ORIGINAL

Assessment of drug utilization patterns of proton pump inhibitors in a tertiary care hospital: a prospective observational study in a south indian tertiary care hospital, India

Evaluación de los patrones de utilización de medicamentos de los inhibidores de la bomba de protones en un hospital de atención terciaria: un estudio observacional prospectivo en un hospital de atención terciaria del sur de la India

Arezoo Roozegar D, Balakeshwa Ramaiah D

Doctors of Pharmacy, Department of Pharmacy Practice, Karnataka College of Pharmacy, Bengaluru, India

Corresponding author

Arezoo Roozegar Department of Pharmacy Practice, Karnataka College of Pharmacy, Bengaluru, India E-mail: arezoo.roozegar@yahoo.com Received: 1 - X - 2021 Accepted: 5 - XII - 2021

doi: 10.3306/AJHS.2022.37.01.77

Abstract

Objective: The present study is aimed to assess the drug use patterns of proton pump inhibitors in a south Indian tertiary care hospital. **Methodology:** A prospective observational study in 6 months that was conducted in the inpatient department at a tertiary care hospital, treatment chart of inpatients will be review for prescribed patterns of proton pump inhibitors, relevant information will be noted in a predefined data collection form. All of the detail will be used to calculate the result of the study.

Result: 124 patients under randomized, prospective, and observational study are collected in this study .therefore from this sample 73 patients (59%) were male and 51(41%) patients were female, four groups of ages 18 to 30 years old (10.48%), 31 to 50 years old (25%), age of 51 to 70 years old (42.7%) and ages above than71 (21.7%). gastrointestinal disease 16.93%, respiratory disease 50%, alcoholism 2.41%, heart disease 27.42%, veins & vessel &gland disorders 49.19%, kidney disease 25.8%, nerve and brain damages 22.5%, liver disease7.25%, inflectional disease 34.67%, diabetic Mellitus 24.2% and other rare diseases 11.3% were the diagnosis of patients, 164 proton pump inhibitors are used during treatment, these drugs are as 124 pantoprazole (75.6%), 37 Omeprazole (22.56%), 2 rabeprazole (1.2%), 1 lansoprazole (0.6%).wherefore these shows that the pantoprazole and omeprazole are most favorite drug to be prescribed by the physicians, gastroesophageal reflex disease in 63 (50.8%) patient, gastric ulceration in 2 (1.6%) patient, inflectional disease in 59 (47.58%) patients was the indications of PPIs and they are given in injections (75.6%) and (24.4%) orally.

Conclusion: Based on data collected in this study Proton pumps inhibitors are mostly used in males and they are prescribed for respiratory disease, veins disorders, and diabetic Mellitus diagnoses; pantoprazole and omeprazole are the most PPIs prescribed by the doctors and they are prescribed in intravenous more than others routs. It was found the use of PPIs in a wide range of indications; therefore, PPIs generally are indicated for gastroesophageal reflux disease and inflectional disease in great value in mean indications.

Keywords: Proton pump inhibitors, pantoprazole, drug utilization.

Resumen

Objetivo: El presente estudio tiene como objetivo evaluar los patrones de uso de medicamentos de los inhibidores de la bomba de protones en un hospital de atención terciaria del sur de la India.

Metodología: Se trata de un estudio observacional prospectivo de 6 meses de duración que se realizó en el departamento de hospitalización de un hospital de atención terciaria, en el que se revisarán las historias clínicas de los pacientes internos para determinar los patrones de prescripción de los inhibidores de la bomba de protones y se anotará la información pertinente en un formulario de recogida de datos predefinido. Todos los detalles se utilizarán para calcular el resultado del estudio.

