presentan DSP y no está determinado manualmente ni manométricamente el punto de corte para determinar hipertono, normotono o hipotono¹². Butrick refiere que la debilidad provoca IU, fecal y POP; la hipertonia produce vejiga dolorosa y DPC¹³.

Ozdemir estableció que el valor normal de manometría de SP es 30-60 mm Hg, bajo si 12-30 mm Hg, y anormalmente bajo si menor a 12 mm Hg¹⁴, lo que coincide con Sartore¹⁵. El valor disminuye en mayores de 40 años y con la paridad^{14,15}.

Quarty sostiene que las mujeres incontinentes presentan una fuerza de 21.7 cm H₂O; las parturientas 35 cm H₂O y las no parturientas 47 cm H₂O¹⁶. Esto refuerza nuestra hipótesis en considerar la normalidad entre el rango 30-45 mm Hg.

Tabla II: Efecto de la rehabilitación multimodal (BFB + RF + NMTP) sobre las distintas variables de resultado en pacientes con DPC (dolor pélvico crónico) n=43; IUE (incontinencia urinaria de esfuerzo) n=40; IUU (incontinencia urinaria de urgencia) n=55 y POP (prolapso de órganos pélvicos) n=52.

Variable	Pre	Post	p
DPC (dolor pélvico crónico) n=43			
EVA dolor (0-10) media ± DE	8 ± 1.57	4.97 ± 2.43	0.0001*
P máxima mm Hg (media ± DE)	45.49 ± 17.28	51.83 ± 22.31	0.0045*
P media mm Hg (media ± DE)	9.18 ± 3.91	10.7 ± 5.13	0.0075*
IUE (incontinencia urinaria de esfuerzo) n=40			
P máxima mm Hg (media ± DE)	23.75 ± 13.12	28.42 ± 14.32	0.0001*
P media mm Hg (media ± DE)	4.3 ± 2.68	6 ± 3.39	0.0001*
FUD (media ± DE)	8.52 ± 3.72	6.32 ± 1.49	0.0001*
FUN (media ± DE)	2.17 ± 1.41	0.72 ± 1.06	0.0001*
IUU (incontinencia urinaria de urgencia) n=55			
P máxima mm Hg (media ± DE)	27.52 ± 14.21	30.85 ± 15.56	0.0060*
P media mm Hg (media ± DE)	5.18 ± 3.17	6.52 ± 3.67	0.0011*
FUD (media ± DE)	10.45 ± 4.20	6.8 ± 2.39	0.0001*
FUN (media ± DE)	2.85 ± 1.6	0.78 ± 0.89	0.0001*
POP (prolapso de órganos pélvicos) n=52			
P máxima mm Hg (media ± DE)	21.17 ± 13.10	24.01 ± 12.06	0.0069*
P media mm Hg (media ± DE)	4.30 ± 3.23	5.17 ± 3.04	0.0007*
Grado de POP (media ± DE)	2.21 ± 0.63	2.03 ± 0.76	0.0019*

EVA, escala visual analógica. DE, desviación estándar. P, prueba estadística T de Student, * p < 0.05. FUD, frecuencia urinaria diurna (normal <8/día). FUN, frecuencia urinaria nocturna (normal <2/noche). POP, prolapso de órganos pélvicos.

Observamos que las pacientes con DPC son más jóvenes que en IUE, IUU y POP. Weidner y Abrahams sostienen que la IUU aumenta con la edad y es más común en gente mayor^{17,18}. Además, con la edad disminuye la fuerza y el tono. Esto explicaría porque las DSP hipotónicas aparecen a los 55 años (IUE 54.4 años, POP 55.4 años, IUU 56.36 años), mientras que las DSP hipertónicas se dan en mujeres más jóvenes (en nuestro estudio 46.3 años)¹⁹.

Con la edad aumentan las fibras tipo I (tónicas) y disminuyen el tipo II (fásicas); por lo que las mujeres presentan más riesgo de incontinencia por la debilidad de las fibras tipo II¹⁶. Además, la deficiencia de estrógeno disminuiría la presión de reposo uretral, lo que produciría IUE¹⁶.

No hemos utilizado la palpación manual como medida de resultado porque la escala de Laycock modificada es subjetiva²⁰. Así, un balance muscular subjetivo de 0/5 se correspondería manométricamente con una contracción de 0 a 9 mm Hg (valor más objetivo)²¹.

Las mujeres incontinentes presentan menor fuerza de contracción vaginal máxima (EMGs) que las mujeres sanas ($p < 0.001$)¹⁹. La fuerza máxima del SP disminuye por décadas¹⁹. Por esto, en nuestro estudio las mujeres con DPC (46.3 años y 45.49 mm Hg) tendrían más fuerza que las mujeres con IUE (54.4 años y 23.75 mm Hg), POP (55.4 años y 21.17 mm Hg) e IUU (56.36 años y 27.52 mm Hg).

El fundamento del BFB [+] se basa en que la debilidad del SP está relacionado con POP, IU, fecal y alteraciones sexuales. Hemos demostrado que el BFB mejora la fuerza y disminuye la incontinencia en IUE e IUU^{9,22,23}. Jorge-Ferreira también ha demostrado que el BFB incrementa la fuerza en DSP de 11 a 19.2 mm Hg ($p < 0.01$)²⁴.

El fundamento del BFB [-] se basa en la teoría de contracción/relajación (Jacobson, 1938) la cual normalizaría el tono y sería útil en las DSP hipertónicas³. Esta teoría originó la técnica de relajación post-isométrica descrita por Lewis (1986), por la cual la rigidez de un músculo se reduce después de una contracción voluntaria²⁵. Naess y Bo han observado que luego de 3 contracciones voluntarias máximas, el tono de la musculatura del SP disminuye, objetivado por manometría y por EMGs². La contracción del BFB (+) y la relajación del BFB (-) disminuirían la hipertonicidad de las DSP en un 59-80%²⁶. Además, el ejercicio mejora la función sexual por la hipertrofia generada por el músculo elevador del ano, mejorando la función de soporte y resistencia. El ejercicio incrementa el flujo sanguíneo favoreciendo la recuperación de las células y tejidos dañados²⁷. Voorham-Zalm sugiere que los músculos débiles deben fortalecerse (BFB [+]) mientras que el tono elevado debe trabajarse con relajación y coordinación del SP (BFB [-]) para romper el ciclo dolor-

contractura-dolor²⁸. Esto explicaría porque el BFB (+) y (-) ha mejorado la fuerza máxima y disminuido el dolor en nuestro estudio.

Debemos fortalecer el SP porque los aumentos súbitos de presión abdominal sin contracción compensatoria producirían pérdida de orina. Una contracción abdominal suave produciría una fuerza de 20 cm H₂O, el saltar o correr 90 cm H₂O y el toser 125 cm H₂O²⁹.

El tratamiento multimodal disminuyó el prolapso de 2.23 ± 0.63 a 2.03 ± 0.76 grados ($p = 0.0019$). Braekken sostiene que los ejercicios del SP mejoraron 1 grado el POP en el 19% de los pacientes tratados a diferencia de un 8% en los controles³⁰. Li y Ge sostienen que los ejercicios del SP mejoraron tanto los síntomas como los grados del POP en sus grupos tratados³⁰.

Una limitación del estudio es no haber evaluado otros parámetros tales como la fuerza pasiva, la velocidad de contracción y la resistencia. Sin embargo, los valores de fuerza máxima han resultado ser significativamente diferentes en las DSP hipertónicas (con punto de corte > 45 mm Hg) de las DSP hipotónicas (< 30 mm Hg). Es necesario valorar estas variables en una serie más grande para comprobar la tendencia observada en este estudio.

Conclusiones

Existen diferencias etarias y manométricas entre los pacientes con DSP hipertónicas (DPC) e hipotónicas (IUE, IUU y POP). El punto de corte $>$ de 45 mm Hg y $<$ de 30 mm Hg podrían ayudar a clasificar tales patologías. El algoritmo de tratamiento multimodal (BFB [+], RF y NMTP) es capaz de mejorar la fuerza y disminuir el dolor en los pacientes con DPC. El BFB (-) con RF y NMTP es capaz de mejorar la fuerza, disminuir la FUD y FUN y disminuir el grado de prolapso en los pacientes con IUE, IUU y POP.

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Conflicto de intereses

Los autores declaran no tener conflicto de intereses.

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ORIGINAL

The latest achievements of operative surgery in the development of modern medicine and dentistry: challenges of implementing artificial intelligence

Los últimos logros de la cirugía operatoria en el desarrollo de la medicina y la odontología modernas: retos de la aplicación de la inteligencia artificial

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Abstract

Aim: to investigate the novel medical advancement in surgery. We also aim to investigate the various modern challenges of implementing artificial intelligence in medicine.

Methods: In our review, we involved English studies from common databases such as Web of Science, Scopus, Google Scholar, Pubmed, and the Cochrane Library using the following keywords "advancement", "artificial intelligence", "innovations in surgery", and "operative surgery" till November 2023.

Scientific novelty: There are published studies that have tried to determine the role of new technologies in the field of surgery; however, there is a lack of studies that have attempted to identify a comprehensive analysis of these innovations and their integration into healthcare services. In our article, we tried to evaluate the role of new technologies in modern medicine and dentistry, especially in the surgical field.

Conclusion: Newly advanced technologies have greatly benefited in developing overall healthcare services, especially in the surgical field. AI has several applications in the field of surgery, which has significantly impacted the current healthcare systems.

Key words: innovations in surgery, artificial intelligence, operative surgery.

Resumen

Objetivo: investigar los novedosos avances médicos en cirugía. También se pretende investigar los diversos retos modernos de la aplicación de la inteligencia artificial en medicina.

Métodos: En nuestra revisión, involucramos estudios en inglés de bases de datos comunes como Web of Science, Scopus, Google Scholar, Pubmed y Cochrane Library utilizando las siguientes palabras clave "avance", "inteligencia artificial", "innovaciones en cirugía" y "cirugía operatoria" hasta noviembre de 2023.

Novedad científica: Existen estudios publicados que han intentado determinar el papel de las nuevas tecnologías en el campo de la cirugía; sin embargo, faltan estudios que hayan intentado identificar un análisis exhaustivo de estas innovaciones y su integración en los servicios sanitarios. En nuestro artículo, intentamos evaluar el papel de las nuevas tecnologías en la medicina y la odontología modernas, especialmente en el ámbito quirúrgico.

Conclusiones: Las nuevas tecnologías avanzadas han contribuido en gran medida al desarrollo de los servicios sanitarios en general, especialmente en el ámbito quirúrgico. La IA tiene varias aplicaciones en el campo de la cirugía, lo que ha repercutido significativamente en los sistemas sanitarios actuales.

Palabras clave: innovaciones en cirugía, inteligencia artificial, cirugía.

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Introduction

Enhancing and strengthening healthcare services is considered one of the main and important goals for all societies worldwide. Because of recent technological advancements, healthcare services have seen major improvement over the previous several decades, from patient examination to recent advances in diagnostic and treatment modalities, including medical and surgical options^{1,2}. The healthcare system provides medical services through an integrated strategy, including hospital facilities, medical professionals, and modern equipment³. Recent innovations and advancements in medical technology applications have provided the general population with higher-quality services, better care, and improved quality of life⁴⁻⁶. Among these advances, the innovations in 3D printing and nanotechnology have enabled the creation of customized implants and medication delivery systems. At the same time, wearable technology and telemedicine have enhanced the accessibility, ease, and customization of healthcare^{7,8}.

To implement the Future of Surgery Commission's recommendations, the Royal College of Surgeons of England is actively involved. The degree of complexity of the various medical interventions that aim to improve the overall patient's quality of life is one of the most important ongoing surgical issues worldwide⁹. Over time, there has been an increase in the demand for healthcare services, leading to general shortages of personnel and supplies in the medical system. To enable patients and even doctors to receive the best and most adequate healthcare services, this prompted interest in incorporating modern technological services into the medical systems¹⁰. Artificial intelligence (AI) plays an essential role in enhancing healthcare services in all aspects, from diagnosis to treatment involving operations improvement^{11,12}. Recently, there has been evidence that AI can be beneficial in evaluating medical imaging, patient symptoms, and investigations from electronic medical records (EMRs). It can also correlate these factors to determine the disease's diagnosis and prognosis¹³.

Research focus

In our review, we focused on studying innovations, recent advances in medicine, and integrating new technologies in surgery. We also investigate the roles and applications of artificial intelligence in operative surgery.

Research problem

There is a significant shortage in both healthcare facilities and providers. Therefore, there is increasing interest in integrating the novel technologies in surgery. There is fear that these advancements in medicine would replace physicians. However, others suggest that these innovations significantly impact the improvement of the healthcare services provided.

Research questions

1. What is the recent medical status?
2. What are the new advancements in medicine and surgery?
3. What is the role of artificial intelligence and recent technologies in operations?
4. What are the challenges of implementing artificial intelligence in the healthcare system?

Research aim

Our study aims to investigate the novel medical advancement in surgery. We also aim to investigate the various modern challenges of implementing artificial intelligence in medicine.

Literature review

The rapid progress of modern technology and research worldwide has aided in advancing medical care regarding how we diagnose, treat, and anticipate illness prognosis. It also increases our understanding of illnesses, leading to more personalized therapy¹⁴. These advancements have definitely benefited surgical practice, particularly in several aspects of surgery. However, there is still a need for increased awareness of these developments among physicians and academics globally, particularly in underdeveloped countries¹⁵. In the last ten years, remarkable advancement was achieved in global surgery, and serious and evidence-based national policies for scaling up surgical services worldwide are currently being formed¹⁶. Developing an accurate country-based assessment of the surgical disease burden, establishing an appropriate estimate of the current needs is an essential step in developing the healthcare service¹⁷. Recently, increased efforts have aimed to update and get the most benefits of modern medical technologies. This includes the use of modern machines, robots, and AI technologies in all medical aspects, including surgeries. There is fear that AI machines replace human clinicians. In 2018, a study investigating the role of AI in recent healthcare services showed that the most significant benefits of AI were shown in image analysis, virtual assistants, robotic-assisted operations, and clinical decision support¹⁸.

Although there are fears that AI will replace human existence, according to a recent study that evaluated the potential for automation across various sectors, health, and education are the areas where robots are least likely to replace humans¹⁹. Clinical competence and the critical requirement for interaction with others will never, in all likelihood, render clinicians obsolete. Although AI will increasingly be utilized to solve specific repeated issues, most notably in the diagnosis process, it appears improbable that it will replace surgeons soon.

Robots

Nowadays, A surgical robot is capable of performing the whole surgical procedure independently. However, dealing with the unpredictable consequences of such

operations is a very distant possibility. At the same time, Robots in the operating room are very intricate and sophisticated instruments used by surgeons and their teams, not replacements for human presence²⁰. The high cost of robots remains a major challenge, but hospital networks, especially those with smaller facilities, have a good chance of working together to share this important resource. Regarding the remote surgery, China has already succeeded in this field, with a surgeon performing an entire operation on a patient thousands of miles away using remote robotic help over 5G networks. Although this remarkable achievement has not been utilized in most countries yet, augmented reality (AR) photographs utilization of to convey real-time information to specialized surgeons in another place seeking their advice to finish complicated surgeries is currently available in the UK²¹.

Laparoscopy

Minimally invasive surgical techniques have become popular in practically all medical fields over the last 30 years. Laparoscopic surgery is one of the earliest and most commonly used minimally invasive procedures since the first laparoscopic surgery in gynecology in 1962²². It is believed that laparoscopic surgery is considered one of the greatest innovations and advances in the surgical field. It has resulted in a revolution in the employment

of digital and robotic technologies in surgical practice. Compared to 'open' surgeries, it has significantly reduced patient recovery times. Even more remarkable, significant gains have been obtained while concurrently improving surgical quality²³. Notably, a recent report published by Bingmer et al. revealed a significant 462% rise in laparoscopic patients performed by general surgeons over the last years, from 2000 to 2018²⁴. Laparoscopic operations are significantly associated with fewer wound infections, less pain VAS score, shorter post-operative hospitalization, lower rates of morbidity and death, an earlier return to work, and an overall improvement in quality of life²⁵. However, there were safety concerns when laparoscopy was first utilized. Fortunately, many of the first reported problems have become relatively rare as surgical teams have advanced past their learning curves over time²⁶. New laparoscopic technologies are constantly being developed, primarily to improve patient clinical results and/or decrease costs. Laparoscopy has potential disadvantages, such as narrowing the operation visual field, limiting the tactile sensation, injuring the internal structures, and the major vessels, making it challenging²². **Figures 1 and 2** show the rise in proportion over the study period now taken up by laparoscopic procedures and the explosive rise of minimally invasive surgery and the progressive replacement of open technique, respectively.

Figure 1: illustrates the increase in the percentage of laparoscopic surgeries performed over the study period²⁷.

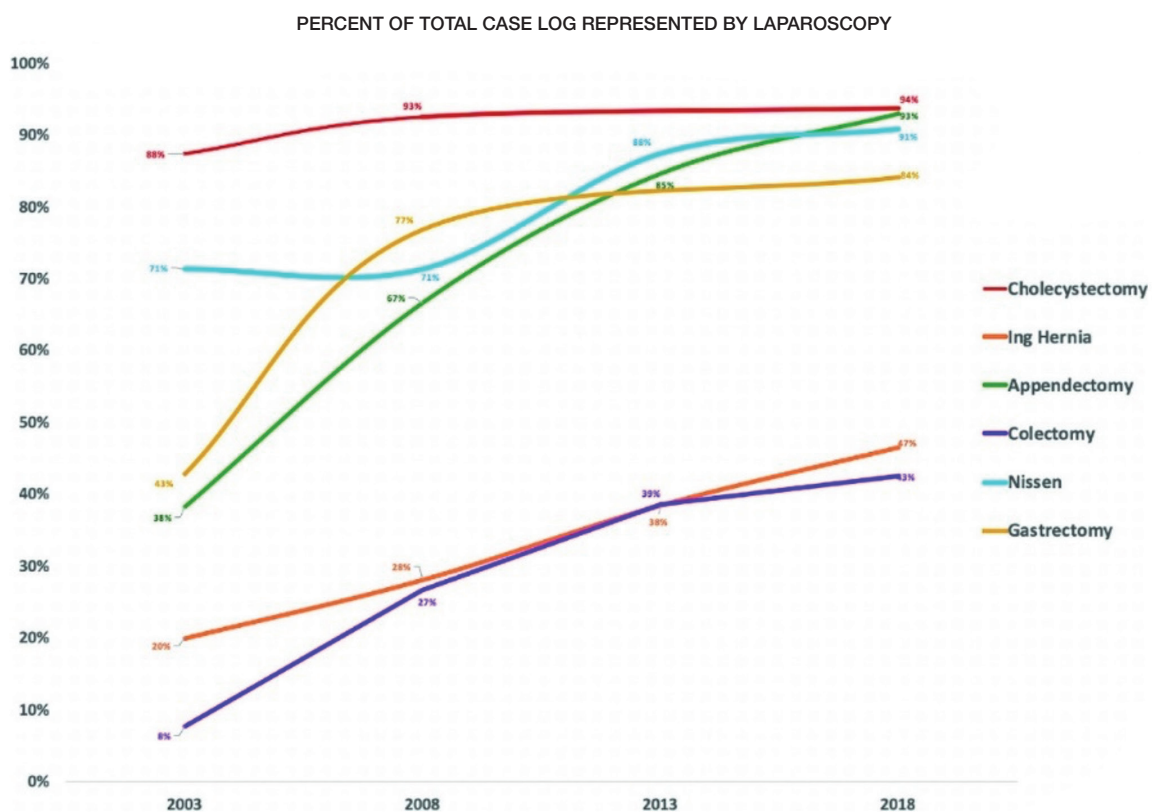
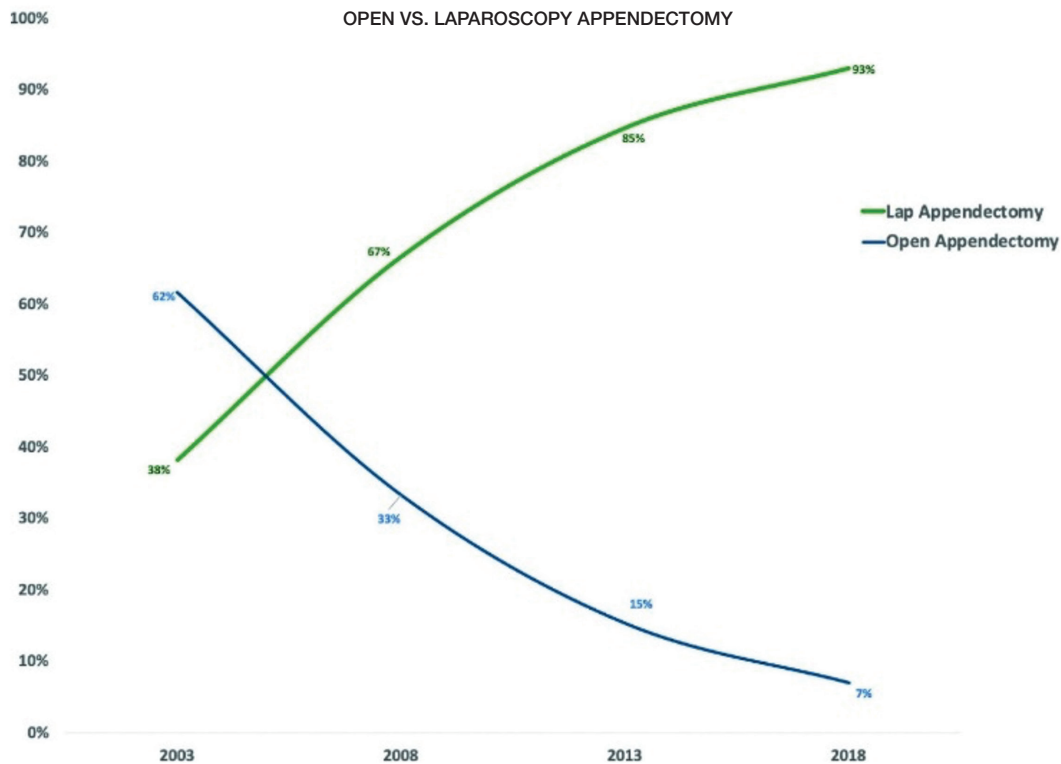


Figure 2: Illustrates how open operations are gradually being replaced with minimally invasive surgery, which is growing in popularity²⁷.

3D printing

3D printing is an additional innovation that has the potential to alter both surgical planning and the variety and efficacy of available implants. Data from patient imaging technologies may be extracted using 3D printing software, which can then be utilized to produce customized, custom surgical guides and implants that replace or stabilize diseased body parts or anatomical structures. It is anticipated that 3D planning and printing technologies will become extensively accessible, and the printed items will be sufficiently durable to be sent to all hospitals for local surgical teams to utilize. This technology may increase the safety and efficacy of surgeries in addition to providing the opportunity for surgical techniques that are now too difficult or yield poor results. Using this advanced technology, patients may have more options, higher expectations, and customized management. Giving patients access to 3D models might help them understand more about the medical procedures they are going to have, which would allow for more informed consent²⁸. A Cross-Sectional Multispecialty Review in 2022 showed the advantages of 3D printing in planning complex medical procedures and training medical professionals. These advantages are improving understanding of the specific anatomy of each patient, simulation-based education and training, improved planning before surgery, mock simulated surgeries, creation of surgical guidelines, creation of implants customized for each patient, and bioprinted structures or organs²⁹.

Stem cells

Among the great advancements in medicine is the use of stem cells in various diseases. There are rapidly increasing efforts and research in the field of stem cell therapy. It is considered the only treatment option for certain disorders such as hemolytic anemias, leukemia, and bone marrow failure. It is also considered a reliable treatment option for other diseases. However, its utilization is still limited as major obstacles face us due to the hazards associated with a bad reaction between the donor and host cells. It has shown a promising effect in children with major disorders in the immune system in Great Ormond Street Hospital³⁰.

Ophthalmologists could make benefit from stem cell therapy in their surgeries. In the Academy of Medical Sciences, a fellow at Moorfields Eye Hospital, Prof Robin Ali, could use stem cell transplants to cure macular degeneration, which is usually a non-curable condition. Their results were promising, and they reported a significant vision improvement in the patients involved³⁰. This raised the hope of treating the difficult retinal disorders. Moreover, Osaka University doctors in Japan restored the sight of a patient in one eye who used stem cell-derived corneal tissue to implant for the first time. To date, corneal transplantation from a dead person is the only available treatment option for severe corneal diseases. Living donors can provide transplantable cells. Rejection rates should also be far reduced since the stem cells mature to take on the features of the host body, unlike 20% of transplant recipients who reject their new cornea³¹.

Artificial intelligence in the field of surgery

The definition of AI is the computational modeling of human cognitive functions, including self-learning, reasoning, and self-correction. These characteristics imply that AI has enormous potential for technologically progressing fields throughout all sectors of human civilization, as seen by the incorporation of this technology into the daily lives of people worldwide³². Exponential advancements in data storage, processing power, and data digitization have begun to transform medicine at a rate faster than human ability³³. Pattern recognition is used in machine learning (ML), utilizing both supervised and unsupervised learning to predict outcomes. In contrast, deep learning (DL) has allowed AI to develop into image identification, processing, and bioinformatics learning³⁴. Healthcare options combined with AI analysis, such as those described before, have the potential to improve patient care and reduce morbidity and mortality rates in emergency surgery through a variety of means, including diagnostics³⁵.

Materials and Methods

General background

The recent innovations and advancements in medical technology applications provided higher quality services, better care, and improved quality of life to the general population. Among these advances, innovations in 3D printing and nanotechnology have enabled the creation of customized implants and medication delivery systems, while wearable technology and telemedicine have enhanced the accessibility, ease, and customization of healthcare. AI plays an important role in enhancing healthcare services in all aspects, from diagnosis to treatment involving operations improvement. Recently, there has been evidence that AI can be very helpful in evaluating medical imaging, patient symptoms, and investigations. It can also correlate these factors to determine the disease's diagnosis and prognosis.

Recently, there have been increased efforts that aim to update and get the most benefits of modern technologies in medicine. This includes the use of modern machines, robots, and AI technologies in all medical aspects, including surgeries.

Inclusion criteria

1. All study designs of the articles were included, such as case series, randomized clinical trials, case-control, or systematic review.
2. We included studies evaluating the role of new technologies in the surgical field.
3. Most included studies should be recent, from 2018 to 2023.

Exclusion criteria

1. Studies and articles that were not peer-reviewed, as well as proposals, procedures, letters, and opinions.

2. Old studies that were conducted before 2010.
3. Studies unrelated to our topic or their aim were not related to ours.

Information sources

We utilized the following online databases: Web of Science, Scopus, Google Scholar, Pubmed, and the Cochrane Library using the following keywords "advancement", "artificial intelligence", "innovations in surgery", and "operative surgery" till November 2023. We collected studies using each set of keyword combinations to create an unbiased collection of publications. The references included in this paper were chosen because they are relevant to our topic.

Data collection

The included studies were reviewed following three stages. The first involved using EndNote Software to import the findings from electronic databases into a Microsoft Excel sheet. The articles entered into the Excel sheet were screened for titles and abstracts in the second stage. The third stage involved screening the included citations from Stage 2's full text. In addition, we manually checked the included publications' references for any potentially overlooked studies.

Statistical analysis

We conducted a qualitative study of the previously published studies. We could not do a quantitative analysis because our study is a narrative review. The outcomes that will be measured in the quantitative analysis must be specified, and more than two studies reporting data on these outcomes must be located and compared to draw a conclusion. We attempted a quantitative analysis in our research, but we could not identify specific results relevant to our subject or papers that presented similar data. To get strong evidence and current results and conclusions, we conducted a qualitative analysis of papers relevant to our topic, presented their findings, and compared them.

Results and discussion

Laparoscopic surgery (LS) and robotic surgery (RS) are used to perform various surgical procedures. RS is controlled like laparoscopic tools but with additional axial flexibility, fatigue resistance, repeatability, and stability^{36,37}. The ultimate goal for RS would be autonomous AI instruments; they are now supervised, but with success: the Da Vinci system in prostatectomy, the Smart Tissue Autonomous Robot "STAR" robot that can stitch bowel. Robots are being developed for endoscopy to provide triangulation for suturing and knot tying^{38,39}. The belief that robots cannot reproduce surgical competence is breaking down, with robots outperforming "expert" surgeons regarding consistency, spacing, time spent, and blunders⁴⁰.

In 2019, Lin et al. showed the role of AI and imaging in performing surgical procedures. This study reported using CT scans and AI to recreate the necrotic pancreatic regions in pancreatitis and assist drainage⁴¹. Similarly, the planning of difficult or complex procedures might be aided by AI models and imaging, as seen in orthognathic surgery, plastic, and reconstructive surgery. Knoop et al. created a model containing 4261 volunteer faces to identify and treat orthognathic patients⁴². Additionally, AI has been proposed for regeneration, including birth abnormalities. An autonomous device with feedback might enable non-invasive tissue restoration via mechanosimulation. A previous study utilized animals to generate new tissues. They are still working to develop implantable technologies that can restore tissue function⁴³.

AI has the potential to improve surgical education and learning as well. In certain instances, real-time feedback has been provided to surgeons, allowing them to modify the force they apply to delicate tissues. In addition to revolutionizing surgical learning, video recording makes it possible to identify surgical performance using AI^{38,44}. An AI model with skin cancer diagnosis accuracy comparable to dermatologists was developed by Esteva et al.⁴⁵. Using machine learning by Rajkomar et al. to predict hospital readmission rates and patient death may help medical personnel identify patients who require more care. Furthermore, Chung et al. developed an AI model that could predict when psychosis would start in those exhibiting clinical high-risk indicators⁴⁶. A machine learning model was created by Khera et al. to identify individuals who are at a high risk of acquiring heart disease. This might lead to early intervention and preventative measures⁴⁷. A previous review highlighted the recent application of AI in emergency surgery in both diagnosis and management and concluded that AI shows great potential in the field of emergency surgery. An ideal scenario would involve using AI to quickly and effectively refer suitable patients through the emergency department, identify surgical concerns on imaging, and even anticipate the risks of surgery based on the clinical history and vital sign observations, enabling a surgeon to provide a customized risk assessment for each patient. However, we should take into consideration that machines may give misleading information and wrong results and may worsen the overall outcomes⁴⁸.

Globally, surgical and non-surgical procedures for pediatric patients have shown rapid and significant advancement in recent years. Given the available data, pediatric surgeons must stay updated on the newest and greatest practices that yield the best results⁴⁹. Injections of botulinum toxin were used to treat children with persistent constipation, according to a retrospective study conducted in the Netherlands. When preinjection pressure is more than 70 mmHg, botulinum toxin was shown to dramatically lower anal basal pressure. That being said, rectal washout is advised in cases of very increased anal basal pressure⁵⁰. For patients with

moderate to severe hereditary spherocytosis (HS), total splenectomy is the most successful therapy. One conservative procedure that can keep some of the spleen's function intact is partial splenic embolization (PSE). A single center's retrospective analysis included HS patients who underwent complete splenectomy and super-selective PSE (SPSE). They demonstrated that SPSE is safe and beneficial for moderate-to-severe pediatric HS; more extended follow-up periods and more patients are required, though⁵¹. Concerning recent surgical procedures in pediatric surgery patients, a previous case-series study reported the role of Argyle™ Replegic Suction Catheter (RSC), endoscopic esophageal vacuum-assisted closure (EVAC) in treating patients with esophageal perforation (EP). They discovered that EVAC, which is frequently used to treat wounds and adult EP patients, was a viable treatment for pediatric EP. Additionally, they advised a quicker transition to RSC in order to minimize the need for anesthesia during later treatments. They found that the vast majority of patients⁵².

Dental and orthodontist practices have changed significantly with the advancements in the modern technology, allowing them to treat patients in a more effective and efficient manner. Technology has altered the dental treatment process, making it more secure, patient-friendly, and more precise. 3D printing and digital X-rays are examples of these advances. In dentistry, technology is employed for purposes beyond diagnosis and treatment. Furthermore, it has reduced the cost and increased accessibility to dental treatment, especially for those with limited resources. Another technical development that has revolutionized dentistry is digital impressions. Dentists may now take digital images of a patient's dental arch using an intraoral scanner instead of unwieldy and painful analogical impressions. More exact and accurate impressions may be obtained due to this technology, which also decreases the need for follow-up visits and improves patient comfort. The authors of research published in this Special Issue examined the precision of four top intraoral scanners in full-arch digital implant impression⁵³. Three-dimensional printing is another technical advancement that has significantly altered dental care. It has totally changed the way dentists create bridges, crowns, and other dental prosthetic restorations. With the use of 3D printing, dentists may create highly accurate models of a patient's teeth that they can use to plan and create specialized dental restorations. Implementing this technology results in dental restorations that take less time, increasing process efficiency and lowering costs⁵⁴. Dental treatment is now safer and more efficient thanks to new technology, which has also improved patient results. Laser dentistry techniques are a good example of this. Gum reshaping, decay removal, and even root canal therapy are all possible with lasers. Patients may have less bleeding and discomfort because they are less intrusive than conventional dental instruments⁵⁵.

Limitations

The primary issue with this article is that it is a narrative review. The included research results are presented in written paragraphs in a narrative review. They don't undertake any pooled analysis using the data from the summarized studies. Real objectivity and pooled analysis are therefore precluded. A narrative review serves as a collated source of the most widely accepted views at the time of publishing. This may be useful to understand a body of evidence fully. As it does not thoroughly consider the alternative hypothesis, it does not guarantee that the prevailing ideas are true.

Conclusion

Innovative medical technology integration is of worldwide interest. Newly advanced technologies have shown a great beneficial role in developing overall healthcare services, especially in the surgical field. AI has several applications in the field of surgery, which has significantly

impacted the current healthcare systems. We are facing challenges in the development of these enhancements and in implementing AI in modern medicine and dentistry. We should provide potential opportunities for new technologies to reach an improved comprehensive medical service.

Conflict of interest

All authors declare no conflict of interest.

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Ethical statement

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ORIGINAL

Cerrando el círculo de calidad en contingencia por enfermedad ocupacional. Distintas competencias y una problemática común

*Closing the quality circle in contingency for occupational disease
Different competences and a common problem*

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Introducción: Se considera contingencia profesional la materialización de un riesgo que provoca una necesidad de protección por la Seguridad Social. El Daño Laboral viene recogido en la Ley de Prevención de Riesgos Laborales como derivado del trabajo y con motivo u ocasión del mismo.

Objetivo: Revisar el debate médico legal en contingencia profesional, el procedimiento de cambio de contingencia y proponer un protocolo de actuación unificado.

Material y método: Se analiza la legislación vigente, los procedimientos administrativos, los datos de notificación y las competencias de las partes implicadas.

Resultados: Existe una tendencia a la infradeclaración de la contingencia profesional, dificultad para establecer la relación de causalidad y coherencia temporal entre la exposición al riesgo y el daño resultante, especialmente en las enfermedades causadas o agravadas por el trabajo.

Conclusiones: Las competencias entre las distintas partes implicadas requieren unificar criterios con unos mínimos comunes y una actuación coordinada para evitar discrepancias.

Palabras clave: enfermedad profesional, salud laboral, medicina legal, contingencia profesional.

Abstract

Introduction: An occupational contingency is considered to be the materialization of a risk that provokes a need for Social Security protection. Occupational Injury is included in the Law on Prevention of Occupational Risks as deriving from work and as a result of or on the occasion of work.

Objective: To review the legal medical debate on professional contingency, the procedure for changing contingency and to propose a unified action protocol.

Methods: The current legislation, administrative procedures, notification data and the competences of the parties involved were analyzed.

Results: There is a tendency towards under-reporting of occupational contingency, difficulty in establishing the causal relationship and temporal coherence between exposure to the risk and the resulting damage, especially in illnesses caused or aggravated by work.

Conclusions: The competencies between the different parties involved require unification of criteria with common minimums and coordinated action to avoid discrepancies.

Key words: occupational disease, occupational health, legal medicine, professional contingency.

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El concepto de contingencia en las enfermedades relacionadas con el trabajo: profesional vs común

Contingencia profesional es un término utilizado tanto por la ley como por la doctrina y la administración que puede tener significados diferentes, sin que haya una definición legal unificada. Se entiende aquí por contingencia *la materialización de un riesgo que provoca un estado de necesidad protegido por la Seguridad Social*. Hay que diferenciar dos tipos de contingencias:

- Contingencia Común. Situación en la que un trabajador, por un accidente o enfermedad no laboral, se encuentra imposibilitado para el desarrollo de su trabajo y recibe asistencia sanitaria por parte del Sistema Público de Salud. Incluye la enfermedad común y el accidente no laboral.
- Contingencia profesional. Según la legislación española sobre Seguridad Social (Ley General de la Seguridad Social-LGSS)¹, es aquel suceso que tiene su origen en el desarrollo de una actividad laboral y que produce alteraciones de la salud del trabajador. Se hablará de contingencias profesionales cuando el origen del proceso patológico que presenta el trabajador esté relacionado con la exposición a los factores de riesgo presentes en el trabajo.

El concepto de Daño Laboral viene recogido en la Ley 31/95, de Prevención de Riesgos Laborales (LPRL)² en su artículo 4: *se considerarán como «daños derivados del trabajo» las enfermedades, patologías o lesiones sufridas con motivo u ocasión del trabajo*.

Se distinguen 2 tipos de contingencias profesionales:

- **El accidente de trabajo:** *toda lesión corporal que el trabajador sufre con ocasión o a consecuencia del trabajo que ejecute por cuenta ajena* (art. 156.1, LGSS). Dicha lesión corporal podrá ser entendida como una herida, un golpe o una enfermedad y se presumirá, salvo prueba en contrario, que son constitutivas de accidente de trabajo las lesiones que sufra el trabajador durante el tiempo y en el lugar del trabajo. Actualmente, el accidente de trabajo contempla también a las lesiones producidas por la acción lenta y progresiva de un agente (exterior o interior al organismo) sobre el cuerpo humano. Se notifica a través del sistema DELTA³ habilitado por el Ministerio de Trabajo y Seguridad Social.

Las enfermedades no incluidas en el listado de enfermedades profesionales en las que se demuestre un nexo causal ligado al trabajo serán consideradas accidente de trabajo y la notificación se hace a través del sistema PANOTRATSS-Notificación de Patologías No

Traumáticas Causadas por el Trabajo⁴, pudiendo ser:

Enfermedades causadas por el trabajo (art. 156.2e -LGSS): aquellas no incluidas en el cuadro de EP que contraiga el trabajador con motivo de la realización de su trabajo. Corresponde al trabajador demostrar el nexo causal entre trabajo y lesión.

Enfermedades o defectos agravados por el trabajo (art. 156.2f): padecidos con anterioridad por el trabajador (que no tienen su causalidad directa en el trabajo), pero que se agravan o agudizan como consecuencia de una lesión constitutiva de accidente de trabajo. Corresponde a la Mutua Colaboradora de la Seguridad Social (MCSS) establecer el nexo causal entre las lesiones del accidente laboral y el agravamiento de las lesiones previas.

- **La enfermedad profesional:** *la contraída a consecuencia del trabajo ejecutado por cuenta ajena en las actividades que se especifican en el cuadro de enfermedades profesionales aprobado por RD 1299/2006⁵, y que está provocada por la acción de los elementos o sustancias que se indiquen en dicho cuadro para cada enfermedad profesional* (art. 157, LGSS). Se notifica a través del sistema CEPROSS⁶, de comunicación de enfermedades profesionales en Seguridad Social.

Por tanto, la enfermedad ocupacional o laboral es un concepto más amplio que engloba tanto a las enfermedades profesionales (EEPP), incluidas en el RD 1299/2006, como a las enfermedades relacionadas con el trabajo, no incluidas en el mismo. La prueba del nexo causal entre trabajo y lesión es una exigencia ineludible para la determinación de la contingencia profesional, demostrando la influencia de los factores de riesgo laboral en la causalidad o agravamiento de la enfermedad. En cualquier caso, para calificar una enfermedad como laboral es necesario:

1. Un diagnóstico de enfermedad compatible, atendiendo a las características clínicas y pruebas complementarias que definen una enfermedad codificada como tal en el CIE-11 (Clasificación Internacional de Enfermedades, 11^a revisión. Estandarización mundial de la información de diagnóstico en el ámbito de la salud)⁷.
2. Que se cumpla el criterio de exposición al factor de riesgo considerado, porque esté o haya estado presente en el entorno laboral de la persona enferma. Por ejemplo, que se cuente con indicios de exposición a condiciones de trabajo, agentes y/o sustancias, previa a la aparición del daño, en dosis suficiente, valorando los medios de protección utilizados y el historial laboral anterior (otras exposiciones laborales similares o coadyuvantes).
3. Que se cumpla el criterio de temporalidad, que implica que la exposición laboral causal considerada es anterior a la aparición de la lesión o enfermedad, y que el tiempo de exposición al factor de considerado y el periodo de latencia son compatibles con el daño.

4. Que se consideren simultáneamente los factores o patologías coadyuvantes, de forma que no tengan *per se* entidad para causar el daño o no hayan actuado con la entidad suficiente para causarlo.

Los criterios para la calificación y valoración de la enfermedad profesional se basan, no solo en la inclusión de la patología en anexo 1 del RD 1299/2006, sino también en el establecimiento del diagnóstico clínico y pruebas complementarias, la exposición laboral suficiente previa a la aparición de la patología, la correlación coherente entre la patología y el intervalo de tiempo entre la exposición y el efecto, así como a la ausencia de factores extralaborales que hayan actuado con la suficiente intensidad para constituir la base de un diagnóstico diferencial⁹.

Situación actual en España de la notificación de enfermedades profesionales

La enfermedad profesional ha tenido en España una regulación legal tardía. El primer listado de EEPP adaptado a la legislación europea, el del R. D. 1995/78 de 12 de mayo⁹, seguía manteniendo una restricción (la necesidad de que la ocupación apareciese listada), que hizo que el número de declaraciones fuese bajo. Con el R. D. 1299/2006 de 10 de noviembre se suprimió dicha restricción y se pensó que el número de enfermedades declaradas aumentaría. Sin embargo, otros factores entre los que destacan los económicos, han hecho que, lejos de crecer el número de enfermedades profesionales declaradas, éste haya ido en descenso¹⁰. En ese sentido, hay que destacar que, en España, la obligación de declarar las EEPP corresponde mayoritariamente a la MCSS por la que opta la empresa para asumir la protección de las contingencias profesionales, es decir, es la misma entidad, de gestión privada, la que declara o no las EEPP y la que debe cubrir las prestaciones sanitarias y económicas de los casos declarados.

Esta tendencia a la infradeclaración se sigue manteniendo en la actualidad y destaca el importante descenso en la notificación de enfermedades profesionales en 2020, con el inicio de la pandemia de COVID-19 (**Tabla I**).

Tabla I: Evolución de la notificación de enfermedad profesional 2012-2021.

Año	con baja	sin baja	total
2012	7.486	8.178	15.664
2013	7.599	9.197	16.796
2014	8.112	9.148	17.260
2015	9.073	10.065	19.138
2016	9.786	10.714	20.500
2017	10.140	10.909	21.049
2018	11.382	12.700	24.082
2019	12.877	14.415	27.292
2020	8.669	9.731	18.400
2021	9.342	11.039	20.381

Fuente: observatorio de enfermedades profesionales (CEPROSS) y de enfermedades causadas o agravadas por el trabajo (PANOTRATSS) informe anual 2022.

En 2022 se notificaron en DELTA 1.196.425 de accidentes de trabajo, de los cuales 564.701 fueron sin baja y 631.724 con baja.

En ese mismo año se notificaron en las estadísticas de la seguridad social 26.778 enfermedades causadas por el trabajo: 22.408 (83,7% del total) enfermedades profesionales y 4.370 (16,3%) patologías no traumáticas causadas o agravadas por el trabajo.

Se observa, por tanto, una notable diferencia en la notificación de contingencia profesional comparando el accidente de trabajo y la enfermedad profesional que induce a reflexionar sobre las causas.

De los daños derivados del trabajo, los accidentes son la parte más visible, dada la inmediatez de sus efectos, que hace evidente el origen laboral del daño producido.

Las enfermedades profesionales generan sufrimientos y pérdidas en el mundo del trabajo, pero permanecen prácticamente invisibles comparadas con los accidentes laborales.

La identificación del origen profesional de una enfermedad conlleva la toma de decisiones clínicas o de epidemiología clínica aplicada basándose en las evaluaciones de riesgo, el conocimiento de las tareas que realiza el trabajador, el tiempo dedicado a las mismas, y las medidas de protección y de seguridad existentes en el medio de trabajo, a lo que se une el hecho de que la determinación del origen de una enfermedad no es una ciencia exacta, sino una cuestión de juicio basado en un análisis crítico de los elementos disponibles: la intensidad de la asociación con el factor de riesgo, la concordancia, la especificidad, el horizonte temporal adecuado, el gradiente y la plausibilidad biológica.

La dificultad es mayor si se considera que, en la mayoría de las enfermedades profesionales causadas por exposiciones laborales, intervienen también causas no relacionadas con el trabajo. Esto hace que la problemática sea global. En la mayoría de los países industrializados las estadísticas oficiales registran sólo una parte de las enfermedades derivadas del trabajo y se estima que los sistemas de indemnización compensan menos del 10% de los casos de EEPP¹¹.

Aspectos médico legales

El debate más complejo desde un punto de vista médico legal se da en las enfermedades causadas o agravadas por el trabajo, habitualmente no reconocidas desde el principio como contingencia profesional por la MCSS o por el servicio de salud que atiende al trabajador.

En ocasiones, una patología se cataloga en un primer momento como enfermedad común, aunque se trate en realidad de una contingencia profesional, porque haya sido causada por la actividad laboral que realiza esa persona o por elementos o sustancias con las que el trabajador está en contacto durante su jornada laboral.

La calificación de una enfermedad como contingencia común o como contingencia profesional tiene implicaciones importantes en el tratamiento que se dará al trabajador durante la enfermedad y en el seguimiento tras la curación o estabilización del proceso. También la prestación económica que recibe el trabajador durante el periodo de incapacidad temporal (IT) o en caso de incapacidad permanente (IP) es distinta si es por contingencia común o profesional, así como los requerimientos precisos para percibir la prestación, ya que si la IP deriva de accidente de trabajo no precisa periodo de carencia.

Si un daño para la salud de un trabajador se ha catalogado como enfermedad común y, dadas las características de este, se considera que debe revisarse el caso para determinar su posible origen laboral, para ello, ha de solicitarse la apertura de un **procedimiento de determinación o cambio de contingencia**. Se trata de un procedimiento administrativo que se desarrolla de conformidad con lo previsto en el Real Decreto 1430/2009¹². Este procedimiento puede iniciarlo el trabajador por vía administrativa ante el Instituto Nacional de la Seguridad Social (INSS), con la presentación de una solicitud acompañada de los documentos e informes médicos que se estimen convenientes para informar sobre su caso y apoyar su reclamación. También puede iniciarlo de oficio el propio INSS o incluso la Mutua.

El INSS dispone de 4 días hábiles para ponerse en comunicación con la Mutua que atiende a la empresa o institución en la que trabaja el solicitante, para que ésta recabe todos los antecedentes del caso e informe sobre la contingencia de la que se deriva la enfermedad y los motivos que la causaron. El equipo de Valoración de Incapacidades (EVI) emitirá un informe en el que se pronuncia sobre la contingencia que originó la incapacidad o suspensión del trabajador. Este informe se presentará al director provincial del INSS.

