Original article

Effective PPI Therapy: Ensuring Appropriate Dosage of PPI in Patients with Different Comorbidities in Medicine, Surgery and Gastroenterology Ward

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Abstract

Background:
Proton pump inhibitors (PPIs) are widely prescribed medications used to treat conditions related to excessive stomach acid, such as gastroesophageal reflux disease (GERD), peptic ulcers, and Zollinger-Ellison syndrome. Despite their efficacy in managing acid-related disorders, the appropriate use of PPIs, particularly concerning the correct dosage remains a critical issue in clinical practice.

Objective:
This study aimed to assess the effectiveness of PPI therapy by ensuring appropriate dosage of PPI in patients with different comorbidities in medicine, surgery, and gastroenterology wards in Dhaka Medical College Hospital.

Methods:
This cross-sectional observational study was conducted at the Department of Pharmacology and Therapeutics, Dhaka Medical College, Dhaka, from July 2019 to June 2020. A total of 600 patients were selected as study subjects by purposive sampling technique. Data were collected and evaluated considering USFDA-approved indications, and the systematic review by Scarpignato et al. recommendations. Data were analyzed using descriptive statistics. Analysis of data was carried out by using Statistical Package for Social Science (SPSS) 22.0 for Windows.

Results:
Among 255 patients, who were prescribed PPIs for an appropriate indication, 129 (50.6%) patients were given PPIs in an appropriate dose, whereas the dose was inappropriate in 126 (49.4%) patients. The appropriate dose was followed mostly in the gastroenterology department (83.1%), followed by the medicine department (47.3%). Whereas in the surgery department, only 35% of patients were given PPIs with an appropriate dose and the difference in the usage of appropriate doses of PPIs among the three departments is significant with p-value <0.001. The most common comorbid condition was diabetes (110; 18.3%), followed by hypertension (91; 15.2%) and stroke (24; 4.0%).

Conclusion:
This study estimates that only 50.6% of the 255 patients received the appropriate PPI dosage. The gastroenterology department had the highest adherence to appropriate dosing (83.1%). Diabetes was the most common comorbidity among patients (18.3%), followed by hypertension (15.2%) and stroke. These results highlight the need for improved adherence to PPI dosing guidelines across departments to enhance therapy effectiveness.

Keywords: Proton pump inhibitor, Appropriate dosage, Indication, Comorbidities

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Introduction:

The management of acid-related diseases has been transformed by the advent of proton pump inhibitors (PPIs) in clinical practice. Since omeprazole was introduced in 1989, the need for elective surgery to treat ulcer disease has nearly disappeared due to effective acid suppression. Additionally, despite the increased use of

non-steroidal anti-inflammatory drugs (NSAIDs) among the aging population, the occurrence of NSAID-associated gastropathy has significantly decreased. The robust evidence supporting the efficacy of PPIs and their favorable safety profile has, however, led to their overuse in both hospital and primary care settings.[1] There are six PPIs named omeprazole, esomeprazole, lansoprazole, dexlansoprazole, pantoprazole, and rabeprazole which are approved by the United States Food and Drug Administration (USFDA) (2014) for clinical purposes.[2] Recent studies have shown that the incidence of inappropriate use of PPIs ranges from 40-70%.[3] In a US study,[4] guidelines for PPI prescription were followed in only 39% of inpatients' prescriptions, with a difference between academic and non-academic hospitals (compliance with guidelines being 50% vs 29% respectively). All Wales Medicine Strategy Group (AWMSG)[5] found that PPI use in Wales continued to increase by nearly 25% over the last 6 years, which was 14% higher than in England. Another study in Dhaka Medical College found that 71.5% of patients were prescribed PPIs inappropriately during their discharge.[6] Two main concerns regarding inappropriate use of PPIs are drug expenditure, which has risen dramatically in recent years, and growing safety concerns.[1] Worldwide, PPIs are one of the most widely prescribed drugs, with about $13B in annual sales.[7] A recent literature review has demonstrated the risk for adverse drug reactions and drug interactions with inappropriate use of PPIs.[8] Over recent years evidence has emerged showing some previously unrecognized toxicities of PPIs.[9] The various mild and self-limiting side effects of PPIs are nausea, loose stool, headache, abdominal pain, muscle and joint pain, and dizziness.[10] Long-term effects include fracture, Clostridium difficile infection, pneumonia, acute interstitial nephritis, chronic kidney disease, hypomagnesemia, vitamin B12 deficiency, cardiovascular events, subacute cutaneous lupus erythematosus, cancer, and higher mortality.[5] PPIs get metabolized through hepatic P450 cytochromes and lead to drug interactions by increasing their half-life and thus causing harmful systemic effects.[10] So, PPI therapy needs to be evidence-based. Decisions on indication of PPI therapy should be sound and PPIs should only be prescribed when there is an appropriate dosage. However, in the current situation, PPI consumption is overwhelming worldwide, which invites studies to be carried out to examine the prescribing pattern of PPIs in hospitalized patients. This study aimed to assess the effectiveness of PPI therapy by ensuring appropriate dosage of PPI in patients with different comorbidities in medicine, surgery, and gastroenterology wards in Dhaka Medical College Hospital.