Resultado: En este estudio se recogen 124 pacientes en el marco de un estudio aleatorio, prospectivo y observacional. Por lo tanto, de esta muestra 73 pacientes (59%) eran hombres y 51 (41%) eran mujeres, cuatro grupos de edades de 18 a 30 años (10,48%), de 31 a 50 años (25%), de 51 a 70 años (42. Enfermedades gastrointestinales 16,93%, enfermedades respiratorias 50%, alcoholismo 2,41%, enfermedades cardíacas 27,42%, trastornos de las venas y los vasos sanguíneos 49,19%, enfermedades renales 25,8%, daños nerviosos y cerebrales 22,5%, enfermedades hepáticas 7,25%, enfermedades infecciosas 34,67%, diabetes mellitus 24. El diagnóstico de los pacientes fue de un 2% y de otras enfermedades raras de un 11,3%. Durante el tratamiento se utilizaron 164 inhibidores de la bomba de protones, de los cuales 124 eran pantoprazol (75,6%), 37 omeprazol (22,56%), 2 rabeprazol (1,2%) y 1 lansoprazol (0,6%). Por lo tanto, esto demuestra que el pantoprazol y el omeprazol son los fármacos preferidos por los médicos, la enfermedad de reflejo gastroesofágico en 63 (50,8%) pacientes, la úlcera gástrica en 2 (1,6%) pacientes, la enfermedad infecciosa en 59 (47,58%) pacientes fueron las indicaciones de los IBP y se administran en inyecciones (75,6%) y (24,4%) por vía oral.

Conclusiones: Según los datos recogidos en este estudio, los inhibidores de la bomba de protones se utilizan sobre todo en los hombres y se prescriben para enfermedades respiratorias, trastornos venosos y diagnósticos de diabetes mellitus; el pantoprazol y el omeprazol son los IBP más prescritos por los médicos y se prescriben por vía intravenosa más que por otras vías. Se constató el uso de los IBP en una amplia gama de indicaciones; por lo tanto, los IBP están indicados generalmente para la enfermedad por reflujo gastroesofágico y la enfermedad infecciosa en gran valor en las indicaciones medias.

Palabras clave: Inhibidores de la bomba de protones, pantoprazol, utilización de medicamentos.

Introduction

The World Health Organization (WHO) defines drug utilization research (DUR) as "the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences"¹. The ultimate goal of DUR is to evaluate whether the drug treatment is rational or not which may provide insights into the various aspects of prescribing patterns such as frequency, dosage, duration of therapy, indication quality, determinants, and outcome of drug use. DUR is used as a potential tool in the evaluation of the healthcare systems as well as a powerful exploratory tool to explain the role of drugs in society. PPIs are one among the most commonly prescribed class of medications in both outpatient and inpatient treatments. These medications are used for long-lasting suppression of gastric acid by inhibiting the hydrogen-potassium adenosine triphosphatase enzyme system, which makes the stomach acidic, and is found in the cells that line the stomach. Over the past few years, the prescriptions for the Proton Pump Inhibitors (PPIs) have consistently increased in the hospital and ambulatory care settings. Studies have shown that the incidence of irrational use of PPIs ranges from 40-70%².

Proton pump inhibitors (PPIs) were developed in the '80s and their use has continuously grown. They represent the first choice in the treatment of acid-related diseases and are currently the most prescribed drugs in the world. Over the past 10 years, there has been a significant increase in their use throughout the world [3,4]. For the treatment of acid-related diseases, various inhibitors of gastric acid emission and killing specialists have been created. At first, killing medications containing aluminum or magnesium, and anticholinergic specialists were utilized. Nonetheless, the effects of those for acid restraint are restricted and their utilization frequently has adverse effects, including cardiovascular occasions, loose bowels, and constipation^{5,6}.

Proton pump inhibitors are the most generally prescribed class of meds in the United States, and they represent >\$10 billion in yearly medical care costs. PPIs are prescribed by a wide scope of primary and specialty care clinicians for a scope of manifestations related to acid reflux sickness. The far-reaching utilization of PPIs has as of late earned consideration from the American Board of Internal Medicine's "Choosing Wisely" mission to promote appropriate stopping of PPIs when appropriate. PPI prescribing guidelines do not promote one PPI formulation over others, as evidence shows similar symptom relief between different PPI formulations. The active ingredients in generic drugs are the same as in brand name drugs and the FDA requires that generic drug manufacturers must prove the bioequivalence of a generic and brand name formulation cost-effectiveness investigations have discovered that conventional PPIs financially overwhelm