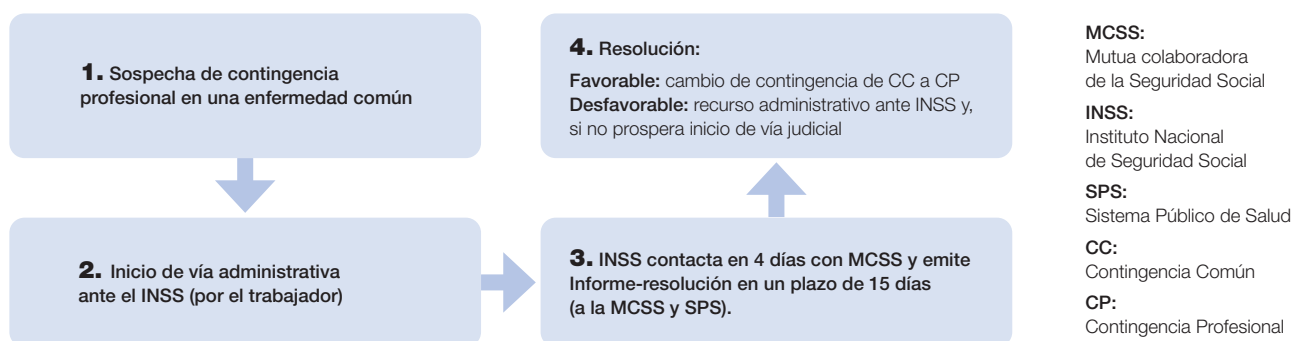
La normativa indica que el INSS emitirá su resolución en un plazo máximo de 15 días y la comunicará al interesado, a la empresa en la que este trabaja, a la Mutua y al Servicio Público de Salud, aunque en la práctica, el proceso suele alargarse varios meses.

Si la resolución es favorable al trabajador, la contingencia será considerada como profesional desde el momento en que se inició el proceso de IT. La Mutua está obligada a reembolsar al trabajador la diferencia que exista a su favor, ya que la indemnización que el trabajador recibe por una situación de contingencia profesional que, por lo general es superior a la que recibe por una baja por contingencia común.

En el caso de que la resolución que emita el INSS no haya sido favorable al solicitante, éste tiene la opción de llevar su caso a la vía judicial. Para ello, debe presentar una demanda ante los juzgados de lo Social o Contencioso (según se trate de personal laboral o funcionario) en un plazo de 30 días después de que la solicitud haya sido desestimada en la vía administrativa (**Figura 1**).

El procedimiento para solicitar el cambio de contingencia común a profesional no es complicado, pero tiene unos tiempos bastante ajustados y exige cumplir una serie de requisitos y documentos, por lo que es un proceso que debe ser atendido de manera inmediata y con mucha atención por parte del interesado.

Figura 1: Procedimiento de solicitud de cambio de contingencia de enfermedad común (CC) a contingencia profesional (CP).



Propuesta de colaboración

Ajustada a las competencias y obligaciones de cada entidad, organismo y profesional afectado (Figura 2).

Corresponde a los empresarios: garantizar la seguridad y la salud de los trabajadores a su cargo en todos los aspectos relacionados con el trabajo, integrando la actividad preventiva en la empresa y dotando a su organización de los medios necesarios.

Corresponde a los servicios de prevención de riesgos laborales: actuar en prevención, conjuntamente técnicos y sanitarios; vigilancia de la salud para la detección precoz de los daños derivados del trabajo y las personas especialmente sensibles en función del puesto de trabajo; notificación de los daños a la salud detectados, especialmente la EEPP o de su sospecha, derivando a la Mutua y facilitando el retorno al trabajo, ajustándose a los estrictos criterios de protección del trabajador dentro de las competencias inherentes a la especialidad (medicina y enfermería del trabajo).

Corresponde a las mutuas colaboradoras de la seguridad social: gestionar las contingencias profesionales, incluyendo su asistencia y rehabilitación; comunicación oficial de las enfermedades profesionales (incluidas en el RD 1299/2006) a CEPROSS, ajustándose a los criterios comunes.

Corresponde a la inspección sanitaria de salud laboral: la vigilancia, inspección y control del cumplimiento de los aspectos sanitarios de la normativa sobre prevención de riesgos laborales y, en lo concerniente a EEPP, la tramitación de las sospechas comunicadas de estas enfermedades, siguiendo los criterios comunes.

Corresponde a los sanitarios del sistema nacional de salud: colaboración con los sanitarios del SPRL, en prevención, comunicación de los daños a la salud detectados que sospechen que son EEPP, ajustándose a los criterios comunes.

Corresponde al INSS-equipos de valoración de incapacidades: calificar y determinar las contingencias profesionales: los accidentes de trabajo (especialmente las enfermedades ocasionadas o agravadas por el trabajo, no incluidas en el RD1299/2006) y las enfermedades profesionales incluidas en el citado RD, ajustándose a los criterios comunes.

Corresponde a la inspección de trabajo y seguridad social: vigilancia, inspección y control del cumplimiento de la normativa sobre prevención de riesgos laborales y, en lo concerniente a EEPP, teniendo en cuenta los criterios comunes, partiendo de la base de la complejidad que conlleva la multicausalidad de muchos procesos.

Figura 2: Propuesta de Protocolo.



Corresponde al ámbito judicial: valorar la actuación pericial tomando como referencia a los Médicos del Trabajo como expertos, en base a su especial conocimiento de las condiciones laborales, las relaciones de causalidad entre exposición a determinados riesgos y desarrollo o empeoramiento de patologías específicas junto con otros datos relevantes incluidos en la historia clínica laborales de las personas atendidas, siempre ajustándose a los criterios comunes.

Conclusiones

Las enfermedades profesionales y ocupacionales son en el momento actual el aspecto con mayor infradeclaración en salud laboral.

La determinación de contingencia profesional en el caso de las enfermedades ocupacionales es un proceso que

requiere un consenso de actuaciones y unos criterios unificados.

Se propone un protocolo de consenso en los criterios relativos a contingencia profesional por enfermedad que unifiquen las actuaciones atendiendo a las diferentes competencias de cada entidad u organismo involucrado

Son criterios de consenso: establecer la exposición al riesgo en tiempo e intensidad necesaria, la coherencia en la temporalidad requerida entre exposición y daño resultante y establecer un correcto diagnóstico diferencial con patologías intercurrentes.

Conflicto de intereses

Los autores declaran no tener conflicto de intereses.

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ORIGINAL

A survey of public knowledge, attitudes and practices towards the seasonal influenza vaccine in North Macedonia

Encuesta sobre conocimientos, actitudes y prácticas de la población en relación con la vacuna contra la gripe estacional en Macedonia del Norte

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Abstract

Introduction: Vaccination against seasonal influenza is the most effective way to prevent infections, hospitalization, morbidity, and mortality. The objective of the study was to assess the knowledge, attitude, and practices of the North Macedonia adult population towards seasonal influenza vaccine.

Materials and methods: A prospective cross-sectional study in November-December 2022 among the adult population of North Macedonia was conducted. A total of 1012 respondents filled in the 4-item semi-structured questionnaire. The questionnaire collected information on de-mographics, knowledge, attitudes, and practices towards the influenza vaccine. The chi-square test was used to test for associations and logistic regression was used to determine the effect of variables on the possibility of vaccination.

Results and discussion: The median age of the respondents was 36 years, predominantly female (73.5%). Only 7.8% of respondents received the influenza vaccine in the previous season (2021/2022) and 12.4% planned to vaccinate in the current season. A statistically significant difference between the vaccinated and non-vaccinated individuals was established in terms of age groups and the presence of comorbidity ($\chi^2=11.246$, $p=0.004$). The vaccinated respondents significantly more often tend to consider the influenza vaccine as safe ($\chi^2=5.026$, $p=0.025$) and effective ($\chi^2=11.247$, $p=0.001$). Respondents who had comorbidities, who considered the vaccine as effective, and were not afraid of possible side effects were 3 times, 2.0 times, and 1.8 times more likely respectively to have received an influenza vaccine. Additionally, the respondents who tend to rely more on social media and internet as the main source of information regarding the flu vaccine were 0.5 times more likely to have rejected the vaccine.

Conclusion: Addressing influenza vaccine safety, efficacy, patient-specific recommendations and encouraging effective physician communication and counselling are some of the key areas for increasing knowledge and awareness.

Key words: influenza vaccine, knowledge, attitudes, practices, vaccination, hesitancy.

Resumen

Introducción: La vacunación contra la gripe estacional es la forma más eficaz de prevenir infecciones, hospitalizaciones, morbilidad y mortalidad. El objetivo del estudio era evaluar los conocimientos, la actitud y las prácticas de la población adulta de Macedonia del Norte respecto a la vacuna contra la gripe estacional.

Materiales y métodos: Se realizó un estudio transversal prospectivo en noviembre-diciembre de 2022 entre la población adulta de Macedonia del Norte. Un total de 1012 encuestados rellenaron el cuestionario semiestructurado de 4 ítems. El cuestionario recogía información sobre datos demográficos, conocimientos, actitudes y prácticas con respecto a la vacuna antigripal. Se utilizó la prueba chi-cuadrado para comprobar las asociaciones y la regresión logística para determinar el efecto de las variables sobre la posibilidad de vacunación.

Resultados y discusión: La mediana de edad de los encuestados fue de 36 años, con predominio de mujeres (73,5%). Sólo el 7,8% de los encuestados recibió la vacuna antigripal en la temporada anterior (2021/2022) y el 12,4% tenía previsto vacunarse en la temporada actual. Se estableció una diferencia estadísticamente significativa entre los individuos vacunados y no vacunados en cuanto a grupos de edad y presencia de comorbilidad ($\chi^2=11,246$, $p=0,004$). Los encuestados vacunados tienden significativamente más a considerar la vacuna antigripal como segura ($\chi^2=5,026$, $p=0,025$) y eficaz ($\chi^2=11,247$, $p=0,001$). Los encuestados que tenían comorbilidades, que consideraban que la vacuna era eficaz y que no temían los posibles efectos secundarios tenían 3 veces, 2,0 veces y 1,8 veces más probabilidades, respectivamente, de haberse vacunado contra la gripe. Además, los encuestados que tendían a confiar más en las redes sociales e Internet como principal fuente de información sobre la vacuna de la gripe tenían 0,5 veces más probabilidades de haber rechazado la vacuna.

Conclusiones: Abordar la seguridad y eficacia de la vacuna antigripal, las recomendaciones específicas para cada paciente y fomentar la comunicación y el asesoramiento eficaces por parte de los médicos son algunas de las áreas clave para aumentar el conocimiento y la concienciación.

Palabras clave: vacuna antigripal, conocimientos, actitudes, prácticas, vacunación, indecisión.

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Introduction

Influenza is a contagious respiratory disease caused by influenza viruses that infect the upper respiratory tract. These viruses circulate during the winter months in the northern hemisphere, and they can affect all age groups, responsible for one of the most wide-spread diseases in the world causing significant morbidity and mortality. Worldwide, the annual epidemics are estimated to result in about 3 to 5 million cases of severe illness, and about 290.000 to 650.000 respiratory deaths¹. In industrialized countries, most deaths associated with influenza occur among people aged 65 or older². The effects of seasonal influenza epidemics in developing countries are not fully known, but research estimates that 99% of deaths in children under 5 years of age with influenza-related lower respiratory tract infections are found in developing countries³. Every year epidemics caused by the influenza viruses are registered in Europe mostly during the winter months and the influenza A-type virus has pandemic potential.

Vaccination against seasonal flu is the most effective way to prevent infections, hospitalization, morbidity, and mortality from this disease^{4,5}. A 2021 study showed that among adults hospitalized with flu, vaccinated patients had a 26% lower risk of intensive care unit (ICU) admission and a 31% lower risk of death from flu compared with those who were unvaccinated⁶. Moreover, vaccination in the elderly has been shown to reduce the risk of death from influenza-related complications by 80%⁷.

To increase protection for more people, the World Health Organization (WHO) and the U.S. Center for Disease Control and Prevention (CDC) have issued new recommendations that persons aged 6 months and older be encouraged to get the influenza vaccine. Individuals in high-risk groups should have the influenza vaccine every year to lower their risk of serious complications^{8,9}.

For the season of 2021/2022, the total number of flu or flu-like diseases among the North Macedonia adult population amounts to 3 960 patients (I=178,4/100.000), which compared to the same period of season 2020/2021 (n=1 127) notes an increase of 3.3 times, and in relation to the last 10 seasons 2012/2022 (n=26 322), notes a decrease of 86.0%¹⁰.

A total of 49,320 persons received an influenza vaccine during the 2021-2022 influenza season. This is an increase of 8.3% compared to the season 2020-2021 when 45.561 doses were administered overall, and by 11.5% compared to the 2019-2020 season. The administration of influenza vaccine doses to older adults over 65 has increased by 100%, which is what caused the overall increase. Contrarily, the number of doses given to pregnant women, people with chronic illnesses, and children aged 6 months to 5 have been drastically reduced¹¹.

The objective of the study was to assess the knowledge, attitude, practices and possible factors influencing the uptake of the seasonal influenza vaccine of the North Macedonia adult population.

Materials and methods

Study design and settings

In the period of November 2022 - December 2022 a cross-sectional study using a semi-structured questionnaire was conducted in North Macedonia. For recruiting the participants, we used a random convenience sampling method using social media to distribute the questionnaire. The sample size was calculated using G* Power version 3.1.9.7. The margin of error (the maximum difference between the sample results and the total population) and the confidence interval (the probability that the sample accurately reflects the attitudes of the targeted population) were set at 5% and 95%, respectively. The number of participants needed for our study was estimated to be 902. The total sample size during our study was 1012 respondents over 18 years of age.

Questionnaire design

A 4-item semi-structured questionnaire was constructed in the Macedonian language. It was prepared using Google Forms and was disseminated through an electronically generated link. Before filling out the survey, the possible respondents had to provide informed consent for participation in the study and there was an option to drop out from the study at any time before submitting the questionnaire. The first part of the survey collected information about the demographics of the respondents such as age, gender, financial situation, education, and financial situation. The second section assessed the knowledge of the participants regarding the main characteristics of influenza (seasonality, risk groups, and recommendations for vaccination. In the third section, we collected information about the practices for vaccination with a flu vaccine- vaccination with a flu vaccine in the previous influenza season and intention to receive the vaccine in the following season. The last section of the questionnaire collected information about the attitudes and beliefs of the respondents towards influenza and the flu vaccine.

Participants and eligibility criteria

1) Age \geq 18 years 2) voluntary participation without payment and with the option to withdraw at any time up until the submission of the data.

Statistical analysis

Data was entered and analyzed using SPSS software, version 25.0 (IBM Corp, Armonk NY, USA). Standard descriptive statistics was used to summarize the demographic characteristics of the respondents. The

qualitative variables were represented using numerical values in the form of absolute and relative frequencies, as well as totals and percentages (n, %). The Kolmogorov-Smirnov test was utilized to ascertain the distribution of the sampled patients. The Chi-Square test was employed to examine the presence of an association between two nominal variables. Statistical tests were considered to have statistical significance if the p-value was less than 0.05. A binominal logistic regression was used to determine the effect of the different variables on the possibility of vaccination.

Ethical considerations

The study received an exemption of the Ethical Committee of the Ss. Cyril and Methodius University in Skopje as it met one of the criteria for exemption (an anonymous survey or interview that do not involve collection of identifiable data).

Results

A total of 1012 people took part in the survey. The median age of the respondents was 36 years (25th percentile 24 yrs.; 75th percentile 48 yrs.), predominantly female (n=747, 73.8%). More than one-quarter of all participants reported that they are smokers (n = 304, 30%), and 7,8% (n = 79) reported having a comorbidity. The most common comorbidity among the participants was diabetes (n=36, 3.56%). The demographics of all respondents are presented in **table I**.

When asked whether they have been vaccinated with an influenza vaccine in the previous winter season

2021/2022, only 7.8% (n=79) of the participants gave a positive answer. We further asked the respondents if they plan to receive the influenza vaccine and 12.4 % (n=125) of them gave a positive response. When exploring the distribution of respondents in different age groups we found a statistically significant difference among the vaccinated and non-vaccinated individuals ($\chi^2=11.246$, $p=0.004$). There is also a statistically significant difference between the two groups regarding the presence of comorbidity (**Table I**).

The respondents showed an overall good knowledge of the characteristics of influenza infection in terms of contagiousness, possible complications, seasonality, and recommended groups for influenza vaccination. Most participants correctly identified the aetiology of influenza (93.7%, n = 948). Most of the participants (79,2%, n = 802) were aware that the influenza vaccine is received once a year, and 76.6% (n = 775) knew that influenza appears at a certain time of the year. Only 62.1% (n = 628) correctly identified at what time of year it is recommended to receive the influenza vaccine. The vaccinated respondents showed a better knowledge when it came to the recommendations for vaccination, and they were significantly more aware that there are specific at-risk groups in the population who should receive the influenza vaccine ($\chi^2=3.923$, $p=0.048$) (**Table II**).

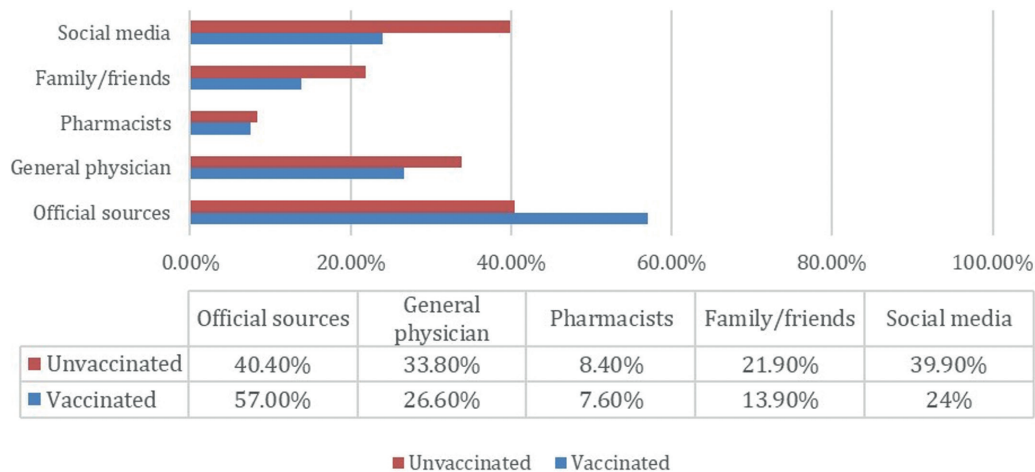
When asking the participants on the sources of information about influenza, our results showed that the most trusted source were official sites of the Ministry of Health (MH) and WHO, CDC (41,8%, n = 422) followed by Internet/ social media (38,6%, n = 390) and general physician (33,1%, n = 336) (**Figure 1**).

Table I: Demographic characteristics of the respondents (n=1012).

Variables	All respondents (n=1012)	Vaccinated (n=79)	Non-vaccinated (n=933)	p-value
Age	36 (24;48)	39 (24;56)	36 (24;48)	0.876
Age group n (%)				0.004
18-30 y.o.	379 (37.4)	32 (8.4)	347 (91.6)	
30-50 y.o	424 (41.9)	21 (4.9)	403 (95.1)	
>51 y.o	209 (20.7)	26 (12.4)	183 (87.6)	
Gender n (%)				0.092
Male	265 (26.2)	27 (10.2)	238 (89.8)	
Female	747 (73.8)	52 (7.0)	695 (93.0)	
Education n (%)				0.323
University degree	642 (63.4)	44 (6.8)	598 (93.2)	
Middle school	346 (34.2)	33 (9.5)	313 (90.5)	
Primary school	24 (2.4)	2 (8.3)	22 (91.7)	
Financial situation, n (%)				0.136
Comfortable	51 (5.0)	7 (13.7)	44 (86.3)	
Good	610 (60.3)	41 (6.7)	569 (93.3)	
Difficult	351 (34.7)	31 (8.8)	320 (91.2)	
Smoking, n (%)				0.746
Yes	304 (30.0)	25 (8.2)	279 (91.8)	
Comorbidities, n (%)				0.000
Yes	78 (7.7)	16 (20.5)	62 (79.5)	

Table II: Knowledge of the participants regarding influenza and the influenza vaccine (n=1012).

Variable	Vaccinated (n=79)	Non-vaccinated (n=933)	p-value
Influenza is caused by a virus, n (%)			
Yes	70 (7.4)	878 (92.6)	0.054
Flu can lead to serious complications, n (%)			
Yes	62 (7.4)	774 (92.6)	0.216
Influenza can be prevented with a vaccine, n (%)			
Yes	68 (7.8)	801 (92.2)	0.956
How often should we vaccinate? n (%)			
Once a year	64 (8.0)	738 (92)	0.547
Influenza is more common in the winter months, n (%)			
Yes	59 (7.6)	716 (92.4)	0.678
There are specific at-risk groups of the population recommended to receive the vaccine., n (%)			
Yes	77 (8.3)	849 (91.7)	0.048

Figure 1: Primary sources of information about the influenza virus and the influenza vaccine of the respondents (n=1012).

We then further explored the main source of information of the vaccinated and non-vaccinated respondents and there were some statistically significant differences. A higher share of people who decided to receive the influenza vaccine trust official sources such as MH, WHO, and CDC for information regarding the influenza vaccine compared to non-vaccinated (n=45, 57.0 vs. n=378, 40.4% $\chi^2=8.099$, p=0.004). Additionally, the respondents who haven't received the vaccine significantly more trust internet and social media as the main source of information about the vaccine compared to the vaccinated individuals (n=368, 39.4% vs. n=19, 24.0% $\chi^2=6.968$, p=0.008).

The attitudes of the respondents towards the influenza vaccine were explored with several statements using a 5-level Likert scale. A statistically significant higher share of vaccinated individuals considered the influenza vaccine as safe (n=50, 63.2% vs n=468, 50.1%, $\chi^2=5.026$, p=0.025). A similar significant difference in the attitudes of the vaccinated and non-vaccinated

respondents was established when they were asked if they considered the influenza vaccine as effective in preventing an illness (n=52, 65.8 for vaccinated vs. n=431, 46.2% for non-vaccinated $\chi^2=11.247$, p=0.001). Positive is the fact that 605 respondents stated that they would recommend the influenza vaccine to family or friends (n=605, 59.8%). More than half of the respondents (62,2%, n = 630) were willing to receive the influenza vaccine after recommendations and advice from their general physician (**Table III**).

A multiple logistic regression was performed to determine the possible association between flu vaccination as the dependent variable (vaccinated vs. non-vaccinated) with the responses of the respondents on the statements of vaccine and the flu itself-safety, effectiveness, side effects, seriousness of the diseases (completely agree/agree vs disagree/completely disagree), and the three most cited sources of information about the flu vaccine as independent variables (official sources, general physician, social

media and internet). Additionally, to the model gender and the presence of comorbidities were added. The logistic regression model was statistically significant $\chi^2(3) = 41.864, p < 0.001$). The model correctly classified 92.3% of the cases. Respondents who had comorbidities were 3 times more likely to have received an influenza vaccine and this was the strongest predictor for vaccination. The participants who considered the

vaccine as effective in preventing illness and were not afraid of possible adverse events following vaccination were 2.0 times and 1.8 times more likely to have been vaccinated respectively. Additionally, the respondents whose main source of information for influenza were social media and internet were 0.5 time more likely to have refused to get vaccinated with a flu vaccine (Table IV).

Table III: Attitudes of the respondents towards the influenza vaccine.

Questions	Vaccinated group (n=79)	Non-vaccinated group (n=933)	p-value
The influenza vaccine is safe, n (%) Agree/Completely agree	50 (9.6)	468 (90.4)	0.025
If I get the Flu/Influenza, I can be seriously ill for more than a week, n (%) Agree/Completely agree	46(9.0)	467 (91)	0.163
The flu is a more serious illness than a bad cold, n (%) Agree/Completely agree	51 (8.0)	588 (92)	0.786
The vaccine cannot always prevent the onset of influenza, n (%) Disagree/Completely disagree	42 (8.3)	463 (91.7)	0.546
Concerned of side effects of the vaccine, n (%) Agree/Completely agree	29 (9.1)	291 (90.9)	0.311
The vaccine is effective, n (%) Agree/Completely agree	52 (10.8)	431 (89.2)	0.001
Would recommend the vaccine to family or friends, n (%) Yes	60 (9.9)	545 (90.1)	0.002
Would get the influenza vaccine if the GP recommend it, n (%) Yes	64 (10.1)	566 (89.9)	0.000

Table IV: Multiple linear regression model on the likelihood of receiving the influenza vaccine.

Model	Unstandardized Coefficients		Wald	df	Sig.	Exp(B)	95% Confidence Interval for B	
	B	Std. Error					Lower Bound	Upper Bound
Constant	-2.441	1.213	4.046	1	0.044	0.087		
Gender								
Female (baseline)								
Male	1.263	1.164	1.179	1	0.278	0.283	0.029	2.765
Comorbidities								
No (baseline)								
Yes	1.169	0.324	13.01	1	0.000	3.218	1.705	6.072
Flu is a serious disease								
Disagree/Completely disagree (baseline)								
Agree/Completely agree	0.515	0.283	3.305	1	0.069	1.674	0.961	2.917
Considers the vaccine as safe								
Disagree/Completely disagree (baseline)								
Agree/Completely agree	0.270	0.318	0.718	1	0.397	0.764	0.409	1.425
Afraid of vaccine side effects								
Agree/Completely agree (baseline)								
Disagree/Completely disagree	0.585	0.268	4.772	1	0.029	1.794	1.062	3.032
Considers the vaccine as effective								
Disagree/Completely disagree (baseline)								
Agree/Completely agree	0.716	0.312	5.253	1	0.022	2.046	1.109	3.772
Main source of information- official authorities								
No (baseline)								
Yes	0.322	0.273	1.383	1	0.240	1.379	0.807	2.358
Main source of information- general physician								
No (baseline)								
Yes	0.467	0.290	2.594	1	0.107	1.596	0.904	2.818
Main source of information- social media, internet								
No (baseline)								
Yes	0.601	0.301	3.995	1	0.046	0.548	0.304	0.988

Discussion

Seasonal influenza vaccination is the primary and the most effective way to prevent influenza and its potentially serious complications. The results from our study revealed an overall vaccination rate of only 7.8% which is suboptimal. Low vaccination rates are a worldwide public health problem. European countries are likewise having difficulty meeting the specified immunization goals for influenza¹². A study from Bulgaria showed that only 11% of the respondents have been vaccinated with an influenza vaccine which is a result similar to ours¹³. Our study's findings show rates that are much lower than those of other nations, including Germany (40.4%), France (37.5%), Spain (56.4%), and Italy (48.6%)^{14,15}. A recent study from North Macedonia exploring the effect of the COVID-19 pandemic on the influenza vaccine uptake showed an increase in the administered vaccine doses by 8.3% but still the vaccination coverage is extremely low (2.5%)¹¹. Due to this, the development of a national program to boost influenza vaccination coverage is of crucial importance.

In our study only 20.5 % of the respondents with comorbidities have received the influenza vaccines which is significantly lower than the recommendations of the European Union regarding the target vaccination rates of the high-risk group of 75%¹⁵. According to recent data, acceptance rates have reportedly reached around 44% among high-risk categories in the European region¹⁶. In the logistic regression analysis, the presence of comorbidity proved to be strongly associated with the likelihood of influenza vaccination and the respondents with comorbidities were 3 times more likely to have the vaccine administered. Therefore, from both a governmental and healthcare professional standpoint, greater attention must be placed on immunizing high-risk groups in North Macedonia.

The respondents in our study had an overall good knowledge regarding influenza and the recommendations for vaccination and there was no association between the knowledge of the participants and the possibility of vaccination that has been established in similar studies^{16,17}.

When analyzing the attitudes of the survey respondents towards the influenza vaccine we established that the vaccinated individuals tend to consider significantly more often the influenza vaccine as safe ($n=50$, 63.2% for vaccinated vs $n=468$, 50.1% for non-vaccinated, $\chi^2=5.026$, $p=0.025$) and effective in preventing the occurrence of infection ($n=52$, 65.8 for vaccinated vs. $n=431$, 46.2% for non-vaccinated $\chi^2=11.247$, $p=0.001$). The respondents who tend to believe the influenza vaccine is effective had 2.0 times higher chance for vaccination. This result correlates with the results from similar studies^{18,19}.

One of the concerns among the respondents regarding the influenza vaccine was the fear of possible side effects after vaccination ($n=320$, 31.6%). The respondents from our study who were not afraid of possible side effects were 1.8 times more likely to have received the vaccine. A similar study done in Turkey showed that around 50% of the participants avoid the vaccination due to this reason²⁰. Additionally, a German study conducted on the general public reported that "fear of side effects" and "vaccination was not necessary" were the most reported concerns influencing influenza vaccine uptake²¹.

Another important factor that might influence the vaccination uptake is the source of information. Among the studied respondents the main source of information were official authorities such as MH, WHO, CDC, followed by social media, and physicians as third main source. These results correspond to other similar studies^{22,23}.

When asked what their main source of information is regarding influenza and the influenza vaccine the vaccinated respondents significantly more often tend to rely on official sources such as MH, WHO, and CDC ($n=45$, 57.0 vaccinated vs. $n=378$, 40.5% non-vaccinated $\chi^2=8.099$, $p=0.004$) whereas the non-vaccinated respondents prefer the internet and social media statistically significantly more often compared to the vaccinated individuals ($n=368$, 39.4% vs. $n=19$, 24.0% $\chi^2=6.968$, $p=0.008$) and those relying on social media were 0.5 times more likely to have rejected to receive the vaccine. It is important to note that 60.6% of the non-vaccinated respondents would be willing to receive the influenza vaccine if recommended by their GPs. Our findings are in line with earlier research that demonstrates that recommendations from medical professionals are one of the most powerful motivators for influenza vaccination²⁴⁻²⁷. Particularly doctors have a critical role in encouraging their patients to adopt appropriate attitudes and practices about influenza vaccination²⁴. This research encourages doctors to have open discussions with their patients about their attitudes and opinions towards influenza vaccination.

This study is a crucial step in educating scientists and decision-makers in the nation about the level of public knowledge regarding influenza and its vaccine, as well as the low vaccination rate. As was already mentioned, the media significantly affects how the general population thinks about vaccination²⁸. By utilizing the country's available multi-media content, such as explainer videos, flyers, or SMS text messages to inform the public about influenza and the availability of influenza vaccines, the country can achieve equitable access to information about influenza infection and influenza vaccine.

Conclusions

This study discovered that the participants in our study had low vaccination rate despite having an appropriate level of flu vaccine knowledge. It is essential to increase the flu vaccination rate among residents of North Macedonia to reach a consistent population-immunity level. Addressing influenza vaccine safety, efficacy, ideal vaccination administration times, patient-specific vaccination recommendations, encouraging effective physician communication and counseling, and using social media platforms to disseminate information from authentic and dependable sources are some of the key areas for increasing knowledge and awareness as well as combating false information about the influenza

vaccination. Medical professionals should be constantly reminded of the importance of screening and guiding patients on vaccinations.

Acknowledgments

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Conflict of Interest

None

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ORIGINAL

Comparing the veneer shear bond strength to the enamel labial surface according to the occlusal-gingival level and cutting depth (an in vitro study)

Comparación de la resistencia a la cizalladura de la carilla a la superficie labial del esmalte en función del nivel oclusal-gingival y de la profundidad de corte (estudio in vitro).

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Abstract

Background and objectives: Veneer restoration success depends on tooth surface, thickness, cement, and preparation. Preserving tooth structure is vital to avoid debonding and ensure a good prognosis. This study aims to explore the shear bond strength of veneers based on the occlusal-gingival level and cutting depth of the enamel labial surface, comparing their success rates.

Methods: This in vitro study, conducted at Sulaymaniyah's Shorsh Dental Teaching Hospital from February to November 2023, involved the classification of thirty upper premolars into three groups. These thirty premolars were further distributed across three groups, each consisting of 10 teeth. Each tooth was partitioned into occlusal and gingival halves for bonding purposes. In Group 1, diamond bur grinding was performed, Group 2 utilized 0.5 mm depth guide burs with smoothing, and Group 3 employed 1 mm depth guide burs with smoothing. Subsequently, 10% zirconia-reinforced lithium silicate blocks were bonded to the teeth, and the shear bond strength was assessed after cementation and thermocycling.

Results: The study compared values between the occlusal and gingival halves within the three groups. Statistically significant differences were identified in Group 2 ($P < 0.05$), where the highest mean in G2O was 25.25, indicating noteworthy variations between the occlusal and gingival subgroups. However, no statistically significant differences were observed in Group 1 and Group 3 ($P > 0.05$). The mean for the occlusal halves was 17.5 for G1 and 19.0 for G3, while the means for the gingival halves were recorded as 12.0 for G1 and 13.0 for G3. The most substantial mean difference in bond strength related to cutting depth on occlusal halves was observed when comparing G2 to G1, with a difference of 7.75. Conversely, the lowest mean difference was noted on the gingival halves of G3 and G1, which was 1. An analysis of failure modes revealed that 9 out of 10 teeth in G1G, G1O, and G2O exhibited adhesive ceramic failure, constituting approximately 15%. Group 3 displayed the highest occurrence of adhesive tooth failure in the gingival half, with 6 teeth showing this failure in G3G, accounting for about 10%.

Conclusion: The shear bond strength of veneers is notably influenced by both the cutting depth and the location of the preparation, whether it is at the occlusal or gingival region. This influence on shear bond strength can exert a substantial impact on the overall treatment outcome.

Key words: Dental Bonding, Enamel Thickness, Preparation Depth, Shear Bond Strength, Veneers.

Resumen

Antecedentes y objetivos: El éxito de la restauración con carillas depende de la superficie dental, el grosor, el cemento y la preparación. Preservar la estructura dental es vital para evitar la descementación y garantizar un buen pronóstico. Este estudio pretende explorar la fuerza de adhesión al cizallamiento de las carillas en función del nivel oclusal-gingival y la profundidad de corte de la superficie labial del esmalte, comparando sus tasas de éxito.

Métodos: Este estudio in vitro, realizado en el Shorsh Dental Teaching Hospital de Sulaymaniyah entre febrero y noviembre de 2023, consistió en la clasificación de treinta premolares superiores en tres grupos. Estos treinta premolares se distribuyeron a su vez en tres grupos, cada uno de los cuales constaba de 10 dientes. Cada diente se dividió en mitades oclusales y gingivales con fines de adhesión. En el Grupo 1 se realizó un tallado con fresa de diamante, en el Grupo 2 se utilizaron fresas guía de 0,5 mm de profundidad con alisado y en el Grupo 3 se emplearon fresas guía de 1 mm de profundidad con alisado. Posteriormente, se adhirieron a los dientes bloques de silicato de litio reforzados con zirconia al 10%, y se evaluó la resistencia de la adhesión al cizallamiento tras la cementación y el termociclado.

Resultados: El estudio comparó los valores entre las mitades oclusal y gingival dentro de los tres grupos. Se identificaron diferencias estadísticamente significativas en el Grupo 2 ($P < 0,05$), donde la media más alta en G2O fue de 25,25, lo que indica variaciones notables entre los subgrupos oclusal y gingival. Sin embargo, no se observaron diferencias estadísticamente significativas en los Grupos 1 y 3 ($P > 0,05$). La media de las mitades oclusales fue de 17,5 para el G1 y de 19,0 para el G3, mientras que las medias de las mitades gingivales se registraron como 12,0 para el G1 y 13,0 para el G3. La diferencia media más sustancial en la fuerza de adhesión relacionada con la profundidad de corte en las mitades oclusales se observó al comparar G2 con G1, con una diferencia de 7,75. Por el contrario, la diferencia media más baja se observó en G2 con G1. Por el contrario, la diferencia media más baja se observó en las mitades gingivales de G3 y G1, que fue de 1. Un análisis de los modos de fracaso reveló que 9 de cada 10 dientes de G1G, G1O y G2O presentaron fracaso de la cerámica adhesiva, lo que constituye aproximadamente el 15%. El grupo 3 mostró la mayor incidencia de fracaso adhesivo dental en la mitad gingival, con 6 dientes que mostraron este fracaso en G3G, lo que representa aproximadamente el 10%.

Conclusiones: La resistencia de adhesión al cizallamiento de las carillas está notablemente influenciada tanto por la profundidad de corte como por la ubicación de la preparación, ya sea en la región oclusal o gingival. Esta influencia en la fuerza de adhesión al cizallamiento puede ejercer un impacto sustancial en el resultado global del tratamiento.

Palabras clave: Adhesión dental, grosor del esmalte, profundidad de preparación, fuerza de adhesión al cizallamiento, carillas.

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Introduction

Patient demand is a paramount consideration for dentists, with a prevailing trend toward a preference for less invasive dental procedures. Minimally invasive dental treatments prioritize the improvement of aesthetics while concurrently minimizing the removal of tooth structures. In such treatments, the quantity of remaining enamel post-tooth preparation assumes a pivotal role in preserving the integrity of dental restorations¹.

A reliable bonding process yields several benefits, including high retention strength, a stable restoration, and reduced micro leakage. However, bonding to dentin has been reported to be more intricate and less dependable, primarily due to the heterogeneous nature of dentin². This characteristic poses a significant challenge in establishing a robust connection between modern adhesives and dentin. The troublesome nature of dentin is exemplified by the deposition of hydroxyapatite on a mesh of collagen fibers with hydrophilicity².

The foundation of aesthetic dentistry rests on adhesion to dental structures, encompassing both enamel and dentin³. Collagen fibers play a pivotal role in dentin adhesion. Preserving these fibers from degradation allows them to form a micro-mechanical bond with adhesives, ensuring the maintenance of good dentin bonding. Despite advancements in bonding to dentin, many authors emphasize the continued importance of considering bonding to enamel during tooth preparation^{4,5}.

The depth of preparation is a critical factor that determines the proportion of enamel surface on the adhesive interface, constituting one of the most crucial elements influencing debonding and the maintenance of adequate bonding strength⁶. Previous studies have consistently demonstrated that the predictability and success of bonding procedures are positively correlated with a higher presence of enamel⁷.

Easily obtained and highly stable, these terms are a description of a successful adhesion to enamel which has been reportedly identified in routine clinical procedures of twenty-first-century adhesive dentistry.

The length and orientation of enamel prisms also play a role in influencing the etching depth, thereby impacting the bonding strength. The depth, direction, and quantity of enamel prisms exhibit variations corresponding to the crown's occlusal-gingival level, potentially influencing the bond strength between the veneer and tooth structure^{8,9}.

Given the scarcity of studies in this domain, particularly within the Middle East, this investigation was deemed necessary to explore the relationship between shear bond strength of veneers and tooth structure concerning the occlusal-gingival surface at various depths.

Materials and methods

This research employed an experimental study design conducted between February 2023 and November 2023 in Sulaymaniyah, Shorsh dental teaching center. Thirty upper premolars extracted for orthodontic purposes were utilized in this study. Inclusion criteria for the selection of upper premolar teeth were established, requiring individuals to be between 14 and 25 years of age and their teeth to be free from cracks or defects. Any tooth falling outside of the specified age range or presenting significant structural problems was excluded from participation in the study.

In this study, thirty upper premolars extracted for orthodontic purposes were obtained from patients aged 14 to 25 years. Before experimentation, these teeth underwent examination to ensure the absence of cracks or defects, followed by cleaning to remove debris or remnant tissue. Subsequently, the teeth were stored in distal water. The samples were categorized into three groups, each consisting of ten teeth.

To prepare the specimens, selected teeth were embedded in cylinders of cold-cure acrylic blocks (Palaxtreme, Kulzer) with dimensions of 10 mm in diameter and 25 mm in height from the cemento-enamel junction. The first group (G1) involved the grinding of intact teeth using a fine (red) cutting diamond bur (ecoline, E850-F018), applied to the surface once without exerting pressure. The second group (G2) had depth guide burs of 0.5 mm utilized on all buccal surfaces, followed by smoothing with fine-cutting diamond burs (ecoline, E850-F018). The third group (G3) underwent preparation with depth guide burs of 1 mm on all buccal surfaces, followed by smoothing with fine-cutting diamond burs (ecoline, E850-F018). All preparations were conducted using a surveyor with a handpiece turbine fixed to it under cooling water, positioned one mm above the cemento-enamel junction, with the bur aligned parallel to the tooth's vertical long axis.

A standardized etching procedure was carried out on the labial surfaces of all specimens using 37% phosphoric acid (Spident, Fineetch) for 15 s, followed by thorough washing with water and drying with oil-free air pressure. Ivoclar Universal Bond was then applied to all etched surfaces. Sixty blocks of lithium silicate reinforced with 10% zirconia Celtra Duo (ZLS) LT A1C14 CEREC Dentsply were prepared for the ceramic specimens, polished, and fired according to the manufacturer's instructions. The fitting surfaces of all prepared ceramic blocks were etched with 10% hydrofluoric acid (FGM), cleaned, and dried. Saline (Bisco, Bis-silane) was applied to the fitting surfaces of the blocks.

Two prepared blocks were randomly selected for each tooth and bonded to the labial surface: one to the occlusal third and the other to the cervical third, using dual-curing

Figure 1: The shear bond strength test was conducted utilizing a universal tensile testing machine.

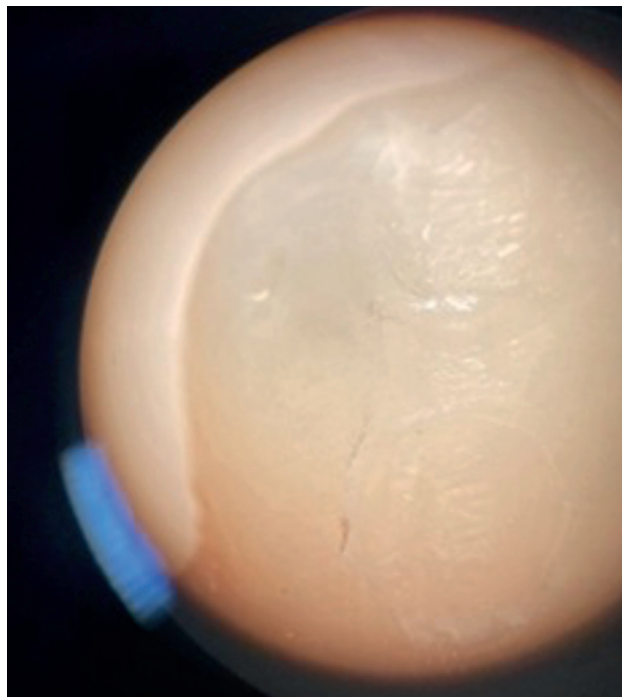


resin cement (Biscotti, duo-link). Cementation involved a 5 kg load application, with a light cure applied at the time of cementation and during the removal of excess material. The specimens were stored in distal water at room temperature for one week, followed by thermocycling (1500 cycles at 5 and 55°C with a dwell time of 30 s). Subsequently, all specimens underwent investigation to measure shear bond strength (SBS) using a chisel end-shaped metal with a 2 mm wide head attached to a universal tensile testing machine, operating at a speed of 1 mm/min until bond rupture. As seen in **figure 1**.

Following the completion of the shear bond test, the collected specimens underwent detailed analysis to identify the specific failure modes. The results, as depicted in **figure 2** are categorized as follows: adhesive tooth resin cement, indicating debonding at the interface between the prepared tooth surface and resin cement; adhesive ZLS resin cement, characterized by debonding between the ceramic fitting surface and the prepared tooth surface; cohesive, involving internal fractures within the ZLS, tooth structure, or resin; mixed-tooth resin cement, reflecting failures in both the tooth structure and adhesive interface; and mixed ceramic, denoting failure at the adhesive interface of the ceramic surface.

Ethical approval for this study was obtained from the ethics committee (Kurdistan higher council) prior to the commencement of the research. The study was conducted

Figure 2: Adhesive tooth failure.



in accordance with ethical guidelines and principles, ensuring the protection of participants' rights, confidentiality, and informed consent. All participants provided informed consent before their inclusion in the study.

The collected data were subjected to comprehensive statistical analysis. The normality distribution of the data was rigorously tested, and paired sample t-tests were employed to compare values between the occlusal half (O) and gingival half (G) of the groups. Additionally, one-way ANOVA revealed no significant differences among the three groups in both the incisal and gingival regions ($P > 0.05$). Pearson's chi-square test was used to analyze the mode of failure.

Results

The comparison of occlusal half (O) and gingival half (G) values within the three groups was conducted through paired sample t-tests. The results demonstrated a notable distinction between the occlusal half (O) and gingival half (G) subgroups in Group 2 ($P < 0.05$). Conversely, no statistically significant difference was identified between the occlusal half (O) and gingival half (G) subgroups in Groups 1 and 3 ($P > 0.05$), as outlined in **table I**.

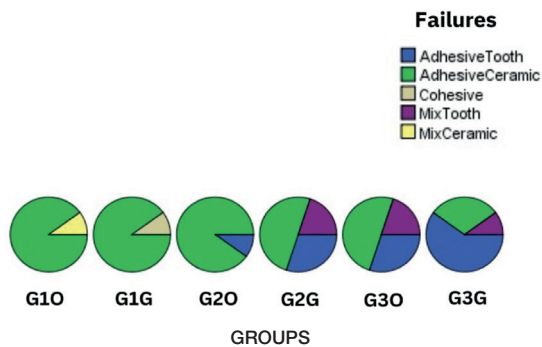
Table I: Assessing the bond strength in megapascal (MPa) based on the depth of tooth structure and its positional variation.

Groups	Subgroups	No.	Mean	St. Dev.	t	p value
Group 1	G1O	10	17.5	11.18034	1.575	0.150
	G1G	10	12.0	4.21637		
Group 2	G2O	10	25.25	12.71755	2.954	0.016
	G2G	10	15.50	4.68449		
Group 3	G3O	10	19.0	6.99206	1.695	0.124
	G3G	10	13.0	5.50252		

The application of one-way ANOVA revealed a lack of statistically significant difference among the three groups in both the occlusal and gingival halves ($P > 0.05$). Further analysis of the results indicated no significant disparities between the corresponding subgroups of Groups 1, 2, and 3 (G1O-G2O, G1O-G3O, G2O-G3O, G1G-G2G, G1G-G3G, and G2G-G3G), as outlined in **table II**.

The analysis of the mode of failure indicated a noteworthy association between the groups and the type of failure, established through the Pearson Chi-Square test ($P = 0.030$). Notably, the G3G group displayed the highest frequency of adhesive tooth failure in comparison to the other groups. Specifically, the G1O group exclusively manifested instances of mixed ceramic failure, while cohesive failure was solely observed in the G1G group. These findings are detailed in **table III** and visually depicted in **figure 3**.

Figure 3: The bond mode failure.



Discussion

This study sought to investigate the influence of the preparation cutting depth and position within the tooth structure on the shear bond strength (SBS) of ZLS ceramics. Rigorous inclusion criteria were applied to select natural teeth to ensure standardization of the experimental setup.

Although both shear bond strength (SBS) and micro-tensile bond strength (μ TBS) tests are frequently utilized for bond testing, micro-tensile bond strength testing is generally considered more reliable. However, in this particular study, the shear bond strength (SBS) test was chosen due to the anticipated higher occurrence of veneer failure, potentially induced by shear forces⁶.

In this study, the etchable ZLS glass ceramic was employed, aiming to enable a minimally invasive design by bonding it to the tooth structure using resin cement¹⁰. This approach was chosen to facilitate the application of the ceramic in cases who waiting for orthodontic treatment was not feasible, particularly in addressing crowded teeth. Varying cutting depths have been explored to effectively accommodate the alignment of crowded teeth. Furthermore, the placement of the ceramic block on both the occlusal and gingival halves was designed to evaluate the impact of enamel type on bond strength, taking into consideration the prism direction and length¹¹. Before undergoing testing procedures, the ZLS blocks were subjected to a 10-minute furnace treatment to enhance their strength to 370 MPa, following the manufacturer's instructions.

Table II: Assessing bond strength in relation to the cutting depth within the tooth structure.