treatment methodologies with more expensive PPI formulations⁷⁻¹⁰. PPIs are the most generally utilized drug for gastric acid hindrance on the planet. All the PPIs accessible in India, including omeprazole, esomeprazole, lansoprazole, and rabeprazole, have a benzimidazole core in their molecules alongside different sorts of branch structures. Omeprazole was the first proton pump inhibitor (PPI) found and has been accessible in Europe for acid suppression since 1988. Subsequently, other drugs have been identified and several alternatives are currently available: lansoprazole, pantoprazole, rabeprazole, dexlansoprazole, and esomeprazole^{4,7}.

In the current setting, the consumption of PPIs is overwhelming; studies have to be carried out to examine the prescribing pattern of the PPIs in hospitalized patients. Hence, the present study aimed to assess and evaluate the utilization patterns of PPIs in the inpatient department of a south Indian tertiary care hospital.

Materials and methods

It is a prospective observational study conducted in the inpatient department at a tertiary care hospital. All of the Prescriptions and treatment charts of inpatients will be review for prescribed patterns of proton pump inhibitors (PPIs). And references projects and books will be used as tools to review the prescription and case chart. The admission register will be reviewed for prescription of any PPIs. When the required data are found, then it is noted in performed data form. All medically relevant information will be noted in a predefined data collection form. Alternatively, the demographic data and the detailed history of the patient regarding past, present, family, personal, and drug history were taken. The other details like the present diagnosis, reason for the present admission will be also noted during 6 months. Patients of both genders who are admitted into the inpatient wards in the Hospital, between the age group of 18-87 years were included in the study. The detailed information such as dosage, frequency, route, indication, and any other relevant information will be retrieved and entered into the data collection form. and at the end of collection data, all of the detail will be used to calculate the result of the study⁸⁻¹⁰.

Result and discussion

Despite advances occurred in medical sciences¹¹⁻¹⁵, diverse diseases have been threated the human health¹⁶⁻¹⁹. In this regard, drug utilization is the best way to treat and control the patterns of diseases, globally. Drug utilization is so important in medical facilities^{20,21}.

Totally 124 patients under randomized, prospective, and observational studies are collected in this study.

therefore, from this sample 73 patients (59%) were male and 51 (41%) patients were female. Patients are divided into four groups of ages as 18 to 30 years old (no: 13 (10.48%)), 31 to 50 years old (no: 31 (25%)), age of 51 to70 years old (no: 53 (42.7%)) and ages above than 71 (no: 27 (21.7%)) (**Table I**).

Table I:	demogerapl	hy of patients
Table I:	demogerapl	hy of patients

Categorized age of patients					
Patient demography	No of participants	Percentage			
age of 18_30	13	10.48%			
age of 31_50	31	25%			
age of 51_70	53	42.70%			
age Above 71	27	21.70%			
Categorized of the gender of patients					
Male	73	59%			
Female	51	41%			
Total Patients	124	100%			

Most of the patients are presented and collected from medicine ward (male 33 numbers (26.6%)-female 26 numbers (20.96%)) and intensive care unit (ICU) (male 13 numbers (10.48%)- female 14 numbers (11.29%)) and High intensive care unit(HICU) (male 27 numbers (21.77%) – female 11 numbers (8.87%)).Within all samples (124 patients) of study for proton pumps inhibitors there was no allergy report after use of PPIs during study procedure, diagnosed with gastrointestinal disease 16.93%, respiratory disease 50%, alcoholism 2.41%, heart disease 27.42%, veins & vessel & gland disorders 49.19%, kidney disease 25.8%, nerve and brain damages 22.5%, liver disease7.25%, inflectional diseases 34.67%, diabetic Mellitus 24.2% and other rare diseases 11.3% (**Table II**).