Dependent Variable	Comparison	Groups	Mean Difference	Std. Error	Sig.	95% Confidence Interval	
O	1	2	-7.75	4.73022	0.247	-19.4782	3.9782
		3	-1.5	4.73022	0.946	-13.2282	10.2282
	2	1	7.75	4.73022	0.247	-3.9782	19.4782
		3	6.25	4.73022	0.396	-5.4782	17.9782
	3	1	1.5	4.73022	0.946	-10.2282	13.2282
		2	-6.25	4.73022	0.396	-17.9782	5.4782
G	1	2	-3.5	2.16025	0.255	-8.8562	1.8562
		3	-1	2.16025	0.889	-6.3562	4.3562
	2	1	3.5	2.16025	0.255	-1.8562	8.8562
		3	2.5	2.16025	0.488	-2.8562	7.8562
	3	1	1	2.16025	0.889	-4.3562	6.3562
		2	-2.5	2.16025	0.488	-7.8562	2.8562

Table III: The mode of bond failure.

Groups	Failures					Total
	Adhesive Tooth	Adhesive Ceramic	Cohesive	Mix Tooth	Mix Ceramic	
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	
G3O	6 (10%)	3 (5%)	0 (0%)	1 (1.67%)	0 (0%)	10 (16.67%)
G3G	3 (5%)	5 (8.33%)	0 (0%)	2 (3.33%)	0 (0%)	10 (16.67%)
G2O	3 (5%)	5 (8.33%)	0 (0%)	2 (3.33%)	0 (0%)	10 (16.67%)
G2G	1 (1.67%)	9 (15%)	0 (0%)	0 (0%)	0 (0%)	10 (16.67%)
G1O	0 (0%)	9 (15%)	1 (1.67%)	0 (0%)	0 (0%)	10 (16.67%)
G1G	0 (0%)	9 (15%)	0	0 (0%)	1 (1.67%)	10 (16.67%)
Total	13 (21.67%)	40 (66.67%)	1 (1.67%)	5 (8.33%)	1 (1.67%)	60 (100%)

The results indicate that the attachment position of the ceramic block, whether towards the occlusal or gingival aspect of the tooth structure, influences the bond strength. Notably, a significant difference was observed between G2U and G2L, whereas no significant differences were observed between G1 and G3. This discrepancy may be attributed to the exposure of enamel prisms in the upper half of G2, as opposed to the lower half where cutting might have exposed more dentin structure⁹.

Recent research has highlighted that the enamel thickness in the incisal portion of a tooth is 0.79mm, while it measures 0.56mm on the facial and palatal aspects. In the process of preparing ceramic veneers, it is common to expose dentin at the incisal edge, a phenomenon supported by existing literature^{7,12}. These findings align with the outcomes of our study, particularly in the assessment of shear bond strength (SBS) in three distinct preparation groups.

Although achieving optimal aesthetic results may necessitate a more substantial reduction of tooth structure, this often leads to the unavoidable exposure of dentin^{6,13}. It is widely acknowledged that bonding to enamel is vital for the long-term success of ceramic laminate veneers⁷. When veneers are primarily bonded to dentin, there is a high risk of failure^{7,14,15}.

The absence of a significant difference between the lower preparation locations for G1 and G3 may be attributed to the comprehensive bonding of both the upper and lower areas to the enamel in Group 1. In contrast, in Group 3, the bonding primarily involves the dentin area in both the occlusal and gingival halves.

The results of our study coincide with earlier research, illustrating the notable influence of preserving enamel on the shear bond strength (SBS) of ceramic laminate veneers⁶.

In particular, a recent study highlighted the necessity for comprehensive infra-enamel preparation and the preservation of a minimum of 40% of enamel to attain optimal bond strength. Moreover, it is recommended that the preparation margins be situated in healthy enamel to enhance bonding strength and diminish the potential for secondary caries resulting from micro-

leakage. These findings align consistently with our examination of SBS^{6,16,17}.

In the comparison of failure modes based on the preparation depth in the occlusal or gingival halves of the labial surface, no significant differences were observed across all groups. This lack of distinction may be attributed to the uniformity in cutting performed within the same structure, whether in the enamel of the occlusal half or proximal to the dentin layer of the gingival half. A study conducted by Nenand et al, reported that approximately 16.7% of cases exhibited exposed dentin at the cementsoenamel junction⁹.

The analysis of failure modes revealed a notable occurrence of adhesive failure at the ceramic-resin interface in groups G1O, G1G, and G2O. This is likely due to the robust bonding interface between the resin and enamel structure in these groups. In contrast, G3G exhibited the highest percentage of adhesive failure at the tooth-resin interface, possibly stemming from the exposed dentin in that area, resulting in a lower bond strength.

Acknowledging the study's limitations, it is clinically advisable to place all preparations in the enamel structure, as they may contribute to enhanced bonding and reduced adhesive failure.

Conclusions

In light of the study's limitations, it can be deduced that both the depth and location (occlusal or gingival) of the preparation significantly influence the bond strength of resin-bonded ceramics to the tooth structure.

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Conflict of interest

The authors declare no conflict of interest regarding the publication of this study.

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ORIGINAL

The assessment of the quality of primary care using the SERVQUAL scale: A cross-sectional study in Morocco

*La evaluación de la calidad de la atención primaria mediante la escala SERVQUAL:
Un estudio transversal en Marruecos*

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Abstract

Objectives: The quality of healthcare is essential for an optimal level of patient satisfaction. The present study aimed to assess the quality of services in primary healthcare centers in Marrakech, Morocco.

Methods: We conducted a cross-sectional study from June 2021 to January 2022. The SERVQUAL scale was used in a survey involving patients recruited in community health centers in Marrakech. The data collected were entered and analyzed using Jamovi 1.6. Statistical analyses included descriptive and bivariate analyses ($p < 0.05$).

Findings: Out of a total of 624 participants, 64.6% were women, and 75% were affiliated with an urban community health center. The gaps between perceptions and expectations of quality were negative for tangibles (-2.52), reliability (-2.48), and assurance (-2.40), respectively. Except for six items related to reliability and empathy, most items exhibited negative quality gaps. Significant associations were found between the community health center location and all dimensions, between the reference history for specialized consultation and the perception of assurance, and finally, between financial difficulty in seeking care and the perception of tangibles ($p < 0.05$).

Conclusions: The present study showed that tangibles, reliability, and assurance had the most negative gaps. These results suggest that patients had higher expectations than their perceptions.

Key words: Quality of health care, primary care, SERVQUAL, patient satisfaction, community health centers.

Resumen

Objetivos: La calidad de la asistencia sanitaria es fundamental para un nivel óptimo de satisfacción del paciente. El presente estudio tuvo como objetivo evaluar la calidad de los servicios en los centros de atención primaria de salud en Marrakech, Marruecos.

Métodos: Realizamos un estudio transversal desde junio de 2021 hasta enero de 2022. Se utilizó la escala SERVQUAL en una encuesta en la que participaron pacientes reclutados en centros de salud comunitarios de Marrakech. Los datos recopilados se ingresaron y analizaron utilizando Jamovi 1.6. Los análisis estadísticos incluyeron análisis descriptivos y bivariados ($p < 0,05$).

Resultados: De un total de 624 participantes, el 64,6% eran mujeres y el 75% estaban afiliados a un centro de salud comunitario urbano. Las brechas entre percepciones y expectativas de calidad fueron negativas para los tangibles (-2,52), la confiabilidad (-2,48) y la garantía (-2,40), respectivamente. Excepto seis ítems relacionados con la confiabilidad y la empatía, la mayoría de los ítems exhibieron brechas de calidad negativas. Se encontraron asociaciones significativas entre la ubicación del centro de salud comunitario y todas las dimensiones, entre el historial de referencia para consulta especializada y la percepción de seguridad y, finalmente, entre la dificultad financiera para buscar atención y la percepción de bienes tangibles ($p < 0,05$).

Conclusiones: El presente estudio mostró que los tangibles, la confiabilidad y la seguridad tenían las brechas más negativas. Estos resultados sugieren que los pacientes tenían expectativas más altas que sus percepciones.

Palabras clave: Calidad de la atención en salud, atención primaria, SERVQUAL, satisfacción del paciente, centros de salud comunitarios.

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Introduction

Primary care entails a holistic approach, considering both the biomedical aspects of the condition and the individual as a whole. Achieving this comprehensive approach requires surmounting two educational challenges for healthcare providers. Firstly, there is a need to enhance their communication abilities. Secondly, it is essential to bolster their capacity to provide patient-centered care¹.

In this context, healthcare professionals with a high degree of empathy have a positive effect on patient satisfaction². Additionally, it is recognized that patients' trust in the services they receive is an essential component of perceived quality³. Better communication is associated with higher scores, whereas the technical quality of care is not significantly associated with the overall assessment of care⁴. However, clinical quality is paramount to patient outcomes. However, service quality perceptions - only sometimes directly related to actual quality - are more likely to be the primary cause of their utilization^{4,5}.

As a result, the quality of health care is primarily derived from the individual's perceptions. Indeed, patients' perceptions of the quality of care are shaped by collective and traditional beliefs as well as the influence of peers⁶. For instance, despite the expansion of healthcare coverage, rural women prefer to have children at home instead of visiting a maternity center nearby^{7,8}. In Bangladesh, women believe that the quality of care in urban and peri-urban facilities is superior to that in local facilities⁷. Conversely, in Morocco, women prefer to give birth at home due to cultural traditions and financial concerns. They know that a transfer to a hospital maternity ward would incur additional expenses for the family⁸. As a result, health systems must not only enhance the actual quality of health care provided but also attempt to bridge the discrepancy between perceived quality and actual quality⁶.

In fact, the quality of healthcare can determine patient satisfaction. Within the literature, technical and functional aspects are acknowledged as essential components of health care⁹⁻¹³. Moreover, it has been documented that patients generally cannot differentiate between functional quality and technical quality¹⁴.

To evaluate perceived quality, there are multiple scales available, with the most common being SERVQUAL, developed by Parasuraman *et al.* (1985). SERVQUAL is designed to assess functional quality, not technical quality¹⁶. Each collection of items impacts the relative importance of five dimensions to patients: tangibility, reliability, responsiveness, assurance, and empathy¹⁷.

These five aspects of service quality apply to service providers in general: (i) Tangibility, which concerns physical facilities, equipment, and personnel appearance; (ii) Reliability, which is the ability to perform the service

accurately and consistently; (iii) Responsiveness, which is the willingness to help customers and provide prompt service; (iv) Assurance, which is the knowledge, courtesy, and ability of employees to inspire confidence; and (v) Empathy, which is the provision of caring, individualized attention to patients^{9,12,17}.

SERVQUAL, a model used to assess the quality of primary care services in multiple countries such as Botswana¹⁸, Romania¹⁹, Greece²⁰, and India²¹, was applied in this study to evaluate the quality of primary care in Marrakech, Morocco.

Methods

Study design and population

We conducted a cross-sectional study in Marrakech. The sample size was determined using a population proportion formula, considering the total population of Marrakech²², a 95% confidence interval (CI), and a 5% error rate. The calculated minimum sample size was 600. Accounting for a 20% non-response rate, the final sample for the study totaled 624 participants. These participants were selected from 54 community health centers (CHC) in Marrakech, and eligible for the study were patients aged 18 years and older.

Data collection

Data collection was done from June 2021 to January 2022 using a questionnaire that contained two parts: (a) sociodemographic variables, such as CHC location, age, sex, education level, social insurance, purpose of visit, prior referral, and financial difficulty in seeking healthcare, and (b) SERVQUAL scale. Data were collected in Arabic dialect translation of the validated Arabic version of SERVQUAL by Al-Daor & Munusamy (2019). The dialectal Arabic version was read and revised by a consensus committee.

SERVQUAL is a questionnaire of 44 questions that attempts to measure the gap between expectations and perceptions. The first set (the first 22 items) is concerned with customers' expectations, while the second set is concerned with their perceptions of utilizing these services. In SERVQUAL, responses to each question are recorded on a 7-point scale (1 = Strongly disagree; 2 = Disagree; 3 = Slightly disagree; 4 = Neutral; 5 = Slightly agree; 6 = Agree; 7 = Strongly agree). Mauri *et al.*²⁴ define service quality (SQ) as the gap between the patient's perception (P) and expectation (E), and it is calculated using the following formula: $SQ = (P - E)$.

Data analysis

The data were analyzed using Jamovi software (Version 1.6). Descriptive statistics were used to summarize participants' characteristics. A paired T-Test analysis ($P < 0.05$) of the gaps between perceptions and

expectations of quality was conducted for the dimensions and items of the SERVQUAL. The independent samples T-Test analysis ($P < 0.05$) was conducted to evaluate the association between participants' characteristics and SERVQUAL dimensions.

Ethics Considerations

Ethical approval was obtained from the Ethics Committee of the Marrakech Faculty of Medicine (Reference: 021/20). Informed consent was obtained from all participants, who were informed about the study's purpose, potential risks, and their right to withdraw at any time.

Findings

The mean age was 46.7 (± 16.4 years). Women represented 64.6% of the participants. Most participants (75%) were affiliated with an urban CHC. Furthermore, 29.5% of participants were illiterate, and 46.6% had RAMED coverage, a Medical Assistance Regime for economically disadvantaged persons. Regarding the purpose of the visit, 32.7% of participants came to the CHC for vaccination, 24.8% for chronic diseases, and 16.2% for general medical consultation. 69.9% of

participants had prior referrals from the health center for specialized consultation, while 72.1% reported a prior financial difficulty in seeking medical care (**Table I**).

Paired t-test analysis showed that the gaps between quality perception and expectation were negative for tangibles (-2.52), reliability (-2.48), and assurance (-2.40), respectively. However, they were, respectively, positive and close to zero for empathy (0.020) and responsiveness (0.34). Except for empathy, the differences in other dimensions were statistically significant ($P < 0.001$) (**Table II**).

Furthermore, the results of the same-item analysis showed that most of them had negative quality gaps, except for items related to reliability (1, 2, 3) and empathy (1, 3, 4). The three most unfavorable gaps were physical assets, i.e., equipment condition (-2.93), and reliability, i.e., service delivery on first contact (-2.93), and service delivery on time promised (-2.85). Statistically significant differences were found among participants' perceptions and expectations regarding various aspects of quality of service (**Table III**).

Table I: Sociodemographic characteristics of the participants (n=624).

Characteristics	Categories	N	%
Sex	Male	221	35.4
	Female	403	64.6
CHC Location [§]	Urban	468	75.0
	Rural	156	25.0
Education level	Illiterate	184	29.5
	Primary	89	14.3
	College	114	18.3
	High school level	94	15.1
	Baccalaureate	95	15.2
	University	48	7.7
Social insurance	Mutual Insurance	210	33.7
	Without Mutual Insurance	76	12.2
	RAMED [¶]	291	46.6
	Private Insurance	47	7.5
Purpose of visit	Vaccination	204	32.7
	Family planning	58	9.3
	Prenatal or Postnatal consultation	59	9.5
	Screening [‡]	47	7.5
	General consultation	101	16.2
	Consultation for chronic disease	155	24.8
Prior Referral	Yes	436	69.9
	No	188	30.1
Prior financial difficulty in seeking care	Yes	450	72.1
	No	174	27.9

[§]CHC: Community Health Center, [¶]RAMED: Medical Assistance Regime for economically disadvantaged persons, [‡]Screening concerns Human Immunodeficiency Virus, breast cancer, and cervical cancer.

Table II: Mean level of participants' perceptions, expectations, and service gaps in SERVQUAL Dimensions.

Dimensions	Perceptions	Expectations	Service gaps	Paired T-Test	
	Mean (SD)	Mean (SD)	Mean (SD)	t	p-value
Tangibles	3.44 (1.40)	5.96 (0.29)	-2.52 (1.43)	-44.13	<.001
Reliability	3.25 (1.33)	5.72 (0.31)	-2.48 (1.35)	-45.70	<.001
Responsiveness	3.42 (1.44)	3.08 (0.41)	0.34 (1.50)	5.64	<.001
Assurance	3.69 (1.49)	6.09 (0.32)	-2.40 (1.54)	-39.00	<.001
Empathy	3.27 (1.44)	3.25 (0.57)	0.02 (1.56)	0.32	0.747

SD: Standard Deviation.

Table III: Mean level of participants' perceptions, expectations, and service gaps in SERVQUAL items.

Items	Perceptions	Expectations	Service gaps	Paired T-Test	
	Mean (SD)	Mean (SD)	Mean (SD)	<i>t</i>	<i>p-value</i>
Tangibles					
1. Adequacy of equipment in health center	3.10 (1.58)	6.03 (0.28)	-2.93 (1.61)	-45.44	<.001
2. Cleanliness of CHC environment	3.19 (1.582)	5.98 (0.39)	-2.79 (1.64)	-42.55	<.001
3. Neat and professional appearance of CHC staff	4.05 (1.532)	5.86 (0.55)	-1.81 (1.60)	-28.17	<.001
4. Visual appealing and comfort of physical facilities	3.44 (1.562)	5.99 (0.23)	-2.55 (1.58)	-40.32	<.001
Reliability					
5. When health service is promised, it is done	3.19 (1.52)	6.04 (0.30)	-2.85 (1.54)	-46.02	<.001
6. Discipline of staff	3.30 (1.51)	6.10 (0.31)	-2.80 (1.53)	-45.85	<.001
7. Delivery of service right in the first time	3.11 (1.51)	6.04 (0.19)	-2.93 (1.52)	-48.10	<.001
8. Provision of health services at the time promised	3.29 (1.54)	4.33 (0.78)	-1.03 (1.70)	-15.14	<.001
9. Keeping patient/user records correctly without mistake	3.34 (1.52)	6.11 (0.32)	-2.77 (1.54)	-44.96	<.001
Responsiveness					
10. Information provided on when services will be performed	3.44 (1.56)	2.89 (0.58)	0.55 (1.67)	8.20	<.001
11. Provision of prompt service	3.35 (1.55)	3.13 (0.45)	0.21 (1.63)	3.29	.001
12. Staff are always willing to help	3.38 (1.53)	2.10 (0.41)	1.28 (1.60)	19.90	<.001
13. Accessibility of staff when needed	3.52 (1.55)	4.21 (0.56)	-0.68 (1.64)	-10.43	<.001
Assurance					
14. Patients/Users trust staff	3.68 (1.56)	6.13 (0.33)	-2.44 (1.60)	-38.02	<.001
15. Patients/Users feel safe with staff	3.70 (1.54)	6.13 (0.33)	-2.43 (1.58)	-38.41	<.001
16. Staff politeness and courtesy	3.67 (1.56)	6.13 (0.33)	-2.46 (1.61)	-38.24	<.001
17. Administration's support of staff's functions	3.73 (1.54)	5.99 (0.48)	-2.26 (1.61)	-34.92	<.001
Empathy					
18. Giving individual attention to each patient/user	3.69 (1.55)	2.99 (0.511)	0.70 (1.65)	10.59	<.001
19. Staff give personal attention to patients/users	2.80 (1.56)	2.95 (0.53)	-0.14 (1.65)	-2.20	.028
20. Understanding of the specific needs of patients/users	3.26 (1.62)	2.24 (0.57)	1.02 (1.72)	14.73	<.001
21. Staff have patient/user's best interests at heart	3.35 (1.61)	2.54 (0.89)	0.81 (1.84)	11.03	<.001
22. Operating hours appropriate to all	3.23 (1.62)	5.51 (1.23)	-2.28 (2.03)	-28.11	<.001

SD: Standard Deviation.

Discussion

Morocco has a healthcare system functions with a hierarchical framework, starting with primary healthcare facilities at the first level. These facilities include both urban and rural CHC and local hospitals. They offer preventive, promotional, and outpatient curative care²⁵. Additionally, ensuring high-quality care and services has always been a fundamental aspect of national strategies. However, it has also presented a notable obstacle^{26,27}.

The study findings indicated that there was a negative gap between the perceptions and expectations of service quality for tangibles (-2.52), reliability (-2.48), and assurance (-2.40). This indicates that the participants had high expectations for these aspects. However, a meta-analysis has demonstrated that assurance and empathy had the most significant expectation variations²⁸. Nonetheless, other studies have shown that tangibles and reliability also exhibited negative gaps^{18,29}, with reliability having the most negative gap^{18,29,30}. In rural regions, primary care facilities in Morocco were occasionally unwelcoming¹, to the extent that patients did not feel safe³¹. Additionally, patients reported a need for more equipment and supplies^{31,32}. However, it is established that the quality of equipment does not have a significant impact on the evaluation of the service quality provided³³. On the other hand, the gap in reliability does have a significant impact on both the quality of service provided and patient satisfaction³⁰. Furthermore, the present

study showed that empathy (0.02) and responsiveness (0.34) had positive but near-zero gaps. This result did not corroborate with the results of other studies, as the gaps between these two dimensions were among the most negative^{18,34}. This suggests that healthcare service is also perceived in terms of the humane touch during care delivery³⁴. The gaps between perceptions and expectations regarding empathy have a significant impact on satisfaction rather than on the overall quality of the service provided³⁰. However, empathy is one of the most critical factors that predict patient centrality and empowerment³⁵. Regarding responsiveness, a study conducted in Morocco on the Quality Cycle showed that the overall performance in terms of responsiveness only reached 39%³⁶. Moreover, another study had shown that patients were referred from CHC for specialized consultation, while general practitioners could have provided follow-up care³⁷.

Again, the results showed that the quality gaps were negative for most items, except for items related to responsiveness (10, 11, and 12) and empathy (18, 20, and 21). This result did not corroborate with the results of other studies since all quality gaps related to the items were negative^{18,29}. The three most negative gaps were related, respectively, to tangibles, notably the adequacy of equipment (-2.927), and reliability, notably regarding service delivery at the first contact (-2.926), and service

delivery at the promised time (-2.847). In other studies, the three items with the most negative quality gaps were related to tangibles¹⁸, reliability, and responsiveness²⁹. In this study, the differences were statistically significant regarding all aspects of healthcare service quality.

Using the SERVQUAL model, healthcare professionals would better understand their patients' expectations while identifying gaps in service delivery and implementing corrective measures. This approach will improve the quality of services provided and ultimately increase patient satisfaction³⁸.

Strengths and limitations

This study is the first in Morocco to be focused on the assessment of the quality of primary care services. By comparing expectations with perceptions, the findings reveal critical areas for improvement, enabling decision-making based on evidence and better patient care. Nevertheless, this study had limitations. Firstly, the adoption of a cross-sectional research design. Indeed, cross-sectional studies are conducted at a single point in time. It would be potentially useful to conduct a longitudinal study to track the evolution of patients' and users' expectations and perceptions over time. Secondly, the results of the present study can be extrapolated to other developing countries like Morocco, but it would be challenging to make this extrapolation.

Conclusion

This study showed that tangibles, reliability, and assurance had, respectively, the most negative gaps. This suggests that there was difficulty in meeting patients' expectations regarding these dimensions since expectations were

excessive compared to perceptions. More effort should be made to enhance the physical workplace environments of primary healthcare professionals, invest in skill development, and implement a performance-based reward system. Additionally, there is a need to strengthen the safety of clinical practices through legal and regulatory measures. However, further research is needed to understand better the factors that predict the quality of primary care services at the national level.

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Competing interests

The authors declare that they have no competing interests.

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Author contribution statement

H. El Mouaddib designed the study, interpreted the data, and wrote the manuscript. M. Sebbani participated in the design, the statistical analysis, the interpretation, and in the revision of the manuscript. L. Adarmouch and M. Amine participated in the design, and in the revision of the manuscript. All authors had access to the data and a role in writing the manuscript. Furthermore, all authors have read and approved the final version of the manuscript.

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ORIGINAL

Prevalencia de los índices de adiposidad corporal (BAI) y volumen abdominal (AVI). Según características metabólicas y factores de riesgo

*Prevalence of body fat (BAI) and abdominal volume (AVI) indices.
According to metabolic characteristics and risk factors*

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Resumen

Introducción: La obesidad ha alcanzado proporciones pandémicas y conlleva un aumento del riesgo cardiometabólico. La resistencia a la insulina y la enfermedad cardiovascular representan dos peligros para la salud pública.

Método: Estudio transversal en 193.462 trabajadores. Se valora síndrome metabólico con: NCEP/ATP-III, IDF y JIS. Se valora resistencia a la Insulina con: TGL/HDL, TyG y METS-IR. Se estima su correlación con los índices BAI y AVI. Se utilizó SPSS 27.0, considerando significación estadística $p < 0,05$.

Resultados: Los valores medios de BAI son más elevados que los de AVI, aumentando con la presión arterial y glucemia basal. Son más altos en con IDF y con METS-IR. Existe una moderada o débil correlación entre presión arterial y diabetes con los tres criterios de resistencia a la insulina ($< 0,60$). AVI y BAI guardan una buena correlación (entre 0.61 – 0,80) con METS IR y, moderada o débil (inferior a 0.60) con TyG y con TGHDL. En Síndrome metabólico se observa moderada concordancia de JIS con NCEP-ATP II (0,456) y con IDF (0,558) y considerable concordancia entre IDF y NCEP-ATP II (0,638).

Conclusiones: Los valores medios BAI y AVI aumentan con hipertensión arterial y diabetes, con valores altos en los tres criterios de síndrome metabólico y con los tres de resistencia a la insulina. Existe buena o muy buena correlación entre los índices AVI y BAI con METS-IR. Los criterios de Síndrome metabólico IDF y NCEP-ATP II muestran una buena correlación entre sí, siendo menor entre JIS con NCEP-ATP II y con IDF.

Palabras clave: Síndrome metabólico, resistencia a la insulina, diabetes, hipertensión, índice AVI; índice BAI.

Abstract

Introduction: Obesity has reached pandemic proportions and leads to increased cardiometabolic risk. Insulin resistance and cardiovascular disease represent two public health hazards.

Methods: Cross-sectional study in 193,462 workers. Metabolic syndrome was assessed with: NCEP/ATP-III, IDF and JIS. Insulin resistance was assessed with: TGL/HDL, TyG and METS-IR. Correlation with the BAI and AVI indexes was estimated. SPSS 27.0 was used, considering statistical significance $p < 0.05$.

Results: The mean values of BAI are higher than those of AVI, increasing with blood pressure and basal glycemia. They are higher with IDF and with METS-IR. There is a moderate to weak correlation between blood pressure and diabetes with the three insulin resistance criteria (< 0.60). AVI and BAI have a good correlation (between 0.61 - 0.80) with METS IR and a moderate or weak correlation (less than 0.60) with T&G and TGHDL. In metabolic syndrome, moderate concordance of JIS with NCEP-ATP II (0.456) and with IDF (0.558) and considerable concordance between IDF and NCEP-ATP II (0.638) were observed.

Conclusions: The mean BAI and AVI values increase with hypertension and diabetes, with high values in the three metabolic syndrome criteria and with the three insulin resistance criteria. There is a good or very good correlation between the AVI and BAI indices with METS-IR. The metabolic syndrome criteria IDF and NCEP-ATP II show a good correlation with each other, being lower between JIS with NCEP-ATP II and with IDF.

Key words: Metabolic syndrome, insulin resistance, diabetes, hypertension, AVI index, BAI index.

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Introducción

La obesidad ha alcanzado proporciones pandémicas con evolución creciente en las últimas décadas, lo que a su vez ha llevado a un aumento en el riesgo de condiciones cardiometabólicas concomitantes. Se considera un desajuste evolutivo determinado genéticamente y con influencia concomitante de la dieta y el estilo de vida modernos; siendo factor clave la hipertrofia masiva de adipocitos para adaptarse al exceso de grasa. La obesidad se asocia, tanto con un exceso de cantidad como con la disfunción del tejido adiposo blanco, particularmente en los depósitos adiposos viscerales¹.

El control sostenido del peso corporal en personas con obesidad mejora su estado de riesgo cardiometabólico, pero es necesario individualizar nuevos índices específicos en función del sexo, basados en parámetros como la circunferencia de la cintura, el índice de masa corporal y con los valores de triglicéridos, colesterol y sus fracciones, que expresen indirectamente la función de la grasa visceral².

La resistencia a la insulina (RI) y la enfermedad cardiovascular (ECV) representan dos peligros para la salud pública, especialmente en las sociedades occidentales. Se ha establecido una relación causa-efecto vinculando la RI con la ECV. La RI implica el desarrollo de trastornos cardiometabólicos como: obesidad, dislipidemia, inflamación de bajo grado, disfunción endotelial e hipertensión, todos ellos factores predisponentes para la ECV³.

Un diagnóstico clínico de obesidad visceral, resistencia a la insulina o síndrome metabólico no es suficiente para evaluar el riesgo global de enfermedad cardiovascular. Para lograr este objetivo, se ha de prestar atención a los factores de riesgo clásicos y, considerar el riesgo adicional derivado de la presencia de obesidad abdominal y síndrome metabólico, definiéndose dicho riesgo global como riesgo cardiometabólico⁴.

Es objetivo de este trabajo determinar la correlación en una población laboral entre los valores medios de los índices de adiposidad corporal (BAI) y volumen abdominal (AVI) con factores de riesgo cardiometabólico: hiperpresión arterial y diabetes; resistencia a la insulina valorada con las escalas: Triglicéridos/HDL (TGL/HDL), Triglicéridos e índice de glucosa (TyG) y Puntuación metabólica para resistencia a la insulina (METS-IR); síndrome metabólico valorado con: los criterios de: Programa Nacional de Educación sobre el Colesterol/Panel de Tratamiento de Adultos III (NCEP/ATP-III), la Federación Internacional de Diabetes (IDF) y la declaración provisional conjunta (JIS).

Metodología

Estudio en 193.462 empleados (116.407 hombres y 77055 mujeres) de nueve regiones de España (Islas Baleares, Andalucía, Canarias, Comunidad Valenciana, Cataluña, Madrid, Castilla-La Mancha, Castilla y León y País Vasco) de diferentes sectores profesionales (hostelería, construcción, comercio, sanidad, administración pública, transporte, educación, industria y limpieza), durante los exámenes de salud de las empresas participantes. El periodo de recogida de datos fue desde enero de 2019 hasta septiembre de 2021.

Son criterios de inclusión: tener una edad comprendida entre 18 y 67 años, no estar en situación de baja laboral por enfermedad o de baja en la empresa por cualquier otro motivo y aceptar participar voluntariamente en el estudio.

El personal sanitario registra los datos de antecedentes clínicos y familiares durante los exámenes de salud, siguiendo la Ley Orgánica de Protección de Datos Personales y garantía de los derechos digitales 2018 (LOPD)⁵.

La tensión arterial se determinó en decúbito supino con un esfigmomanómetro automático OMRON M3 calibrado tras 10 minutos de reposo (tamaño del manguito ajustado a la circunferencia del brazo). Se realizaron tres mediciones a intervalos de 1 minuto y se calculó la media de las tres. Se clasifica la presión arterial aplicando los criterios del séptimo informe del Joint National Committee para la Prevención, Detección, Evaluación y Tratamiento de la Hipertensión Arterial JNC-7⁶.

Las muestras de sangre se obtuvieron por venopunción periférica tras un ayuno de 12 horas y se enviaron a laboratorios de referencia donde se procesaron en un plazo de 48-72 horas. Se clasifican las cifras de glucemia aplicando los criterios de la asociación americana de diabetes ADA⁷.

Para el cálculo de Resistencia a la Insulina se han utilizado tres escalas:

Triglicéridos/HDL que calcula la relación TGL/HDL atendiendo a la siguiente fórmula: triglicéridos en ayunas (mg/dl)/colesterol-HDL (mg/dl). El diagnóstico de diabetes se ha basado atendiendo a los niveles de glucosa plasmática 2 horas post-sobrecarga ≥ 200 mg/dl⁸.

Triglicéridos e índice de glucosa (TyG) calculado siguiendo la fórmula: $\ln(TG [mg/dL] \times glucosa [mg/dL]) / 2$. El punto de corte para el índice TyG se ha establecido en 8,8 en hombres y 8,7 en mujeres⁹.

Puntuación metabólica para resistencia a la insulina- Metabolic Score for Insulin Resistance (METS-IR), se obtiene utilizando el inverso de la suma de los logaritmos de la insulina en ayunas y la glucosa en ayunas: $1/$

$(\log(\text{insulina en ayunas } \mu\text{U/mL}) + \log(\text{glucosa en ayunas mg/dL}))^{10}$.

Para el diagnóstico del Síndrome metabólico se utilizaron las definiciones y criterios de: National Cholesterol Education Program/Adult Treatment Panel III (NCEP/ATP-III)¹¹, la International Diabetes Federation (IDF)^{12,13} y el Joint Interim Statement (JIS)¹⁴.

El Índice de volumen abdominal- Abdominal volume index(AVI): utiliza la fórmula propuesta por Guerrero-Romero et al: $AVI = [2 \times (\text{cintura-cm})^2 + 0,7 (\text{cintura-cadera-cm})^2] / 1.000^{15}$.

El Índice de adiposidad corporal-body adiposity index (BAI). Utiliza la fórmula propuesta por Bergman RN et al: $BAI = (\text{circunferencia de la cadera}) / (\text{altura}) (1.5) - 18^{16}$.

Se realizó un análisis descriptivo de las variables categóricas, calculando la frecuencia y la distribución de cada variable. En el caso de las variables cuantitativas, se calcularon la media y la desviación típica. Para evaluar la normalidad de la muestra se aplicó la prueba de Kolmogorov-Smirnov. Para el estudio estadístico se realizó un análisis univariante empleando la t-student y la chi cuadrado. El análisis estadístico se realizó con el programa SPSS 29.0, siendo el nivel de significación estadística aceptado de 0,05. La correlación entre las diferentes escalas de resistencia a la insulina se obtuvo

aplicando el coeficiente de Pearson. Se valora el grado de concordancia de los tres criterios de síndrome metabólico aplicando el índice kappa de Cohen.

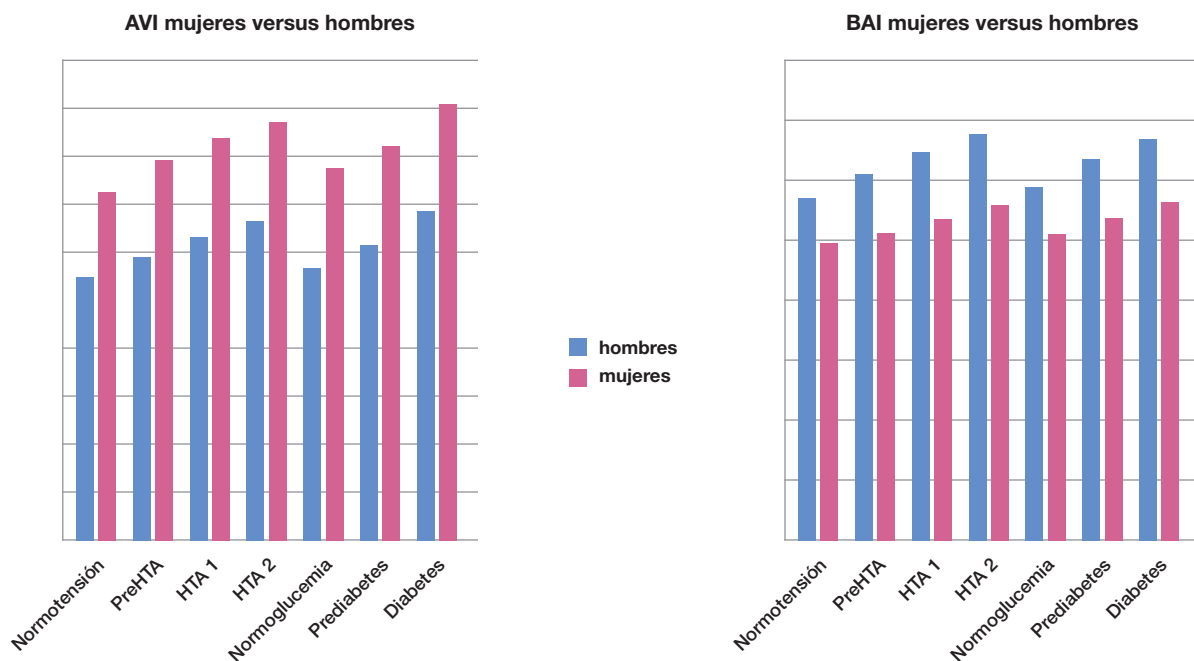
El estudio fue aprobado por el Comité Ético de Investigación Clínica del Área de Salud de Baleares (IB 4383/20).

Resultados

Estudio descriptivo transversal en una población laboral de 193.462 personas, con mayoría de hombres (116.407 hombres y 77.055 mujeres), edad media de 39 años en mujeres y 39.8 años en hombres, en ambos sexos de nivel formativo básico y pertenecientes a la clase social III. El IMC está en parámetros de sobrepeso, algo más altos entre los hombres (26,8) que en las mujeres (25,2). Los niveles de presión arterial, glucemia basal, colesterol y fracciones y triglicéridos se encuentran dentro de la normalidad, siendo más altos en los hombres. Las mujeres practican más actividad física y tienen mayor adherencia a dieta mediterránea. La mayoría de la población es no fumadora.

Los valores medios de BAI son siempre más elevados que los de AVI, algo superiores en las mujeres y van aumentando en ambos sexos según lo hacen las cifras de presión arterial y glucemia basal (**Gráfico 1**).

Gráfico 1: AVI y BAI mujeres versus hombres según comorbilidades (HTA y diabetes).



Los valores medios más altos en síndrome metabólico de AVI y BAI en ambos sexos se obtienen con IDF (**Gráfico 2**) y los de resistencia a la insulina con METS-IR (**Gráfico 3**), en ambos casos son más altos los de AVI en hombres y los de BAI en mujeres (**Tabla I**).

Tanto en hombres como en mujeres existe una moderada o débil correlación entre la presión arterial y la diabetes con los tres criterios de resistencia a la insulina (inferior a 0,60 en todos los casos).

AVI y BAI guardan una buena correlación (entre 0.61 – 0,80) con METS IR en ambos sexos y, moderada o débil (inferior a 0.60) con TyG index y con TG/HDL (**Tabla II**)

En Síndrome metabólico, el grado de concordancia de los tres criterios según el índice kappa de Cohen muestra Moderada concordancia de JIS con NCEP-ATP II (0,456) y con IDF (0,558). Considerable concordancia entre IDF y NCEP-ATP II (0,638) (**Tabla III**). Valoración del Índice de Kappa Cohen para expresar cualitativamente la fuerza de la concordancia, según Landis y Koch²² 0,00=pobre

Tabla I: Valores medios de AVI y BAI según tensión arterial, diabetes, síndrome metabólico y resistencia a la insulina.

Mujeres									
VARIABLES			n	AVI		BAI			
				Media (dt)	p	Media (dt)	p		
HTA	Normotensión		42237	10,99 (2,03)	<0.0001	28,57 (4,42)	<0.0001		
	PreHTA		28220	11,89 (2,58)		30,47 (5,04)			
	HTA 1		4856	12,64 (3,00)		32,34 (5,54)			
	HTA 2		1742	13,32 (3,20)		33,94 (5,98)			
Diabetes	Normoglucemia		71043	11,39 (2,35)	<0.0001	29,42 (4,84)	<0.0001		
	Prediabetes		5712	12,38 (2,84)		32,01 (5,43)			
	Diabetes		300	13,77 (4,23)		33,59 (6,04)			
Síndrome metabólico	SM ATPIII	No	74142	11,30 (2,13)	<0.0001	29,43 (4,79)	<0.0001		
		Si	2913	15,90 (4,38)		34,66 (6,01)			
	SM IDF	No	73802	11,24 (2,09)		<0.0001		29,38 (4,73)	<0.0001
		Si	3253	16,80 (3,23)		35,30 (6,11)			
	SM-JIS	No	72494	11,23 (2,10)		<0.0001		29,32 (4,72)	<0.0001
		Si	4561	15,36 (3,62)		34,53 (5,87)			
Resistencia a la insulina	METS-IR	normal	72786	11,19 (1,98)	<0.0001	29,05 (4,30)	<0.0001		
		alto	4269	16,42 (3,64)		39,44 (5,01)			
	TG/HDL	normal	61557	11,19 (2,08)		<0.0001		29,15 (4,73)	<0.0001
		alto	15498	12,61 (3,22)		31,52 (5,31)			
	TyG	normal	68578	11,25 (2,10)		<0.0001		29,32 (4,81)	<0.0001
		alto	8477	13,30 (3,70)		32,12 (5,31)			
Hombres									
VARIABLES			n	AVI		BAI			
				Media (dt)	p	Media (dt)	p		
HTA	Normotensión		28339	14,62 (2,68)	<0.0001	24,70 (3,56)	<0.0001		
	PreHTA		63486	15,72 (3,21)		25,58 (3,74)			
	HTA 1		18487	16,74 (3,58)		26,81 (4,00)			
	HTA 2		6095	17,50 (3,85)		27,93 (4,21)			
Diabetes	Normoglucemia		97741	15,54 (3,17)	<0.0001	25,45 (3,77)	<0.0001		
	Prediabetes		17494	16,49 (3,64)		26,79 (4,06)			
	Diabetes		1172	18,19 (4,21)		28,21 (4,28)			
Síndrome metabólico	SM ATPIII	No	106120	15,22 (2,72)	<0.0001	25,43 (3,74)	<0.0001		
		Si	10287	20,71 (4,30)		28,25 (4,13)			
	SM IDF	No	102916	15,04 (2,67)		<0.0001		25,33 (3,69)	<0.0001
		Si	13491	20,79 (3,12)		28,34 (4,10)			
	SM-JIS	No	102640	15,10 (2,67)		<0.0001		25,34 (3,70)	<0.0001
		Si	13767	20,25 (3,83)		28,24 (4,09)			
Resistencia a la insulina	METS-IR	normal	106615	15,23 (2,79)	<0.0001	25,18 (3,45)	<0.0001		
		alto	9792	20,91 (3,76)		31,15 (3,83)			
	TG/HDL	normal	89714	15,05 (2,58)		<0.0001		25,28 (3,75)	<0.0001
		alto	26693	17,92 (4,28)		27,05 (3,91)			
	TyG	normal	87868	15,03 (2,59)		<0.0001		25,26 (3,73)	<0.0001
		alto	28539	17,78 (4,21)		27,00 (3,94)			

dt= desviación típica HTA=hipertensión arterial; AVI= Índice de volumen abdominal- Abdominal volumen index, BAI= Índice de adiposidad corporal-body adiposity index; Síndrome Metabólico; NCEP/ATPIII=Adult Treatment Panel III; IDF= International Diabetes Federation; JIS= Joint Interim Statement; Resistencia a la insulina: Triglicéridos/ colesterol HDL (TG/HDL), Triglicéridos-Glucosa (TyG), Valoración metabólica de resistencia a la insulina (METS-IR), Significación estadística p<0,05.

Gráfico 2: AVI y BAI mujeres versus hombres según síndrome metabólico (ATPIII, IDF, JIS).

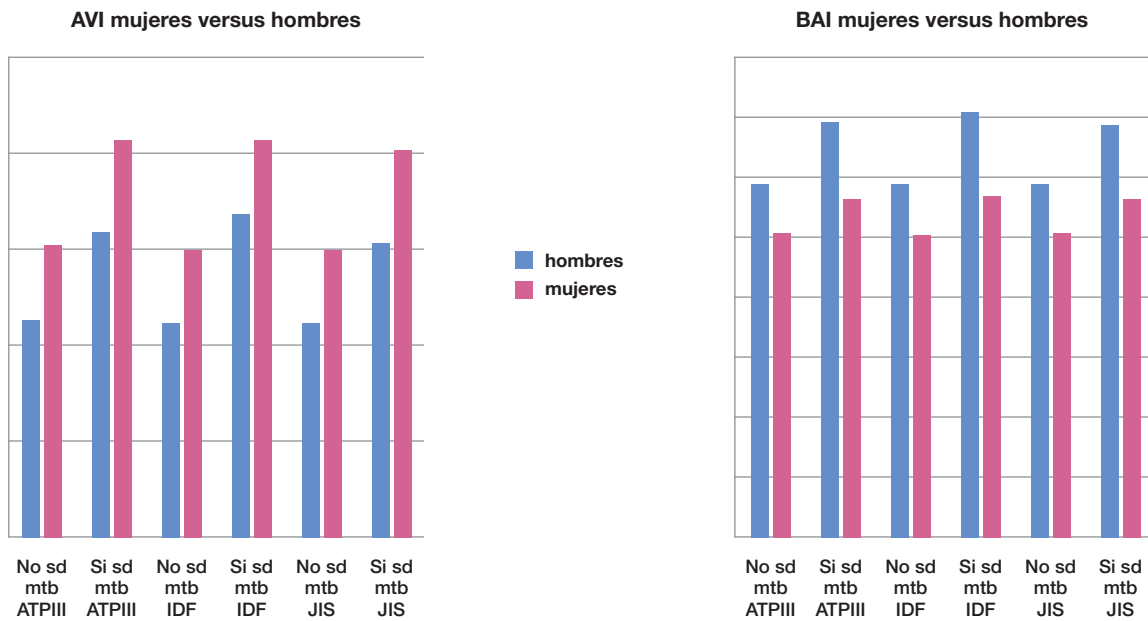


Gráfico 3: AVI y BAI mujeres versus hombres según resistencia a la insulina (METS-IR, TG/HDL, TyG).

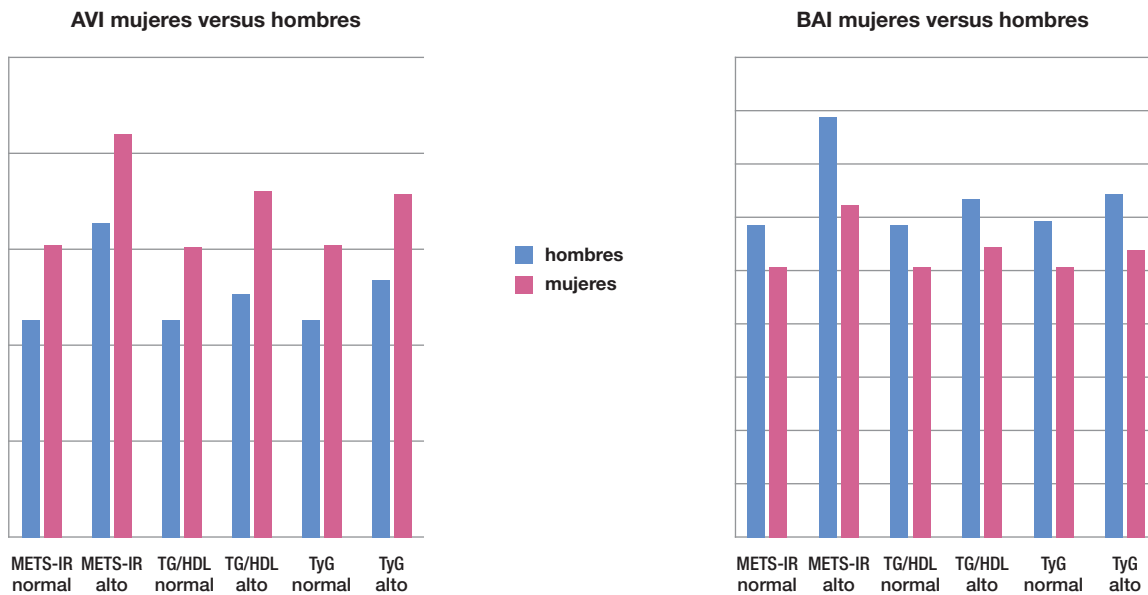


Tabla II: Coeficiente de correlación de Pearson entre BAI y AVI y los valores de tensión arterial, diabetes y de resistencia a la insulina.

Mujeres								
	TAS	TAD	GLUCOSA	AVI	BAI	TyGindex	METSIR	IATGHDL
TAS	1	,753**	,172**	,249**	,275**	,208**	,386**	,192**
TAD		1	,186**	,277**	,287**	,236**	,412**	,208**
GLUCOSA			1	,158**	,163**	,416**	,307**	,161**
AVI				1	,487**	,302**	,692**	,317**
BAI					1	,238**	,704**	,221**
TyG index						1	,474**	,847**
METS-IR							1	,466**
IA TG/HDL								1
Hombres								
	TAS	TAD	GLUCOSA	AVI	BAI	TyGindex	METSIR	IATGHDL
TAS	1	,702**	,177**	,230**	,214**	,201**	,348**	,162**
TAD		1	,194**	,263**	,240**	,250**	,388**	,192**
GLUCOSA			1	,156**	,156**	,381**	,318**	,155**
AVI				1	,404**	,427**	,699**	,425**
BAI					1	,248**	,648**	,198**
TyG index						1	,582**	,816**
METS-IR							1	,535**
IA TG/HDL								1

Tabla III: Coeficiente de concordancia Kappa Cohen entre los tres criterios de valoración de síndrome metabólico.

	Síndrome metabólico NCEP-ATP III	Síndrome metabólico IDF	Síndrome metabólico JIS
Síndrome metabólico NCEP-ATP III	1	0,638	0,456
Síndrome metabólico IDF		1	0,558
Síndrome metabólico JIS			1

concordancia, 0,01-0,20 leve concordancia, 0,21-0,40=concordancia aceptable, 0,41-0,60 moderada concordancia, 0,61-0,80 considerable concordancia y 0,81-1,00 casi perfecta concordancia. Síndrome Metabólico; NCEP/ATPII=Adult Treatment Panel III; IDF= International Diabetes Federation; JIS= Joint Interim Statement

Discusión

La obesidad es bien conocida como un potencial factor de riesgo cardiometabólico. Se prevé que para 2030 hasta el 57,8 % de los adultos en todo el mundo tengan sobrepeso u obesidad. El índice de masa corporal es muy útil pero, a pesar de su uso generalizado; es solo una medida sustituta de la grasa corporal, no ofrece una indicación real de la composición corporal y, a veces, se ve afectada por la edad, el género y las diferencias étnicas. Para medir la obesidad central, se han propuesto una variedad de índices¹⁷.

En nuestro trabajo hemos utilizado dos de estos índices: el BAI y el AVI y su relación con la repercusión metabólica, especialmente con síndrome metabólico y con resistencia a la insulina.

La obesidad es un factor de riesgo importante, especialmente para el desarrollo de diabetes, hipertensión

y de las enfermedades cardiovasculares. Los índices de adiposidad visceral (VAI) y de adiposidad corporal (BAI), junto con otros se han asociado significativamente con complicaciones de la diabetes como albuminuria y enfermedad renal avanzada. Por ello se propone su uso para la detección temprana en los programas de salud pública que permitan reconocerlas y tomar las medidas adecuadas para prevenir complicaciones posteriores¹⁸.

En nuestro trabajo, los valores medios de los dos índices, AVI y BAI aumentan en ambos sexos según ascienden las cifras tensionales y los valores de glucemia, siendo los valores medios más altos los que se asocian con hipertensión arterial y con diabetes.

En nuestro estudio, los valores medios de AVI y BAI son más altos en ambos sexos con síndrome metabólico y con los tres criterios, especialmente con IDF, donde se obtienen los valores más altos.

La presencia de sobrepeso en hombres e incluso peso corporal normal en mujeres se corresponde con un aumento de volumen de tejido visceral en el abdomen. El síndrome metabólico se define como un grupo de factores de riesgo metabólicos coexistentes, como: obesidad central, trastornos de los lípidos, trastornos de los hidratos de carbono e hipertensión arterial. Es responsable del desarrollo de la resistencia a la insulina

y se ha demostrado una correlación entre adiposidad, especialmente con acumulación de grasa abdominal y el índice de masa corporal en personas con síndrome metabólico y, en relación con la hipertensión, trastornos de lípidos y trastornos de carbohidratos. Desde un punto de vista preventivo se debe considerar la introducción de profilaxis primaria y detección precoz en personas de riesgo incrementado para limitar el desarrollo de diabetes mellitus tipo 2 y enfermedades cardiovasculares¹⁹. Los índices AVI y BAI pueden resultar de utilidad en esta labor preventiva.

En este trabajo, los valores medios de AVI y BAI son más altos con resistencia a la insulina con las tres escalas utilizadas y, especialmente con METS-IR.

La relación de la obesidad con la resistencia a la insulina y los problemas cardiometabólicos relacionados está presente en la bibliografía científica. Tradicionalmente, el depósito de grasa visceral se ha considerado uno de los principales responsables del desarrollo de resistencia a la insulina. Recientemente, la evidencia apoya el papel funcional del tejido adiposo en el desarrollo de complicaciones metabólicas independientemente del volumen o distribución del tejido adiposo. La disminución de la capacidad de diferenciación y angiogénesis de los adipocitos, junto con la hipertrofia de los mismos, puede desencadenar un círculo vicioso de inflamación que conduce a la disfunción del tejido adiposo subcutáneo y al depósito de grasa ectópica. El cambio del estilo de vida continúa siendo la intervención más importante en la práctica clínica para mejorar la función del tejido adiposo y evitar el desarrollo de resistencia a la insulina y las complicaciones cardiometabólicas relacionadas²⁰. Por ello las actuaciones, como la que aquí presentamos en prevención primaria cobran especial trascendencia y el uso de índices que complementen al índice de masa corporal son de utilidad, especialmente por su accesibilidad y facilidad en su manejo.

En la sociedad occidental, el síndrome metabólico es un desafío clínico y de salud pública y representa un grupo de factores de riesgo interrelacionados que predicen enfermedades cardiovasculares y diabetes mellitus. Existe un claro vínculo entre el Síndrome Metabólico y la Resistencia a la Insulina²¹.

En este trabajo hemos relacionado ambos trastornos, el síndrome metabólico y la resistencia a la insulina con indicadores específicos de adiposidad: BAI y AVI que puedan servir como herramientas de apoyo en la detección precoz de riesgo por adiposidad y que, en salud laboral permitan iniciar actuaciones preventivas y de promoción de la salud de forma

precoz. Teniendo en cuenta la alta prevalencia de trastornos metabólicos (trastorno del metabolismo de la glucosa, hipertensión, dislipidemia, obesidad, etc.), la atención médica preventiva debe centrarse en actuar en prevención primaria y con cambios en el estilo de vida para reducir la obesidad y el acumulo de grasa corporal y visceral, evitando complicaciones posteriores como aumento de morbilidad y el consiguiente gasto sanitario y sociolaboral.

Se considera fortaleza de este trabajo el tamaño de la muestra poblacional estudiada y la utilización de índices de adiposidad como el BAI y el AVI, reconocidos por su capacidad predictiva en obesidad y sus complicaciones posteriores.

Se considera una limitación la falta de datos comparativos entre diferentes sectores laborales y la exclusión de una parte de la población general, las personas menores de 18 y mayores de 66 años, por lo que se debe tener precaución al interpretar los resultados y aplicarlos a la población global. No se puede establecer una relación temporal con este diseño transversal y, sería necesario realizar un estudio prospectivo posterior para evaluar la efectividad de los índices AVI y BAI como herramientas predictivas en diferentes poblaciones laborales y sectores profesionales y, por ello también en población general no trabajadora.

Conclusiones

Los índices de adiposidad corporal (BAI) y de volumen abdominal (AVI) muestran diferencias entre hombres y mujeres y aumentan sus valores medios con hipertensión arterial y diabetes.

Los valores medios de AVI y BAI aumentan con los tres criterios de síndrome metabólico: ATP III, IDF y JIS y con los tres de resistencia a la insulina: METS-IR, TG HDL y TyG.

Existe una buena o muy buena correlación entre los índices AVI y BAI con METS-IR. Los criterios de Síndrome metabólico IDF y NCEP-ATP II muestran una buena correlación entre si. Siendo menor la obtenida entre JIS con NCEP-ATP II y con IDF.

Conflicto de intereses

No existen conflictos de intereses.

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ORIGINAL

Nuevos sistemas robóticos, ¿Qué tenemos disponible actualmente y qué nos aportan?

New Robotic Systems: What is Currently Available and What Do They Contribute?

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Resumen

Introducción: La aparición de nuevos sistemas quirúrgicos robóticos disponibles para su uso por los urólogos conlleva la necesidad de conocer sus características y sus diferencias con el ya establecido robot Da Vinci.

Material y métodos: Se realiza una revisión no sistemática en la herramienta de búsqueda bibliográfica PUBMED/MEDLINE, acotando la búsqueda a los últimos cinco años. Hemos utilizado el término MeSH "Robotic surgical procedures" (11.762), y otros términos como: "Robotic Surgery" (15.595), "Robotic Surgery AND Urology" (3.807) y "New Robotic System" (3511). Con los resultados obtenidos, realizamos una búsqueda específica sobre los sistemas robóticos encontrados para uso en cirugía urológica abdominal, con el objetivo de analizar la evidencia científica disponible en el uso de dichas plataformas en urología.

Resultados: Se analizan los distintos sistemas robóticos disponibles en el mercado, marcando las diferencias en cuanto a tipo de consola y mandos, tipo de óptica, tecnología de vídeo y control de cámara, disposición y tipo de brazos, características de los instrumentos quirúrgicos y ventajas entre ellos. Repasamos los retos de futuro que nos encontraremos los urólogos con la irrupción de estas nuevas plataformas.

Conclusiones: Existen nuevos sistemas robóticos disponibles para su uso en Europa cuyo ritmo de implantación dependerá de las ventajas que aporten a los hospitales. Dada la escasa evidencia disponible actualmente no se puede afirmar con seguridad que los sistemas analizados se comporten de manera comparable al sistema Da Vinci. Son necesarios estudios aleatorizados que comparen los resultados oncológicos y funcionales entre diferentes sistemas para poder llegar a conclusiones precisas.

Palabras clave: Procedimientos quirúrgicos robóticos, tecnología biomédica, urología, economía y organización de sistemas sanitarios.

Abstract

Introduction: The emergence of new robotic surgical systems available for use by urologists requires understanding their characteristics and differences compared to the established Da Vinci robot.

Materials and methods: A non-systematic review was conducted using the PUBMED/MEDLINE bibliographic search tool, limiting the search to the last five years. The MeSH term "Robotic surgical procedures" (11,762) was used, along with other terms such as "Robotic Surgery" (15,595), "Robotic Surgery AND Urology" (3,807), and "New Robotic System" (3511). With the obtained results, a specific search was conducted on the robotic systems found for use in abdominal urological surgery, aiming to analyze the available scientific evidence for the use of such platforms in urology.

Results: Different robotic systems available in the market are analyzed, highlighting differences in console and control types, optics, video technology, camera control, arrangement and type of arms, characteristics of surgical instruments, and advantages among them. Future challenges for urologists with the emergence of these new platforms are reviewed.

Conclusions: New robotic systems are available for use in Europe, and their rate of implementation will depend on the advantages they bring to hospitals. Given the limited evidence currently available, it cannot be confidently stated that the analyzed systems behave comparably to the Da Vinci system. Randomized studies comparing oncological and functional outcomes among different systems are necessary to draw precise conclusions.

Key words: Robotic Surgical Procedures, Biomedical Technology, Urology, Health Care Economics and Organizations.

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Contexto

La urología ha vivido en las últimas décadas una de las mayores revoluciones en los tratamientos quirúrgicos, por la irrupción de la cirugía laparoscópica y posteriormente por el desarrollo de sistemas quirúrgicos robóticos. Desde la realización de los primeros casos vía laparoscópica en el año 1991¹, la técnica se ha popularizado en todo el mundo. Sin embargo, este abordaje requiere una difícil curva de aprendizaje, necesaria para dominar la técnica laparoscópica. Los sistemas robóticos se crearon con la idea de sobreponerse a esta, y facilitar el acceso a este tipo de cirugía a un mayor número de urólogos².

Durante las últimas dos décadas, el sistema robótico Da Vinci (SRDV) (Intuitive Surgical, EEUU) ha sido el único disponible para su uso en cirugía abdominal, con la salida al mercado de hasta 5 modelos del mismo desde el año 2002. En el año 2019 expiraron las patentes más importantes de la primera versión del SRDV, generando una carrera entre diferentes empresas para desarrollar nuevas plataformas.

El aumento de las indicaciones de la cirugía asistida por robot (CAR) en otras especialidades como: cirugía general³, ginecología⁴, cirugía torácica⁵ u otorrinolaringología⁶, ha llevado a la expansión cada vez mayor del número de CARs realizadas en nuestro país, así como del aumento exponencial del número de robots quirúrgicos distribuidos por la práctica totalidad de la geografía española.

Objetivo

Aparte del SRDV, en estos momentos están disponibles diferentes sistemas robóticos para su utilización en CAR abdominal en Urología. El objetivo de esta revisión es analizar los diferentes sistemas robóticos disponibles para su uso actualmente en Europa.

Adquisición de evidencia

Hemos realizado una revisión no sistemática en la herramienta de búsqueda bibliográfica PUBMED/MEDLINE, acotando la búsqueda a los últimos cinco años. Hemos utilizado el término MeSH "Robotic surgical procedures" (11.762), y otros términos como: "Robotic Surgery" (15.595), "Robotic Surgery AND Urology" (3.807) y "New Robotic System" (3511). Con los resultados obtenidos, realizamos una búsqueda específica sobre los sistemas robóticos encontrados para uso en cirugía urológica abdominal: Da Vinci (Intuitive surgical), Versius (CMR surgical), Hugo (Medtronic), Senhance (Asensus), Avatera (Avateramedical), Dexter (Distalmotion), Revo I (Meerecompany), Hinotori™ (Medicaroid), MicrohandS, con el objetivo de analizar la evidencia científica disponible en el uso de dichas plataformas en urología. Contactamos con las diferentes compañías para recibir información técnica y fotografías de sus sistemas.

Síntesis de evidencia

Después de la búsqueda realizada hemos encontrado 9 sistemas robóticos disponibles para su uso en humanos, aunque con limitaciones en cuanto a su utilización según los mercados donde han obtenido licencia para su uso. Por lo tanto, analizaremos principalmente los disponibles y con certificación de uso a nivel europeo.

Se describen todas las plataformas en función del siguiente esquema:

- Tipo de consola y mandos.
- Tipo de óptica, tecnología de vídeo y control de la cámara.
- Disposición y tipo de brazos.
- Características de los instrumentos quirúrgicos.

Da Vinci

La compañía Intuitive Surgical tiene su base en California, Estados Unidos. Fue fundada en 1995 y obtuvo el marcado europeo **CE** para la primera generación de sus sistemas robóticos en el año 2003. Actualmente tenemos disponible la 4ª generación que engloba las versiones Xi, X y SP. Analizaremos la versión Xi al tener la tecnología más novedosa de la compañía comercializada en Europa, ya que el modelo SP no dispone de marcado **CE**.

EL SRDV Xi se compone de una consola cerrada inclusiva (**Figura 1**), desde la que el cirujano en posición sentada manipula los brazos robóticos mediante unos mandos tipo anillo que se acoplan a los dedos del cirujano. También dispone de varios pedales para el control de la cámara, la aplicación de la energía, el embrague y el cambio de brazo. La unidad de visualización está incluida en la consola con tecnología 3D HD. Dispone de unos controles que permiten adaptar la posición de trabajo del cirujano según las preferencias de este, para mejorar la ergonomía.

Figura 1: Consola del sistema robótico Da Vinci. (Imagen cedida por Intuitive).



La cámara endoscópica 3D es de un tamaño de 8 mm y permite su uso en cualquiera de los 4 brazos robóticos facilitando la cirugía multicuadrante. La cámara permite el uso de fluorescencia con verde de indocianina, como la versión anterior, y el movimiento de la cámara es controlado por el cirujano desde los mandos de la consola. El resto del equipo al lado del paciente tiene visión de la cirugía mediante una pantalla 2D sobre la torre de control.

Los 4 brazos robóticos dependen de una única columna móvil o carro del paciente (**Figura 2**), que se desplaza por quirófano sobre una base con ruedas. En esta última versión del SRDV se ha perfeccionado el diseño de los brazos ocupando menos volumen al ser más pequeños, largos y delgados lo que conlleva una disminución de las posibilidades de choque entre ellos.

Figura 2: Columna móvil con brazos robóticos del sistema Da Vinci. (Imagen cedida por Intuitive).



EL Da Vinci Xi tiene un amplio catálogo de instrumentos que permiten una articulación con 7 grados de libertad mediante la tecnología Endowrist®. El tamaño de los instrumentos permite su uso a través de un trócar de 8 mm, a excepción de la endograpadora robótica que precisa un trócar de 12 mm. Dispone de una amplia variedad de instrumentos que incluyen diferentes pinzas de agarre y portaagujas, tijeras, pinzas bipolares, pinzas selladoras, aplicadores de clips y endograpadoras.

Existe abundante evidencia científica sobre su uso en el campo de la urología⁷⁻¹⁰, donde puede ser usado prácticamente para la realización de cualquier cirugía abdominal¹¹⁻¹³.

Versius

La empresa Cambridge Medical Robotics (CMR) surgical tiene su base en Cambridge, Reino Unido. Fue fundada en 2014 y ha desarrollado el sistema robótico Versius, que obtuvo el marcado CE en marzo de 2019

para su uso en cirugía urológica, ginecológica y en cirugía general. Dicho sistema se compone de una consola abierta (**Figura 3**) desde la que se controlan los instrumentos quirúrgicos mediante un mando ergonómico con forma de joystick que dispone de diferentes botones (no se utilizan pedales para control de los brazos) y una unidad de visualización abierta con una pantalla 3D. El diseño ergonómico de la consola permite adaptar la posición de la misma según las preferencias del cirujano, de pie o sentado.

Figura 3: Consola del sistema robótico Versius. (Imagen cedida por CMR surgical).



Consta de una cámara endoscópica de 10 mm que ofrece una visión 3D que requiere del uso de gafas 3D por parte del cirujano. No está disponible actualmente la posibilidad de fluorescencia. El movimiento de la cámara se controla desde los mandos de la consola. El resto del equipo al lado del paciente tiene visión de la cirugía mediante una pantalla 2D.

El diseño de los brazos robóticos es modular con cuatro módulos independientes (**Figura 4**) que se pueden mover por el quirófano sobre una base con ruedas.

Figura 4: Módulo independiente con brazo robótico Versius. (Imagen cedida por CMR surgical).



Los instrumentos quirúrgicos permiten una articulación de 7 grados de libertad en la punta del instrumento. Se utilizan a través de trócares de 5 mm, como único requisito, dichos trócares deben poseer balón de fijación para evitar cambios en la posición de los instrumentos. Existe una amplia variedad de pinzas de agarre, pinzas bipolares, portaagujas y tijeras todos ellos con 7 grados de libertad.

La evidencia científica disponible sobre el uso de este sistema en urología consiste actualmente en estudios preclínicos^{14,15}. En cirugía general y ginecología ya se han publicado las primeras series de casos con el uso de esta tecnología¹⁶⁻¹⁸, reportando principalmente su seguridad y reproducibilidad. Es probable que la implantación progresiva de nuevos sistemas robóticos Versius, principalmente en Reino Unido haga que aumente el número de series publicadas.

Hugo

La empresa Medtronic tiene su base en EEUU e Irlanda. Fue fundada en 1949 y es una de las compañías de tecnología sanitaria más importantes en relación a ventas a nivel mundial. Tiene una amplia experiencia en el desarrollo de dispositivos médicos y ha desarrollado el sistema robótico Hugo. Ha obtenido el marcado CE autorizando su venta para realizar cirugías urológicas y ginecológicas en octubre de 2021.

El sistema Hugo (**Figura 5**) se compone de una consola abierta para su manejo en la posición de sentado, desde la que se manipula los instrumentos quirúrgicos. Dispone de unos mandos ergonómicos con botones, que permiten un agarre similar al de una pistola (**Figura 6**), así como diferentes pedales desde los que se controlan la cámara, las fuentes de energía y el brazo auxiliar. Consta, además de una unidad de visualización abierta para el cirujano con tecnología 3D HD.

Como óptica utiliza una cámara endoscópica de Karl Storz® 3D TIPCAM® S, con un diámetro de 10 mm, que permite la visualización en 3D HD, pudiendo ser colocada en cualquiera de los brazos robóticos. Como con el sistema Versius, es necesario el uso de gafas

Figura 5: Sistema robótico Hugo, de izquierda a derecha: Módulo con brazo robótico, consola con mandos y pedales, unidad central de procesamiento con pantalla, sistema de insuflado y generador electroquirúrgico. (Imagen cedida por Medtronic).



3D con marcadores reflectantes por parte del cirujano. El control de la cámara se realiza desde los propios instrumentos de la consola, combinando el movimiento con los mandos y el pedal correspondiente. Dispone de un monitor interactivo con un multiplicador de la rotación y ajustes de escala de movimiento.

El sistema robótico Hugo es un sistema modular multipuerto con hasta 4 módulos independientes. Al igual que el sistema Versius, los módulos tienen una base sobre ruedas que permiten su movilidad por el quirófano sin dificultad. Una característica de este robot es que cada brazo robótico tiene seis articulaciones, que le permiten obtener una amplia variedad de movimientos para adaptarse a la posición del paciente.

Dispone de una amplia variedad de instrumentos quirúrgicos como portaagujas y otras pinzas de agarre que permiten 7 grados de libertad en la punta del instrumento. Actualmente no dispone de endograpadora ni de pinza para colocación de clips de polímero. La duración de los instrumentos es variable, siendo algunos de un solo uso y otros de múltiples usos. Requiere del uso de trócares especialmente diseñados para esta plataforma.

También consta de una torre con pantalla 2D como unidad central de procesamiento donde se aloja el sistema de insuflado y un generador electroquirúrgico Valleylab® para los instrumentos quirúrgicos.

Dado la reciente obtención del marcado CE para su uso en cirugía urológica y ginecológica, la evidencia disponible es escasa. En urología se han publicado dos series de casos, el primero con diferentes cirugías¹⁹ donde se estudiaba su versatilidad y seguridad, y el segundo estudio se centraba en la realización de prostatectomías radicales con linfadenectomía²⁰. En ambos estudios con pacientes seleccionados, se demostró la seguridad y factibilidad de realizar cirugías urológicas con este sistema robótico.

La compañía tiene acuerdos de colaboración previa con hospitales nacionales e internacionales de referencia mediante el programa *Integrated Health Solutions*, por lo que es probable que aumenten el número de dispositivos en uso y así la evidencia disponible.

Figura 6: Mandos de control del sistema robótico Hugo. (Imagen cedida por Medtronic).



Senhance

La empresa Asensus surgical tiene su base en EEUU (cambió su nombre previo de Transenterix en febrero del año 2021). Está centrada en el desarrollo de sistemas quirúrgicos robóticos. En el año 2015 adquirió la empresa italiana SOFAR SpA que había desarrollado el sistema robótico TELELAP-ALF-X. Posteriormente cambiaron el nombre del sistema robótico a Senhance que obtuvo el marcado CE para su uso en cirugía general, ginecología, urología y cirugía torácica en el año 2016.

EL sistema robótico se compone de una consola abierta para el cirujano, que dispone de un sistema de mandos con la forma de la base de un portaagujas y pedales que permiten el control de los instrumentos quirúrgicos (**Figura 7**). La unidad de visualización consta de una pantalla 3D 4K.

La cámara endoscópica es de un tamaño de 10 mm. El control de la misma se realiza mediante el movimiento ocular a través de unas gafas 3D con sensores, lo que permite desplazar la imagen de la cámara mediante el movimiento de la cabeza del cirujano. Se puede usar la fluorescencia con verde de indocianina mediante un adaptador especialmente diseñado que proporciona la compatibilidad con el endoscopio PINPOINT® (Stryker®).

Figura 7: Sistema robótico Senhance, de izquierda a derecha: Tres módulos independientes con brazos robóticos y consola del sistema. (Imagen propiedad de Asensus).



Consta de un sistema modular independiente de hasta 4 brazos robóticos, con una base sobre ruedas que permiten su desplazamiento por el quirófano.

Los instrumentos son similares a los utilizados en laparoscopia convencional, sin disponer de grados de libertad en la punta, a excepción de una pinza de agarre atraumática y un portaagujas. El tamaño del portaagujas es de 10 mm y de un solo uso. Una de las características singulares de esta plataforma es que los instrumentos transmiten la sensación táctil al cirujano mediante tecnología háptica, permitiendo conocer las diferencias en cuanto a resistencia de los tejidos. Los tamaños de los instrumentos quirúrgicos son de 3, 5 y 10 mm y reesterilizables sin límites de uso en su mayor parte, por lo que el coste es menor que en otros sistemas.

Incluye también una torre laparoscópica donde se encuentran los sistemas de energía e insuflado y de una pantalla de visualización para el resto del equipo quirúrgico.

Al haber transcurrido más tiempo desde que ha recibido el marcado CE comparado con los otros sistemas robóticos analizados, disponemos de una mayor evidencia con respecto a los resultados de su uso. Las mayores series de casos publicadas corresponden a cirugía general^{21,22} y ginecología^{23,24}. No obstante ya existen series sobre su uso en prostatectomía radical²⁵ y en patología del tracto urinario superior²⁶. Cabe destacar el trabajo de Kulis *et al*²⁷ donde compara el uso de este sistema robótico con la cirugía laparoscópica para realizar la prostatectomía radical extraperitoneal, no observando diferencias a nivel de seguridad ni factibilidad en más de 100 casos. La propia compañía ha estimulado la utilización de un registro de las cirugías usando su plataforma en las distintas especialidades quirúrgicas, focalizándose principalmente en la seguridad, y evaluando que los procesos realizados sean seguros y reproducibles²⁸.

Avatera

La empresa Avateramedical fue fundada en 2011 en Alemania con la idea de obtener un sistema robótico europeo. El sistema Avatera obtuvo el marcado CE para su uso en cirugías urológicas y ginecológicas en 2019.

El sistema robótico Avatera (**Figura 8**) tiene muchas similitudes con el SRDV, consta de una consola abierta desde la que se controla los movimientos de los brazos robóticos mediante un sistema de mandos, tipo anillo que se acoplan a los dedos del cirujano, y con el movimiento de la muñeca. La unidad de visualización dispone de un sistema binocular con tecnología 3D HD similar al usado en la microcirugía permitiendo que el cirujano tenga las orejas y la boca sin obstrucción de ningún tipo.

La cámara endoscópica es 3D, de un tamaño de 10mm, y la resolución de la imagen obtenida por la cámara es HD. Los movimientos de la cámara se realizan mediante los mandos y los pedales de la consola.

Los 4 brazos robóticos dependen de una columna móvil única o carro del paciente, en la que se colocan los instrumentos y el endoscopio.

Figura 8: Sistema robótico Avatera, de izquierda a derecha: Consola con visor binocular y columna móvil de la que dependen los cuatro brazos robóticos. (Imagen cedida por Avateramedical).



Los instrumentos disponibles son un disector tipo *Maryland* bipolar, unas tijeras de *Metzenbaum* bipolares, una pinza de agarre atraumática y un portaagujas, todos de un solo uso y de tamaño de 5 mm que permiten 7 grados de libertad en la punta del instrumento.

Con respecto a la evidencia científica sobre este nuevo sistema actualmente no existen artículos publicados sobre su uso en un contexto clínico ni de desarrollo. Recientemente ha sido utilizado en el Hospital de Leipzig en sus primeros casos en urología según la propia web de la compañía²⁹, pero no disponemos de datos sobre ello.

Dexter

La empresa Distalmotion tiene su base en Suiza, y fue fundada en 2012 a partir del laboratorio robótico del instituto suizo de tecnología de Lausana. Su sistema robótico Dexter obtuvo el marcado **CE** para su uso en diciembre del año 2020.

El sistema se compone de una consola (**Figura 9**) que puede elevarse o descender por lo que permite su utilización en posición de pie o sentado. Los mandos de control son de tipo anillo y se acoplan a los dedos del cirujano de forma similar a los del SRDV. La unidad de visualización permite obtener imágenes con tecnología 2D o 3D.

Figura 9: Sistema robótico Dexter, de izquierda a derecha: Consola del sistema, dos módulos independientes con brazos robóticos y soporte robótico de cámara endoscópica. (Imagen cedida por Distalmotion).



No dispone de cámara endoscópica propia. El control de la cámara puede hacerse por el ayudante de igual manera que en la cirugía laparoscópica o mediante un soporte robótico adaptable a cualquier cámara endoscópica laparoscópica que se fija a la mesa quirúrgica y se controla desde la consola. Esto permite el uso en 2D, 3D o con fluorescencia. Requiere el uso de gafas para la visión en 3D.

El diseño de los 2 brazos robóticos independientes es modular con ruedas incorporadas por lo que se pueden desplazar sin dificultad por el quirófano.

Los instrumentos son de 8.3 mm y permiten 7 grados de libertad. Son de un solo uso y compatibles con cualquier plataforma de energía, permitiendo el uso de energía monopolar o bipolar. Posee dentro de su catálogo de dos pinzas de agarre, tipo *Grasper* y *Maryland* bipolar, portaagujas, tijeras y gancho monopolar.

No disponemos de ninguna publicación en la literatura sobre el uso de este sistema, aunque según la página web de la compañía se ha comenzado a usar en el marco de un estudio clínico por el servicio de cirugía general del Hospital de Lausana.

Diferencias entre los sistemas robóticos

A pesar de la hegemonía del SRDV en las últimas décadas, nuevas plataformas robóticas han emergido en este campo y buscan ser competidoras por el liderazgo del mercado. Las nuevas generaciones de robots quirúrgicos pueden llevar a una reducción de los costes que permitan aumentar el acceso a la CAR. Asimismo, buscan solucionar algunas de las limitaciones que presenta el SRDV, como la dificultad de comunicación con el equipo debido a la consola cerrada, las limitaciones de posicionamiento de los brazos por la posibilidad de choque entre ellos²⁰, la falta de retroalimentación háptica, la necesidad de trócares de 8 o 12 mm y el elevado coste del sistema³⁰. El desarrollo de sistemas modulares, consolas abiertas, instrumentos de menor tamaño y posibilidades de adquisición por uso por procedimiento, son algunos de los avances que aportan estos nuevos sistemas (**Tabla I**).

Tabla I: Resumen de los sistemas robóticos analizados y sus características principales.

Sistema robótico	Compañía	Marcado CE	Características principales
Da Vinci Xi	Intuitive	2014	Columna móvil, instrumentos y cámara de 8 mm, unidad visualización cerrada, amplia variedad de instrumentos con 7 grados de libertad. Posibilidad de uso de fluorescencia.
Versius	CMR surgical	2019	Modular, instrumentos 5 mm, unidad de visualización abierta, instrumentos con 7 grados de libertad. Brazos en 4 módulos independientes de tamaño reducido.
Hugo	Medtronic	2021	Modular, instrumentos 5 mm, unidad visualización abierta, instrumentos con 7 grados de libertad. Brazos en 4 módulos independientes.
Senhance	Asensus	2016	Modular, instrumentos de 5 mm, instrumentos de cirugía laparoscópica sin grados de libertad, unidad de visualización abierta, sensibilidad háptica.
Avatera	Avateramedical	2019	Columna móvil de la que dependen los brazos robóticos, instrumentos de 5 mm con 7 grados de libertad, consola abierta, instrumentos de un solo uso.
Dexter	Distalmotion	2020	Modular con 2 brazos robóticos, instrumentos de 8 mm de un solo uso con 7 grados de libertad, visualización abierta, soporte robótico endoscópico adaptable a cualquier tipo de sistema de endoscopia laparoscópica

Implantación en hospitales

El número de cirugías realizadas a nivel mundial con el SRDV a comienzos del año 2022 ha sobrepasado la cifra de los 10 millones, con más de 6800 sistemas instalados globalmente y con una rápida expansión en los últimos años. En la península ibérica se ha llegado, según datos de la compañía, a más de 100 sistemas instalados, con previsión de aumentar su número en el corto plazo. Los SRDV instalados en España actualmente se encuentran en hospitales de gran volumen o en centros privados.

Los nuevos sistemas analizados se enfrentan al problema de un gran competidor como es el SRDV, un producto eficiente y consolidado, con gran implantación, una amplia red de mantenimiento y soporte técnico, unas posibilidades de entrenamiento variadas y evidencia científica de alto nivel.

Las dos estrategias de implantación de estos nuevos sistemas pueden ser: Implantarlos en hospitales que no dispongan de esta tecnología o bien introducirse en el mercado de los hospitales que ya lo poseen. Dada la necesidad de demostrar su eficiencia y generar evidencia científica de alto nivel para aumentar su impacto en el mercado, pensamos que esta segunda estrategia va a ser la tomada inicialmente, al menos por las compañías más potentes, para asegurarse los mejores resultados posibles y así poder pasar a un mercado más global posteriormente.

En la publicación de Liatsikos *et al*³¹ se analizan las potenciales oportunidades de implantación del sistema robótico Avatera señalando que para poder competir con el SRDV tiene que ofrecer una capacidad técnica comparable, disminuir los costes de adquisición del sistema robótico y abaratar el uso de sus instrumentos y el mantenimiento.

Retos en la formación

Ya hace más de una década Valero *et al*³² remarcaban la importancia de crear un proceso de formación en CAR dentro de los programas de residencia. Actualmente en España nos encontramos con pocos centros que

incluyan esta formación de manera habitual. En una reciente encuesta realizada desde la Asociación Española de Urología entre residentes cuyos hospitales tenían SRDV, únicamente el 12,77% afirmaban que su servicio disponía de un programa de formación robótica reglada. (Datos pendientes de publicación). Esto contrasta con aproximadamente el 54% de los residentes de EE.UU. que disponen de entrenamiento específico³³. Debemos dar pasos en la implementación de estos programas formativos en nuestro país.

Retos en la innovación

La competición entre sistemas puede acelerar la llegada de innovación como puede ser la posibilidad de utilizar fluorescencia con diferentes marcadores como marcador de PSMA que nos permitiría ver exactamente los límites de la prostatectomía en pacientes con riesgo de extensión extracapsular o afectación linfática³⁴, el uso de inteligencia artificial que permita conjugar los hallazgos de las pruebas de imagen con el campo quirúrgico³⁵, los sistemas de navegación intraoperatoria a tiempo real o los procesos automatizados que podrían llevar a que el propio sistema realizara de forma parcial o total la cirugía³⁶.

Conclusión

Existen nuevos sistemas robóticos disponibles para su uso en Europa cuyo ritmo de implantación dependerá de las ventajas técnicas y económicas que aporten en los hospitales. Dada la escasa evidencia disponible actualmente no se puede afirmar con seguridad que los sistemas analizados se comporten de manera comparable al SRDV. Son necesarios estudios aleatorizados que comparen los resultados oncológicos y funcionales entre diferentes sistemas para poder llegar a conclusiones precisas.

Conflicto de intereses

Los autores declaran no tener conflicto de intereses.

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ORIGINAL

Hospitalización en Salud Mental infantil y adolescente en Baleares: características clínicas

Hospitalization in Child and Adolescent Mental Health in the Balearic Islands: clinical characteristics

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Entre los principales motivos de ingreso en población infanto-juvenil estaría la protección ante un riesgo de la integridad física, valorar de manera intensiva la patología y necesidad de descartar cuadro orgánico. El objetivo de este estudio es conocer el perfil clínico de los menores que ingresan en nuestra unidad de hospitalización.

Se realiza estudio de 225 pacientes, ingresados durante los años 2017-2018 a través de la revisión sistematizada de informes de alta.

El perfil obtenido es el de una mujer entre 15-17 años de edad, con diagnóstico de trastorno relacionado con trauma y factores de estrés o por trastorno destructivo del control de los impulsos y de la conducta. Casi un 70% de los ingresos son motivados por ideas y/o conductas autolíticas y alteraciones conductuales, de este subgrupo solo 12,1% padecía un trastorno mental grave. De los resultados obtenemos como principales factores precipitantes de ingresos: baja tolerancia a la frustración, falta de estrategias de afrontamiento, desregulación emocional, fracaso de los modelos educativos, y desbordamiento de la capacidad de contención del entorno (sociofamiliar y educativo). Por lo que planteamos si dichos factores se están abordando desde los recursos adecuados o es necesario una mayor optimización de los recursos existentes o la promoción de otros alternativos con la implantación de programas específicos e intensivos a nivel comunitario y otros a nivel secundario como prevención del suicidio, que permitan dar una respuesta íntegra y evitar el ingreso por el estigma o consecuencias.

Palabras clave: Hospitalización, salud mental infanto-juvenil.

Abstract

Among the main reasons for admission to the child and adolescent population would be protection against a risk to physical integrity, intensive assessment of the pathology and the need to rule out an organic condition. The objective of this study is to know the clinical profile of minors admitted to our hospitalization unit.

A study was carried out on 225 patients, admitted during the years 2017-2018 through the systematized review of discharge reports. The profile obtained is that of a woman between 15-17 years of age, with a diagnosis of a disorder related to trauma and stress factors or a destructive disorder of impulse control and behavior. Almost 70% of admissions are motivated by self-harming ideas and/or behaviors and behavioral alterations; of this subgroup, only 12,1% suffered from a serious mental disorder. From the results we obtain the main factors precipitating income: low tolerance for frustration, lack of coping strategies, emotional dysregulation, failure of educational models, and overflow of the containment capacity of the environment (socio-familial and educational). Therefore, we propose whether these factors are being addressed with adequate resources or whether greater optimization of existing resources or the promotion of other alternatives is necessary with the implementation of specific and intensive programs at the community level and others at the secondary level such as suicide prevention, which allow for a comprehensive response and avoid admission due to stigma or consequences.

Key words: Hospitalization, child and adolescent mental health.

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Introducción

Alrededor del 10-20% de los niños y adolescentes padece, según datos de la OMS, algún trastorno mental^{1,2}.

En un medio similar al nuestro, como es Reino Unido, según el informe emitido por el National Health Service (NHS) sobre la población de entre 5 a 19 años en el año 2017, uno de cada ocho (12,8%) individuos evaluados presentaba criterios para al menos un trastorno mental, y un 5% presentaba criterios diagnósticos para dos trastornos o más. Las tasas de trastorno mental aumentaban progresivamente con la edad, siendo el grupo de mujeres de entre 17-19 años el más vulnerable³.

En la práctica asistencial, ante la detección o sospecha de un trastorno mental, son varios los factores clínicos, pero también del entorno, que pueden llevar a recurrir a un ingreso hospitalario. Las guías clínicas recomiendan minimizar el uso de las hospitalizaciones en esta población, unidades específicas cuando sea posible, y reservar este recurso para situaciones que se valoren individualmente^{4,5}. La Convención sobre los derechos del Niño de 1989, proclamada por la Asamblea General de la ONU, cuyo cumplimiento está garantizado por la Constitución Española de 1978 (en sus artículos 39 y 49), recoge este derecho a una protección y atención adecuadas (incluyendo los medios) a la salud física, psíquica y social de los menores. La valoración de la pertinencia del ingreso de los menores por motivos psiquiátricos queda también regulada según la ley (LEC 1/2000 del 7 de enero), que en España establece el requerimiento de autorización judicial⁶.

Entre las principales situaciones recomendables la hospitalización, están las en las que hay riesgo para la seguridad (del paciente o terceros), sobre todo para la integridad física, ante un sistema de soporte que no puede realizar la contención o el manejo apropiados. La seguridad del paciente y/o su entorno pueden verse especialmente comprometidas ante cuadros de agitación, en presencia de agresividad o ideación suicida, trastornos de la conducta alimentaria con compromiso físico grave, o en aquellos casos en los que el menor es víctima de su entorno (malos tratos, abusos, negligencias, Münchaussen por poderes...). Pero la presencia de alguno de estos elementos no debe motivar una hospitalización, si el ambiente en que se produjo puede modificarse adecuadamente para la contención^{4,5}.

La posibilidad de acometer un ingreso hospitalario se puede plantear cuando se requiere observar de manera intensiva la patología para su diagnóstico y abordaje, y en los casos en que haya que descartar organicidad del cuadro clínico^{4,5}.

Por otro lado, un ingreso de un menor en una unidad de hospitalización psiquiátrica puede tener distintos efectos negativos como un mayor estigma, posible

efecto contagio, ganancias secundarias que refuercen la problemática del menor, por ello se deben realizar una evaluación clínica pormenorizada, con un balance adecuado riesgo/beneficio que justifique la decisión del ingreso en unidad de hospitalización.

En nuestra práctica clínica habitual en la Unidad de Hospitalización de Psiquiatría infanto-juvenil, hemos observado en últimos 5 años un aumento progresivo de la demanda de este recurso. La apreciación en los últimos tiempos es que el requerimiento de este recurso se ha incrementado en parte ante las limitaciones de la contención estructural/ambiental de alteraciones conductuales y emocionales, ante cuyo manejo la red actual de dispositivos, tanto de salud mental como socio-comunitarios, se ve desbordada.

Como unidad de hospitalización de salud mental infanto-juvenil de referencia para la Comunidad Autónoma de las Islas Baleares, nos interesa conocer cuál es el perfil de los menores ingresados, con el objetivo de que ello permita diseñar estrategias de intervención intensivas a nivel comunitario que disminuyan el número de ingresos, reingresos y/o la estancia media, minimizando el impacto que puede tener un ingreso psiquiátrico en esta población más vulnerable.

Métodología

Participantes

La muestra para el estudio estuvo constituida por un total de 225 pacientes, ingresados por uno o varios periodos de tiempo en la Unidad de Hospitalización del Instituto Balear de Salud Mental Infantil y Adolescente (IBSMIA) durante los años 2017 y 2018.

Dicho dispositivo constituye la única Unidad de Hospitalización de Salud Mental Infanto-juvenil disponible en el momento actual en las Islas Baleares, y da cobertura a todos los menores de la Comunidad Autónoma (según el INE, la población de Baleares en 2018 de 0-19 años era de 228.082 habitantes, no disponiéndose de datos para la franja específica de 0-18 años).

Todos los sujetos estudiados eran menores de edad cuando ingresaron en la Unidad.

Materiales

A partir de los informes de alta de hospitalización de los sujetos, se constituyó un registro de variables para el estudio de las características sociodemográficas (edad, sexo, absentismo escolar) y clínicas (motivo de ingreso; consumo de tóxicos, consumo de cannabis; seguimiento previo por IBSMIA; antecedentes familiares en Salud Mental; diagnóstico principal al alta; presencia de ideación, conducta y/o comunicación suicida), así como las herramientas terapéuticas (tratamiento psicofarmacológico al alta, reingresos) y otros recursos

empleados (implicación de Servicios Sociales, notificación al Servicio de Protección del Menor, notificación a la Fiscalía de Menores). Los informes aludidos contienen, de manera sistemática, las variables objeto de estudio.

Para los pacientes que habían requerido más de un ingreso hospitalario en el periodo, se tomaron los datos de alta tras su primera hospitalización (empleándose los informes posteriores, solo, para la descripción de las variables asociadas al reingreso –número de reingresos e intervalo de tiempo transcurrido hasta el siguiente– y la estancia media total).

Los diagnósticos fueron realizados según criterios del Manual DSM-5, y agrupados según las categorías diagnósticas recogidas en dicho manual.

Procedimiento

Este estudio se realizó mediante revisión sistematizada de los informes de alta por facultativos de la Unidad de Hospitalización (psiquiatra y psicólogo clínico), confeccionándose una base de datos anónima, en la que se recogieron las variables mencionadas.

A partir de la información obtenida por este procedimiento, se elaboró un estudio descriptivo centrado en las variables de sexo, edad y absentismo escolar y los aspectos clínicos de la población descrita, y los recursos terapéuticos y sociales empleados.

Análisis de los datos

Los estadísticos descriptivos de este estudio fueron calculados mediante el uso de Excel

Resultados

Los 225 sujetos de la muestra generaron en total 328 hospitalizaciones durante el periodo de estudio. El 75% (168) de los pacientes requirieron un único ingreso en el periodo; sin embargo, el 25% (57) tuvieron más de un ingreso en la unidad y dieron lugar, en total, a casi el mismo número de ingresos (160).

La población estudiada tenía una edad superior a los 12 años, el 96% (216), solo el 4% (9) eran menores de esa edad. El grupo de edad con mayor número de ingresos correspondió al constituido por los pacientes entre 15-17 años, el 67,6% (152). (Figura 1). En cuanto al sexo, la razón mujeres: hombres fue de 2,31:1.

La estancia media de los ingresos fue de 11,05 días. Los motivos de ingreso más habituales fueron la ideación o comportamientos suicidas el 49,8% (112), seguidos por las alteraciones conductuales en segundo lugar el 19,5% (44) y las restricciones alimentarias/descompensaciones bulímicas en tercer lugar, el 16% (36).

De los sujetos ingresados, casi la mitad un 49,3%

(111) refirió ideación suicida, con comunicación de esta por parte de un 36% (81). Un 42,7% (97) realizaron conductas autolíticas, de ellos sin finalidad suicida en un 25,8% (58), con finalidad suicida en un 8% (18) y no determinada en un 8,9% (20). (Figura 2).

Al alta, los diagnósticos principales registrados más frecuentemente fueron: los trastornos relacionados con traumas y factores de estrés un 17,3% (39), seguidos por los trastornos destructivos del control de los impulsos y de la conducta 16,4% (37), los trastornos alimentarios y de la ingestión de alimentos un 16% (37), los trastornos de la personalidad/rasgos de personalidad disfuncional el 13,8% (31) y los trastornos del neurodesarrollo 12% (27). Con menor frecuencia se detectaron otras patologías como los trastornos del espectro de la esquizofrenia y otros trastornos psicóticos 8% (18), los trastornos depresivos 5,3% (12), los trastornos de ansiedad 1,8% (4), los trastornos relacionados con sustancias y trastornos adictivos 1,8% (4), el trastorno bipolar y trastornos relacionados 1,3% (3), el trastorno obsesivo-compulsivo y otros trastornos relacionados 0,4% (1), los trastornos de síntomas somáticos y trastornos relacionados 0,4% (1), y otros pacientes sin cumplir criterios diagnósticos de trastorno mental 5,3% (12). Un 41,3% de los pacientes presentaba algún diagnóstico comórbido, además del diagnóstico principal. (Figura 3).

Más de la mitad de los pacientes fueron dados de alta con tratamiento psicofarmacológico, con al menos un fármaco 34,7% (78) o más 24,4% (55). En torno a una cuarta parte de los pacientes, el 25% (57) requirió al menos un reingreso en el periodo de estudio (2017-2018). El 61,4% (35) de esos 57 pacientes requirieron sólo un reingreso en la unidad; el 16% (9) necesitaron 3 ingresos durante un año, el 10,5% (6) precisaron 4 ingresos, el 5% (3) requirieron 5, y el 7% (4) precisaron más de 5 ingresos durante ese periodo.

Aproximadamente la cuarta parte de la muestra estudiada consumía algún tóxico de forma habitual 24,9% (56) siendo, en particular, el consumo de cannabis casi igual de prevalente 21,8% (49). La presencia de antecedentes familiares psiquiátricos se detectó en un 60% (135) de los pacientes.

La mayoría de los pacientes estudiados 65,8 % (148) habían realizado seguimiento ambulatorio en el IBSMIA.

Se registró el absentismo escolar en un 16% (36) de los pacientes, mientras que un 76,4% (172) mantuvieron la actividad académica. No se dispone de información recogida sobre el restante 7,6% (17).

En cuanto a la implicación de los servicios sociales, esta se dio en un 26,7% (60) de los pacientes. En varios de los casos, se procedió a la notificación a otras entidades como el Servicio de Protección del Menor el 30,2% (68) o la Fiscalía de Menores un 22,2% (50).

Figura 1: Distribución de la muestra de pacientes ingresados en Unidad de Hospitalización Infanto-Juvenil IBSMIA, entre 2017-2018, según grupos de edad.

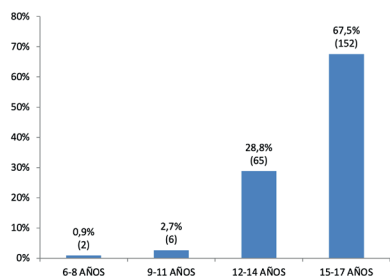


Figura 2: Presencia de ideación, comunicación y conductas autolíticas, entre los pacientes ingresados en Unidad de Hospitalización Infanto-Juvenil IBSMIA, en 2017-2018.