Table II: Categorized of ward preser	ited of	PPIs.
--------------------------------------	---------	-------

Ward presented	No of participants		Percentage	
	Male	Female	Male	Female
Highly intensive care unit (HICU)	27	11	21.77%	8.87%
Intensive care unit (ICU)	13	14	10.48%	11.29%
Medicine	33	26	26.60%	20.96%
Total	73	51	59%	41%

164 proton pump inhibitors are used during treatment, these drugs are 124 pantoprazole (75.6%), 37 Omeprazole (22.56%), 2 rabeprazole (1.2%), 1 lansoprazole (0.6%). wherefore there are shows that pantoprazole and omeprazole are the most favorite drug to be prescribed by the physicians in the hospital. proto pumps are prescribed in different diseases by the physicians, it was found the use of PPIs in a wide range of indications, generally, we made classifications on basic use of PPIs, therefore they can be as a gastroesophageal reflex disease in 63 (50.8%) patient, gastric ulceration in 2 (1.6%) patient, inflectional disease in 59 (47.58%) patients (**Table III**).

Table III: Categorized patient diagnosis.

Patient diagnosed	No of participants	Percentage
gastrointestinal disease	21	16.93%
respiratory disease	62	50%
alcoholism	3	2.41%
heart disease	34	27.42%
veins & vessel &gland disor	61	49.19%
kidney disease	32	25.80%
nerve and brain damages	28	22.50%
liver disease	9	7.25%
infectional disease	43	34.67%
diabetic Mellitus	30	24.20%
other rare diseases	14	11.30%

For a totally of 124 patients 164 proton pump inhibitors are used during treatment, these drugs are 124 pantoprazole (75.6%), 37 Omeprazole (22.56%), 2 rabeprazole (1.2%), 1 lansoprazole (0.6%).wherefore these shows that the pantoprazole and omeprazole are most favorite drug to be prescribed by the physicians in the hospital, which is presented in **table IV**.

Table IV: Categorized of PPIs used.

Drug name	No of PPIs	Percentage
pantoprazole	124	75.60%
omeprazole	37	22.56%
rabeprazole	2	1.20%
lansoprazole	1	0.60%
Total drugs	164	100%

Within this study proto pumps are prescribed in different diseases by physicians and it was found the use of PPIs in a wide range of indications, generally, we made classifications on basic use of PPIs, therefore they can be as a gastroesophageal reflex disease in 63 (50.8%) patient, gastric ulceration in 2 (1.6%) patient, inflectional disease in 59 (47.58%) patients, these are presented in **table V**.

Most of the frequency of PPIs was given to 110 patients once a day (67.07%) which was more than twice (32.92%) (59 patients) in a day. They are given in injections (75.6%) and (24.4%) orally. These drugs are given most likely in

Table V: Categorized of PPIs indication use.

Drug indications	No of participants	%	No of participants		Percentage	
			Male	Female	Male	Female
gastroesophageal reflex disease	63	0.508	36	27	29.03	21.77
gastric ulceration	2	0.016	1	1	0.8	0.8
inflectional disease	59	0.4758	36	23	29.3	18.54

injections by the physician. Tablets, intravenous, and capsules are given as PPIs dosage forms, this results that most of PPLs are used in the intravenous dosage form (**Table VI**).

Table VI: Categorized of ward presented of PPIs

Categorized of the frequency for PPIs						
Frequency	no of drug	percentage%				
Once in a day	110	67.07%				
Iwice a day	54	32.92%				
Categorized of the route of PPIs						
Injections	124	75.60%				
Orally	40	24.40%				
Categorized of the dosage form of PPIs						
Intravenous	124	0.756				
Tablet	35	0.2134				
Capsule	5	0.0304				

The majority of drug-drug interactions were caused by atorvastatin + pantoprazole 25 (23.4%), followed by propranolol + pantoprazole 19 (17.8%). The frequency and outcomes of the potential drug-drug interactions involving PPIs are summarized in **table VII**.

According to the severity classification of drug-drug interactions, the study showed 87% moderate, 10% minor,

and 3% major interactions. The results were compared with those observed in the Airee et al., (2016) study. Major interactions were caused by rabeprazole + clopidogrel, which increased the risk of thrombosis, and pantoprazole + cilostazol, which increased the cilostazol exposure²².