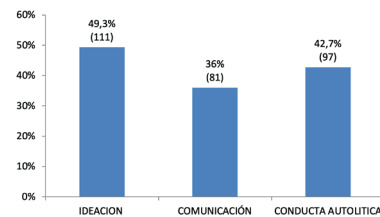
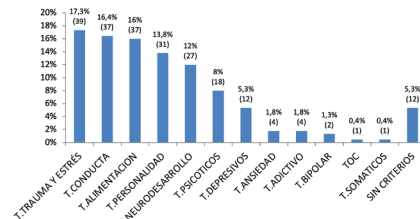


Figura 3: Diagnósticos según DSM V entre los pacientes ingresados en Unidad de Hospitalización Infanto-Juvenil IBSMIA, en 2017-2018.



De los resultados mostrados previamente, se ha extraído que un 69,3% (156) de los ingresos de los dos años de estudio son motivados por ideas y/o conductas autolíticas y alteraciones conductuales. Del análisis de este grupo mayoritario de pacientes (en función de sus diagnósticos al alta), se concluyó que sólo un 12,2% (19) de los 156 pacientes de ellos padecía un trastorno mental grave (trastorno psicótico, trastorno bipolar o trastorno depresivo mayor). Un 70,51% (110) recibieron alguno de los siguientes diagnósticos al alta: trastornos de la conducta, trastornos relacionados con el estrés, trastornos de personalidad, trastorno relacionado con el consumo de sustancias o sin criterios diagnósticos para trastorno mental. En este otro grupo de pacientes, destaca la presencia en un 61,8% (68) de antecedentes familiares psiquiátricos.

Por lo que el perfil que obtenemos en nuestra unidad es el de una mujer con edad comprendida entre los 15-17 años, que ingresa principalmente por ideación o comportamiento suicida, con diagnóstico al alta de trastorno relacionado con trauma y factores de estrés o por trastorno destructivo del control de los impulsos y de la conducta. La mayoría tiene antecedentes familiares de salud mental y han tenido algún tipo de contacto previo con la red de salud mental infanto-juvenil con anterioridad.

Discusión

En conclusión, la mayor parte de los pacientes requirieron al menos un ingreso hospitalario a consecuencia del riesgo suicida o por alteraciones de conducta, sin padecer, en la mayor parte de los casos, un trastorno mental grave. Esta tendencia es concordante con los resultados de otros estudios^{7,8}. Los diagnósticos mayoritarios de estos pacientes nos orientan hacia otra serie de conflictos o dificultades como las principales generadoras de hospitalizaciones: las problemáticas intrafamiliares y sociales, la baja tolerancia a la frustración, la desregulación emocional, la falta de estrategias de afrontamiento y los comportamientos disruptivos (especialmente en la etapa adolescente), el fracaso

de los modelos educativos, el desbordamiento de la capacidad de contención del entorno (sociofamiliar y educativo), etc.

Estos resultados invitan también a la reflexión acerca de la utilización de los recursos de Salud Mental, y en particular a la de las hospitalizaciones psiquiátricas, en los menores. Al recomendar el uso limitado de los ingresos en esta población, destaca el uso requerido de estos dispositivos para abordar problemas conductuales y emocionales en ausencia de trastorno mental grave, transfiriendo la incapacidad del entorno para realizar una contención adecuada.

La cuestión sobre la adecuación de los recursos podría concretarse aún más. Se plantea si algunos problemas, como las alteraciones de conducta o los trastornos relacionados con estrés, que germinan o se perpetúan y repercuten en el entorno del paciente, se abordan con los medios adecuados: si existen y se emplean recursos eficaces en el ámbito comunitario, si la hospitalización es el recurso adecuado para generar los cambios necesarios, o si este recurso puede tener efectos negativos sobre la evolución de la situación atendida, son cuestiones que surgen de la observación realizada. El número de ingresos requeridos por algunos pacientes en ausencia de trastorno mental grave, podría ser un signo de la insuficiencia o inadecuación de los recursos o dispositivos sanitarios, sociales y educativos, implicados en la actuación sobre este perfil de menores. Como se mencionaba, el ingreso puede tener efectos negativos, que han de ser tomados en cuenta y confrontados a los beneficios verdaderamente esperables. En este sentido, la hospitalización puede constituir una experiencia ansiógena o traumática en algunas ocasiones^{4,5,9}. En otros casos, puede resultar contraproducente debido al efecto contagio¹⁰, aunque los estudios disponibles al respecto son escasos y no permiten establecer una conclusión clara acerca de la magnitud de este efecto^{11,12}. También se ha apreciado, en algunos pacientes con múltiples hospitalizaciones, la aparición de ganancia secundaria que perpetúa la problemática y la dependencia del recurso¹⁰.

En otra línea, se propone una mayor optimización de los recursos existentes o la promoción de otros alternativos que pudieran favorecer una atención más concreta y holística. Dentro de la red de salud mental, una de estas estrategias podría ser la potenciación de los hospitales de día para aquellos pacientes con necesidades clínicas y terapéuticas complejas. Otra medida podría ser la implantación de programas específicos e intensivos de prevención secundaria, como los dirigidos a la prevención del suicidio, que permitan dar una cobertura íntegra y proporcional a problemas determinados.

No obstante, la multitud de factores que influyen sobre las principales demandas de atención (problemáticas intrafamiliares, fallos de los modelos educativos, abusos sexuales, maltrato en sus diferentes formas y entornos, consumo de tóxicos, ...), sugieren también la necesidad de una amplia intervención comunitaria. En este sentido, se trataría de auspiciar estrategias de prevención primaria y secundaria a través de la implicación de las familias, los centros de enseñanza, Servicios Sociales, y otras instituciones de carácter público. En esta línea, existen múltiples programas de intervención a todos los niveles que han demostrado resultados positivos (académicos, intervenciones familiares en domicilio, programas intensivos para mejorar el comportamiento y la relación de los menores con sus padres o cuidadores, programas de prevención de maltrato...) ¹⁰, y que podrían mejorar el manejo de algunas problemáticas que implican en su génesis a otros sistemas y que, en el momento actual, se están abordando mayoritariamente desde la red de salud mental.

Con respecto a las limitaciones de este estudio, cabe señalar que, aunque se revisó el cumplimiento de los

criterios diagnósticos según el manual DSM-5 para cada caso, no se emplearon escalas específicas para medir síntomas. Además, existe un posible sesgo asociado a la percepción de los examinadores. Por otro lado, al ser un estudio descriptivo, las variables analizadas pueden tener un impacto sobre los resultados obtenidos, que no se contrasta con un test de hipótesis. Queda por tanto la posibilidad de plantear un futuro estudio con carácter analítico.

Conclusiones

La mayoría de los ingresos acometidos en los últimos dos años en la Unidad de Hospitalización infanto-juvenil en la que se ha realizado el estudio, no están motivados por la presencia de patología mental grave (i.e., trastornos psicóticos, trastorno bipolar, trastorno depresivo mayor...). Tras la demanda aparentemente subyace, con mayor frecuencia, la insuficiencia de la contención estructural y/o ambiental de alteraciones conductuales y emocionales.

A tenor de los resultados, desde nuestro punto de vista, sería aconsejable la optimización de los recursos disponibles, en la medida en que estos sean suficientes y den cobertura a la demanda concreta en el medio adecuado, implicando no sólo a los servicios sanitarios sino también a familiares, Servicios Sociales, centros académicos y otras instituciones públicas.

Conflicto de intereses

Los autores declaran no tener conflicto de intereses.

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Synchronous versus asynchronous methodology in nursing students: a comparative study

Metodología sincrónica versus asincrónica en estudiantes de enfermería: un estudio comparativo

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Abstract

Objectives: This study aimed to assess the influence of self-regulation and self-efficacy on two different e-learning models, asynchronous vs synchronous.

Methods: 201 nursing students were randomly assigned (1:1) to a synchronous working group (SG) versus an asynchronous working group (AG). Sociodemographic variables, self-efficacy and self-regulation were collected. Comprehension was assessed with a multiple-choice test. Linear regression was used to identify influential covariates, and test scores were compared using propensity scoring and inverse probability weighted regression.

Results: There were no differences between synchronous and asynchronous interventions. Age ($\beta = -0.04$), employment status ($\beta = 1.16$) and level of performance self-regulation strategies ($\beta = 0.31$) predicted the level of knowledge acquired. After adjusting for the scores of both groups, no differences were found in the knowledge test scores.

Conclusions: There are no differences between the two e-learning models. Regardless of the type of model, level of self-regulation, employment status and age have an impact on e-learning.

Key words: e-learning, synchronous learning, asynchronous learning, self-efficacy, self-regulation.

Resumen

Objetivos: Este estudio tuvo como objetivo evaluar la influencia de la autorregulación y la autoeficacia en dos modelos diferentes de aprendizaje electrónico, asíncrono y sincrónico.

Métodos: 201 estudiantes de enfermería fueron asignados aleatoriamente (1:1) a un grupo de trabajo sincrónico (SG) versus un grupo de trabajo asíncrono (AG). Se recogieron variables sociodemográficas, autoeficacia y autorregulación. La comprensión se evaluó con una prueba de opción múltiple. Se utilizó la regresión lineal para identificar covariables influyentes y las puntuaciones de las pruebas se compararon mediante puntuación de propensión y regresión ponderada de probabilidad inversa.

Resultados: No hubo diferencias entre las intervenciones sincrónicas y asíncronas. La edad ($\beta = -0,04$), la situación laboral ($\beta = 1,16$) y el nivel de estrategias de autorregulación del desempeño ($\beta = 0,31$) predijeron el nivel de conocimientos adquiridos. Después de ajustar por las puntuaciones de ambos grupos, no se encontraron diferencias en las puntuaciones de las pruebas de conocimientos.

Conclusiones: No existen diferencias entre los dos modelos de e-learning. Independientemente del tipo de modelo, el nivel de autorregulación, la situación laboral y la edad tienen un impacto en el e-learning.

Palabras clave: aprendizaje online, aprendizaje sincrónico, aprendizaje asíncrono, autoeficacia; autorregulación.

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Introduction

During the COVID-19 pandemic, many universities were affected and had to suspend face-to-face classes from the beginning¹. According to statistics provided by UNESCO in 2020, the COVID-19 pandemic affected more than 190 countries and almost 1.5 billion students². On March 9, 2020, in an effort to protect public health in the midst of the COVID-19 pandemic, the Autonomous Community of Madrid became the first region in Spain to suspend face-to-face classroom activities as of March 11. Then, five days later, on March 14, the Spanish government declared a state of emergency, resulting in the suspension of face-to-face education nationwide³. During this time, online learning emerged as a solution to minimise the impact on students' academic progress⁴. While online education has been recognized as a promising and effective method for teaching nursing students^{5,6}, the transition to fully online courses during the COVID-19 crisis presented a unique challenge. The functioning of online courses and the mental states of individuals can differ significantly from those in normal times⁷. Of particular note is the situation of international students currently engaged in distance learning from resource-limited home countries, where institutional readiness in terms of technological and infrastructural support may not always be available⁸. This circumstance adds an additional layer of complexity to cross-national online education. The mandated shift to distance learning during the lockdown required a rethinking of both teaching-learning methods and processes. In addition, the reopening of schools, accompanied by the necessary sanitary measures, brought about a profound change in the perception of learning and teaching⁹. This process has been generalized to many other countries (10–12). In a survey of 700 universities and institutions in 8 countries, 95% of institutions had offered online learning during the COVID-19 pandemic, and 80% intended to increase investment in technology over the next 5 years¹³.

E-learning is a concept that emerged in the 1990s as a form of distance learning using the Internet and technology, where the main aim is to ensure independent learning without the need for constant teacher intervention¹⁴. This concept has undergone a long evolution, from the design and publication of multimedia resources, the use of Learning Management Systems (LMS) with content on platforms (defined as virtual classrooms), the use of Web 2.0 (which enhances social interaction) and cloud computing, more focused on open content, which has generated new methodologies for Massive Online Open Courses (MOOCs)¹⁵.

There are two types of e-learning: asynchronous and synchronous. Synchronous learning refers to online or distance learning that takes place in real time, with students attending scheduled classes. Asynchronous learning uses technology to facilitate the exchange of information and online learning resources by promoting

communication and peer interaction in a timeless manner, thus removing the spatial and temporal limitations of synchronous methodology and allowing students to learn anytime, anywhere^{16,17}. However, no differences have been found between the two types of e-learning in the academic performance of medical students^{18,19}. The success of e-learning depends to a large extent on the learner's ability to direct and manage his or her own learning process. This requires the student to set appropriate goals and strategies to achieve them. This methodology encourages autonomy, independent learning and self-regulated thinking rather than traditional modes²⁰. As a result, the most efficient and effective students in this learning model achieve better results²¹. There are few studies that assess self-efficacy in online learning environments in a multidimensional way^{22,23}. Most studies have focused on the development of technology for learning²⁴⁻²⁶ or on students' competence in using the Internet^{27,28}, but none of these studies has focused on evaluating the influence of general self-efficacy and self-regulatory processes on the e-learning process, either synchronous or asynchronous.

For these reasons, the aim of this study was to evaluate, in the context of teaching during the COVID-19 pandemic, in our environment, the degree of assimilation of content taught through synchronous e-learning compared to asynchronous e-learning taught simultaneously to two groups of students, as well as to know the influence of self-regulation and self-efficacy on the results obtained.

Methods

Design and setting

A comparative study was carried out in October 2021, in a single University centre in Madrid, Spain.

Population

The study population consisted of all first-year nursing students at a public university in Madrid, Spain (N=201). Students who did not want to participate or did not sign the informed consent form were excluded from the study. Students were randomly assigned (1:1) to a synchronous working group (SG) before an asynchronous working group (AG). For randomization, a list of random numbers was generated using the statistical-epidemiological program Epidat v. 4.2.

The reasons for exclusion were not completing the previous questionnaires or not completing the asynchronous course.

Variables

At baseline, the following socio-demographic variables were collected: gender (male or female), age (years), living arrangement (with parents, friends, partner, only)

and employment status (full-time, part-time, none and including volunteer work to explore its influence on academic performance). In addition, two validated self-report questionnaires were administered to all participants to measure self-efficacy and self-regulation:

- The Inventory of Self-Regulation Learning Processes (IPAA) (Rosario et al., 2007): an instrument to assess the use of self-regulation strategies by subjects in the three phases of this process (planning, execution and evaluation). It consists of 12 items in Likert format with five alternatives: 1 (never), 2 (few times), 3 (sometimes), 4 (many times) and 5 (always). The score in each variable (planning, execution and evaluation) is obtained from the mean of the subject's responses to the set of items assessing each of these dimensions. Therefore, the maximum score in each variable is five and the minimum is one. The internal consistency of the scale is adequate ($\alpha = 0.87$)²⁹.
- General self-efficacy scale (Schwarzer & Jerusalem, 1995). The scale consists of 10 items that are scored on a Likert scale with four alternatives: 1 (never), 2 (rarely), 3 (often), 4 (always). The maximum score is 40 and the minimum score is 10. The scale has adequate internal consistency indices ($\alpha = 0.90$) and a unidimensional structure³⁰.

Procedure

Prior to the experience, students completed the informed consent and self-efficacy and self-regulation questionnaires. Both groups were then exposed to an academic lesson, each in their respective modality. For the AG, the lesson was delivered in an asynchronous e-learning format by watching a 40-minute video on health content creation and dissemination, based on the principles of mobile learning³¹. The video was created by an expert in audiovisual communications and digital content distribution. In this group, the students had the opportunity to send e-mails to the professors with questions about the content of the video. Students watched the video on their own devices, allowing them to pause and rewind as many times as they needed to if they did not understand certain parts. The video was watched in class to ensure that students completed the task and to assess their knowledge acquisition.

The SG received the same content synchronously via a webinar where they could ask questions to the presenter in a traditional classroom setting. The webinar consisted of an online class through the Microsoft Teams platform, where the instructor interacted directly with the students and explained the content directly online. Students could ask the instructor questions through an online chat facility. In addition to chat questions, students were able to ask final questions directly to the presenter via the online platform at the end of the webinar. The study was conducted with

both groups on the same day, in different classrooms and at the same time. At the time of both lessons, all students in both groups were physically present in the classrooms. During the course of the study, there were no COVID-19-related restrictions, such as limitations on the number of students and social distance in our center. In both groups, the students were accompanied by a professor to solve any technical problems that might arise during the lesson. At the end of the lesson, the students completed a 10-question test with 3 possible answers and a single correct answer on the assimilation of the content covered in the lesson. This knowledge test was administered on the virtual campus but was conducted in person within the classroom, under the supervision of a professor. This arrangement ensured that students were unable to share information or answers during the test.

Statistical analysis

The results of the categorical variables were presented as absolute frequencies (n) and percentages (%). Quantitative variables were presented as means and typical deviations. The characteristics of the participants were compared using the chi-squared test for categorical variables and univariate T-Student and ANOVA tests for continuous quantitative variables. Linear regression was used to identify covariates (socio-demographic factors, self-efficacy and self-regulation) that might influence the results. In order to adjust the test scores for the type of educational intervention and the covariates that were significant in the linear regression models, the propensity score matching technique (logistic regression model) was used, which selects the individuals in a paired form based on the values obtained in each covariate, and inverse probability weighted regression (simple linear regression model), which weighted each observation by the values obtained in the covariates, with different weights (the model gives high weight to subjects who obtain low values in the covariates and low weight to those who obtain high values). The results were considered statistically significant with a significance level of $p < 0.05$. All data analyses were performed using SPSS version 24 for Windows.

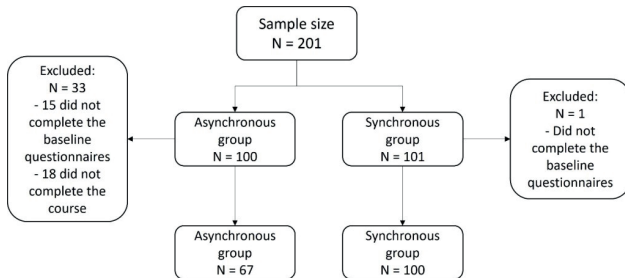
Ethical and legal aspects

The tenets of the Declaration of Helsinki on biomedical research involving human subjects have been always followed. All students were informed of the aims and conditions of the research and signed an informed consent form stating that participation was completely voluntary and anonymous, that they were free to withdraw from the study at any time without giving any reason, and that participation did not entail any advantage or disadvantage for the students. In accordance with current legislation on the protection of personal data, the confidentiality and privacy of the data have always been respected. Data were entered into secure databases and access to data was restricted to researchers. Data analysis was restricted to the purposes of this study. The research protocol was approved by the University Research Committee.

Results

Of the total number of students (201), 167 completed the study, 100 in the SG and 67 in the AG (Figure 1). 85.6% (n = 143) were women.

Figure 1: Distribution of students by groups.



Note: AG: Asynchronous group. SG: Synchronous group.

The mean age was 20.72 (6.86) years. Most students lived with their parents (73.05%), and half (56.3%) did not work or volunteer (Table I).

No differences were found between the groups in self-efficacy scores and in all subscales of self-regulation (planning, execution and evaluation) (Table II).

No differences were found in the age of the participants between the groups (IG: 19.62 vs. GC: 21.46; $t = -1.89$; $p = 0.06$) or by gender ($X^2 = 0.08$; $p = 0.78$), type of cohabitation ($X^2 = 2.88$; $p = 0.41$) or employment status ($X^2 = 0.83$; $p = 0.84$). There were no differences in the scores between the groups on the test following the

synchronous and asynchronous interventions (AG: 8.00 vs. SG: 7.95; $t = 0.24$; $p = 0.81$).

In the simple linear regression model to predict the effect of covariates on test scores, the regression equation for age was statistically significant, indicating that 39% of the variability in test scores was due to age differences, which were inversely related to test scores ($\beta = -0.04$). A statistically significant association was also found for the work variable ($F_3, 146 = 8.19$; $p = 0.002$), those who did not work in a remunerated and continuous way had a higher score than those who did work in a remunerated and continuous way ($\beta = 1.16$), explaining a variability in scores of 14.4%. No statistically significant associations were found between the level of self-efficacy and the processes of self-regulation of learning (planning and evaluation) with the test scores. However, the regression equation was statistically significant for the execution processes ($F_1, 148 = 4.06$; $p = 0.046$), the higher the score on the execution subscale, the higher the score on the test ($\beta = 0.31$), explaining 26.7% of the variability in the test scores.

Finally, the scores obtained by each group on the test were adjusted using the propensity and scoring technique, considering the scores obtained on the IPAA execution subscale, age and employment status. After adjusting for the covariates in the model, the difference between the groups' test scores did not reach statistical significance ($t = -0.60$, 95% CI: -0.61, 0.37; $p = 0.55$). In the inverse probability weighted linear regression model adjusting for IPAA performance scores, age and employment status, no statistically significant differences were observed between the groups in the test scores ($F_{1, 148} = 0.88$; $p = 0.35$).

Table I: Sociodemographic data between groups.

	Synchronous Group	Asynchronous Group	Total	p-value
	N=100 M (SD) / n (%)	N=67 M (SD) / n (%)	N=167 M (SD) / n (%)	
Age	21.46 (8.02)	19.62 (4.45)	20.72 (6.86)	0.95
Employment situation				0.86
Part-time paid job	12 (12.00%)	9 (13.43%)	21 (12.57%)	
Does not work	55 (55.00%)	38 (56.72%)	93 (55.69%)	
Full-time paid job	15 (15.00%)	7 (10.45%)	22 (13.17%)	
Volunteer	18 (18.00%)	13 (19.40%)	31 (18.56%)	
Type of cohabitation				0.56
With friends	15 (15.00%)	8 (11.94%)	23 (13.77%)	
With parents	71 (71.00%)	51 (76.12%)	122 (73.05%)	
In couple	10 (10.00%)	3 (4.48%)	13 (7.78%)	
None	2 (2.00%)	2 (2.99%)	4 (2.40%)	
Alone	2 (2.00%)	3 (4.48%)	5 (2.99%)	
Gender				0.78
Woman	85 (85.00%)	58 (86.57%)	143 (85.63%)	
Men	15 (15.00%)	9 (13.43%)	24 (14.37%)	

Table II: Differences in the self-efficacy and self-regulation scales by groups.

	Asynchronous Group	Synchronous Group	95% CI	p-value
	M (SD)	M (SD)		
General Self-efficacy Scale	29.39 (4,04)	29.62 (4,06)	(-1.71, 0.84)	0.50
Planning (IPAA)	3.80 (0,70)	3.71 (0,69)	(-0.15, 0.23)	0.66
Execution (IPAA)	4.00 (0,62)	3.96 (0,60)	(-0.15, 0.24)	0.66
Assessment (IPAA)	3.72 (0,76)	3.80 (0,79)	(-0.33, 0.17)	0.54

Note: IPAA: The Inventory of Self-Regulation Learning Processes.

Discussion

According to our results, we did not observe any differences in the scores of a knowledge test between the two e-learning based teaching strategies (synchronous vs. asynchronous). Regardless of the e-learning technique used, age, employment situation and level of self-regulation strategies affect test scores in such a way that the older the student, the lower the score; students who do not work continuously obtain better grades than those who work; and students who use more self-regulation strategies in the execution dimension obtain higher scores on multiple-choice knowledge tests.

The students who achieve better results are those who use more self-regulation strategies, which seems to confirm the idea that learning through active online strategies depends to a large extent on the student's ability to manage their own learning process through the use of executive strategies^{20,21}. Therefore, self-regulation of learning mediates between context, student characteristics and performance³² to better explain differences in performance between students and as a means of improving academic success³³.

We found no differences between groups in levels of self-efficacy, and no associations were found between grades and scores on the self-efficacy scale. However, other studies have found direct relationships between levels of self-efficacy and academic performance in terms of students' tendency to choose more difficult and challenging academic tasks^{24,34}. In addition, in a survey of 200 nursing students, Kim et al found that self-directed learning in online learning was a predictor of academic success³⁵. Razzak et al. found that students receiving online instruction in physiology preferred the asynchronous method to the synchronous method in which they adequately achieved the learning objectives³⁶. In a survey of 4 Korean universities, Park et al. found that the variables that predicted online learning success were learning flow, learning engagement, and self-directed learning³⁷. These findings reinforce the line of our results, that academic success depends on self-regulation through learning strategies. Vodovar et al, evaluating medical students, observed that students preferred the combination of online modality with face-to-face learning modality. In this combined modality, students attended more and had better academic success³⁸.

In a design very similar to ours, Mao et al. found no differences in outcomes between one online learning modality and the other, but did find that the level of active participation (participation in online discussions) was associated with better academic outcomes¹⁸. Similar to our study, Farros et al. found no differences between synchronous and asynchronous modalities in a test-based knowledge test¹⁹.

Based on the results obtained and the publications in this field, it is necessary to emphasise that, in order to improve

the academic learning process, a series of elements must be included: the use of open social networks that facilitate the process of self-direction of learning by students; the creation of activities with interactive and attractive content; the establishment of flexible deadlines for the submission of work in order to organise time; the use of technology and training in its use; and the support of self-regulation processes³⁹.

Study limitations and Future lines

This study was conducted with a sample of students from a single centre and a single degree, so the results cannot be generalized to other student populations. Studies with larger samples of students and other disciplines should be carried out to confirm the results of our study. In addition, it is important to contrast the data obtained from our two e-learning modalities with face-to-face learning to compare the influence of self-efficacy and self-regulatory processes on academic performance. The results obtained are from a single training session, which is characterized by its limited time frame. Ideally, these findings should be incorporated into more comprehensive training programs that provide a thorough understanding of content assimilation across different instructional models.

Educational Practice Implications

The study shows that there are no significant differences in knowledge acquisition between the two e-learning methods. Although asynchronous methods are less expensive and offer greater flexibility, making them a viable alternative for moderately complex topics, synchronous methods involve live instruction with the ability to resolve doubts immediately. Surprisingly, delivering content through recorded video that allows students to review at their own pace produces similar levels of comprehension and content acquisition. Disadvantages of synchronous methods include potential disruptions caused by student questions; a challenge not present in asynchronous settings. Efficiency is enhanced in asynchronous methods when alternative communication channels are allowed to resolve questions. To enhance the asynchronous approach, it is suggested that instructional videos be straightforward and that communication channels be provided for students to interact with instructors, thus promoting a more supportive learning environment.

Conclusions

In conclusion, there are no differences in academic performance in nursing students between both e-learning models. There is no evidence to confirm that nursing students who complete their education through a synchronous course score higher on a test of subject knowledge than those who complete their education asynchronously. Irrespective of the type of model, levels of self-regulation, employment status and age have an impact on e-learning.

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Conflict of interest

The authors declare that they have no competing interests.

Author contributions

LIMS: Conceptualisation, Methodology, Writing-Original draft preparation. FJGG: Conceptualisation, Methodology, Writing-Original and Editing. PRGD: Data curation, Visualisation, Software, Validation. CVA: Translation, Validation, Writing-Reviewing and Editing. GM: Writing-Reviewing and Editing; AMM: Writing-Reviewing and Editing. All authors have made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human subjects/patients were approved by the Ethics and Research Committee of the Faculty (approval number: FEFP 20/21, on 4 November 2020). All participants included in the study were informed, verbally and in writing, of the study objectives and conditions. Written informed consent was obtained from all participants.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to data protection policy but are available from the corresponding author on reasonable request.

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ORIGINAL

LC3 siRNA-Mediated Impressed Autophagy in GBM Cells Enhances the Efficacy of Temozolomide: Inhibits Proliferation, Clone Formation and Migration of U87-MG Cells

La autofagia impresa mediada por ARNip de LC3 en células GBM mejora la eficacia de la temozolomida: inhibe la proliferación, la formación de clones y la migración de células U87-MG

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Abstract

Objective: Autophagy is a catabolic process for degrading dysfunctional proteins and organelles and closely associated with cancer cell survival under therapeutic, metabolic stress, hypoxia, starvation and lack of growth factors, contributing to resistance to therapies. However, the role of autophagy in Glioblastoma (GBM) is not clarified.

Methods and results: In the present study, we investigated the role of autophagy in highly aggressive and metastatic GBM cells and demonstrated that the knockdown of light chain 3 (LC3) with LC3-siRNAs which is considered as potential markers of autophagic activity, inhibited autophagy and significantly suppressed cell proliferation, colony formation, migration in GBM cells. Also, combination of Temozolamide (TMZ) and LC3-siRNA significantly inhibited autophagic activity, cell proliferation, colony formation, migration in GBM cells. Furthermore, knockdown of LC3 led to inhibition of multiple proto-oncogenic signaling pathways, including cyclin D1, integrin- β 1/Src, and PARP1. Our findings suggest for the first time that LC3 are required for cell proliferation, survival, migration and may contribute to tumor growth and progression in by targeting cyclin D1, integrin- β 1, Src, and PARP1 oncogenic signaling in GBM cells.

Conclusion: Overall, these results suggesting, LC3-targeted combination treatments may be a potential therapeutic strategy for GBM and enhanced the efficacy of TMZ.

Key words: GBM, U87-MG, LC3-siRNA, Temozolamide, autophagy.

Resumen

Objetivo: La autofagia es un proceso catabólico para degradar proteínas y orgánulos disfuncionales y está estrechamente asociada con la supervivencia de las células cancerosas bajo estrés terapéutico, metabólico, hipoxia, inanición y falta de factores de crecimiento, contribuyendo a la resistencia a las terapias. Sin embargo, el papel de la autofagia en el glioblastoma (GBM) no está claro.

Métodos y resultados: En el presente estudio, investigamos el papel de la autofagia en células de GBM altamente agresivas y metastásicas y demostramos que el knockdown de la cadena ligera 3 (LC3) con LC3-siRNAs que se considera como marcadores potenciales de la actividad autofágica, inhibió la autofagia y suprimió significativamente la proliferación celular, la formación de colonias, la migración en células de GBM. Asimismo, la combinación de temozolamida (TMZ) y LC3-siRNA inhibió significativamente la actividad autofágica, la proliferación celular, la formación de colonias y la migración en células GBM. Además, el knockdown de LC3 condujo a la inhibición de múltiples vías de señalización proto-oncogénicas, incluyendo ciclina D1, integrina- β 1/Src, y PARP1. Nuestros hallazgos sugieren por primera vez que LC3 son necesarios para la proliferación celular, la supervivencia, la migración y pueden contribuir al crecimiento tumoral y la progresión en la ciclina D1, integrina- β 1, Src, y PARP1 señalización oncogénica en células GBM.

Conclusiones: En general, estos resultados sugieren que los tratamientos combinados dirigidos a LC3 pueden ser una estrategia terapéutica potencial para GBM y mejorar la eficacia de TMZ.

Palabras clave: GBM, U87-MG, LC3-siRNA, Temozolamida, autofagia.

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Introduction

Glioblastoma (GBM) is the most common¹, aggressive tumor characterized by poor prognosis and high recurrence rates, and is the most lethal type of primary brain tumors with a poor prognosis. The heterogeneity, high proliferation rates and aggressive behavior of GBMs make treatment difficult in GBM patients^{2,3}. Traditional treatment strategies for GBM patients are based on surgical resection of the tumor, temozolamide-based chemotherapy, radiotherapy, or a combination of these options^{4,5}. However, despite conventional chemotherapy and radiotherapy, patient response is still not at the desired level. Therefore, although great advances have been made in the treatment of GBM, the life expectancy of patients is very low^{4,6}.

Although temozolamide (TMZ) is the first-line therapy used in the chemotherapy of GBM, natural and acquired resistance conferred by multiple mechanisms causes treatment failure^{7,8}. To protect against TMZ cytotoxicity, GBM cells are thought to defend themselves against TMZ by inducing autophagy^{9,10}. Therefore, it is suggested that autophagy-targeted therapies in GBM will increase the efficacy of conventional therapies^{9,11-13}.

Autophagy is consistently used by both normal and cancer cells and is an evolutionarily conserved catabolic process involving lysosome-dependent degradation of defective cytoplasmic materials and organelles¹⁴⁻¹⁶. In normal cells; autophagy can play a role as a tumor suppressor mechanism for eliminating toxic materials, damaged organelles, misfolded proteins, and reducing oxidative stress and protecting cells from genetic damage¹⁷. And also, autophagy may act as a survival pathway under conditions such as starvation, hypoxia and therapy-induced stress in tumor cells¹⁵. Because of autophagy in cancer cells, it is suggested that suppression of autophagy will increase the anti-cancer therapeutic effect¹⁸⁻²⁰.

Autophagy is a highly complicated process regulated by expression of at least 15 genes and consists of several well-coordinated phases, including initiation, nucleation, elongation and fusion with lysosome. In these phases several autophagy-related (Atg) genes/proteins including microtubule-associated light chain 3 (LC3, homolog of yeast Atg8 gene) play an important role and are often considered as potential markers of autophagic activity^{14,16}. LC3 exists in two forms, LC3-I and LC3-II (a LC3- phospholipid conjugate). LC3-I is localized in the cytoplasm under normal conditions. When autophagy is induced by various stresses (such as starvation, hypoxia and growth factor deprivation), a cytosolic form of LC3 (LC3-I) is converted to LC3-II, by conjugation of a lipid molecule called phosphatidyl ethanolamine (PE) for incorporation into membrane of autophagosomes. Therefore, LC3-II is a marker of autophagy^{14,15,21}. We also believe that LC3 can be used as a therapeutic target in

cancer. However, data on LC3 in glial tumors are scarce and further research is needed on this subject.

In the present study, we investigated the role of LC3 in GBM cells, and demonstrated that LC3 gene is involved in promotion of cell proliferation, colony formation and migration in highly metastatic GBM cells. In addition, we found that LC3 expression is involved in expression of cyclin D1, integrin- β 1 and PARP proteins as well as the activity of Src, all of which are well known as mediators of the cell cycle, cell survival, and cell migration. Further more we demonstrated that LC3-siRNA and TMZ combination significantly suppressed GBM cell proliferation, colony formation and migration more and LC3 specific siRNAs enhanced effect of TMZ in GBM cells. Overall, our findings suggesting for the first time that LC3 may contribute to GBM cell growth, survival and progression, and also combination of LC3-siRNA and TMZ may be a good alternative therapeutic strategy in GBM therapy.

Materials and methods

Cell lines, culture conditions, and reagents

Human U87-MG (cat# HTB-14) cell was purchased from the American Type Culture Collection (Manassas, VA, USA). U87-MG cell line was cultured in Dulbecco's Modified Eagle's Medium (DMEM)/F12 supplemented with 10% fetal bovine serum (Sigma-Aldrich, St. Louis, MO). Temozolamide (TMZ) (CAS: 85622-93-1 was purchased from Sigma-Aldrich (St. Louis, MO) and was dissolved in Dimethyl sulfoxide (DMSO) (Sigma Aldrich, D2650) to prepare stock solution. The stock solution of TMZ was diluted within FBS free medium and applied to U87-MG cells at different concentrations for 72h.

Transfection with siRNA

Two different small interfering RNAs (LC3#1 siRNA, SASI_Hs02 00356118_AS, 50nM, Sigma-Aldrich LC3#2 siRNA, SASI_Hs01 00212378_AS, 50nM, Sigma-Aldrich) targeting LC3 gene and non-silencing control siRNA (Cat# WD00909801) were purchased from Sigma-Aldrich. Exponentially growing U87-MG GBM cells were plated 24h before transfection and transfected with two different LC3 siRNAs or control siRNA at a final concentration of 50 nM for 72h, using HiPerFect Transfection Reagent (Qiagen, Valencia, CA) according to the manufacturer's protocol. Non-silencing control siRNA-transfected cells were used as negative controls²²⁻²⁵. After treatment, the cells were harvested and processed for further analysis.

Western blot analysis

For western blot analysis, cells were seeded in T-25 culture U87-MG cells were transfected with siRNAs (50 nM) for 72h. Then, the cells were collected, washed twice in ice-cold phosphate-buffered saline (PBS) and lysed in a lysis buffer at 4°C. The protein concentrations were measured with a protein assay kit (DC kit; Bio-

Rad, Hercules, CA). A total of 40 µg of protein from each sample was separated by Sodium dodecyl sulfate (SDS) - polyacrylamide gel electrophoresis with a 4-20% gradient and transferred to polyvinylidenedifluoride membranes. The membranes were blocked with a blocking buffer (0.1 Triton X-100 with 5% dry milk in Tris-buffered saline-Tween 20 (TBS-T) for 60min. After being washed with TBS-T, the membranes were probed with the following primary antibodies: LC3 (2775S, Cell Signalling) Cyclin-D (60186-1-IG, Proteintech), Integrin-β (12594-1-IG, Proteintech), pSrc (2101S, Cell Signalling), Src (11097-1-AP, Proteintech), and β-actin (60008-1-IG, Proteintech). After being washed with TBS-T, the membranes were incubated with horseradish peroxidase-conjugated anti-rabbit (Bio-Rad, #170-6515) or anti-mouse secondary antibody (Biorad, #1706515). β-actin was used as a loading control. All antibodies were diluted in TBS-T containing 5% dry milk. Chemiluminescence detection was performed with Clarity Western ECL Substrate (Biorad) and the blots were visualized with a ChemiDoc MP Imaging System (Biorad) and quantified with a densitometer using the ChemiDoc MP Imager application program (Biorad)²³⁻²⁶.

Cell viability and proliferation assays

Cell viability and proliferation were measured by MTS (3-(4, 5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium) assay (Promega, Madison, WI) as described previously [24-26]. U87-MG cells were seeded in 96-well plates (1.20 x10³ cells/well) and treated with increasing doses of TMZ (10, 20, 40, 80, 100, 200, 400, 500 and 600 µM). Also, U87-MG cells were seeded in 96-well plates (1.20 x10³ cells/well) and transfected with siRNAs (50 nM) for 72h. Furthermore, U87-MG cells were seeded in 96-well plates (1.20 x10³ cells/well) and treated with TMZ (20 and 40 µM) and at the same time transfected with siRNAs (50 nM) for 72h. Following treatments, a solution containing MTS and phenazine methosulfate (20:1 v/v) was added to the cells. After 3h of incubation at 37°C, the number of viable growing cells was estimated by measuring absorption at 490 nm using Elisa Reader based on generation of formazan by the cells²³⁻²⁶.

Detection of Acidic Vesicular Organelles (AVOs)

Autophagosomes were detected by formation of acidic vesicular organelles (AVOs). AVOs were acridine orange staining was performed²⁷. Briefly, cells were seeded in 6-well plates (1x10⁵ cells/2 ml medium). U87-MG cells were treated with TMZ (20 and 40 µM) for 72h. Also, U87-MG cells were seeded in 6-well plates (1x10⁵ cells/2 ml medium) and transfected with siRNAs (50 nM) for 72h. Furthermore, cells were seeded in 6-well plates (1x10⁵ cells/2 ml medium) and treated with TMZ (20 and 40 µM) and at the same time transfected with siRNAs (50 nM) for 72h. Following treatments, the cells were stained with 1 µg/ml acridine orange for 15min AVO staining was examined using a fluorescence microscope (Nikon Eclipse Ti)^{24,28}.

Colony formation and Clonogenic assays

U87-MG cells were seeded in 6-well plates (1.5 x 10³ cells/ well) and treated with TMZ (20 and 40 µM) and incubated at 37°C for 2 weeks to form colonies. Also, cells were seeded in 6-well plates (1.5 x 10³ cells/well) transfected with a non-silencing control siRNA or LC3 siRNAs (50 nM) and grown for 2 weeks. Furthermore, cells were seeded in 6-well plates (1.5 x 10³ cells/well) and treated with TMZ (20 and 40 µM) and at the same time transfected with siRNAs (50 nM) and grown for 2 weeks. Then, the cells were washed with PBS and stained with crystal violet, and visible colonies were counted^{23-26,28}.

Cell migration and motility assay

U87-MG cells were seeded in 6-well plates (5 x 10⁵ cells/well) and treated with TMZ (20 and 40 µM) for 72h. Also, cells were seeded in six-well plates (5 x 10⁵ cells/well) and transfected with the control siRNA or two different LC3 siRNAs (50 nM) for 72h. Furthermore, U87-MG cells were seeded in 6-well plates (5 x 10⁵ cells/well) and treated with 20 and 40 µM TMZ at the same time transfected with siRNAs for 72h. Following treatments each cell monolayer was carefully scratched using a 20-µl sterile tip and cellular debris was removed by washing with medium, which was then replaced with fresh medium. Cells in the scratched area were imaged at start and 24h using light microscopy, and the distance traveled by cells at the leading edge of the wound was measured at each time point. The results were expressed as average distance between the edges of the gap^{23,24}.

Statistical analysis

All experiments were conducted at least in triplicate, and the results were summarized as means with Standard Deviations (SD). Statistical significance was determined using the Student-t test. P- values less than 0.05 were considered statistically significant.

Results

TMZ inhibits MDA-MB-231 Cell Proliferation, Colony Formation and Migration

We first treated cells with TMZ in increasing concentration (10, 20, 40, 80, 100, 200, 400, 500 and 600 µM) for 72h. The MTS analysis revealed that TMZ treatment reduced cell proliferation of U87-MG cells compared to untreated (NT) and DMSO-treated control cells (**Figure 1**).

We found that 20 µM and 40 µM concentrations of TMZ treatment led to about 20% and 25% reduction in cell viability, respectively, in U87-MG cells compared to NT and DMSO-treated cells.

We then investigated the effects of TMZ on colony formation of U87-MG cells. TMZ treatment 20, 40 µM led to a significant reduction in the number of colonies in TMZ cells compared DMSO-treated cells, and 20 µM

and 40 μM concentrations of TMZ treatment led to about 30% and 40% reduction in cell viability, respectively, of U87-MG cells compared to NT cells and DMSO-treated cells (**Figure 2**). However, TMZ treatment at doses starting at 400 μM and 600 μM led to almost complete elimination viable cells.

We also investigated the effects of TMZ on motility and migration of U87-MG cells using wound healing or scratch assay. After 72h of treatment with TMZ (20, 40 and 80 μM), a single scratch wound was created in wells and the cells were monitored for 24h. While the control cells treated with DMSO, the wounded areas completely closed by migrating into the open areas, TMZ treated cells had a larger open areas with much less number of cells at 24h time point. In treated cells with TMZ in increasing concentrations (20, 40 and 80 μM), the width of the wound was found to be between mean 120-150 μm compared to NT and DMSO-treated cells (**Figure 3**).

TMZ inhibits autophagic activity in U87-MG cells

GBM cells represent highly aggressive and metastatic phenotype of brain tumors that are known to be relatively resistant to chemotherapeutics^{29,30}. The development of resistance often limits the therapeutic benefit of temozolomide, particularly in GBM. A number of resistance mechanisms have been proposed including the development of cytoprotective autophagy. Therefore, we first investigated the effect of TMZ on autophagic activity.

Autophagy is characterized by the formation of acidic vesicular organelles (AVOs), which represent formation of autophagolysosomes. AVOs were detected by acridine orange (AO) staining, which stain nuclear and cytoplasm with bright green color, while it stains AVOs with bright red color^{24,25,28}. After treatment with TMZ, (20 and 40 μM) U87-MG cells were examined by inverted fluorescence microscope (Nikon Eclipse Ti-E) using green filter. FITC, excitation wavelength: 465-495 nm; dichroic mirror (DM): 505 nm) and red filter (Tx Red, excitation wavelength: 540-580 nm; dichroic mirror (DM): 595 nm). The percentage of cells with redfluorescence stains (indicating AVOs) was calculated. We found that that TMZ treatment led to about only 30% reduction of autophagosome formation in U87-MG cells compared with control cells (DMSO-treated cells) by AO staining (**Figure 4**). Therefore, we thought that continued autophagic activity may reduces the therapeutic effects of TMZ against GBM cells.

LC3 siRNA inhibits autophagic activity and suppresses cell proliferation, colony formation and migration in U87-MG cells

LC3 considered important mediators of autophagy^{24,31,32}. Therefore, to clarify the function of LC3 and autophagic process in cells, we knocked down LC3 in U87-MG cells and investigated the effects on cell proliferation, clonogenicity and migration compared to the control cells transfected with control siRNA. We first demonstrated

that siRNA mediated knockdown of LC3 using two different siRNAs (72h). The siRNAs targeted LC3 mRNA efficiently reduced expression of LC3-I and LC3-II proteins (**Figure 5**). These results showed that the LC3 siRNAs can effectively knockdown LC3 expression in the U87-MG. Also, we found that LC3#2 siRNA suppressed expression of LC3 more than LC3#1 siRNA in cells.

Next, to investigate the effect of LC3 silencing in inhibition of autophagy we also evaluated autophagy induction in U87-MG cells. The cells were seeded in a six-well plates and transfected with LC3, or control siRNA for 72 hours. and stained with AO to detected AVOs by fluorescent microscopy. Knockdown of LC3 efficiently suppressed autophagy as evidenced by reduced AVO formation compared to control siRNA transfected cells (**Figure 4**).

Then, we tested the effect of LC3 knockdown on cell proliferation, viability and colony formation or clonogenicity. To this end, U87-MG were transfected by LC3 siRNAs and 72h later cell viability was detected by MTS assay. Cell viability was significantly reduced after LC3 knocked down in U87-MG cells as examined by MTS assay (**Figure 1**).

We next examined the effects of LC3 siRNAs on cell colony formation in U87-MG cells by using a clonogenic assay. Knockdown of LC3 in U87-MG cells resulted in a marked reduction of colony formation (**Figure 2**).

Then, to assess whether autophagy is involved in cell motility migration of GBM cells, we performed an in vitro scratch or wound healing assay. GBM cells were seeded in a six-well plates and transfected with LC3 siRNAs. 72h after transfections, a single scratch wound was created in the well, and the cells were monitored for 24h. While some cell migration was observed in the wounded (sctracted) areas in control cells (control siRNA transfected) and the wounded areas were completely closed by migration of cells (24h), in LC3 knocked down cells, indicating that cells with reduced LC3 expression were unable to migrate (**Figure 3**). These data demonstrated that autophagy is essential for survival, proliferation, colony formation and migration of GBM cells.

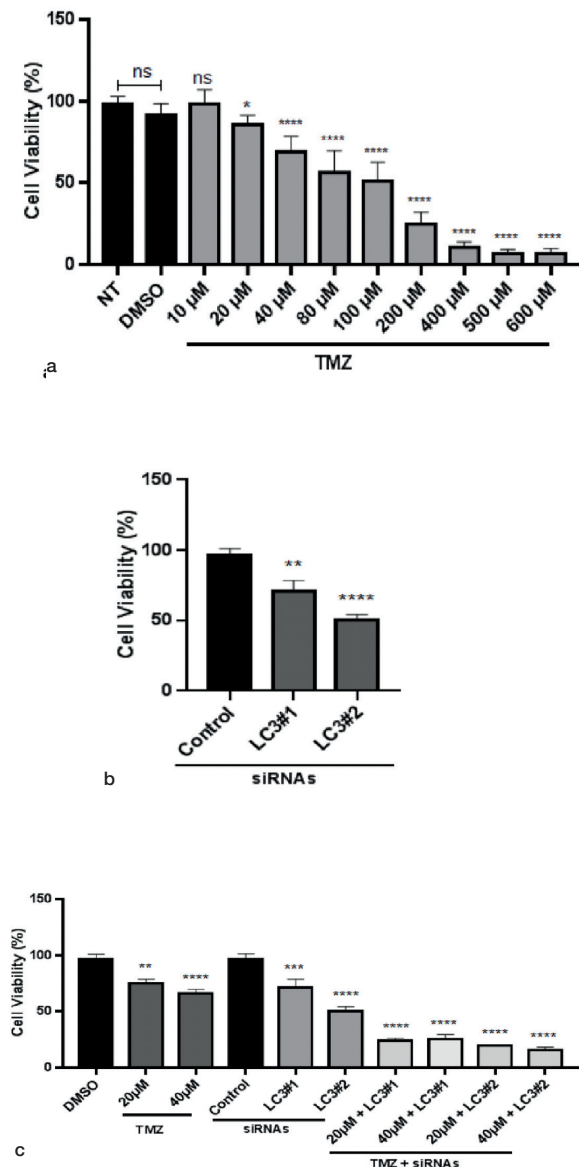
Combination of LC3 siRNA and TMZ significantly suppresses autophagic activity and inhibits cell proliferation, colony formation and migration in U87-MG cells

Glioblastoma multiforme (GBM) remains one of the most challenging solid cancers to treat due to its highly aggressive and drug resistant nature²⁹. Therefore, to test whether suppressed LC3 increases the sensitivity of cells to TMZ, we investigated the effect of the combination of TMZ and siRNA on cell viability, clonogenicity and migration. To this end, U87-MG cells were seeded in 96-well plates (1.20×10^3 cells/well) and treated with 20 and 40 μM TMZ and at the same time transfected with siRNAs (50 nM) for 72h later cell viability was detected by

MTS assay. The MTS analysis revealed that LC3 siRNA and TMZ combination treatment significantly reduced cell proliferation of U87-MG cells compared to LC3-siRNA transfected and TMZ treated cells (Figure 1).

We next examined the effects of LC3-siRNA and TMZ combination treatment on cell colony formation in U87-MG cells by using a clonogenic assay, LC3 siRNA and TMZ combination treatment in U87-MG cells resulted in a marked reduction of colony formation (Figure 2).

Figure 1. LC3-siRNA and TMZ combination treatment inhibits cell proliferation in U87-MG cells. Cells were treated with increasing concentration of TMZ, and cell proliferation was evaluated after 72 h by MTS assay (a). U87-MG cells were transfected with indicated siRNAs and proliferation/ cell viability was detected by an MTS assay. LC3-siRNA-mediated knockdown of autophagy gene inhibits U87-MG cell proliferation/viability (b). Cells were treated with LC3-siRNA and TMZ combination, and cell proliferation was evaluated after 72 h by MTS assay. Combination of LC3-siRNA and TMZ significantly inhibit U87-MG cell proliferation (c). The data are presented as means with standard deviations. (ns: non-significant, *p < 0.05, **p < 0.01, ****p < 0.0001).



Even, LC3 siRNA and TMZ combination treatment led to almost complete elimination of colony formation. Then, to identify the effects of LC3 siRNA and TMZ combination treatment on cell motility and migration, U87-MG cells were treated with 20, 40 and 80 μ M TMZ and at the same time transfected with siRNAs (50 nM) for 72h. In LC3-siRNA and TMZ combination treatment in U87-MG cells were unable to migrate (Figure 3).

Figure 2. LC3-siRNA and TMZ combination treatment inhibits colony formation in U87-MG cells. Cells were treated TMZ and evaluated for colony formation by crystal violet staining at the end of the 14 days in U-87MG cells (a). U87-MG cells were transfected with two different LC3-siRNAs or control siRNA and evaluated for colony formation by crystal violet staining at the end of the 14 days (b). Cells were treated with LC3-siRNA and TMZ combination, and was evaluated for colony formation by crystal violet staining at the end of the 14 days (c). Colony areas measured densitometrically and image J at the at the end of the 14 days. The data are presented as means with standard deviations (d) (ns: non-significant, ****p < 0.0001).

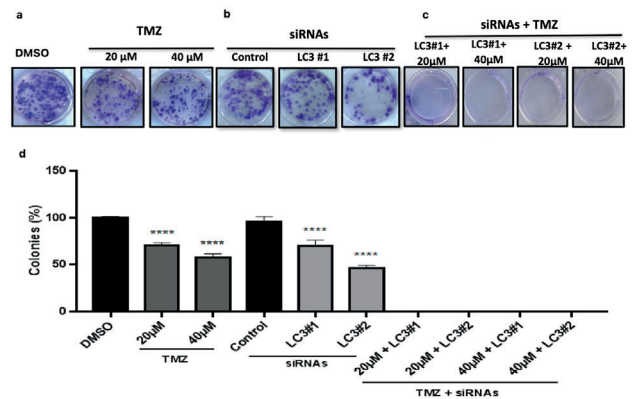
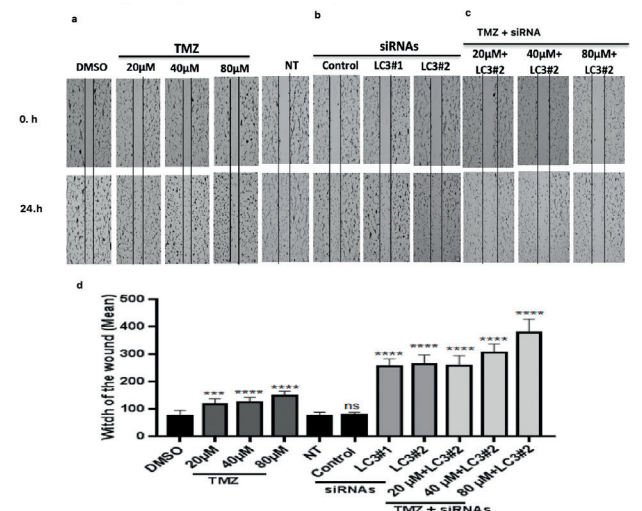


Figure 3. LC3-siRNA and TMZ combination treatment inhibits migration in U87-MG cells. Cells were treated with TMZ and evaluated after 72 h for migration and visualized by light microscopy. (a). Cells were transfected with two different LC3 siRNAs. The cell migration was visualized by light microscopy (b). Cells were treated with LC3-siRNA and TMZ combination, and cell migration was visualized by light microscopy (c). Cell migration was measured by a scratch wound healing assay. A single scratch was made in the center of the confluent cell monolayer. Images were taken immediately (0 h), and after 24 h of scratching the cultures. The bar graph shows the percentages of the migrating cells to scratched/wounded area, and the data are presented as means with standard deviations (d) (ns: non-significant, ****p < 0.0001).



To investigate the effect of combination of LC3-siRNA and TMZ in inhibition of autophagy we also evaluated autophagy induction in U87-MG cells. The cells were seeded in a six-well plates and transfected with LC3-siRNA treated with 20 and 40 μ M TMZ for 72 hours were stained with AO to detected AVOs by fluorescent microscopy. LC3-siRNA and TMZ combination efficiently suppressed autophagy as evidenced by reduced AVO formation (Figure 4).

These results showed that LC3-siRNA by suppressing autophagy and increased sensitivity and efficiency against TMZ in U87 cells.

Figure 4. LC3-siRNA and TMZ combination treatment decreases autophagy in U87-MG cells. Formation of acidic vesicular organelles (AVO) were detected in U87 cells following TMZ treatments by AO staining and fluorescent microscopy (a). Formation of AVO in transfected cells with indicated siRNAs were demonstrated by AO staining and fluorescent microscopy (b). Cells were treated with LC3-siRNA and TMZ combination, and formation of AVO was visualized by AO staining and fluorescent microscopy (c). The data are presented as means with standard deviations (d) (ns: non-significant, ****p <0.0001).

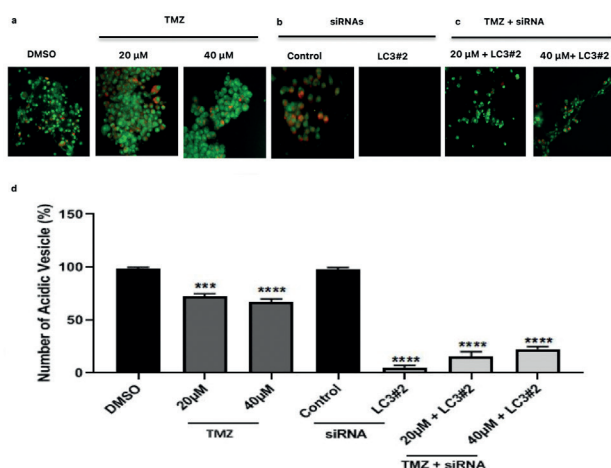
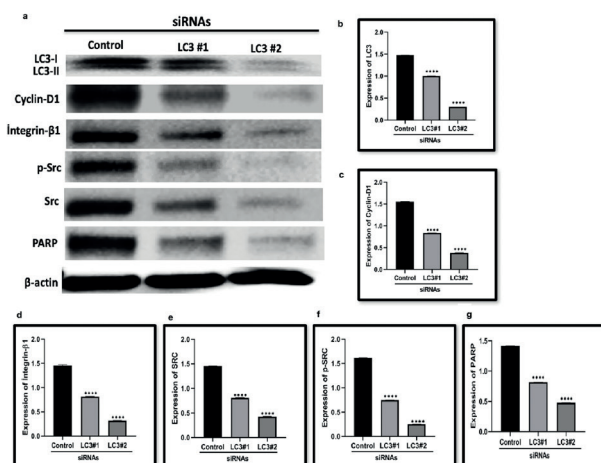


Figure 5. Down-regulation of autophagy by LC3 siRNAs inhibits expression of mediators of the cell cycle, cell survival, and cell migration. Cells were transfected with 50 nM LC3 siRNA or control siRNA. Protein extracts were isolated 72 h after transfection. β -Actin was used as a loading control. Knockdown of LC3 by siRNA decreased expression levels of Cyclin D, Integrin β 1 and p-Src, Src and PARP. α / β -Tubulin was used as a loading control. The data are presented as means with standard deviations (d) (ns: non-significant, ****p <0.0001).



Knockdown of LC3 inhibits mediators of the cell cycle, survival, and cell migration/invasion in U87-MG cells

To elucidate the molecular mechanisms by which autophagy inhibition reduces cell survival, migration and invasion we investigated related signaling pathways after knockdown of autophagy-regulating gene (LC3). We found that inhibition of autophagy markedly reduced the expressions of cyclin D1, which promotes the cell cycle by inducing G1 phase, Integrin- β 1/p-Src, both of which are the most important mediators of cell survival, migration and invasion²³⁻²⁵, PARP, which is involved in DNA repair and cell death, and plays an important role in GBM (Figure 5). Overall, our findings suggest that LC3 may provide protumorigenic effects by inducing important signaling pathways in U87-MG cells.

Discussion

Genomic studies on tumour cells from GBM patients have shown that mutations in multiple signalling pathways have an effect on regulating autophagy (33). Furthermore, in GBM cell cultures, autophagy has been observed to be frequently activated as a stress response upon treatment with therapeutic agents³⁴. Cellular and xenograft experiments suggest that autophagy plays an important role in GBM^{12,35}. Mouse studies have also shown that autophagy is necessary for GBM growth³⁶.

The present study showed that suppression of LC3, the main element of autophagy mechanism, by two different siRNAs significantly inhibited cell proliferation, viability and migration. Thus, it was shown that autophagy inhibition via LC3 inhibits cell proliferation, clone formation and migration in GBM cells.

In addition, the present study showed that suppression of LC3 expression in GBM cells via two different LC3-siRNAs suppressed CyclinD1/Integrin β 1/Src signalling expression, which is involved in cell proliferation, viability, and migration, and PARP expression, which plays an important role in DNA repair and cell death.

As previously reported, TMZ is an alkylating agent used in the first line chemotherapy of GBM⁷. However, although TMZ is the first-line chemotherapy for glioma patients, natural and acquired resistance provided by multiple mechanisms leads to treatment failure. Studies have shown that TMZ induces autophagy¹⁰. It has also been shown that pharmacological inhibition of autophagy at different stages has different results on TMZ-induced autophagy. However, in the present study, TMZ (20 and 30 μ M) was found to suppress autophagy by 30% in U87-MG cells. Accordingly, it was found that cell viability decreased by approximately 20-25% in cells treated with 20 and 30 μ M TMZ. For all these reasons, inhibition of the autophagic process is thought to significantly affect the antitumour effect of TMZ¹⁰.

In the light of all these, it was thought that suppression of LC3 by two different LC3-siRNAs, which are markers of autophagy, and LC3-siRNA-mediated suppressed autophagy would increase the anticarcinogenic activity of TMZ in U87-MG cells. LC3-siRNA and TMZ were co-administered simultaneously. The combination of LC3-siRNA and TMZ significantly decreased cell viability, clonogenic formation and migration compared to TMZ-treated cells. This result indicated that LC3-siRNA-mediated suppressed autophagy may increase the sensitivity of U87-MG cells to TMZ.

In addition, our study demonstrated for the first time that when the expression of LC3 was suppressed by two different LC3 siRNAs, the expression of PARP protein was also significantly suppressed. Poly (ADP-ribose) polymerase 1 (PARP) is a protein involved in DNA repair and cell death and is generally highly expressed in cancers³⁷. Our results showed that autophagy promoted cell survival by preventing apoptotic cell death in GBM cells. Our study also showed for the first time that suppression of LC3 expression in GBM cells through two different LC3-siRNAs suppresses CyclinD1/Integrin β 1/Src^{22,23} expression, which is involved in cell proliferation, viability, adhesion and migration, and leads to inhibition of Src-phosphorylation.

GBMs are aggressive brain tumours characterised by poor prognosis and high recurrence rates and are the most lethal type of primary brain tumours with poor prognosis. The heterogeneity, high proliferation rates and aggressive behaviour of GBMs make the treatment of GBM patients difficult. Therefore, although great advances have been made in the treatment of GBM, the survival of patients is still very low^{4,6}.

Conventional treatment strategies for GBM patients are based on tumour resection (neurosurgery), TMZ-based chemotherapy, radiotherapy or a combination

of these options⁴. However, patients respond poorly to conventional chemotherapy and radiation.

In particular, temozolomide (TMZ) is used as an effective chemotherapeutic in the treatment of GBM^{38,39}. However, GBM cells become resistant to TMZ-induced cytotoxicity and this resistance limits the efficacy of TMZ^{9,40}. To protect against TMZ cytotoxicity, GBM cells are thought to defend themselves against TMZ by inducing autophagy^{9,10}. Therefore, autophagy-targeted therapies in GBM are suggested to improve the efficacy of conventional therapies^{9,11,13}.

Conclusion

Our results showed that LC3, and thus autophagy, promotes important oncogenic biological processes such as GBM cell survival, proliferation, migration and resistance to apoptosis and that LC3-siRNA-mediated suppression of autophagy significantly blocks these mechanisms and that autophagy may be a critical factor in the progression of GBM and that LC3, and thus autophagy, represents a potential therapeutic target in the treatment of GBM. LC3-targeted combination therapies may be a potential therapeutic strategy for GBM and may enhance the efficacy of TMZ. Therefore, our results suggest that the combination of LC3-siRNA and TMZ may be a novel therapeutic strategy for the treatment of GBM. Further research is needed for this, and it is suggested that these results obtained in vitro should be transferred to in vivo environment and their effects in the living body should be revealed.

Conflict of interest

The authors declare that they have no competing interests.

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ORIGINAL

Enfermedad de la Peyronie y radiofrecuencia capacitiva resistiva: estudio piloto y evaluación preliminar

Peyronie's disease and capacitive resistive radiofrequency: pilot study and preliminary evaluation

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Resumen

Objetivo: a) valorar el efecto de la radiofrecuencia capacitiva resistiva (TECAR terapia) más terapia manual sobre el dolor, la curvatura y el tamaño de la placa en una serie de pacientes con enfermedad de la Peyronie (PE); b) reportar efectos adversos.

Material y métodos: estudio prospectivo a 8 pacientes, edad media 53.87 ± 13.44 años. Criterios inclusión: a) mayores de 18 años; b) EP de 6 meses; c) curvatura $> 30^\circ$ según Test de Kelami; d) dolor mayor a 3 según escala visual analógica (EVA). Criterio exclusión: a) marcapasos cardíaco o neuroestimulador sacro. Variables de resultado: a) dolor (EVA 0-10); b) curvatura del pene (Test de Kelami); c) tamaño de la placa evaluado por ecografía lineal. Estas variables se analizaron al inicio y al término del tratamiento. Tratamiento, 12 sesiones de Radiofrecuencia capacitiva resistiva (TECAR terapia), 15 minutos tipo resistivo, 2 veces / semana.

Resultados: Se pautaron 12.87 ± 6.64 sesiones (rango 8-24 sesiones). Ningún paciente reportó efectos adversos (0%). El dolor disminuyó de 6.25 ± 1.03 a 1.25 ± 1.75 puntos ($p=0.0002$). El tamaño de la placa disminuyó de 9.4 ± 5.12 a 3.06 ± 2.68 mm ($p=0.0462$). La curvatura disminuyó de 48.75 ± 16.85 a 38.12 ± 17.30 grados ($p=0.0081$).

Conclusión: Un protocolo de 12 sesiones de radiofrecuencia resistiva es capaz de disminuir el dolor, la curvatura y el tamaño de la placa fibrótica en una pequeña serie de pacientes con EP. No se han reportado eventos adversos tras este protocolo. Interesa ampliar la muestra para confirmar la tendencia observada en este estudio.

Palabras clave: Enfermedad de Peyronie, radiofrecuencia capacitiva resistiva, tecarterapia.

Abstract

Objective: a) to assess the effect of capacitive resistive radiofrequency (TECAR therapy) plus manual therapy on pain, curvature and plaque size in a series of patients with Peyronie's disease (PD); b) report adverse effects.

Material and methods: prospective study of 8 patients, mean age 53.87 ± 13.44 years. Inclusion criteria: a) over 18 years of age; b) 6-month PD; c) curvature $> 30^\circ$ according to the Kelami Test; d) pain greater than 3 according to the visual analogue scale (VAS). Exclusion criteria: a) cardiac pacemaker or sacral neurostimulator. Result variables: a) pain (VAS 0-10); b) penile curvature (Kelami test); c) plaque size assessed by linear ultrasound. These variables were analyzed at the beginning and at the end of the treatment. Treatment, 12 sessions of resistive capacitive Radiofrequency (TECAR therapy), 15 minutes resistive type, 2 times / week.

Results: 12.87 ± 6.64 sessions were scheduled (range 8-24 sessions). No patient reported adverse effects (0%). Pain decreased from 6.25 ± 1.03 to 1.25 ± 1.75 points ($p=0.0002$). Plaque size decreased from 9.4 ± 5.12 to 3.06 ± 2.68 mm ($p=0.0462$). The curvature decreased from 48.75 ± 16.85 to 38.12 ± 17.30 degrees ($p=0.0081$).

Conclusion: A protocol of 12 resistive radiofrequency sessions reduced pain, curvature, and the size of the fibrotic plaque in a small series of patients with PD. No adverse events have been reported after this protocol. It is interesting to expand the sample to confirm the trend observed in this study.

Key words: Peyronie's disease, capacitive resistive radiofrequency, tecartherapy.

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Introducción

La enfermedad de la Peyronie (EP) es una patología progresiva que origina curvatura y dolor del pene durante la erección. Se llama así en honor a Francois de la Peyronie, cirujano francés y fundador de la Real Academia de Cirugía, quien la describió en 1749. Sin embargo, esta patología fue previamente descrita en 1561 en una carta entre Andreas Vesalius y Gabriele Fallopio¹.

Dependiendo del país, se cree que la EP afecta del 0.3% al 20.3% de la población; así por ejemplo, en Estados Unidos de América, 1 de cada 10 hombres podrían padecer esta enfermedad^{1,2}. La EP puede causar dolor con o sin erección, incapacidad para la penetración, disfunción eréctil, estrés emocional, depresión, dificultades de pareja y para tener relaciones sexuales³.

La EP se debe a inflamación y fibrosis de la túnica albugínea, la cual es la capa que recubre los cuerpos cavernosos y permite al pene erectarse durante la excitación^{1,3}. La etiología es desconocida, aunque se atribuyen a factores genéticos y microtraumatismos repetidos¹. La presentación es más frecuente a los 50 años³.

El diagnóstico es eminentemente clínico. A la observación, con el pene en erección (por autofotografía) se puede objetivar la desviación o curvatura del pene, que según el Test de Kelami, es leve si $< 30^\circ$, moderado entre $30-60^\circ$, severo si $> 60^\circ$ ⁴. A la palpación, se puede objetivar y localizar la placa; mientras que por ecografía se puede apreciar la calcificación de la túnica albugínea, además de medir el tamaño de la misma^{1,3}.

Se han descrito comorbilidades asociadas tales como la diabetes, enfermedad cardiovascular y trastornos fibroproliferativos tales como enfermedad de Dupuytren, Ledderhose y esclerodermia¹.

Están descritas dos fases en la EP. La fase activa se caracteriza por la aparición de la curvatura y se acompaña de dolor durante la erección. En la fase estabilizada desaparece, se palpa la placa y la curvatura se estabiliza⁵.

Para evitar la progresión de la EP en la fase aguda se han propuesto varias terapias orales tales como la vitamina E, el para amino benzoato de sodio, tamoxifeno, colchicina, carnitina y pentoxifilina; con resultados muy variados⁵. En la fase estabilizada se han propuesto infiltraciones perilesionales tales como corticoides, verapamilo, colagenasa derivada de *Clostridium histolyticum*, Interferón (IFN- α) e Iloprost (prostaciclina sintética). También se han propuesto terapias físicas tales como la terapia de succión de vacío, aparatos para tracción de pene, iontoforesis y ondas de choque extracorpóreas⁵. Los pacientes que fracasen a los tratamientos conservadores descritos previamente son candidatos a la cirugía. Se ha

descrito técnicas tales como la plicatura, la exéresis de la placa fibrosa y colocación de injerto^{1,5}. Pacientes con mala función eréctil son candidatos a prótesis de pene⁵.

Actualmente existe un creciente interés en el manejo de la EP. En Urología el principal tratamiento no quirúrgico de la EP es la colagenasa de *Clostridium histolyticum*, la cual disminuye la curvatura al menos en un 30%³; pero, desde que se ha decidido dejar de comercializar el producto en Europa a partir del 31 diciembre del 2019 por motivos puramente comerciales⁶, los especialistas en el manejo de la EP han decidido buscar otras alternativas conservadoras. En ese sentido, Pavone ha presentado recientemente un estudio de tolerabilidad de la radiofrecuencia capacitiva resistiva (TECAR terapia) en el manejo de la EP realizado en 70 pacientes⁷; además ha presentado un reciente estudio randomizado en 96 pacientes evaluando el efecto terapéutico sobre la EP, actuando básicamente sobre el dolor⁵.

El objetivo del presente estudio es valorar en un protocolo preliminar el efecto de la radiofrecuencia resistiva (TECAR terapia) más terapia manual sobre el dolor, la curvatura y el tamaño de la placa en una serie de pacientes, además de reportar efectos adversos, en caso de suceder.

Material y métodos

Hemos estudiado prospectivamente a 8 pacientes con una edad media de 53.87 ± 13.44 años. Los pacientes autorizaron el tratamiento y firmaron el consentimiento informado. El estudio ha sido autorizado por el Comité de ética del Hospital.

Los criterios de inclusión fueron: a) mayores de 18 años; b) con EP de 6 meses; c) curvatura $> 30^\circ$ según Test de Kelami⁴; d) dolor mayor a 3 según escala visual analógica (EVA).

El criterio de exclusión fue: a) presencia de marcapasos cardíaco o neuroestimulador sacro, los cuales contraindican de manera absoluta la técnica.

Las variables de resultado fueron: a) dolor medido por EVA (0-10); b) curvatura del pene evaluada por autofotografía (Test de Kelami⁴); c) tamaño de la placa evaluado por ecografía lineal. Estas variables se analizaron al inicio y al término del tratamiento.

Los pacientes recibieron 12 sesiones. El tratamiento consistió en la aplicación de radiofrecuencia capacitiva resistiva (TECAR terapia) a 448 KHz (Indiba Activ Recovery, Barcelona, España). El fundamento del tratamiento es que la TECAR terapia produce estimulación celular, vasodilatación y aumento de la temperatura del área tratada, lo cual estimula los procesos de reparación y replicación celular^{5,7}. Los pacientes recibieron 2 sesiones/semana hasta completar 12 sesiones. El

tiempo de tratamiento fue de 15 minutos de modalidad resistiva, colocando el aplicador que corresponda sobre la placa fibrótica, acompañado de terapia manual. La intensidad del tratamiento se estableció entre una escala de sensibilidad analógica subjetiva (SAS) entre 6-7, donde el 0 significa "sin sensación térmica" y 10 equivale a "la mayor sensación térmica posible"^{5,7}.

Para el análisis estadístico de los casos utilizamos el programa SPSS v.20 (IBM, Michigan, USA). Para valorar las variables cualitativas se usaron porcentajes; mientras que para las variables cuantitativas se utilizaron medias y desviaciones estándar. Para evaluar el cambio de las variables cuantitativas antes y después del tratamiento se utilizó la prueba estadística U de Mann-Whitney. La significación estadística se estableció al 95% ($p < 0.05$).

Resultados

Se han analizado a 8 pacientes con EP. Las características básicas de la muestra se describen en la **tabla I**. La edad media de la muestra fue 53.87 ± 13.44 años. Los pacientes recibieron 12.87 ± 6.64 sesiones (rango de 8 a 24 sesiones) y ninguno de los pacientes tratados reporto efectos adversos (0%).

Tabla I: Características principales de los pacientes tratados (n=8).

Variabes	Valor	DE
Edad	53,87	13,44
Tiempo enfermedad	6,2	1,8
Número sesiones	12,87	6,64
Tolerabilidad (%)	100	
Reacciones adversas (%)	0	

DE, desviación estándar. %, porcentaje.

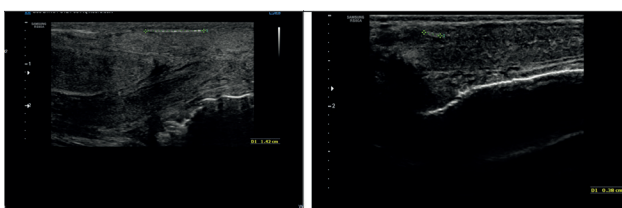
El dolor disminuyó de 6.25 ± 1.03 a 1.25 ± 1.75 puntos y con diferencia estadística ($p=0.0002$). El tamaño de la placa disminuyó de 9.4 ± 5.12 a 3.06 ± 2.68 mm y con diferencia estadística ($p=0.0462$). La curvatura, evaluada por el Test de Kelami (autofotografía) disminuyó de 48.75 ± 16.85 grados a 38.12 ± 17.30 grados, y de manera estadísticamente significativa ($p=0.0081$). **Tabla II y figura 1**.

Tabla II: Características principales de los pacientes tratados (n=8).

Variabes de resultado	Antes	Después	P
Dolor EVA 0-10	$6,25 \pm 1,03$	$1,25 \pm 1,75$	*0,0002
Curvatura (grados)	$48,75 \pm 16,85$	$38,12 \pm 17,30$	*0,0081
Tamaño placa (mm)	$9,4 \pm 5,12$	$3,06 \pm 2,68$	*0,0462

P, significación estadística. *, $p < 0.05$.

Figura 1: Se aprecia en este paciente, que tras 12 sesiones de Radiofrecuencia capacitiva resistiva, la placa de calcificación disminuyó de 14,2 mm a 3,8 mm.



En esta serie, las variables dolor, tamaño de placa y curvatura del pene han disminuido tras radiofrecuencia de manera significativa ($p < 0.05$).

Discusión

Hasta donde sabemos, este es el primer estudio que demuestra que 12 sesiones de radiofrecuencia capacitiva resistiva (TECAR terapia) es capaz de disminuir el dolor, la curvatura y el tamaño de la placa fibrosa en una pequeña serie de pacientes, en un estudio piloto y reporte preliminar.

La EP es una fibrosis cicatricial de la túnica albugínea, sin comprometer al tejido eréctil. Aunque la etiología es aún desconocida, se aceptan como factores predisponentes los microtraumatismos y los factores genéticos. La prevalencia es del 2 al 9% en los varones de entre 40 y 70 años, con una incidencia de 30/100.000 habitantes⁸. Nuestra serie presenta en promedio una edad de 53.87 años, lo que coincide con otras series publicadas.

La EP cursa con una fase aguda o inflamatoria que puede durar hasta 18 meses, y en la que aparecen: dolor a la erección o al roce, placa palpable, curvatura, retracción o estrechamiento del pene y disfunción eréctil. La fase de estabilización es la etapa crónica, en la que se estabiliza la curvatura y remite el dolor⁸. Por lo general, los pacientes solicitan consulta durante los 6 meses del inicio de los síntomas⁹, como ha sucedido en nuestra serie (6.2 meses).

Si no se aplica tratamiento en la fase aguda, la fase natural de la enfermedad va hacia la progresión en un 30 a 48% de los casos⁹; sin embargo, algunos autores reportan curación espontánea en 7 a 29% de los pacientes⁴, mientras que otros reportan tan solo una curación espontánea de sólo 3.2 al 12% de los casos¹⁰.

En el tratamiento de la EP se han sugerido diversas opciones conservadoras, que incluyen la terapia oral, los agentes tópicos, las inyecciones intralesionales, la tracción del pene y las ondas de choque. Sin embargo, la ausencia de ensayos controlados, el pequeño tamaño muestral y la diversidad de parámetros evaluados han hecho que tales deficiencias metodológicas arrojen resultados contradictorios, lo cual limita realizar recomendaciones clínicas más sólidas sobre ellos¹¹. Además, según las Guías Clínicas actuales basadas en la EUA (European Urology Association), la AUA (American Urology Association) y la Sociedad Internacional de Medicina Sexual, la EP continúa siendo un desafío clínico y terapéutico ya que la terapia actual solo se dirige a modificar la curvatura peneana sin valorar el dolor ni la disfunción sexual⁸.

En ese sentido, la FDA (Food and Drug Administration) y la EMA (European Medicines Agency) han aprobado

a Xiaflex/Xiapex (colagenasa de *Clostridium histolyticum*) como el único fármaco seguro y efectivo, el cual es capaz de disminuir en al menos un 30% la curvatura peneana (disminuye 20° la curvatura, según el estudio de García-Cruz¹¹). Desafortunadamente, debido a la suspensión en la comercialización de la colagenasa de *Clostridium histolyticum* en Europa desde 31 diciembre 2019⁸, los investigadores nos hemos visto en el dilema de buscar nuevas opciones terapéuticas de tipo conservador para el manejo de la EP.

En el tratamiento conservador de la EP, la AUA recomienda terapia anti inflamatoria no esteroidea. Como tratamiento oral recomienda Vitamina E, tamoxifeno, procarbazona, ácidos grasos tipo Ω 3, o la combinación de Vitamina E + L-carnitina. Como terapia intralesional recomienda colagenasa de *Clostridium histolyticum*, interferón (IFN- α) y verapamilo¹. La AUA recomienda en los casos severos la opción quirúrgica (plicatura, incisión o exéresis de placa con injerto, o la prótesis de pene)¹. La AUA no hace referencia ni considera a la TECAR terapia (radiofrecuencia capacitiva resistiva) como una opción conservadora en el manejo de la EP.

Para considerar tratamiento conservador o quirúrgico, teniendo en cuenta la clasificación de Kelami⁴, los penes con curvatura < 30° no deberían tratarse, entre 30-60° debería recibir tratamiento conservador, y las curvaturas > 90° deberían recibir tratamiento quirúrgico⁴. Si tenemos en cuenta la clasificación de Levine et al, las placas de grado I (< 3 mm) y de grado II (entre 3 y 15 mm) requieren tratamiento conservador; por el contrario, las placas de Grado III (placas > 15 mm o placas múltiples > 10 mm) requieren tratamiento quirúrgico, sobre todo si los pacientes tienen una función eréctil satisfactoria¹². En nuestra serie, los pacientes presentaban una curvatura de $48.75 \pm 16.85^\circ$ y un tamaño de placa de $9.4 \text{ mm} \pm 5.12 \text{ mm}$; por lo que realizamos tratamiento conservador (TECAR terapia).

Ante la suspensión de la comercialización en Europa de Xiapex/Xiaflex, el único fármaco aprobado por la FDA y la EMA para el manejo de la EP⁸, y ante el dilema de buscar un tratamiento conservador y efectivo para tratar el dolor, la curvatura y disminuir el tamaño de la placa; y teniendo en cuenta las recientes publicaciones de Pavone (2013 y 2017)^{5,7}; nos hemos planteado si un protocolo de 12 sesiones sería efectivo en el manejo la enfermedad de la Peyronie. Hasta donde sabemos, no existen otros trabajos sobre la efectividad de la radiofrecuencia capacitiva resistiva (TECAR terapia) sobre la EP.

Pavone en 2013 planteó un protocolo de 3 sesiones de TECAR terapia (3 minutos capacitivo, 5 minutos resistivo) para valorar la seguridad y tolerabilidad en el manejo de la EP. Evaluó a 70 pacientes, de 60 años en promedio; y observó que el dolor disminuyó en el 80% de los casos, en un 30% (n=21) disminuyó la curvatura, el tamaño de la

placa y mejoró el coito. Además, no se presentó ninguna reacción adversa y reportó un 100% de tolerabilidad⁷.

En 2017 Pavone actualizó los resultados de su protocolo de TECAR terapia en un estudio randomizado de casos y controles en una muestra de 96 pacientes con un promedio de 59 años. Observó una reducción significativa del dolor en un 79.6% de los pacientes. Hubo mejoría numérica aunque no significativa de la disfunción eréctil en el grupo tratado; sin embargo, no se observó ninguna mejoría con respecto a la curvatura⁵.

Maretti en 2020 evaluó la utilidad de la TECAR terapia (15 minutos de terapia resistiva) más hidroelectroforesis con verapamilo y solo TECAR terapia. Realizó un estudio randomizado a 60 pacientes y aplicó 16 sesiones de tratamiento. Maretti observó que ambos grupos de tratamiento mejoraron el dolor, la función eréctil y la curvatura del pene; aunque, en el grupo TECAR terapia más verapamilo, la mejoría en cuanto al dolor y la curvatura fue significativamente mayor¹³.

La diferencia del presente estudio con los de Pavone y Maretti radica en el número de sesiones (3 sesiones Pavone, 16 sesiones Maretti, 12 sesiones el presente estudio)^{5,7,13}. Esto explicaría la disminución significativa de la curvatura y del tamaño de la placa observada en nuestro estudio y el de Maretti¹³. El dolor disminuyó significativamente en ambas series. Del presente estudio se deduce que se necesitan al menos 8 sesiones para originar una remodelación de la placa fibrótica y así disminuir tanto el tamaño como la curvatura. Esto ha sido confirmado en la serie de Maretti¹³.

La radiofrecuencia capacitiva-resistiva es un agente electrofísico que se usa en la rehabilitación desde hace 15 años, aunque aún existe controversia sobre su funcionamiento y hay muy pocas publicaciones que avalen su eficacia en Rehabilitación y sobre todo en la patología del suelo pélvico o en la EP¹⁴. Fernández-Cuadros et. al. afirman que la radiofrecuencia capacitiva y resistiva es ampliamente usada en la práctica clínica por sus efectos térmicos, aliviando el dolor y la inflamación y mejorando la extensibilidad de los tejidos. La termoterapia local eleva el umbral doloroso. Este efecto analgésico se debe a la teoría de la Puerta de Entrada de Melzack y Wall. De acuerdo con esta teoría, la percepción del dolor es modulada en la columna dorsal por la disputa al ingreso de los nervios no-nociceptivos A β de gran diámetro que transmiten información cutánea superficial, mecánica o de estimulación eléctrica y los pequeños nervios nociceptivos A δ y nervios C que transmiten información dolorosa. Los nervios A δ activados por la estimulación térmica de las corrientes capacitiva-resistiva de la radiofrecuencia reducen la transmisión del dolor y por ello la intolerancia al dolor disminuye¹⁴. Esto explicaría por qué la radiofrecuencia resultó efectiva en disminuir el dolor y mejorar la curvatura en los pacientes con EP, como se ha observado en la presente serie.

Existen otros tratamientos conservadores que han intentado disminuir el dolor, la curvatura y el tamaño de la placa, pero no han resultado tan efectivos como nuestro tratamiento (TECAR terapia). García-Cruz demostró que 2 sesiones de colagenasa de *Clostridium histolyticum* disminuyeron la curvatura en 20.63° (de 49.84 a 30.67°) en 31 pacientes; sin embargo, no reportó beneficio sobre el dolor ni sobre el tamaño de la placa¹¹. En 2 estudios sobre iontoforesis transdérmica con dexametasona y verapamilo, Cabello-Benavente et al y Garrido-Abad et al han reportado que esta terapia disminuye el dolor y el tamaño de la placa, mas no así la curvatura^{4,10}. Gallo et al han reportado que un tratamiento multimodal (L-arginina y pentoxifilina oral, verapamilo intralesional y tracción del pene) disminuyó la curvatura en 8°, aumento en 7 mm el tamaño del pene (de 10.3 a 11 cm), mejoró la función eréctil; pero no disminuyó ni el dolor ni el tamaño de la placa⁹. Finalmente, Casabe et al han reportado que las ondas de choque de baja intensidad son capaces de disminuir el dolor en la EP; sin embargo no actúan sobre el tamaño de la placa ni sobre la curvatura⁸.

A manera de resumen, una reciente revisión sobre el manejo de la EP establece que ningún tratamiento oral ni tópico ha mostrado resultados consistentes atener en consideración. En el caso de la modificación de la curvatura, Xiaflex/Xiapex (colagenasa de *Clostridium histolyticum*) es la mejor opción, aunque el estudio que produjo su aprobación en la FDA solo demostró una mejoría de solo 7.7° en la disminución de la curvatura. Para el manejo de la curvatura ventral, el interferón (IFN- α) es la única modalidad que ha demostrado beneficio. Por último, para el manejo del dolor, las ondas de choque son la mejor opción¹³.

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Una limitación del estudio es el pequeño tamaño muestral de la serie. Sin embargo, dado que este es un ensayo piloto más reporte preliminar de los resultados, amerita ampliar el tamaño muestral del estudio para confirmar la tendencia observada en este manuscrito.

Conclusión

Un protocolo de 12 sesiones de radiofrecuencia capacitiva resistiva (TECAR terapia) es capaz de disminuir el dolor, la curvatura y el tamaño de la placa fibrótica en una pequeña serie de pacientes con EP. No se han reportado eventos adversos durante la aplicación de este protocolo. Interesa ampliar el estudio para confirmar la tendencia observada en este estudio.

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Conflicto de intereses

Los autores declaran no tener ningún conflicto de intereses.

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Cómo redactar la metodología en la tesis y su relación con el artículo científico

How to write the methodology in the thesis and its relation with the scientific paper

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Resumen

Introducción: El reconocimiento, congruencia, previsión y organización del método científico para la solución de las diferentes tareas de investigación resulta una de las barreras que dificultan la escritura de tesis por los estudiantes de postgrado en educación. El objetivo de este artículo consiste en ofrecer recomendaciones respecto a cómo planear y redactar el apartado de metodología en las tesis de doctorado y maestría en educación que se elaboran en Cuba, mediante el análisis y la toma de partido en la polémica que al respecto tiene lugar a nivel internacional, contrastándola con la tradición nacional.

Material y métodos: Se aplicó el método analítico sintético al abordar la polémica a nivel internacional y su contraste con la propuesta cubana.

Resultados: Se propone un cambio en el enfoque metodológico de la investigación centrado no exponer cómo fueron usados los métodos sino en determinar desde el inicio cómo serán usados para resolver las tareas planteadas de modo que investigaciones en educación que se equiparen al nivel de rigurosidad que existe internacionalmente.

Conclusiones: Se aconseja realizar un cambio hacia el diseño metodológico como planeación proyectiva que oriente al investigador para encausar las investigaciones en educación.

Palabras clave: metodología de la investigación, artículo científico, informe de tesis, protocolo de investigación.

Abstract

Introduction: The recognition, congruence, forecast and organization of the scientific method for solving the different research tasks is one of the barriers that hinder the writing of thesis by postgraduate students in education. The objective of this article is to offer recommendations regarding how to plan and write the methodology section in the doctoral and master's theses in education that are prepared in Cuba, through analysis and taking sides in the controversy that takes place in this regard. at an international level, contrasting it with the national tradition.

Material and methods: The synthetic analytical method was applied when addressing the controversy at the international level and its contrast with the Cuban proposal.

Results: A change in the methodological approach of the research is proposed, focusing not on exposing how the methods were used but on determining from the beginning how they will be used to solve the tasks set so that research in education is comparable to the level of rigor that exists. internationally.

Conclusions: It is advisable to make a change towards methodological design as projective planning that guides the researcher to conduct research in education.

Key words: Research methodology, scientific article, thesis report, research protocol.

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Introducción

Una de las características emergentes de la sociedad contemporánea es la creciente producción de nuevos conocimientos mediante la investigación, a lo que se incorporan cada vez más personas. El informe mexicano “El Sistema Nacional de investigadores en números” muestra la aceleración en el crecimiento del número de investigadores en un período de 10 años (2006-2016). En 2016 había ya, dos veces más investigadores que en 2006. Esa corresponde a la tasa de crecimiento mayor en relación con iguales períodos anteriores¹. Tal situación también es visible a nivel mundial; en el año 2021 el número de investigadores creció en un 14%².

Otro fenómeno concomitante también es visible a nivel internacional y es que, aunque de manera muy polarizada hacia los países desarrollados, las publicaciones científicas crecieron un 21% en 2019 con relación al 2014³.

Este comportamiento es propio, no solo de las ciencias naturales y de la tecnología, sino también en las ciencias sociales. Como plantea UNESCO “nunca antes ha habido tantos científicos sociales en el mundo”³.

En concordancia con este crecimiento, Toala-Toala, Mendoza y Moreira-Moreira⁴ consideran que “la producción de conocimientos o investigación es una tarea inherente a la universidad” y resaltan la importancia de la enseñanza de la metodología de la investigación. Esto impone retos a las universidades y a los profesores que se encargan de la formación de investigadores.

Los autores de este artículo coinciden con Campos y Chinchilla⁵ cuando plantean que: “la investigación no se logra únicamente con la inclusión de algunos cursos dentro de los planes de estudio, sino mediante el desarrollo riguroso y sostenido de una pedagogía de la investigación, capaz de formar un estudiantado idóneo para pensar y hacer, en sus lugares de trabajo e incluso en su vida social, investigaciones y estudios de calidad”.

Antonijević⁶ llama la atención en cuanto a que: “el objetivo de la educación hoy en día no es solo la adquisición de conocimientos estáticos y conocimientos a nivel de hechos, sino también el desarrollo de diferentes habilidades para aplicarlas de inmediato para resolver cualquier problema particular en la vida profesional o cotidiana de un individuo”.

Los autores de este artículo coinciden con Retamozo⁷ cuando plantea: “La consolidación creciente del campo de la investigación en ciencias sociales y su creciente profesionalización han cambiado en gran medida las condiciones de producción, circulación y reconocimiento del discurso científico. En este contexto, la oferta de posgrados en el área se ha incrementado

notablemente y la realización de especialidades, maestrías y doctorados se ha convertido en una instancia de formación crucial e inevitable en el trayecto formativo de quienes eligen dedicarse a la investigación en instituciones del sistema científico”.

En el cumplimiento de estos retos son actuales varias polémicas a nivel internacional acerca de los reportes de investigación y la formación de investigadores. Una de ellas hace referencia a la correspondencia que se supone debe existir en las diferentes formas de comunicación de los resultados científicos, en particular entre el informe de tesis y los artículos que de la investigación se generan⁷⁻¹¹.

En la experiencia de los autores, como tutores, oponentes y miembros de tribunales de tesis de especialidad, maestría y doctorado, así como revisores de artículos científicos para diferentes revistas del área, se percibe la metodología como uno de los apartados que mayores barreras representa para su planeación y redacción por los investigadores en formación. Esta idea es explorada con mayor profundidad por Asencio e Ibarra¹² quienes racionan “las principales regularidades observadas en lo referido al sustento metodológico”.

Reconocer los diferentes niveles de los métodos, la congruencia en su aplicación y prever las acciones para su aplicación a la solución de las diferentes tareas de una investigación, así como su organización, resultan ser aspectos que presentan bastante dificultad para los estudiantes de pregrado y postgrado.

El apartado metodología de un informe de investigación es uno de los más importantes porque proporciona tanto los métodos como la muestra utilizada, los instrumentos y el modo en que todo eso fue integrado en una única estrategia durante el estudio. Este apartado es la base para la credibilidad del trabajo, pues proporciona las herramientas para replicar el estudio por otros investigadores que den validez al proceso y sus resultados¹³.

El objetivo de este artículo consiste en ofrecer recomendaciones respecto a cómo planear y redactar el apartado de metodología en las tesis de, doctorado y maestría en que se elaboran en Cuba, mediante el análisis y la toma de partido en la polémica que al respecto tiene lugar a nivel internacional, contrastándola con la tradición nacional.

La metodología en el hacer ciencias en Cuba

La forma de redacción del apartado metodología en las tesis elaboradas en Cuba tiene una tradición histórica que se estableció en la década de los noventa del siglo XX, y perdura hasta hoy a pesar de las transformaciones que en la forma de hacer ciencia se han operado durante los años transcurridos desde entonces.

¡Esa tradición se concreta en que la metodología forma parte de lo que se ha llamado el diseño de la investigación* y su redacción es una declaración de los grupos de métodos utilizados (empíricos, teóricos y matemáticos-estadísticos). Para cada grupo de métodos se declaran aquellos que fueron utilizados y cómo fueron utilizados en la investigación.

Esta forma de redacción tiene la ventaja de ser exhaustiva en cuanto a dar a conocer los métodos involucrados durante todo el proceso investigativo y cómo se les aplicó, pero tiene la desventaja de que desmiembra las metodologías mediante las cuales se consiguieron los resultados de la investigación y solo en el cuerpo de la tesis es posible apreciarlo. Es difícil, al obrar de este modo, hacerse una idea, desde el diseño de la investigación, acerca de cómo se procedió.

Rigurosamente, el diseño de la investigación no se redacta para la tesis, sino en las etapas iniciales de la investigación y su función es guiar el proceso investigativo¹⁴, es la planeación de la investigación, y su componente metodológico debería estar dedicado a declarar cómo, utilizando los métodos, se proyecta obtener los resultados expresados en el objetivo general.

Redactar los métodos de la manera establecida en Cuba conduce, en primer lugar, a que el diseño de investigación pierda su carácter de planeación en su aspecto metodológico y, en segundo lugar, a tener que hacer una redacción diferente de este apartado especialmente para la tesis (si se compara con los artículos científicos), lo cual conlleva tiempo y esfuerzos adicionales. "Para el aspirante a doctor aparece como una tarea doble que se antoja imposible"⁸.

¿Tesis y/o artículos científicos?

La mayor visibilidad, en cuanto a la divulgación de los resultados científicos, la tienen los artículos que se publican en revistas de impacto y eso se demuestra con los valores que ofrecen las diferentes métricas bibliográficas. Estudios realizados relativos a las tesis de grado reportan que el promedio de personas que leen una tesis es de 1,6¹⁵.

La diferencia entre esos impactos ha llevado a varios autores a promover y defender la idea de que el informe de tesis debe acercarse más, por su estructura y redacción, a un artículo científico^{8-11,15}.

La posición más radical en esta polémica consiste en considerar que los artículos científicos bien posicionados y que abarquen todo el contenido de la investigación realizada son suficientes para evaluar la formación lograda por un doctorando¹⁶.

Los autores de este artículo consideran que, tanto la producción de artículos científicos como el informe de tesis tienen, además de la científica, una función formativa que no es recomendable soslayar en el área de las ciencias de la educación. Por otro lado, apoyan la idea de que a pesar de que ambas producciones textuales tienen diferencias⁸, existen también congruencias que es necesario tener en cuenta, al menos por dos razones; la primera consiste en responder a una única unidad de elaboración y la segunda lograr mayor eficiencia en la escritura de reportes de investigación y en la formación de los investigadores.