Conclusion

The present study showed the usage pattern of PPIs in a wide range of indications. Based on data collected in this study Proton pumps inhibitors are mostly used in males and they are prescribed for respiratory disease, veins disorders, and diabetic Mellitus diagnoses; pantoprazole and omeprazole are the most PPIs prescribed by the doctors and they are prescribed in intravenous more than others routs. Generally, PPIs are indicated for gastroesophageal reflux disease and inflectional disease in great value in mean indications. Various efforts should be made to reduce the unnecessary use of PPIs to minimize drug interactions, related risks, and health care.

Interests conflict

The authors declare no conflict of interest.

PDDIs involving PPIs	Outcomes of interaction	Number	Percentage
Atorvastatin+ Pantoprazole	Increased blood levels of atorvastatin	25	23.4
Propranolol +Pantoprazole	Increased propranolol exposure	19	17.8
Torsemide +Pantoprazole	Hypomagnesemia	16	15.0
Torsemide +Rabeprazole	Hypomagnesemia	3	2.8
Furosemide +Pantoprazole	Hypomagensemia	14	13.1
Glimepiride +Esomeprazole	-	1	0.9
Fluconazole +Pantoprazole	Increased plasma concentration of cyp2c19	2	1.9
Clopidogrel + Pantoprazole	Increased effectiveness of clopidogrel	9	8.4
Clopidogrel +Rabeprazole	Increased risk of thrombosis	2	1.9
Fluconazole +Rabeprazole	Increased plasma concentration of cyp2cl9	1	0.9
Cefpodoxime +Pantoprazole	Increased blood levels of cefpodoxime	3	2.8
Rifampin +Pantoprazole	Increased blood levels of rifampin	7	6.5
Cyanocobalamin +Pantoprazole	-	4	3.7
Amikacin +Pantoprazole	Hypomagensemia	1	0.9

References

1. World Health Organization. WHO International Working Group for Drug Statistics Methodology, WHO Collaborating Centre for Drug Statistics Methodology, WHO Collaborating Centre for Drug Utilization Research and Clinical Pharmacological Services: Introduction to drug utilization research. Introduction to drug utilization research. Geneva: World Health Organization 2003.

2. Tadvi NA, Shareef SM. Use of proton pump inhibitors in general practice: Is it rationale. International Journal of Medical Research & Health Sciences 2014; 3(1):37-42.

3. Ntaios G, Chatzinikolaou A, Kaiafa G, Savopoulos C, Hatzitolios A, Karamitsos D. Evaluation of use of proton pump inhibitors in Greece. European journal of internal Medicine 2009; 20(2):171-3.

4. Bollavaram C, Bhukya K, Komuravelli S, Valupadas C, Bandaru SB, Eggadi V. Drug Utilization Evaluation of Pantoprazole in Inpatients of Tertiary Care Hospital. Indian Journal of Pharmacy Practice 2021; 14(1):41.

5. Madi L, Ahmed Elhada AH, Alrawashdeh H, Ahmed A. Prescribing Pattern of Proton Pump Inhibitors in Qatar Rehabilitation Institute: A Retrospective Study. J Res Pharm Pract. 2019 Apr-Jun;8(2):101-4.

6. Elnaem MH, Mohamed MHN, bin Nazar AH, binti Ibrahim RNK. Evaluation of proton pump inhibitors prescribing among non-critically ill hospitalized patients in a Malaysian tertiary hospital. Journal of Applied Pharmaceutical Science 2017; 7(12):077-083.

7. van Vliet EP, Otten HJ, Rudolphus A, Knoester PD, Hoogsteden HC, Kuipers EJ, et al. Inappropriate prescription of proton pump inhibitors on two pulmonary medicine wards. Eur J Gastroenterol Hepatol. 2008 Jul;20(7):608-12.

8. Lodato F, Poluzzi E, Raschi E, Piccinni C, Koci A, Olivelli V, et al. Appropriateness of Proton Pump Inhibitor (PPI) prescription in patients admitted to hospital: Attitudes of general practitioners and hospital physicians in Italy. Eur J Intern Med. 2016 May;30:31-6.