Como argumentos que sirvan de apoyo a las ideas anteriores se pueden esgrimir los que se enuncian a continuación. Si un apartado de la tesis se diferencia significativamente en cuanto a su concepción del mismo en un artículo, el doctorando puede comprenderlo como dos cosas diferentes o, en el peor de los casos, provocar en él una contradicción que frene la integración de sus conocimientos y, en consecuencia, el avance. Por otro lado, exige menos esfuerzos redactar una vez el apartado en cuestión y ajustarlo a las particularidades de cada documento, que enfrascarse en la redacción de dos diferentes, es un asunto relativo a minimizar los esfuerzos.

Muñoz y Peiró¹⁰ son muy claros y convincentes al abordar este aspecto. Plantean que la diferencia entre la metodología que se elabora al inicio de la investigación y la que se escribe en el artículo radica en que en el primero se relata cómo realizar el estudio, mientras que en el segundo se relata cómo ese estudio se realizó. Como se puede apreciar la diferencia es en el tiempo verbal, pero hacen referencia a una misma acción.

Los propios autores consideran que "la metodología" debe cumplir dos objetivos:

1. Debe proporcionar toda la información necesaria para que otros investigadores puedan replicar el estudio.
2. Debe proporcionar toda la información necesaria para que otros investigadores puedan evaluar la validez interna y externa de un estudio¹⁰.
3. Lo que se ha hecho por tradición en las tesis escritas en Cuba no responde directamente a ninguno de estos dos objetivos, tal situación se revertiría si se asume en las tesis la forma de redactar la metodología establecida internacionalmente para los artículos científicos.

Acrecentando las polémicas y proponiendo soluciones

Otro aspecto que llama la atención en la bibliografía de metodología de la investigación tiene que ver con el

*Los autores de este artículo recomiendan abstenerse de llamar "diseño de la investigación" a la planeación de la investigación, por cuanto internacionalmente se le llama diseño de investigación al método general que se adopta para verificar la validez de los resultados de la investigación. Se asume el término difundido en Iberoamérica de "protocolo de investigación".

uso de la metodología que se declara. En el enfoque cuantitativo es casi exclusivo para verificar la validez del resultado científico alcanzado. Pero, indudablemente, en otras etapas de la investigación también se aplican metodologías que deben ser reveladas.

En cuanto a la obtención de los resultados de la investigación, habitualmente se declaran métodos generales, como el hipotético deductivo que define el cauce de la mayoría de las investigaciones cuantitativas, o la investigación acción participativa en las cualitativas, y con eso se considera todo resuelto cuando en realidad estos métodos requieren de su concreción en acciones referidas a métodos particulares que difieren de una investigación a otra. Esa es la razón por la que los autores de este artículo, en concordancia con López, Fraga, Rosas, Castro y Thompson¹⁷, consideran que debe declararse una metodología que sea específica de los resultados de la investigación, es decir, qué métodos y cómo se van a usar para obtener los resultados proyectados.

Por otro lado, el planteamiento del problema de investigación también requiere de la planeación de la metodología a seguir para la realización de esta etapa imprescindible y primaria en toda investigación. En la bibliografía se describen estrategias generales para lograr el planteamiento del problema, pero no se han encontrado referencias que recomienden a los investigadores planear para ello una metodología que se ajuste a las condiciones particulares que cada uno de ellos enfrenta.

Encontrar el vacío de la ciencia que se concreta en el problema y justifica la investigación es una de las tareas más arduas para los investigadores¹⁸. Sin una metodología previamente concebida para juntar suficientes datos que permitan precisar la dificultad percibida en la práctica educativa que genera la indagación, su procesamiento y el trabajo con la bibliografía para identificar el vacío, el desempeño del investigador seguramente se mengua, el investigador se desorienta y corre el riesgo de que la fundamentación del problema de investigación quede insuficientemente argumentada.

Qué decir, además, de la conformación del marco teórico, ¿acaso no se necesita también para ello de una metodología?

Desde el inicio en que se decide hacer una investigación y durante el tránsito posterior por las diferentes etapas del proceso investigativo, es posible identificar estrategias metodológicas sin las cuales el proceder del investigador no sería viable. Muchas veces ellas tienen un carácter intuitivo, se realizan por ensayo-error, pero resulta mucho más eficiente y riguroso si el investigador se detiene en cada etapa a planear la metodología que aplicará.

El lector que conoce la tradición cubana seguramente ha notado que este análisis se ha intencionado hacia

las que habitualmente se declaran como tareas en las investigaciones. Y es que, efectivamente, la propuesta de los autores de este artículo va dirigida a considerar que se proyecte una estrategia metodológica para la solución de cada tarea de investigación que se declare en el protocolo de la investigación.

Está claro que la dialéctica del proceso investigativo puede llevar a transformarlas o enriquecerlas durante su decurso en el tiempo, pero ejecutar un proceso planificado, proyectado, pensado previamente, tiene un valor metodológico reconocido. En palabras de Labarrere¹⁹, es evitar la tendencia a la ejecución en la solución de cualquier problema que se revierte, como mínimo, en ahorro de tiempo y esfuerzo.

Esta propuesta está en concordancia con lo que plantean Ronda y Lumbreras²⁰, si se considera la correspondencia que debe existir entre las tareas de investigación y los objetivos específicos, cuando declaran que “la finalidad del apartado de metodología en un proyecto de investigación es explicar el diseño del estudio y los procedimientos que los investigadores llevarán a cabo para dar respuesta a cada uno de los objetivos planteados”.

O también con el siguiente criterio de Retamozo⁷: “en el apartado de la metodología se debe exponer la dinámica de trabajo que conducirá a responder a las preguntas realizadas y cumplir con los objetivos”.

Asumir esta propuesta eleva la coherencia del protocolo de investigación por cuanto las tareas de investigación estarían directamente ligadas con la metodología para su solución. No es una lógica basada en cómo fueron usados los métodos (asumida por tradición), sino en cómo resolver las tareas de investigación y con ello aporta más a la comprensión de la investigación tanto para el lector como para el propio investigador.

Quizás a los lectores esta conclusión les parezca obvia, pero no es sencillo romper los esquemas anclados en una tradición que fue funcional por años. Y es que, inicialmente, el acceso a la bibliografía sobre metodología de la investigación en Cuba era escaso, así como a los artículos científicos publicados en internet, y la visión de otras perspectivas era prácticamente inalcanzable. Ello conllevó a un desarrollo casi únicamente endógeno de las prácticas científicas, influidas prácticamente de manera exclusiva por la bibliografía proveniente del que fuera el campo socialista.

Cuba tuvo su conexión a internet por vía satelital en 2016²¹, solo disponible en la academia de ciencias y a solo 64 kbps. Gradualmente, se fueron conectando las universidades, pero con un ancho de banda insuficiente. La conexión de Cuba por cable de fibra óptica a Venezuela en 2011²² significó un mayor acceso a la información contenida en internet, lo cual ha ido mejorando con el

paso de los años. Sin embargo, ello no ha tenido un impacto, entre otras cosas, en transformaciones en cuanto a la redacción de la metodología en la tesis.

Este artículo es un llamado y un intento de fomentar cambios en la formación de investigadores y en la realización de investigaciones que se equiparen al nivel de rigurosidad que existe internacionalmente. Y no solo invita a ello, sino que propone unos que pudieran ser un paso en ese camino.

Conclusiones

La metodología para la planeación de las investigaciones en Cuba fue el resultado de propuestas propias que incluyó influencias del que fuera el campo socialista por la falta de disponibilidad bibliográfica. A pesar de que a partir del segundo lustro de la década de los noventa del siglo XX el acceso a la bibliografía se ha incrementado en concordancia con la disponibilidad y acceso a internet que se ha incrementado a través de los años, los criterios para la planeación de las investigaciones se han mantenido inalterables, pero los estudios de otras perspectivas demuestran la

necesidad de introducir cambios. En este artículo aborda el apartado de metodología.

Tanto los artículos científicos como la tesis cumplen una función formativa para el investigador. Sin embargo, enfrentar ambas tareas con concepciones no coincidentes en cuanto a la redacción de la metodología significa un obstáculo innecesario. Se propone asumir en las tesis la forma de redacción de la metodología establecida internacionalmente para los artículos científicos.

Un análisis de las etapas del proceso investigativo conduce a considerar que el uso de la metodología no se limita a probar la validez del resultado científico propuesto (que es lo más difundido), sino que existe al menos una metodología para cada tarea de investigación planificada y es recomendación de los autores de este artículo que sea así que se construya lo que se ha denominado diseño metodológico de la investigación, y conseguir con ello que sea verdaderamente una planificación proyectiva que sirva de orientación al investigador.

Conflicto de intereses

Los autores declaran no tener conflicto de intereses.

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SPECIAL ARTICLE

¿Necesitamos un Plan Estratégico de Atención Pediátrica para el Sistema Nacional de Salud?

Do we need a Strategic Pediatric Care Plan for the National Health System?

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Resumen

El modelo de atención a la población pediátrica en el Sistema Nacional de Salud es desde hace tiempo objeto de controversia. La dificultad creciente para cubrir las plazas de pediatría de atención primaria por pediatras se ha convertido en un problema para los gestores de la sanidad pública. A raíz de esta situación, las comunidades autónomas han ido implementando diversas estrategias que modifican el modelo atención y que responden exclusivamente a las necesidades a muy corto plazo de manera reactiva, sin incorporar en el centro del debate a los pacientes. Complicando más la cuestión, la evidencia disponible publicada no cuenta con la significación suficiente para poder establecer recomendaciones. Además, pese a que se habla de la necesidad de una adecuación del modelo de la atención primaria de salud para dar una cobertura adecuada a las necesidades y problemas de salud, no parece que en este planteamiento se esté incluyendo el papel de la atención pediátrica. Llegados a este punto, proponemos iniciar un debate informado para dar una respuesta proactiva al problema con la elaboración de un Plan Estratégico de Atención Pediátrica. Este Plan deberá basarse en estudios en nuestro medio que puedan evaluar la eficiencia de los posibles modelos, ser participativo y tener como objetivo fundamental ofrecer la mejor atención a la población infantil. Además, deberá adaptarse a los nuevos retos sociales y económicos buscando la solvencia del sistema sanitario público.

Palabras clave: Pediatría, Política de Salud, Economía y Organizaciones de la Atención Médica.

Abstract

The model of care for the paediatric population in the National Health System has long been the subject of controversy. The growing difficulty in filling primary care paediatrics posts with paediatricians has become a problem for public health care managers. As a result of this situation, the Autonomous Communities have been implementing various strategies that modify the care model and respond exclusively to very short-term needs in a reactive manner, without incorporating patients into the centre of the debate. Further complicating the issue, the available published evidence does not have sufficient significance to be able to establish recommendations. Furthermore, although there is talk of the need for an adaptation of the primary health care model to provide adequate coverage of health needs and problems, the role of paediatric care does not appear to be included in this approach. At this point, we propose to initiate an informed debate to provide a proactive response to the problem with the development of a Strategic Plan for Paediatric Care. This Plan should be based on studies in our environment that can evaluate the efficiency of possible models, be participatory and have as its fundamental objective to offer the best care to the paediatric population. It must also adapt to the new social and economic challenges, seeking the solvency of the public health system.

Key words: Pediatrics, Health Policy, Health Care Economics and Organizations.

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La infancia constituye una parte esencial de la sociedad y la inversión en su bienestar y adecuado desarrollo repercutirá positivamente en toda la sociedad. Ha de ser objeto de especial protección en todos los ámbitos, entre ellos, y de forma muy importante, el sanitario.

Se trata de un periodo en el que se desarrollarán todos los órganos y sistemas del individuo, así como aspectos tan relevantes como la personalidad, el aprendizaje, el lenguaje o la socialización entre otros. Por tanto, es una etapa crítica del ser humano en todos los sentidos de manera que cualquier intervención positiva o negativa tendrá un gran impacto a lo largo de la vida. Además, los niños y niñas, por su inmadurez, se encuentran en una situación de indefensión y dependencia. Son las decisiones y actos de los adultos las que determinarán el entorno favorable o desfavorable para su adecuado desarrollo tanto físico como psíquico y psicológico.

Por todos estos motivos, son muchas las instituciones que se han posicionado a favor de proteger de forma especial a la infancia proporcionándole el ambiente y las condiciones necesarias para el adecuado desarrollo de todo su potencial. En el ámbito sanitario, es fundamental reconocer a los niños y niñas como seres diferentes a los adultos y por tanto con unas necesidades distintas. Una correcta asistencia sanitaria a la infancia requiere adecuar espacios y materiales y encomendar la atención a profesionales con la capacitación específica en pediatría, tal y como recogen organismos internacionales como la ONU¹ o el Parlamento Europeo², así como el propio Ministerio de Sanidad³.

En abril de 2013 se aprobó por acuerdo de Consejo de Ministros el II Plan Estratégico Nacional de Infancia y Adolescencia 2013-2016 (II PENIA)⁴ que define las líneas estratégicas de desarrollo de políticas estableciendo que la atención a la infancia y adolescencia ha de realizarse de forma coordinada por medio de la cooperación de los distintos agentes implicados en la misma.

Si nos centramos en la atención sanitaria, podemos considerar que el modelo actual de atención pediátrica en el SNS queda definido a partir del Real Decreto 137/1984, de 1 de febrero, de estructuras básicas de salud, de la Ley 14/1986, de 25 de abril, General de Sanidad y ratificado por la Ley 16/2003, de 28 de mayo, de Cohesión y Calidad del Sistema Nacional de Salud.

En la atención pediátrica hospitalaria se ofrecen servicios en función del nivel de complejidad y tamaño de los hospitales. Si bien existe un consenso ampliamente aceptado sobre la estructura y modelo de oferta de servicios⁵.

En este modelo asistencial, el límite de edad pediátrica es hasta los 14 años, no obstante, es habitual que los servicios de pediatría de los hospitales sigan haciéndose cargo de la atención de los niños con patologías crónicas

hasta los 18 años y más, como ocurre en el caso de la oncología pediátrica⁶.

También existe consenso en cuanto a la necesidad de coordinación, cooperación y colaboración entre el ámbito de atención pediátrica hospitalaria y el ámbito de atención pediátrica comunitaria.

Sin embargo, en lo relativo a la prestación sanitaria pediátrica en atención primaria surgen elementos de disenso.

Si bien la aparición de pediatras en el ámbito comunitario se remonta a los años 60 del siglo pasado, antes de las dos referencias normativas que hemos planteado como punto de partida, podemos considerar que la atención pediátrica queda integrada en el primer nivel asistencial a partir de la incorporación de los pediatras y las enfermeras de pediatría en los equipos de atención primaria. Inicialmente la población diana eran los menores de 7 años, aunque posteriormente se amplió hasta llegar a los 14 años.

Sin embargo, un gran inconveniente que se encontró en su día fue la escasez de pediatras titulados para poder ocupar esas plazas de nueva creación, que llevó a autorizar por parte del INSALUD que esas plazas fuesen ocupadas por médicos generalistas (con título previo al año 1995) y posteriormente por especialistas en medicina de familia y comunitaria, o por médicos especialistas con título de especialista en pediatría no homologado en España. No obstante, el acceso de estos profesionales a este tipo de plazas siempre será de forma eventual o interina.

En este contexto se identifica un gran tema de debate y controversia: ¿quién es el profesional sanitario más adecuado para atender a la población de pediatría en los equipos de atención primaria?

Este tema ha sido abordado a lo largo de los años por numerosos estudios desde diferentes puntos de vista. Algunos de ellos simplemente han descrito el modelo de atención de los diferentes países⁷⁻⁹, han reflexionado sobre la importancia de disponer de profesionales con adecuada formación para la atención de pacientes pediátricos en atención primaria¹⁰⁻¹³ o sobre posibles nuevos modelos de atención¹⁴. Otros estudios han analizado las diferencias que han podido encontrar entre la atención prestada por médicos de familia y pediatras sin llegar a decantarse por uno u otro modelo de atención¹⁵⁻²⁰.

Algunos autores han aportado argumentos a favor de que sea el pediatra quien se encargue de la atención de los niños en atención primaria²¹⁻³⁵ pero también hay otros que se postulan a favor de que esta atención sea llevada a cabo por los médicos de familia^{36,37}. Es paradójico como en función de la visión

y posicionamiento sobre el tema que a priori se tenga, los mismos artículos son citados en estos documentos para reafirmar posiciones contrapuestas. Entendemos que esto es reflejo de que, o bien no es posible identificar claramente diferencias, o bien los artículos publicados tienen bajo nivel de evidencia.

Una cuestión relevante en este debate es la dificultad de disponer actualmente del número de pediatras para cubrir todas las plazas de pediatría de atención primaria³⁸. Esta situación se ve agravada por las condiciones en que estos profesionales desarrollan su labor. Un estudio del año 2014 identificó varios puntos negros en este sentido como la distribución de tiempos en la jornada laboral, las condiciones del lugar de trabajo, las cargas de trabajo o la falta de autogestión entre otros³⁹. Esto hace, además, a la Atención Primaria poco atractiva para los nuevos pediatras recién formados con lo que el problema de falta de profesionales se perpetúa.

Diversos documentos que han evaluado y proyectado la necesidad de médicos especialistas en España a medio plazo identifican que la pediatría será una de las especialidades que estarán en equilibrio, con brechas entre la oferta y la demanda/necesidad entre -5% y 5%^{40,41}. Sin embargo, se han identificado problemas de cobertura de plazas en atención primaria, relacionado con el modelo de atención, y con el poco interés que las plazas de atención primaria tienen para los pediatras jóvenes que eligen preferentemente los hospitales⁴⁰.

Ante esta situación, se han ido incorporando otros profesionales, médicos de familia en su mayoría, a las plazas vacantes, a la vez que se han ido desarrollando diferentes estrategias para tratar de dar cobertura a toda la población infantil con un menor número de pediatras. Entre estas estrategias se encuentra la creación de la figura del pediatra de área en atención primaria⁴² o los modelos de áreas integradas. En ambos casos se ha identificado por parte de los profesionales una mayor precariedad laboral, así como, en el caso del pediatra de área de AP, una merma en la calidad asistencial que pueden ofrecer en las condiciones que se les presentan⁴³. La Asociación Española de Pediatría de Atención Primaria (AEPap) ha publicado varios estudios sobre la situación de la pediatría de atención primaria en diferentes comunidades autónomas⁴⁴⁻⁵¹ para posteriormente publicar en varias ocasiones recomendaciones o propuestas organizativas para tratar de mejorar esta situación⁵²⁻⁵⁴. Un estudio⁵⁵ publicado recientemente, propone establecer un modelo de atención en atención primaria basado en el trabajo coordinado del pediatra, la enfermera de atención primaria y la enfermera referente de centro educativo. Esta última permite establecer una atención más integral al abordar aspectos como la educación sexual, emocional y en hábitos saludables, el uso adecuado de las nuevas tecnologías, la promoción de entornos saludables, vacunación e igualdad en el centro educativo con la participación activa del alumnado.

La realidad es que se está introduciendo un cambio en el modelo asistencial de la pediatría en atención primaria que se está implementando sin un análisis integral de la situación, sin una reflexión sobre las posibles alternativas y sin una evaluación del impacto en salud que pueden tener estas decisiones organizativas.

Esta situación es especialmente llamativa si tenemos en cuenta que el Ministerio de Sanidad, Consumo y Bienestar Social publicó en 2019 el documento *Marco Estratégico para la Atención Primaria y Comunitaria*⁵⁶ que posteriormente desarrolló mediante el *Plan de Acción de Atención Primaria y Comunitaria 2022-2023*⁵⁷. Ambos documentos abordan los principales desafíos que tiene la atención primaria que debe adaptarse a los cambios de índole social, económica y tecnológica entre otras y proponen todo un listado de propuestas para llevar a cabo esta transformación. En ambos documentos se ha obviado la atención a la población pediátrica, no hay análisis de la situación de la misma ni propuestas para mejorarla.

Parece lógico iniciar un proceso de reflexión estratégica ante esta situación que debería concluir en la elaboración de un Plan Estratégico de Pediatría que, analice la realidad que tenemos en el SNS, que valore las proyecciones futuras, que dé voz a todos los agentes implicados y que permita consensuar el mayor número de iniciativas para configurar el modelo de la atención pediátrica de los próximos años.

Para ello, previamente se deberá establecer claramente el papel de los pediatras de atención primaria planteando opciones que van desde mantener el modelo actual en el que se establece que la atención de los menores de 14 años se lleva a cabo por pediatras tanto en atención hospitalaria como en atención primaria a explorar nuevos modelos. En este sentido, son muchas las propuestas que se han hecho entre las que se encuentra la reducción del programa del niño sano y la presencia de pediatras en atención primaria con un papel de consultores y más centrados en la atención a la cronicidad en pediatría y la pediatría comunitaria dejando la consulta ordinaria en manos de los médicos de familia.

Llegados a este punto, no parece que vaya a ser fácil responder a la pregunta que formulábamos párrafos atrás sobre ¿quién es el profesional sanitario más adecuado para atender a la población de pediatría en los equipos de Atención Primaria? Se han publicado muchas opiniones más o menos documentadas, muchas editoriales, muchas noticias, pero pocas publicaciones que midan efectividad, eficiencia, resultados en salud, seguridad, adecuación o beneficio con altos niveles de evidencia.

Hay que añadir además la disparidad de modelos organizativos de la atención a la población infantil y la heterogeneidad de los análisis. La comparación entre países tiene dificultades metodológicas no sólo porque se estén evaluando distintos modelos de atención

pediátrica en primaria sino porque esta atención está vinculada a perfiles profesionales que no coinciden ni con los de nuestro país ni entre países europeos.

Igualmente ocurre con los programas formativos, que son distintos (4 o 5 años de especialidad; tronco común y especialidades en la mayoría de países; etc.), Respecto al programa formativo de la especialidad de pediatría en España, ya se hablaba en el año 1979 de la necesidad de que los pediatras se formaran en pediatría comunitaria, pero no fue hasta el año 2006, con la entrada en vigor del nuevo programa formativo, que se reguló la rotación específica obligatoria de los residentes durante 3 meses en atención primaria.

Otro elemento a considerar es el que hace referencia a las enfermeras de pediatría en atención primaria. Conviene recordar que la Enfermería Pediátrica se diferenció como especialidad en España en 1964, pero no es hasta el 2005⁵⁸, cuando se estableció el programa formativo de la especialidad, el cual define el perfil de la enfermera especialista en pediatría y las competencias a adquirir durante el periodo formativo. Las enfermeras especialistas en pediatría tienen, según el programa formativo, una rotación de siete meses en atención primaria destinada a adquirir competencias para la atención de los niños y niñas y la familia en el ámbito comunitario. De forma similar a lo que ocurre para los pediatras, existen artículos que han analizado las ventajas e inconvenientes del modelo de atención con enfermeras de pediatría en atención primaria^{59,60}.

Finalmente, por lo que respecta a las preferencias manifestadas por los usuarios/padres, cabe destacar que disponer de pediatras en atención primaria se ha identificado como una conquista social de bienestar⁶¹, que los padres prefieren elegir a pediatras para que sean atendidos sus hijos⁵ y disponer de una consulta de enfermería pediátrica específica^{62,63}. Si bien, como en todo lo comentado hasta ahora, hay autores que identifican importantes sesgos en este tipo de análisis¹⁹.

Consecuentemente a lo expresado hasta ahora y en base a la evidencia que se ha podido encontrar, entendemos que existen más argumentos a favor de mantener un modelo asistencial con equipos de pediatría en atención primaria, pediatras y enfermeras de pediatría, integrados en los equipos de los centros de salud y encargados de atender a la población menor de 14 años que argumentos en contra de abandonar este modelo. A estos argumentos podríamos añadir las previsiones de necesidades de médicos de familia para los próximos años que identifican un déficit importante de estos profesionales⁴⁰ para la atención de la población adulta.

En cualquier caso, frente a la posibilidad de un cambio de modelo, pensamos que sería deseable impulsar estudios observacionales en nuestro medio que puedan evaluar la eficiencia de pediatras o médicos de familia atendiendo a

la población infantil; medir el impacto que puede tener uno u otro sistema de provisión de los servicios de atención infantil con indicadores adecuados o utilizar los modelos de datos masivos de vida real como aproximación a estudios similares a los ensayos clínicos⁶⁴⁻⁶⁵.

Esto nos debería permitir promover un debate informado sobre el modelo asistencial que querríamos tener para atender mejor a la población infantil.

Aunque el tema de la atención primaria tiene una especial importancia a la hora de replantear el modelo de atención, actualmente existen otra serie de temas que necesitan también ser abordados desde la planificación estratégica sanitaria.

En relación a la atención hospitalaria es necesario avanzar en el reconocimiento de las diferentes áreas de capacitación específica de la especialidad (neonatología, gastroenterología pediátrica, endocrinología pediátrica, etc.) para que los pediatras que las desarrollan puedan recibir la formación más adecuada⁶⁶. Además, es preciso buscar soluciones para los problemas de cobertura de guardias en determinados hospitales comarcales que, al disponer de una plantilla más pequeña, es complicado cubrir las bajas, los permisos de maternidad o las guardias que dejan de hacer los profesionales cuando cumplen los 55 años, lo que provoca serias dificultades para ofrecer cobertura 24x7x365.

Otros temas tienen que ver con la organización y el acceso a determinadas prestaciones complejas y con alto impacto en salud como son la oxigenación por membrana extracorpórea (ECMO), los CSUR pediátricos, la Atención Temprana, o la organización del transporte pediátrico (especialmente en comunidades autónomas de gran dispersión poblacional o con insularidad). Además, cada comunidad autónoma tendrá que tener en cuenta sus características especiales y problemas locales a la hora de diseñar su modelo de atención a la infancia y adolescencia.

Por último, cabría destacar la atención al adolescente como un campo de necesario desarrollo tanto para formar a los pediatras y enfermeras de pediatría como para responder a las demandas de estos pacientes y sus familias o cuidadores.

En este contexto, surge la pregunta con la que damos título a este artículo, ¿necesitamos un Plan Estratégico de Pediatría como instrumento de planificación y coordinación sanitaria para mejorar la salud de la población en edad pediátrica y que defina el modelo de atención más adecuado?

No es la primera vez que se formula esta pregunta y ha habido algunas CCAA que en los últimos años han realizado trabajos en este sentido si bien, por distintas razones, no han conseguido llegar a la publicación de dichos planes⁶⁷.

Distintos elementos son los que se enumeran a la hora de justificar la elaboración de un Plan de la Atención Infantil. Por una parte, los sistemas sanitarios necesitan adaptarse a los cambios demográficos y sociales y tienen que ofrecer respuestas a las necesidades de nuestra población. Las respuestas deben estar sustentadas en la actualización de la evidencia científica, en la innovación, en la seguridad, en las buenas prácticas y en la calidad de la atención. Elaborados adecuadamente, son una herramienta que realmente consigue mejorar el funcionamiento de los servicios sanitarios de modo que son capaces de reducir el impacto de los determinantes sociales en los resultados en salud de la población a la que van dirigidos⁶⁸.

Además, los profesionales, de todos los ámbitos asistenciales que atiendan a la población infantil del SNS, deben disponer de los recursos necesarios para garantizar este tipo de atención.

En definitiva, con este Plan se debería afrontar con eficiencia, sostenibilidad y solvencia los nuevos retos sociales y económicos a los que nos enfrentamos desde el sistema sanitario público, sin dejar de considerar que los costes de oportunidad de implementar unas acciones condicionan aquellas otras acciones que no pueden ser implementadas.

El objetivo fundamental del Plan sería beneficiar en primer lugar a los niños y niñas, a sus familiares y a sus cuidadores. Este objetivo no se alcanzará sin el necesario beneficio que obtendrán también los profesionales que les atienden. Y todo ello debería permitir mejorar la salud no sólo de los niños y niñas sino también de las futuras generaciones de nuestra población.

Para conseguir este objetivo, el Plan debería establecer líneas de actuación que nos permitan desarrollar la atención sanitaria pediátrica de manera eficaz y eficiente, que aseguren la equidad del acceso a los recursos sanitarios y que en definitiva contribuyan a optimizar la

calidad de la asistencia a población pediátrica teniendo en cuenta los recursos disponibles.

Para finalizar, entendemos que los objetivos en este ejercicio de planificación estratégica deberían ser:

- Realizar un análisis de la situación actual de la atención pediátrica en el sistema sanitario público, a partir de la participación de los profesionales implicados para detectar necesidades y puntos susceptibles de mejora, así como también conseguir el consenso entre ellos en el establecimiento de las estrategias que se consideren oportunas. Este análisis debe tratar de identificar los recursos disponibles, especialmente la disponibilidad de profesionales con la capacitación que se considere adecuada en cada caso.
- Incorporar las ideas fuerza que se generarán en el Plan a la visión estratégica que en los próximos años se tendrá de la salud de la población infantil.
- Establecer las prioridades y definir estrategias de intervención que serán objeto de seguimiento y control según el cronograma establecido (corto, medio y largo plazo).
- Alcanzar la coordinación a todos los niveles asistenciales e institucionales. Esto incluirá la necesidad de cambios organizativos, de disponer de escenarios de cooperación, de establecer consensos, de fomentar la participación, de ofrecer transparencia y de promover el buen gobierno.

Conflicto de intereses

Los autores declaran no tener ningún conflicto de intereses relacionado con el artículo.

También declaran que las opiniones expresadas son de exclusiva responsabilidad de los autores y no representan el pensamiento u opinión formal de la institución para la que trabajan.

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CASE REPORT

Ataxia cerebelosa como debut de un cáncer diferenciado de tiroides

Cerebellar ataxia as a debut of differentiated thyroid cancer

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Resumen

Hombre de 60 años con ataxia cerebelosa grave. Las exploraciones por resonancia magnética y tomografía computarizada no revelaron anomalías anatómicas estructurales del SNC. Como hallazgo incidental se observó un nódulo tiroideo izquierdo de 25mm. La PET/TCT con 18F-FDG mostró hipometabolismo cerebeloso e hipermetabolismo tiroideo sugiriendo un síndrome paraneoplásico relacionado con cáncer de tiroides diferenciado oculto. Los anticuerpos anti-mGluR1 séricos positivos confirmaron el diagnóstico. Posteriormente a la tiroidectomía y la terapia con yodo radiactivo, el paciente mostró una mejoría clínica significativa. Una exploración PET/CT con 18F-FDG de seguimiento mostró una normalización parcial del metabolismo cerebeloso y los niveles séricos de anti-mGluR1 volvieron a la normalidad. El caso subraya la utilidad de la PET/CT con 18F-FDG en el diagnóstico de cánceres ocultos y establece una relación entre la ataxia cerebelosa con anticuerpos antineuronales anti-mGluR1 y el cáncer diferenciado de tiroides.

Palabras clave: Ataxia cerebelosa, hipometabolismo cerebeloso, hipermetabolismo tiroideo, PET/TC, síndrome paraneoplásico, cáncer diferenciado de tiroides, anticuerpos anti mGluR1.

Abstract

A 60-year-old male exhibited severe cerebellar ataxia. MRI and CT scans revealed no structural anatomical abnormalities of the CNS. A 25mm left thyroid nodule was observed as an incidental finding. 18F-FDG PET/CT showed cerebellar hypometabolism and thyroid hypermetabolism suggesting a paraneoplastic syndrome related to occult differentiated thyroid cancer. Positive serum anti-mGluR1 antibodies confirmed the diagnosis. After thyroidectomy and radioiodine therapy, the patient showed significant clinical improvement. A follow-up 18F-FDG PET/CT scan showed partial normalization of cerebellar metabolism and serum anti-mGluR1 levels returned to normal. The case underscores the utility of 18F-FDG PET/CT in diagnosing occult cancers and establishes a relationship between cerebellar ataxia with antineuronal anti-mGluR1 antibodies and differentiated thyroid cancer.

Key words: Cerebellar ataxia, cerebellar hypometabolism, thyroid hypermetabolism, PET/CT, paraneoplastic syndrome, differentiated thyroid cancer, anti-mGluR1 antibodies.

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Caso clínico

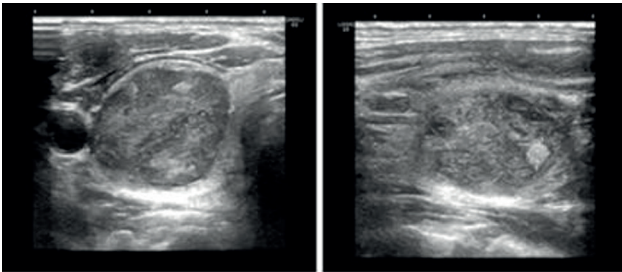
Varón de 60 años diagnosticado de cáncer diferenciado de tiroides tras estudio PET/CT-18F-FDG realizado en búsqueda de neoplasia de origen desconocido, en contexto de ataxia cerebelosa subaguda como probable síndrome paraneoplásico.

En Septiembre/2020 cursó con inestabilidad postural y de la marcha indicándose tratamiento sintomático. Tras empeoramiento clínico (necesidad silla de ruedas-temblor severo en MMSS-etc) en Octubre/2020 acudió a Urgencias del hospital local (H. de Manacor) con ingreso en Neurología por ataxia cerebelosa de origen desconocido.

El diagnóstico diferencial de esta entidad incluye múltiples etiologías: neoplasias- drogas/fármacos- alteraciones hormonales/vitamínicas- enfermedades neurodegenerativas- infecciones-etc¹.

Se realizaron estudios de imagen (RX de tórax-TC craneal-RMN cerebral y columna cervical) con un nódulo tiroideo izquierdo de 25mm como único hallazgo. En ecografía aparecía bien definido, con calificaciones en su interior (**Imagen 1**); visualizándose otros 2 nódulos hipo-ecogénicos en LTD en contexto de un BMN²). Se realizó PAAF del nódulo izquierdo con diagnóstico de lesión folicular de significado incierto (Bethesda III).

Imagen 1: Ecografía de tiroides-Nódulo en LTI.

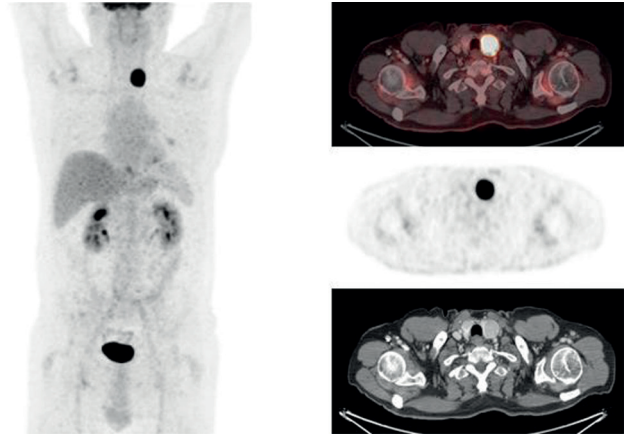


Se cursaron pruebas de laboratorio (sangre y LCR) incluyendo marcadores tumorales resaltando únicamente anticuerpos anti-neuronales a títulos bajos en patrón de IFI. Se remitió la muestra al Hospital Clínic (Barcelona) para ampliar estudio. Informaron positividad para anticuerpos anti-mGluR1 en suero (positivo débil) y LCR (positivo fuerte). Los anticuerpos anti-mGluR1 poseen su diana en la superficie de las células del Purkinje clasificados como anticuerpos tipo 2 (extracelulares), siendo patogénicos y pudiéndose asociar frecuentemente a neoplasia. Se orientó entonces el caso como encefalitis cerebelosa autoinmune, de probable origen paraneoplásico³.

Comenzó tratamiento de 1ª línea con Inmunoglobulinas iv para eliminar anticuerpos sanguíneos estabilizándose la clínica. En Nov/2020 inicio tratamiento inmunosupresor de 2ª línea durante dos años: Rituximab para reducción de linfocitos B-anticuerpos y Ciclofosfamida para reducción de celularidad / infiltrado inflamatorio durante 4 meses.

En Enero/2021 realizó finalmente estudio PET/CT-18F-FDG cerebral y cuerpo completo para búsqueda de neoplasia oculta evidenciando hipometabolismo cerebeloso y un depósito focal intensamente hipermetabólico en lóbulo tiroideo izquierdo (SUVmáx de hasta 52,06) altamente sospechoso de malignidad (**Imagen 2**).

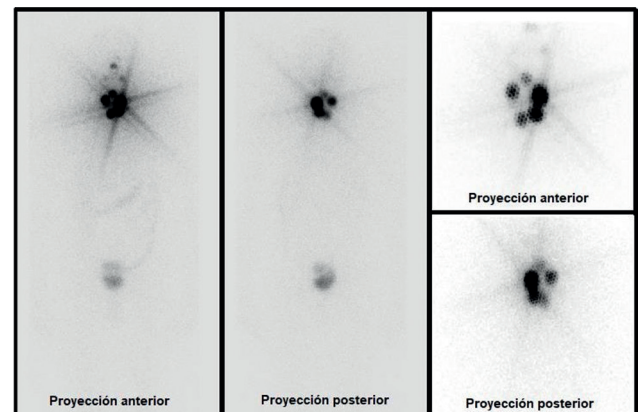
Imagen 2: PET/TC-18F-FDG. Nódulo hipermetabólico en LTI.



Está descrito en la literatura que las captaciones focales tiroideas en PET/CT-18F-FDG tienen una prevalencia de cánceres primarios del 14-63%⁴. Se realizó tiroidectomía total con AP de carcinoma papilar de tiroides variante folicular encapsulado de 2,6cm en LTI con componente solido/trabecular 20%, patrón papilar clásico 8%, patrón de células altas 1% (AJCC 8ªed-pT2NxMx)⁵.

Siguiendo las recomendaciones de ATA-2015 siendo un CDT de bajo riesgo², recibió tratamiento para eliminación de restos con 1110MBq de 131I tras estímulo exógeno con TSH-rh en el Servicio-MNU de referencia^{6,7,8}. El día del tratamiento presentó valores estimulados de TSH>90,47μUI/mL, Tg 2,01ng/ml, sin elevación de los anticuerpos anti-tiroglobulina. Dado de alta a las 24h (tasa de dosis de 17.8mSv/h/1metro) con evidencia de restos de tejido tiroideo normal en ambos lóbulos en rastreo de distribución a las 72h (**Imagen 3**).

Imagen 3: Rastreo de distribución post-tratamiento con radioyodo.



En Abril/2021 el paciente presenta recuperación ad integrum de su sintomatología a nivel clínico, con un estudio PET/CT-18F-FDG cerebral posterior que evidencia la mejoría del metabolismo cerebeloso.

Actualmente persiste asintomático, en seguimiento por Neurología y Endocrinología con monitorización clínico-analítica.

Discusión

Afirmar que la detección de un carcinoma papilar de tiroides en presencia de un síndrome neurológico clásico, en asociación con autoanticuerpos onconeurales bien caracterizados y descartadas otras etiologías no neoplásicas podría cumplir criterio suficiente para definir un trastorno paraneoplásico asociado.

Destacar la rareza del caso clínico presentado, con escasa literatura de síndromes paraneoplásicos cerebelosos secundarios a neoplasias tiroideas, ninguno de ellos relacionado con anticuerpos anti-GluRm1 hasta el momento.

Dado que el CDT es una patología frecuente resulta importante resaltar la existencia de posibles formas de presentación atípicas como su asociación con la ataxia cerebelosa.

Resaltar el papel crucial de la PET/CT-18F-FDG en la detección precoz de neoplasias ocultas en contexto de un proceso paraneoplásico.

Recalcar el significado de una captación focal tiroidea en un PET/CT-18F-FDG, la relación entre morfología/distribución de la captación y la intensidad del metabolismo glicídico con la sospecha de malignidad.

No olvidar el significado de un resultado citológico Bethesda III que conlleva un 10-30% de riesgo de malignidad.

Juicio clínico final

Ataxia cerebelosa por anticuerpos antineuronales (anti-mGluR1) como síndrome paraneoplásico en el debut de un cáncer diferenciado de tiroides.

Conflicto de intereses

Los autores declaran no tener conflicto de intereses.

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CASE REPORT

Purpura fulminans más hematoma del psoas en niño con sepsis por *Acinetobacter baumannii*: una complicación muy infrecuente

Purpura fulminans plus psoas hematoma in a child with Acinetobacter baumannii sepsis: a very rare complication

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Resumen

Los hematomas del psoas (HP) son muy infrecuentes y pueden ocurrir debido a traumatismo, iatrogenia (cirugía lumbar), uso de anticoagulantes o tras desordenes de la coagulación tales como hemofilia o tras coagulación intravascular diseminada (CID) secundaria a sepsis. La púrpura fulminans (PF) es considerada un signo de CID, afectando la piel de los pacientes, sobre todo a nivel de nalgas, muslos y piernas. La incidencia del HP va del 0.1% al 0.6% y se consideran factores de riesgo la edad adulta y ser hemodializados. La clínica característica incluye dolor en la ingle o muslo, impotencia del miembro afectado, parestesias unilaterales y ocasionalmente parálisis del nervio motor. Esta parálisis es frecuente en hematomas crónicos y grandes. Se puede apreciar hematoma periumbilical (signo de Cullen) o en los flancos (signo de Grey Turner). El diagnóstico es eminentemente clínico pero se confirma con ecografía, tomografía o resonancia magnética. La mayoría de los hematomas se resuelven espontáneamente, por lo que el tratamiento es conservador. En caso de hipovolemia o shock, el tratamiento debe ser intervencionista, incluyendo drenaje, embolización o cirugía. Presentamos el caso clínico de un niño de 9 años quien tras presentar PF con alteración grave de los parámetros de hemostasia y coagulación secundario a sepsis por *Acinetobacter baumannii*, y que fue ingresado en UCI por insuficiencia respiratoria, presentó como complicación posterior HP; el cual requirió tratamiento conservador. Resaltamos la importancia de la anamnesis detallada y del examen físico completo para brindar el manejo adecuado de esta patología tan infrecuente pero potencialmente mortal.

Palabras clave: hematoma del psoas, signo del psoas, púrpura fulminans, sepsis, *Acinetobacter baumannii*.

Abstract

Hematomas of the psoas (PH) are very infrequent and may occur due to trauma, iatrogenic (lumbar surgery), use of anticoagulants or after coagulation disorders such as hemophilia or after disseminated intravascular coagulation (DIC) secondary to sepsis. Purpura fulminans (PF) is considered a sign of DIC, affecting the skin of patients, especially at the level of the buttocks, thighs and legs. The incidence of PF ranges from 0.1% to 0.6% and adult age and being hemodialyzed are considered risk factors. The characteristic clinical features include groin or thigh pain, impotence of the affected limb, unilateral paresthesias and occasionally motor nerve palsy. This paralysis is frequent in chronic and large hematomas. Periumbilical hematoma (Cullen's sign) or flank hematoma (Grey Turner's sign) may be seen. The diagnosis is eminently clinical but is confirmed by ultrasound, tomography or magnetic resonance imaging. Most hematomas resolve spontaneously, so treatment is conservative. In case of hypovolemia or shock, treatment should be interventional, including drainage, embolization or surgery. We present the clinical case of a 9-year-old boy who, after presenting PF with severe alteration of hemostasis and coagulation parameters secondary to sepsis due to *Acinetobacter baumannii*, and who was admitted to the ICU for respiratory failure, presented PH as a subsequent complication; which required conservative treatment. We emphasize the importance of detailed anamnesis and complete physical examination to provide adequate management of this rare but potentially fatal pathology.

Key words: psoas hematoma, psoas sign, purpura fulminans, sepsis, *Acinetobacter baumannii*.

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Introducción

El hematoma del psoas (HP) es una complicación muy infrecuente, presentando una incidencia del 0,1 al 0,6%, afectando más frecuentemente a pacientes adultos y hemodializados¹. El HP a pesar de ser infrecuente en niños, es una condición muy grave que presenta una mortalidad en UCI del 30 al 50%², de ahí la importancia de reconocer o descartar su presentación.

Las causas de presentación del HP pueden ser secundarias a traumatismo, uso de anticoagulantes, iatrogenia (cirugía lumbar o disectomía endoscópica), y desordenes de coagulación (hemofilia o coagulación intravascular diseminada [CID])¹.

La púrpura fulminans (PF) es una condición hemorrágica asociada a sepsis o infección previa. Sus signos incluyen necrosis tisular, trombosis de pequeño vaso y CID³. Otros autores consideran a la PF como un signo de CID; y en ese sentido, una terrible complicación de la sepsis severa y del shock séptico, asociado a infección por bacterias Gram negativas tales como meningococo³, malaria^{4,5}, varicela⁶, *Capnocytophaga canimorsus*⁷, *Streptococo pneumoniae*⁸ y *Acinetobacter baumannii*⁹, entre otros.

La PF aunque se relaciona más a episodios de sepsis aguda también puede ser idiopática, manifestarse a los 10 días de una enfermedad infecciosa, o puede ser hereditaria (déficit de proteína C, S y déficit de antitrombina III¹⁰). En cualquier caso, la PF al ser una condición hemorrágica y formar parte del síndrome de CID, puede acompañarse de lesiones purpúricas simétricas en nalgas y muslos; y puede producir hematomas espontáneos debido a la coagulopatía por consumo (disminución de fibrinógeno y aumento de productos de degradación de la fibrina)⁶. Así, el HP puede aparecer en pacientes con alteraciones de la coagulación ya sea por: a) CID diseminada secundaria a infección o sepsis por Gram negativos tal como *Acinetobacter baumannii*; b) enfermedades hematológicas (hemofilia u otras discrasias sanguíneas); c) tratamiento anticoagulante; d) traumatismos musculares¹¹.

El diagnóstico de HP precisa: a) una anamnesis completa; b) una exploración física minuciosa; c) exámenes laboratoriales que valoren el hemograma y los parámetros de coagulación¹². La manifestación clínica más típica comprende dolor lumbar o en fosa ilíaca izquierda, además de dolor a la flexo extensión de la cadera; eventualmente neuropatía femoral, y dependiendo de la cantidad de sangrado, shock hipovolémico¹². El diagnóstico confirmatorio se realiza con ecografía, tomografía o resonancia magnética. La prueba más rentable es la tomografía¹².

Finalmente, el manejo del HP puede ser: a) conservador (reposo absoluto, corrección de la hemostasia,

analgésicos y anti inflamatorios); b) invasivo (drenaje percutáneo, angiografía más embolización y/o cirugía)¹².

El objetivo del presente artículo es presentar el caso clínico de un niño de 9 años quien tras presentar PF con alteración grave de los parámetros de hemostasia y coagulación secundario a sepsis por *Acinetobacter baumannii*, y que fue ingresado en UCI por insuficiencia respiratoria, presentó al alta de UCI e Ingreso en Medicina Interna hematoma espontáneo del psoas, el cual requirió tratamiento conservador, resaltando la importancia de la anamnesis detallada y del examen físico completo para brindar el manejo adecuado de esta patología tan infrecuente pero potencialmente mortal.

Caso Clínico

Presentamos el caso clínico de un niño de 9 años quien de manera insidiosa presentó fiebre, diarrea, dolor torácico y dificultad respiratoria progresiva de 2 días de evolución y que le obligó a ingresar en UCI y ser intubado. A los 3 días previos a la hospitalización o ingreso, aparecieron lesiones purpúricas en pulgar izquierdo, rodilla derecha y dedos de pie derecho, además de lesiones petequiales de 3 mm de diámetro en todo el cuerpo. El examen laboratorial reveló leucocitosis (26,380 /mL), plaquetopenia (55,000/mL) y anemia (Hb 11.4 mg%). El examen bioquímico reveló elevación de transaminasas (TGO y TGP).

A las 24 horas de ingreso en UCI apareció un sangrado por sonda nasogástrica y empeoramiento de los valores hematológicos (plaquetas < 35,000 /mL, leucocitos 33,670/mL y hemoglobina [Hb] 9,8 mg%), confirmándose miositis, miocarditis y shock séptico. A las 48 horas de ingreso, aparecieron púrpuras y petequias en todo el cuerpo, comprometiendo tórax, palmas y plantas. Al 3° día de ingreso se aisló *Acinetobacter baumannii* y se prescribió antibióticoterapia sensible (Meropenem) y se añadió diuréticos para asegurar diuresis por miositis. Al 5° día, tras presentar mejoría de su condición clínica, mejor saturación y la aparición de ventilación espontánea, se decidió su traslado a planta de Hospitalización Pediatría. Los parámetros hematológicos también mejoraron (plaquetas 310,000/mL; Hb 10.1 mg%).