9. Gamelas V, Salvado V, Dias L. Prescription Pattern of Proton Pump Inhibitors at Hospital Admission and Discharge. GE Port J Gastroenterol. 2019 Mar;26(2):114-120.

10. Basyal B, Marasine NR, Sankhi S, Lamichhane R, Uprety B N. Prescribing pattern of proton pump inhibitors among patients visiting the outpatient general medicine clinic in a tertiary care teaching hospital in Nepal. Journal of Health Research 2021 (in press).

11. Rahimi E, Yazdanpour S, Dehkordi FS. Detection of Toxoplasma gondii antibodies in various poultry meat samples using enzyme linked immuno sorbent assay and its confirmation by polymerase chain reaction. J Pure Appl Microbiol. 2014;8(1):421-7.

12. Dehkordi FS, Saberian S, Momtaz H. Detection and segregation of Brucella abortus and Brucella melitensis in Aborted Bovine, Ovine, Caprine, Buffaloes and Camelid Fetuses by application of conventional and real-time polymerase chain reaction. The Thai Journal of Veterinary Medicine. 2012 Mar 1;42(1):13.

13. Ranjbar R, Seif A, Dehkordi FS. Prevalence of antibiotic resistance and distribution of virulence factors in the shiga toxigenic Escherichia coli recovered from hospital food. Jundishapur Journal of Microbiology. 2019;12(5):8.

14. Nejat S, Momtaz H, Yadegari M, Nejat S, Safarpour Dehkordi F, Khamesipour F. Seasonal, geographical, age and breed distributions of equine viral arteritis in Iran. Kafkas Univ Vet Fak Derg. 2015 Jan 1;21(1):111-6.

15. Rahi A, Kazemeini H, Jafariaskari S, Seif A, Hosseini S, Dehkordi FS. Genotypic and phenotypic-based assessment of antibiotic resistance and profile of staphylococcal cassette chromosome mec in the methicillin-resistant Staphylococcus aureus recovered from raw milk. Infection and drug resistance. 2020;13:273.

16. Sheikhshahrokh A, Ranjbar R, Saeidi E, Dehkordi FS, Heiat M, Ghasemi-Dehkordi P, Goodarzi H. Frontier therapeutics and vaccine strategies for sars-cov-2 (COVID-19): A review. Iranian Journal of Public Health. 2020 Jul 11.

17. Ranjbar R, Mahmoodzadeh Hosseini H, Safarpoor Dehkordi F. A review on biochemical and immunological biomarkers used for laboratory diagnosis of SARS-CoV-2 (COVID-19). The Open Microbiology Journal. 2020 Dec 15;14(1).

18. Mirzaie A, Halaji M, Dehkordi FS, Ranjbar R, Noorbazargan H. A narrative literature review on traditional medicine options for treatment of corona virus disease 2019 (COVID-19). Complementary therapies in clinical practice. 2020 Aug 1;40:101214.

19. Halaji M, Farahani A, Ranjbar R, Heiat M, Dehkordi FS. Emerging coronaviruses: first SARS, second MERS and third SARS-CoV-2: epidemiological updates of COVID-19. Infez Med. 2020;28(suppl):6-17. 20. Madi L, Elhada AH, Alrawashdeh H, Ahmed A. Prescribing pattern of proton pump inhibitors in Qatar rehabilitation institute: a retrospective study. Journal of research in pharmacy practice. 2019 Apr;8(2):101.

21. D'Souza AM, Shastry CS, Mateti UV, Kabekkodu S, Chand S. Drug Utilization and Evaluation of Proton Pump Inhibitors in General Medicine Ward of a Tertiary Care Hospital. Journal of Pharmaceutical Sciences and Research. 2019 Jun 1;11(6):2174-9.

22. Airee, R.S., Rawal, A., John, N.N., Binu, K.M., (2016). Drug use evaluation of proton pump inhibitors in a private tertiary care teaching hospital. WJPPS. 5(1), 922-30.