El 6° día apareció un hematoma espontáneo en la rodilla izquierda de 5 cm de diámetro, y el 7° día apareció dolor abdominal y dolor intenso en el muslo derecho que le impidió conciliar el sueño. El día 8° el dolor abdominal disminuyó pero el dolor en muslo continuó ascendiendo, lo mismo que el volumen del muslo (confirmado por circimetría). Ante la sospecha de que el dolor se haya desencadenado por la presencia de un catéter que se colocó en UCI en la misma zona, se solicitó ecografía la cual descartó insuficiencia arterial (**Figura 1**), y se realizó

interconsulta a Infectología, quien descartó infección o absceso en muslo. Los médicos tratantes también cursaron interconsulta a Psiquiatría, a fin de valorar si estas quejas eran inventadas por el niño, en el afán de conseguir la atención de sus padres.

Durante el día 9 al día 12 de hospitalización, las lesiones purpúricas fueron disminuyendo en tamaño y en número; sin embargo, el dolor en el muslo se incrementaba, le incapacitaba el dormir y le limitaba el apoyar la pierna y caminar por el dolor. Los médicos tratantes realizaron una segunda interconsulta a Psiquiatría para descartar ganancia secundaria.

El día 13° se solicitó interconsulta a Medicina Física y Rehabilitación para valorar el dolor y realizar terapia física y recuperación de la marcha. En nuestra visita apreciamos al paciente con fascies dolorosa, miembro inferior derecho en postura antiálgica (flexo de cadera y rodilla y decúbito lateral izquierdo). (Figura 2). A la movilización activa y pasiva de la cadera (signo del psoas), se apreciaba dolor importante y defensa muscular. No se observó hematoma en abdomen

y el mismo a la palpación era blanda, sin signos de irritación peritoneal. A la palpación se objetivó dolor en tercio superior de muslo derecho, y la bipedestación y la marcha se realizaron con cojera importante por flexo de cadera y rodilla. En decúbito prono el paciente era incapaz de relajar el psoas, se apreciaba un flexo de cadera de 90°. Ante la sospecha de hematoma espontáneo del psoas sugerimos reposo absoluto, analgesia y anti inflamatorios parenterales, termoterapia alternada con crioterapia y se solicitó ecografía y tomografía.

El estudio ecográfico (Figura 3) y tomográfico (Figura 4) confirmaron hematoma del psoas ilíaco derecho. En la ecografía se apreciaba imagen hipoeoica; en la tomografía se apreciaba aumento de volumen del vientre muscular del músculo psoas iliaco derecho. Con esos resultados, sugerimos continuar con tratamiento conservador y reposo para disminuir el dolor y realizar un manejo adecuado de esta complicación grave y potencialmente mortal.

El día 18° se inició bipedestación y marcha con andador. El flexo de cadera disminuyó a 15° y el dolor disminuyó considerablemente. EL día 20°, tras haber conseguido una marcha casi normal, sin apenas cojera, y al no presentar otras complicaciones, se decidió dar de alta médica.

Figura 1: El estudio doppler confirmó permeabilidad de arteria y vena femoral en región inguinal derecha, descartando insuficiencia y/u obstrucción arterial o venosa.

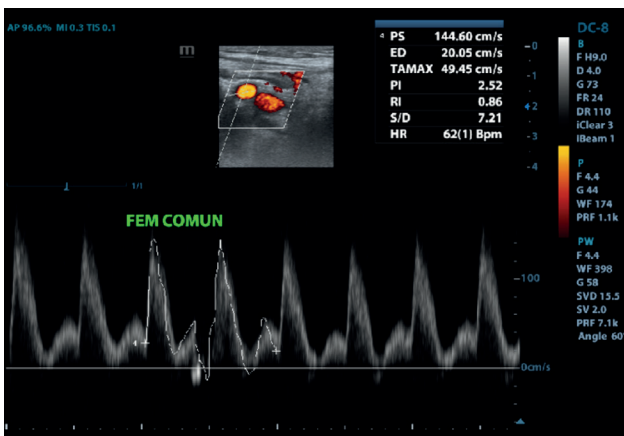


Figura 3: Se aprecia imagen hipoeoica (*) que compromete músculo psoas derecho asociado a colección adyacente (compatible con hematoma). Imagen contralateral muestra ecogenidad normal, sin alteración en la estructura fibrilar ni colecciones asociadas.

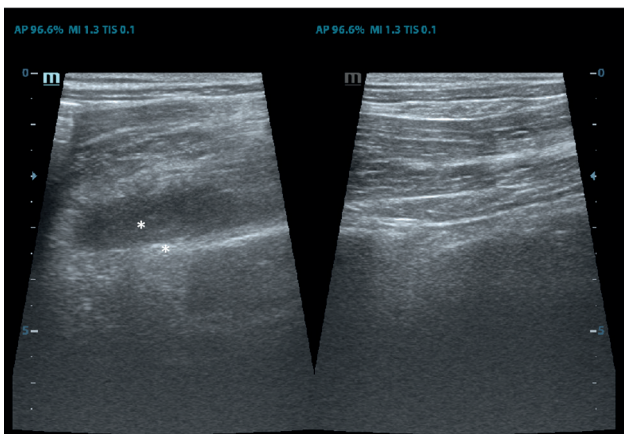


Figura 2: Se aprecia paciente con miembro inferior derecho en postura antiálgica (flexo de cadera y rodilla y decúbito lateral izquierdo).

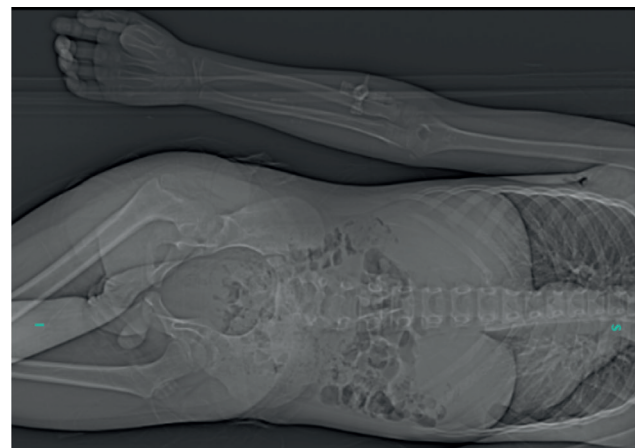
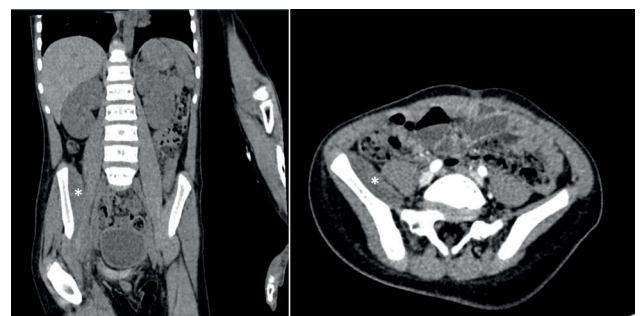


Figura 4: Se aprecia imagen isodensa/hipodensa (*) a nivel de músculo iliopsoas derecho en corte coronal y sagital. Comparar volumen de complejo iliopsoas de lado derecho versus izquierdo, siendo el primero el más voluminoso.



Discusión

En el paciente crítico, la aparición de dolor espontáneo en la región inguinal, tras haber sufrido una alteración de la coagulación por sepsis secundaria a *Acinetobacter baumannii*, acompañado de la presencia de lesiones purpúricas y petequias nos hizo pensar en la posibilidad de hematoma espontáneo del psoas y permitió sugerir un manejo lo más conservador posible, debido a la elevada morbimortalidad que produce esta complicación.

La anamnesis, el examen físico minucioso y el signo del psoas nos orientaron a diagnosticar HP, una complicación muy infrecuente, que puede aparecer en pacientes críticos con alteración de la coagulación por sepsis secundaria a infección por *Acinetobacter baumannii*. Se reporta en la literatura el primer caso de púrpura fulminans por *Acinetobacter baumannii* (bacilo Gram negativo) más hematoma espontáneo del psoas.

La PF es una condición hemorrágica asociada a sepsis secundaria a infección por bacilos Gram negativos³. La PF es un signo de CID, y como tal, la consecuencia de sepsis severa y de shock séptico⁴. La PF hace referencia a la aparición brusca de lesiones purpúricas y equimóticas, dolorosas, rápidamente progresiva y que se asocia a alteración de la coagulación⁶, tal como hemos observado en nuestro paciente pediátrico. Las lesiones purpúricas generalmente son simétricas, afectan más frecuentemente las nalgas y muslos y se autolimitan sólo a la piel⁶.

En nuestro caso clínico se observaron lesiones en mano rodilla y pie derecho. Dado que la PF produce coagulopatía por consumo, el objetivo terapéutico era reponer los factores deficitarios, administrando plasma fresco, heparina y tratamiento anti trombina⁶. *Acinetobacter baumannii* es un cocobacilo aerobio Gram negativo⁹, y como tal puede ser causa de PF, como ha sido documentado en el presente caso clínico.

Los HP son una condición extremadamente rara en niños². Los factores de riesgo son: a) obesidad; b) enfermedad renal crónica o hemodiálisis; c) edad adulta; d) discrasia sanguínea (hemofilia); e) terapia antiagregante; f) terapia anticoagulante^{2,12}. Esta complicación no está descrita en pacientes pediátricos, por ello a importancia de aportar este caso clínico a la literatura. El músculo psoas ilíaco contribuye a la postura con la flexión del tronco y del muslo¹¹. Los hematomas en este músculo son más frecuentes en pacientes con alteración de la coagulación o con terapia anticoagulante; es extremadamente raro en pacientes sin discrasia sanguínea; mientras que en pacientes jóvenes es consecuencia de eventos traumáticos¹. Nuestro paciente aunque joven, no presentó ningún evento traumático conocido.

Las manifestaciones clínicas del hematoma del psoas incluyen dolor en la ingle, cadera o muslo, equimosis periumbilical (Signo de Cullen), equimosis en el flanco

(Signo de Grey Turner), neuropatía femoral, flexión de cadera en posición antiálgica (**Figura 2**), y Signo del Psoas (dolor provocado tras hiperextensión de la cadera) (**Figura 2**). La imposibilidad para extender la cadera origina impotencia funcional del miembro afectado, lo que origina una marcha con cojera o marcha antiálgica¹¹. El HP puede aparecer ocasionalmente en la pared abdominal (Signos de Cullen o de Grey Turner), o en la región inguinal o en el muslo^{11,12}, como sucedió en nuestro caso clínico. Los HP pueden ser cuantiosos, lo que puede producir hipovolemia o incluso shock¹¹. Esto se debe a que el músculo psoas puede alojar hasta 10 veces su tamaño original¹⁴; por eso es que un retraso en el diagnóstico puede tener consecuencias fatales¹⁵, de allí la importancia de hacer un diagnóstico diferencial, como el que planteamos en nuestro caso clínico.

Los HP son complicaciones graves y potencialmente mortales. Salvando esta eventualidad, las complicaciones crónicas del HP son: a) quistes; b) pseudotumores; c) miositis osificante¹⁶. La incidencia del HP en pacientes anticoagulados va del 0.1% al 0.6%; en pacientes en UCI es del 0.38%; y del 0.76% en pacientes con COVID-19¹⁷. En el 38% de pacientes con HP, el sangrado no revierte¹⁵. Esto explicaría la mortalidad del 4% que se observa en los Servicios de Emergencia, y la mortalidad del 30% al 50% en UCI¹⁸. Sunga et. al. sostienen que a los 7 días de evolución del HP, la mortalidad es del 5.6%, mientras que a los 30 días, esta podría elevarse hasta el 10.1%¹⁹.

El diagnóstico del HP es eminentemente clínico, pero precisa confirmación imagenológica^{13,14,16,17,20}. El diagnóstico precoz evitaría complicaciones tales como absceso, compresión nerviosa y cirugías innecesarias [20]. En la ecografía se puede observar engrosamiento o hipogenicidad del músculo psoas^{14,20}. En la tomografía, el HP se observaría como una colección isodensa o hipodensa²⁰. En la RM se puede apreciar también el hematoma y su extensión¹⁶. La resonancia magnética en imagen T2 es más sensible que la tomografía¹¹. La ecografía es la prueba más rentable para estudiar hematoma de partes blandas profundas (músculo psoas)¹¹. Sin embargo, la tomografía es la prueba más accesible y adecuada para el diagnóstico de hematomas intramusculares o retroperitoneales¹³. La angiografía, aunque es una prueba más invasiva, tiene utilidad diagnóstica y terapéutica, ya que podría realizar además embolización del vaso sangrante¹¹. En los pacientes con HP es necesaria una analítica sanguínea completa que incluya hemograma, hemoglobina y hemostasia, para valorar el estado de coagulación del paciente y actuar en consecuencia¹¹.

El tratamiento del HP sigue siendo controversial, y dependiendo de la repercusión hemodinámica, se optará por tratamiento conservador o intervencionista^{11,12}. El tratamiento conservador incluye: a) reposo absoluto; b) corrección de la hemostasia (transfusión sanguínea,

plasma congelado, etc.); c) analgésicos y antiinflamatorios; d) tracción blanda de miembro afecto (para disminuir el dolor)^{11,12}. Si el tratamiento conservador es inefectivo, se procede a instaurar tratamiento invasivo que comprende: a) drenaje percutáneo; b) angiografía más embolización percutánea; c) drenaje quirúrgico^{11,12}. En el presente caso clínico, el paciente pediátrico requirió tratamiento conservador (reposo absoluto, analgesia, crioterapia, termoterapia), con lo cual se logró mejoría clínica.

Conclusión

La sepsis severa por *Acinetobacter baumannii* que presenta como signo de coagulación intravascular diseminada púrpura fulminans en un paciente pediátrico, fue la causa final que provocó hematoma

del psoas como complicación severa e infrecuente, como se ha podido documentar en el presente caso clínico. El signo del psoas fue la prueba física que permitió su sospecha clínica; y la ecografía y la tomografía sirvieron como pruebas confirmatorias. El diagnóstico precoz y el manejo oportuno evitaron un desenlace fatal en el presente caso, a pesar de la alta morbimortalidad que presentan los hematomas del psoas no diagnosticados ni tratados.

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Conflicto de intereses

Los autores declaran no tener conflicto de intereses.

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CASE REPORT

Intoxicación por solución alcalina casera. ¿Conocemos los riesgos de las soluciones de rehidratación oral?

Home alkaline solution poisoning - Do we know the risks of oral rehydration solutions?

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Received: 30 - XII - 2023**Accepted:** 21 - I - 2024**doi:** 10.3306/AJHS.2024.39.03.154**Resumen**

Paciente de 2 años que acude a Urgencias por cuadro de gastroenteritis aguda de 12 horas de evolución con empeoramiento del estado general y letargia en últimas horas. En domicilio inician rehidratación oral con solución alcalina casera. A su valoración en Urgencias, presenta aspecto deshidratado, mal estado general, letargia, taquicardia e hipotensión arterial. Se inicia expansión con suero fisiológico con normalización de las constantes vitales. En resultados analíticos iniciales, presenta alcalosis metabólica hipematrémica grave con intento de compensación respiratoria (pH 7,47, pCO₂ 81 mmHg, HCO₃ 60 mEq/L, EB +30 mmol/L, Na 182 mEq/L, láctico 19 mmol/L) con Cl en orina < 20 mmol/L y parámetros de insuficiencia renal aguda. Elevación moderada de reactantes de fase aguda (PCR 2,8 mg/dL y PCT 3,98 ng/mL). Se inicia antibioterapia con cefotaxima. Se contacta con Unidad de Transporte Pediátrico Balear para traslado a centro de referencia. Ingresa en la Unidad de Cuidados Intensivos de adultos presentando convulsión tónico-clónica generalizada de 30 minutos (tratada con benzodiazepinas y levetiracetam) por lo que se procede a intubación orotraqueal. Presenta cambios pupilares intermitentes (miosis y midriasis) y taquicardia asociada, sugestivos de convulsión, que ceden con midazolam. Posteriormente presenta anisocoría que evoluciona a midriasis bilateral arreactiva. Se realiza TAC craneal urgente que evidencia edema cerebral difuso e isquemia de ganglios de la base. Deterioro hemodinámico que requiere soporte vasoactivo con noradrenalina y adrenalina. Presenta varias paradas cardiorrespiratorias (PCR) con ritmo organizado sin pulso, recuperadas tras reanimación cardiopulmonar avanzada, administración de adrenalina, expansión y bolos de calcio y potasio por hipocalcemia iónica e hipopotasemia, tras lo que se estabiliza y permite traslado aéreo a hospital de referencia con Unidad de Cuidados Intensivos Pediátricos sin precisar sedoanalgesia.

Al ingreso en UCIP persiste alcalosis metabólica grave (pH 7,71 HCO₃ 63,2) con natremia de 166 mEq/L. Precisa correcciones de hipopotasemia e hipocalcemia. Destaca exploración neurológica clínica compatible muerte encefálica. EEG isoelectrico y patrón de flujo reverso en ecografía doppler transcraneal. Evolución a shock refractario y fallo multiorgánico. Se produce nueva parada cardiorrespiratoria y éxitus.

Rehistoriando a los padres del paciente destaca en la rehidratación casera empleada un aporte de entre 14-33 mEq/kg de bicarbonato sódico en menos de 12 horas, que habría originado junto a la deshidratación y la afectación renal las alteraciones del equilibrio ácido-base e hidroelectrolíticas detectadas. No se observó pérdida renal de cloro ni otras causas que las pudieran haber justificado o agravado tras estudio endocrino-metabólico, genético, renal y necropsia.

Palabras clave: Alcalosis metabólica, bicarbonato, solución de rehidratación, letal.

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Abstract

2-year-old patient who comes to the Emergency Department due to a 12-hour episode of acute gastroenteritis with worsening general condition and lethargy in the last few hours. Oral rehydration with homemade alkaline solution is initiated at home. Upon evaluation in the Emergency Department, the patient appears dehydrated, in poor general condition, lethargic, tachycardic, and hypotensive. Intravenous fluid expansion is initiated, achieving normal vital signs. Initial analytical results reveal severe hypernatremic metabolic alkalosis with respiratory compensation attempt (pH 7.47, pCO₂ 81 mmHg, HCO₃ 60 mEq/L, base excess +30 mmol/L, Na 182 mEq/L, lactate 19 mmol/L) with urine chloride < 20 mmol/L and parameters indicating acute renal failure. Moderate elevation of acute phase reactants (PCR 2.8 mg/dL and PCT 3.98 ng/mL) is observed. Cefotaxime antibiotic therapy is started. Pediatric Transport Unit of the Balearic Islands is contacted for transfer to a referral center. While waiting for this team, the patient is admitted to the adult Intensive Care Unit, where he experiences a 30-minute generalized tonic-clonic seizure (treated with benzodiazepines and levetiracetam), which leads to orotracheal intubation. He presents intermittent pupil changes (miosis and mydriasis) associated with tachycardia, which is interpreted as maintained seizure activity, he responds to midazolam. Subsequently, anisocoria develops into bilateral arreactive mydriasis. Urgent cranial CT scan reveals diffuse cerebral edema and basal ganglia ischemia. Hemodynamic deterioration requires initiation of vasoactive support with norepinephrine and adrenaline. Multiple cardiac arrests with organized pulseless rhythm occur, recovered after advanced cardiopulmonary resuscitation, adrenaline administration, and calcium and potassium boluses for ionic hypocalcemia and hypokalemia, stabilizing afterward for aerial transfer to a referral hospital with a Pediatric Intensive Care Unit without the need for sedation or analgesia.

Upon admission to the Pediatric Intensive Care Unit, severe metabolic alkalosis persists (pH 7.71, HCO₃ 63.2) with sodium levels of 166 mEq/L. Correction bolus for hypokalemia and hypocalcemia are required. Clinical neurological examination indicates brain death. Isoelectric EEG and reverse flow pattern on transcranial Doppler ultrasound are noted. Progression to refractory shock and multiorgan failure occurs. A new cardiac arrest and death follow.

Upon rehistory from the patient's parents, the homemade rehydration employed involved an intake of 14-33 mEq/kg of sodium bicarbonate in less than 12 hours, which, along with dehydration and renal involvement, would have caused the detected acid-base and electrolyte imbalances. No renal chloride loss or other justifying or exacerbating causes are observed after endocrine-metabolic, genetic, renal, and necropsy studies.

Key words: Metabolic alkalosis, bicarbonate, oral solution, fatal.

Descripción del caso

Paciente de 2 años de sexo masculino con retraso del crecimiento intrauterino y fallo de medro como únicos antecedentes personales de interés que es atendido en Urgencias por cuadro de fiebre, vómitos y deposiciones diarreicas cuantiosas de 12 horas de evolución. Los padres refieren inicio de la clínica con un vómito aislado sin productos patológicos y, pocas horas después, aparición de deposiciones diarreicas abundantes. Mantiene inicialmente buen estado general. Dada la clínica, la familia inicia rehidratación oral con una solución casera de limonada alcalina con buena tolerancia. Durante el sueño el paciente presenta fiebre con temperatura de hasta 39,8°C y, además, los padres detectan empeoramiento rápido del estado general y dificultad para despertarlo por lo que contactan con el 061 y, según su recomendación, acuden a Urgencias. Los padres niegan posibilidad de intoxicación con algún fármaco o sustancia al alcance del paciente. No sospechan relación de la clínica con ingesta de ningún alimento ni hay otros familiares, convivientes o contactos cercanos recientes con clínica infecciosa.

A su llegada a Urgencias, el pediatra de guardia objetiva mal estado general, aspecto deshidratado, taquicardia de 220 lpm e hipotensión de 60/30 mmHg, por lo que administra expansión de volumen con suero salino fisiológico 0,9%. La gasometría venosa inicial muestra una importante alcalosis metabólica con intento de compensación respiratoria: pH 7,47, pCO₂ 81 mmHg, HCO₃ 60 mEq/L y EB +30. Láctico 19. Se extrae analítica de sangre urgente en la que destaca hipernatremia grave (sodio corregido por glucemia de 182mEq/L) e hiperglucemia 234 mg/dL que condicionan una hiperosmolalidad de 394 mOsm/kg, parámetros de insuficiencia renal aguda (urea 81 mg/dL y creatinina 1,63 mg/dL) y elevación moderada de reactantes de fase aguda (proteína C reactiva 2,8 mg/dL y procalcitonina 3,98 ng/mL). Sin otras diselectrolitemias. El cloro en sangre es de 96 mmol/L y en orina, que tiene un pH de 7, < 20 mmol/L.

Dada la inestabilidad hemodinámica del paciente y las graves alteraciones hidroelectrolíticas y del equilibrio

ácido base, se traslada al paciente a la Unidad de Cuidados Intensivos de adultos y se contacta con la Unidad de Transporte Pediátrico Balear (UTPB) para traslado a centro de referencia. Tras ingreso en la Unidad de Cuidados Intensivos de adultos, presenta una convulsión tónico-clónica generalizada de 30 minutos de duración que cede tras administrar tres dosis de benzodiacepinas (2 vía rectal y 1 endovenosa) y una dosis de carga de levetiracetam intravenoso. Posteriormente, se procede a intubación y conexión del paciente a ventilación mecánica previa administración de sedoanalgesia.

A la llegada de la UTPB, el paciente persiste con aspecto deshidratado y taquicardia de 166 lpm con tensión arterial normal. Presenta mala perfusión periférica e hiperlactacidemia de 20 mmol/L. En la exploración física inicial, se objetivan cambios pupilares intermitentes y alternantes (midriasis y miosis) con reactividad a la luz, por lo que se interpreta la clínica como nueva crisis convulsiva. Se administra una dosis de benzodiacepina intravenosa con lo que se resuelve. Sin embargo, pocos minutos después, presenta anisocoria y posterior midriasis bilateral arreactiva. Ante dicha alteración, se realiza TAC craneal urgente. Durante el traslado para realización de la prueba de imagen, presenta hipotensión arterial súbita de hasta 30/20mmHg con pulso que precisa inicio de soporte vasoactivo con noradrenalina y adrenalina en perfusión. Se suspende sedoanalgesia. Mantiene estabilidad hemodinámica posterior que permite iniciar traslado al hospital de referencia con Unidad de Cuidados Intensivos Pediátricos. Durante el traslado en ambulancia informan de resultados de TAC craneal: edema cerebral difuso con lesiones en núcleos basales y diencefálicas compatible con encefalopatía hipóxico-isquémica aguda (**Ilustración 1**).

Durante el trayecto en ambulancia presenta parada cardiorrespiratoria con actividad eléctrica sin pulso requiriendo maniobras de reanimación cardiopulmonar

Ilustración 1: Imagen del TAC cerebral.



durante 5 minutos (2 ciclos de reanimación y una dosis de adrenalina). A los 10 minutos, presenta una segunda parada cardiorrespiratoria por la que vuelven a iniciarse maniobras de reanimación cardiopulmonar durante 20 minutos precisando en total 4 dosis de adrenalina, 2 bolos de gluconato cálcico y 2 cargas de seroalbúmina al 5%. Se suspende el traslado y se retorna al hospital de origen durante la reanimación.

A la llegada al centro emisor se informa a la familia de la impresión de pronóstico infausto. Durante la transmisión de información, presenta una tercera parada cardíaca con actividad eléctrica sin pulso de 4 minutos que responde a maniobras de reanimación, que incluyen una dosis única de adrenalina y una expansión de seroalbúmina al 5%. Se realiza ecocardiografía a pie de cama durante la reanimación objetivándose una aceptable función y contractilidad cardíaca, que además mejora tras aumento de soporte inotrópico. Se consigue mantener estabilidad hemodinámica dentro de la situación de extrema gravedad, por lo que se decide traslado a hospital de referencia.

Durante el traslado, el paciente presenta pupilas midriáticas arreactivas en todo momento. No se objetivan movimientos ni respiración espontánea. No precisa reinicio de sedación desde su retirada tras la primera parada cardiorrespiratoria. Puede retirarse soporte vasoactivo progresivamente, quedando a su llegada a la Unidad de Cuidados Intensivos Pediátricos únicamente con perfusión de adrenalina. A nivel respiratorio, se mantiene muy estable.

A su ingreso en dicha unidad, presenta escala de Glasgow 3/15 (M1O1V1) y pupilas midriáticas arreactivas. Se inicia registro de electroencefalograma continuo de 2 derivaciones sin actividad eléctrica. Ecografía doppler transcraneal con flujo reverso diastólico bilateral. El paciente presenta una rápida evolución a fallo multiorgánico en las primeras horas de ingreso. Se objetiva elevación de parámetros de daño miocárdico y disfunción cardíaca sisto-diastólica moderada-grave biventricular (fracción de eyección del 25%). Hipotensión progresiva que precisa administrar expansión de volumen y aumentar soporte con drogas vasoactivas sin respuesta. Además, comienza a presentar patrones de electrocardiograma abigarrados con alteración de la repolarización por elevación del segmento ST en todas las derivaciones (excepto II y V6) y con evolución posterior a complejos QRS anchos correspondientes a taquicardia ventricular y que no responden a correcciones iónicas (administración de gluconato cálcico y cloruro potásico por hipocalcemia e hipopotasemia), a la cardioversión eléctrica ni tratamiento con amiodarona. Durante el ingreso, se inicia exploración neurológica reglada compatible con muerte encefálica. Presenta nueva parada cardiorrespiratoria en asistolia a las 20 horas del ingreso. Dada la situación de muerte encefálica, no se inician maniobras de reanimación. El paciente es éxitus.

Discusión

Presentamos el caso de un paciente con clínica de gastroenteritis aguda de corta evolución que desarrolla de forma catastrófica una grave e infrecuente alteración del equilibrio ácido-base e hidroelectrolítica. El análisis de este caso es de gran interés médico para los autores por su excepcionalidad y, sobre todo, por la posibilidad de prevenirlo en otros pacientes.

El determinante del fallecimiento del paciente parece ser una grave alcalosis metabólica hipernatémica de instauración aguda que produjo complicaciones neurológicas y hemodinámicas letales por alteración del medio interno.

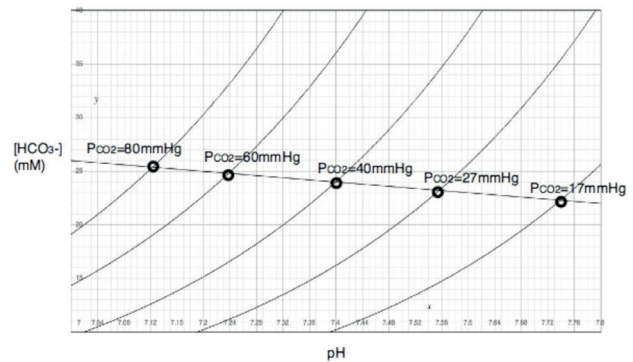
En nuestro caso, se objetivó una alcalosis metabólica grave con un pH de 7,71 y un bicarbonato de 63mEq/L como valores máximos durante su evolución. En la Pediatría son extensamente conocidas la gravedad y consecuencias de la acidosis por su frecuencia. Sin embargo, quizá el conocimiento de la alcalosis metabólica es menor, a pesar de que valores de pH superiores a 7,65 se asocian a un 80% de mortalidad.

Los síntomas de la alcalosis metabólica son secundarios a la propia alcalemia, una situación en la que se desencadenan múltiples procesos patológicos. Entre otros, a nivel respiratorio produce hipoventilación compensatoria con hipoxemia secundaria. A nivel electrolítico, el potasio se desplaza al espacio intracelular y, además, se pierde por la orina produciendo hipopotasemia^{1,2}. El paciente presentaba hipopotasemia de hasta 2,7 mEq/L de difícil reposición, sin conseguir cifras en rango de normalidad en ningún momento. Además, se objetiva una disminución de la concentración de calcio iónico por favorecerse su unión a la albúmina, alteración iónica también observada en nuestro paciente. A nivel cardiaco, puede provocar arritmias y disminución del gasto cardiaco y, consecuentemente, parada cardiorrespiratoria. Igualmente, causa clínica neurológica como irritabilidad, desorientación, convulsiones y coma y aumenta la concentración sanguínea de compuestos nitrogenados neurotóxicos como el amoníaco^{1,3}.

Respecto a los mecanismos de compensación de los trastornos ácido-base, la alcalosis respiratoria da lugar a una compensación a nivel respiratorio. Esquemas como el diagrama de Davenport han intentado reflejar el equilibrio ácido-base y la variación de bicarbonato y presión parcial de dióxido de carbono (CO₂) en caso de activarse mecanismos compensatorios (**Ilustración 2**).

En teoría, la pCO₂ aumenta en 7 mmHg por cada 10 mEq/L de incremento de la concentración sérica de bicarbonato. Sin embargo, una compensación respiratoria adecuada nunca excede los 55-60 mmHg⁴. En el paciente del caso, por tanto, no hablamos de

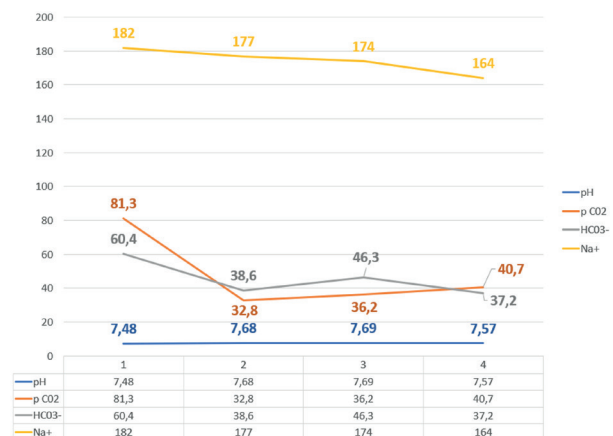
Ilustración 2: Diagrama de Davenport (Davenport, H. W. (1974). The ABC of Acid-Base Chemistry: The Elements of Physiological Blood-Gas Chemistry for Medical Students and Physicians (6th ed.). Chicago: The University of Chicago Press).



compensación, si no de intento de la misma en todo momento ya que la situación de alcalemia no llega a resolverse a pesar de un aumento de pCO₂. La pCO₂ había llegado a tener valor de 81 mmHg por lo que se entiende que ese aumento de pCO₂ no se corresponde únicamente con una compensación *per se*, si no que el paciente presentaba un trastorno mixto de alcalosis metabólica y acidosis respiratoria. Es importante señalar que, a pesar de no resolver la situación de alcalemia, la hipoventilación del paciente ejercía cierto efecto compensador y éste se pierde de forma brusca y con ello aumenta bruscamente el pH tras la intubación y conexión a ventilación mecánica invasiva con parámetros estándar de ventilación (**Ilustración 3**). A su llegada al centro de referencia, se objetiva pCO₂ de 47 mmHg que intenta mantenerse en torno a 55 mmHg en horas posteriores.

Una elevación de bicarbonato plasmático puede producirse como reacción a la pérdida gastrointestinal o renal de hidrogeniones, al movimiento de hidrogeniones al interior de las células o al aporte exógeno de bicarbonato. Además, es necesario que esta concentración de bicarbonato plasmático se mantenga, es decir, que exista alguna condición que comprometa la eliminación renal del exceso de bicarbonato⁵.

Ilustración 3: Representación gráfica de la variación de pH, pCO₂, HCO₃ y Na durante la evolución. A destacar el marcado aumento de pH tras la pérdida de compensación respiratoria.



Se analizan a continuación las posibilidades etiológicas del cuadro. El paciente presentaba vómitos y deposiciones diarreicas abundantes. Sin embargo, el número y cantidad de estos y la corta evolución de la clínica sólo podría explicar parcialmente la alcalosis, pero difícilmente podría explicar las elevadas cifras de bicarbonato alcanzadas. Respecto a la posibilidad de pérdida de hidrogeniones en orina, el pH urinario era de 7 inicialmente y asciende en horas posteriores hasta 8,5, por lo que una eliminación excesiva de hidrogeniones en orina tampoco es causa probable de la alcalosis.

Respecto a posibles aportes exógenos, se corrobora que, tanto en el hospital de origen como en el traslado y en manejo en el hospital de referencia, no se administró bicarbonato.

Se interroga a los padres acerca de la rehidratación oral en domicilio. Refieren que desde el inicio de la clínica esa mañana el paciente ingiere 1 litro de una dilución que contiene 4 cucharaditas de bicarbonato en cada litro de agua. No ofrecen otros líquidos. Asumiendo que 1 cucharadita puede contener de 3 a 7 gramos de bicarbonato sódico, se calculan unos aportes de 14-33 mEq/kg en pocas horas. Es difícil conocer con exactitud cuántos miliequivalentes ingirió el paciente por no conocer la específicamente la composición del bicarbonato de repostería, pero esto podría explicar una alcalosis hipernatémica como la del paciente. Según los padres, ya habían administrado esta solución hacia unos meses por gastroenteritis aguda tras consultar en su Centro de Salud siguiendo supuestamente las recomendaciones les dieron en esa otra ocasión.

Se postula la posibilidad de que exista una tubulopatía renal precipitante y/o agravante de la evolución fatal. El paciente presentó un crecimiento intrauterino retardado y estaba siendo estudiado por un fallo de medro que había sido enfocado a celiacía y déficit de hormona del crecimiento, pero no a posibles tubulopatías como el síndrome de Bartter o la diabetes insípida central.

El paciente no presentaba un hábito poliúrico, por lo que la diabetes insípida central parece un diagnóstico improbable. En cambio, sí podría tratarse de un tipo de síndrome de Bartter clásico con debut por un cuadro de deshidratación severa en contexto de un proceso infeccioso. A favor de esta posible etiología, el paciente presentaba un fenotipo con frente abombada y facies triangular y; en contra, valores de potasio normal a su llegada al hospital emisor. Además, el cloro en sangre estaba discretamente descendido (96 mEq/L) y bajo en orina (< 20 mEq/L) lo que en principio no sugiere la presencia de una tubulopatía renal. Aun así, ante esta posibilidad, se cursa estudio genético por secuenciación masiva orientado a estos diagnósticos del que se obtiene un resultado normal; así como estudio metabólico y hormonal que descarta un exceso de actividad mineralcorticoide. Con ello, queda razonablemente

descartada la existencia de una patología subyacente como causa o agravante del cuadro clínico.

Como se ha señalado, la elevación de bicarbonato en plasma es reversible si se produce una adecuada eliminación renal. Esta eliminación podría haberse visto reducida en el caso de este paciente debido a una insuficiencia renal prerrenal. La propia activación de la actividad del sistema angiotensina-aldosterona secundaria a una depleción de volumen estimula la reabsorción de sodio en los túbulos renales, la reabsorción de bicarbonato y la generación de nuevo bicarbonato. Además, la hipernatremia (que parece también originada por el aporte exógeno de bicarbonato sódico) contribuía también a la alcalosis, ya que el aumento de sodio en el túbulo distal de la nefrona y, por tanto, su mayor reabsorción genera secreción de hidrogeniones y potasio en orina. Además, la depleción de potasio resultante también juega un papel en el mantenimiento de la alcalosis, ya que activa el movimiento de hidrogeniones hacia el interior de las células generando bicarbonato extracelular y un aumento de la secreción renal de hidrogeniones².

Para ir más allá y según lo encontrado en la bibliografía⁴, la variación de la ingesta de cloruro de sodio en la dieta tiene un impacto importante en la capacidad de reabsorción de bicarbonato del riñón. Los sujetos que ingieren una dieta relativamente alta en cloruro de sodio excretan muy fácilmente una carga de bicarbonato de sodio exógeno con un cambio mínimo en el pH sistémico o el nivel de bicarbonato. Sin embargo, en los sujetos que ingieren una dieta baja en cloruro de sodio, la capacidad de reabsorción de bicarbonato del riñón aumenta y una carga de bicarbonato de sodio elevará el pH sérico y el nivel de bicarbonato. Se podría considerar la alta probabilidad de que la dieta de nuestro paciente de 2 años no tuviera alto contenido en sal y que esto pudiera haberle predispuesto a generar una mayor alcalosis.

Es importante comentar también el papel de la hipernatremia en la clínica y morbilidad del paciente, dados los efectos que presenta sobre el sistema nervioso central y los riesgos de una corrección rápida. A nivel clínico, la hipernatremia provoca una clínica caracterizada por sensación marcada de sed, irritabilidad y letargia. Además, puede producir fiebre. A nivel del sistema nervioso central, la hiperosmolaridad extracelular provoca disminución del volumen cerebral y, con ello, tracción y desgarro de venas intracerebrales provocando hemorragias cerebrales. También pueden producirse convulsiones y, como en los casos de corrección rápida de hiponatremias, desencadenar una mielinolisis central pontina y/o extrapontina. Así, el estado letárgico que sufre el paciente y por el que los padres acuden a Urgencias, así como la crisis convulsiva presentada durante su evolución podrían explicarse por esta alteración electrolítica. Sin embargo, la neuroimagen no mostró hallazgos característicos como sangrados intraparenquimatosos, disminución de volumen cerebral, complicaciones trombóticas o mielinolisis.

A pesar de no ser la alteración electrolítica más frecuente, la hipernatremia puede ocurrir en pacientes con gastroenteritis aguda que sufren una pérdida de agua mayor a la pérdida de sodio (en diarreas hipotónicas, por ejemplo) y que no tienen acceso o tolerancia a líquido hipotónico que reponga esa pérdida de agua sufrida. El paciente tenía buena tolerancia a la rehidratación oral según los padres, sin embargo, se trataba de una reposición con un líquido hipertónico que no solventaba el déficit de agua, por lo que es posible que cierto grado de hipernatremia correspondiera a esta causa. Aun así, las cifras tan elevadas de sodio alcanzadas en ese corto periodo de tiempo que duró la clínica (presentó un valor máximo de 182 mEq/L) no se justificarían por ese mecanismo por sí solo. Al igual que en el caso del bicarbonato, sí podrían explicarse por los aportes exógenos excesivos de bicarbonato sódico ingeridos. Como se comentó previamente, el estudio hormonal y genético posterior descartó la presencia de una patología subyacente favorecedora tanto de la alcalosis metabólica como de la hipernatremia. Independientemente de la etiología, sí está claro en este paciente que la instauración de la hipernatremia fue aguda: la clínica y el inicio de los aportes exógenos de bicarbonato sódico ocurrió en un periodo de unas 10-12 horas previo a la consulta en Urgencias. Este hecho permite disipar las dudas sobre si la propia corrección de sodio pudiera haber sido responsable de cierta clínica a nivel del sistema nervioso central (a su llegada al centro de referencia, presentaba una natremia de 167 mEq/L y, en horas posteriores, se mantuvo estable entre 166-169mEq/L). Una hipernatremia aguda grave puede ser corregida con rapidez sin riesgo de edema cerebral. Esto se debe a que los idiosmoles que produce el cerebro para incrementar la osmolaridad intracelular y evitar la deshidratación celular, aún no han tenido tiempo de formarse y acumularse en el caso de una instauración brusca. La formación de estos idiosmoles es la responsable del gradiente osmótico que se da en las correcciones rápidas de hipernatremias de instauración gradual y que provoca el edema cerebral³.

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Juicio clínico final

Por lo tanto y para concluir, la situación de grave alcalosis metabólica fue la causa del éxitus de nuestro paciente y ésta probablemente fue de origen multifactorial: parece que se desencadenó principalmente por una administración exógena excesiva de bicarbonato sódico y se agravó por una situación de deshidratación e insuficiencia renal aguda que podrían haber alterado su excreción.

La alcalosis metabólica grave de rápida instauración puede causar daños neurológicos y cardíacos graves e irreversibles y es necesario conocerla a pesar de su infrecuencia.

No se deben recomendar soluciones caseras de rehidratación cuya preparación pueda inducir a error; ya que pueden causar, en pacientes predispuestos, graves complicaciones como en el caso presentado. Por lo revisado en la bibliografía, hay descritos algunos casos similares, de los cuales hubo 2 pacientes con mismo desenlace fatal^{6,7,8,9,10}. Por el momento no se ha publicado ninguno en nuestro país.

Se podría considerar un objetivo de la presentación de este caso proponer la divulgación de esta entidad, así como de una recomendación oficial colegial dirigida a personal sanitario para evitar la recomendación de soluciones caseras de rehidratación oral que pueden inducir a errores de preparación y, con ello, presentar consecuencias muy graves como la descrita. Esta recomendación sería de especial importancia en la edad pediátrica, donde la amplísima variación de edades y peso de los pacientes obligan a una individualización de las dosis y tipos de tratamiento.

Conflicto de intereses

Los autores declaran no tener conflicto de intereses.

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CASE REPORT

Hydromyelia regarding a case, should we perform an intrapartum epidural?

Hidromielia a propósito de un caso, ¿debemos realizar una epidural intraparto?

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Summary

Hydromyelia, dilation of the ependymal duct, is a random finding that is increasing in incidence due to the use of magnetic resonance imaging. During labour, central locoregional anaesthesia can be performed without increasing the incidence of neurological complications or sequelae. It is important to differentiate it from syringomyelia, a fluid-filled cavity in the spinal cord and lined with glial cells that is usually associated with Chiari syndrome and can produce, with central locoregional anaesthesia, depending on its location, a valvular mechanism of the CSF and increase intracranial pressure.

Key words: Anesthesia, Spinal, syringomyelia, Arnold-Chiari malformation.

Resumen

La hidromielia, dilatación del conducto endimario, es un hallazgo aleatorio cuya incidencia está aumentando gracias al uso de la resonancia magnética. Durante el parto, se puede realizar anestesia locorregional central sin aumentar la incidencia de complicaciones o secuelas neurológicas. Es importante diferenciarla de la siringomielia, una cavidad llena de líquido en la médula espinal y revestida de células gliales que suele asociarse al síndrome de Chiari y que puede producir, con la anestesia locorregional central, dependiendo de su localización, un mecanismo valvular del LCR y aumentar la presión intracraneal.

Palabras clave: Anestesia espinal, siringomielia, malformación de Arnold-Chiari.

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Introduction

Syrinx in the form of a slit or hydromyelia refers to a dilation greater than 6 mm in Magnetic Resonance (MRI) of the central spinal canal, the ependymal duct, which is lined by ependymal cells, and must be differentiated with the term syringomyelia, which comes from the Greek language "syrinx" (reed or tube) and "myelos" (marrow), which refers to the presence of a fluid-filled cavity in the spinal cord and lined with glial cells¹. The predominant classification is based on anatomical characteristics and pathogenesis rather than pathophysiological mechanisms.

The diagnosis of hydromyelia should be made by a complete spinal MRI (cervical, dorsal and lumbar) that includes morphological sequences (T1-, T2-, FLAIR-, T2, Enhanced T1) and a dynamic MRI with a careful study of CSF velocity (CISS, cine-MR sequences)². Plain radiographs and computed axial tomography (CAT) are used to study bone abnormalities.

Treatment of incidental asymptomatic hydromyelia is nonsurgical. It does not represent a disease with an underlying pathology; no clinical or radiological progression has been observed³.

Figure 1: MRI image.



Case

Patient in labour with a history of lumbosciatalgia and broken tailbone after an accident years ago. When reviewing the history, a TSE-T1 TSE-T2 and STIR MRI showed distention of the central ependymal canal between D4-D5 and D9-D10 with a dimension of 1,7mm in D6-D8 and slight physiological cervical lordosis, without presence of central stenosis or existence of masses or pathological collections (Figure 1 and figure 2).

When performing the epidural technique in the previous physical examination, thoracolumbar scoliosis was evident. The epidural technique was performed under asepsis without complications.

During labour, analgesia was administered by continuous infusion of 0.2% ropivacaine plus 0.1 mg of fentanyl at 8 ml/h. No lateralization or extensive motor block was observed, and he remained hemodynamically stable with a VAS level of 2.

As labour did not progress and there were alterations in the foetal monitor, urgent caesarean delivery was indicated. 3 ml of 2% lidocaine, 7 ml of 0.75% ropivacaine plus 0.05 mg of fentanyl were administered, allowing the caesarean section to be performed with a good anaesthetic level.

During the postoperative period, hemodynamic stability was maintained without obvious bleeding, a contracted uterus, and recovery of motor skills and sensitivity in the lower extremities.

Figure 2: MRI image.



Discussion

Epidural anaesthesia is a safe procedure. Knowledge of complications can support efforts to minimize risks. Hydromyelia should be separated from patients with true syringomyelia with an underlying disorder, as they do not share clinical or radiological features.

Post-traumatic syringomyelia is a life-threatening late complication of spinal cord injury. The syrinx extended upward and/or downward from the area of previous trauma. It occurs in approximately 1,1 – 3,2% of spinal injury cases⁴. It is characterized by the development of new neurological symptoms after a variable time interval, around 12 years.

The most typical symptom, although it is not necessarily present, is the decrease in vital sensitivity without loss of gnostic sensitivity.

Surgical treatment is recommended if there is progressive neurological deterioration and consists of drainage of the syrinx⁵.

Idiopathic syringomyelia, in theory, have a higher risk of increased intracranial pressure and brainstem compression and/or disease progression during labor⁶.

It is closely related to the unusually low position of the conus medullaris, idiopathic scoliosis and Chiari syndrome type I, which is a disorder of the hindbrain that can cause altered craniospinal pressures and abnormal flow of cerebrospinal fluid⁷ since they all probably share the same pathogenic mechanism⁸. Anaesthetic complications occur infrequently in patients with ACM-I regardless of anaesthetic management⁹.

New case series studies have emerged supporting that in patients with Chiari I malformation who do not have signs of increased intracranial pressure, the mode of delivery should be based on obstetric rather than neurological considerations. In addition, both the use of epidural and intradural anaesthesia must be available¹⁰.

Conflict of interest

The authors declare that they have no competing interests.

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