Methods:

This cross-sectional observational study was conducted at the Department of Pharmacology and Therapeutics, Dhaka Medical College, Dhaka, from July 2019 to June 2020. The study population comprised all patients admitted to the medicine, surgery, and gastroenterology wards of Dhaka Medical College Hospital. A total of 600 patients were selected as study subjects based on specific inclusion and exclusion criteria, using a purposive sampling technique. Inclusion criteria included patients admitted for 2 days or more in the medicine, surgery, or gastroenterology wards, both genders aged 18 years or older, and those who consented to participate. Exclusion criteria included patients admitted for less than 2 days, those under 18 years of age, and those who refused to give consent. Data were collected using a specially designed form that involved reviewing patients' clinical records, including clinical history, laboratory data, medication charts, and other relevant information, focusing on the dosage for PPI use guided by USFDA[2] and the systematic review by Scarpignato et al.[1] Descriptive statistics were used for data analysis, with continuous data presented as mean ± SD (standard deviation) and nominal data expressed as percentages. Data analysis was performed using SPSS 22.0 for Windows, and results were presented in tables and diagrams. Ethical approval was obtained from the ethical committee of Dhaka Medical College, and informed written consent was acquired from all participants.

Results:

The highest number of respondents (267 patients) were in the age group 41-60 years, followed by the age group 21-40 years (258 patients) and the lowest number of respondents (6 patients) were in the age group ≤20 years. The mean age of our patients was 44.8±13.5 years. In this study male patients were more than female patients with a ratio of 1.3:1 (Table-I).

Table-I: Distribution of respondents by their age and gender (N=600)

Demographic characteristics	no. (%)
Age group (years)	
≤20	6 (1.0)
21-40	258(43.0)
41-60	267(44.5)
61-80	69(11.5)
Mean±SD (range)	44.8±13.5 (18-80)
Sex	
Male	341(56.8)
Female	259(43.2)
Male: Female ratio	1.3: 1

The above table shows that among 600 patients, 241 (40.2%) patients were from the surgery department, 220 (36.6%) patients were from the medicine department and 139 (23.2%) patients were from the gastroenterology department (Figure-1).

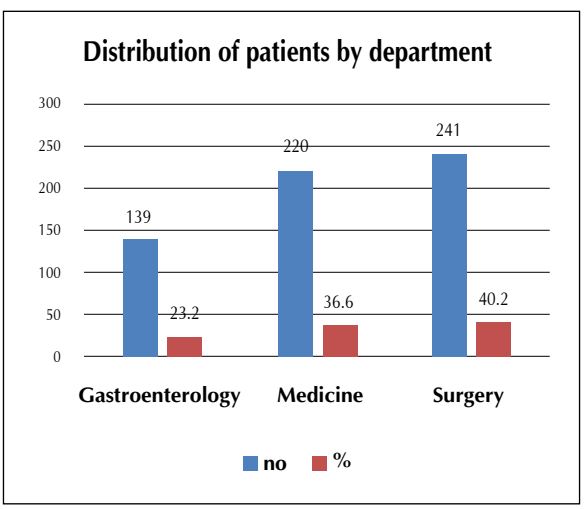

Figure-1: Distribution of the study patients by department (N=600)

Most of the patients (521; 86.8%) were prescribed PPIs, among them 440 (84.5%) were prescribed omeprazole followed by 70 (13.4%) esomeprazole, 6 (1.2%) pantoprazole, 4 (0.8%) rabeprazole and 1 (0.2%) lansoprazole.No patient was prescribed dexlansoprazole in our study. Among 255 patients, who were prescribed PPIs for an appropriate indication, 129 (50.6%) patients were given PPIs in an appropriate dose, whereas the dose was inappropriate in 126 (49.4%) patients (Table-II)

Table-II: Distribution of the study patients by prescription of PPI (N=521/600)

Prescription of PPI	no. (%)
PPIs prescribed	**(n=521)**
Yes	521(86.8)
No	79(13.2)
Individual PPI used	
Omeprazole	440(84.5)
Esomeprazole	70(13.4)
Pantoprazole	6(1.2)
Rabeprazole	4(0.8)
Lansoprazole	1(0.2)
Dexlansoprazole	0(0)
Appropriate indication of PPIs	
Yes	255(48.9)
No	266(51.1)
Appropriate dose of PPIs	**(n=255)**
Yes	129(50.6)
No	126(49.4)

Concerning the co-morbidities, we found 255 (42.5%) patients with different co-morbidities, whereas 345 (57.5%) patients had having single disease condition, most common comorbid condition was diabetes (110; 18.3%), followed by HTN (91; 15.2%) and stroke (24; 4.0%) (Figure-2).

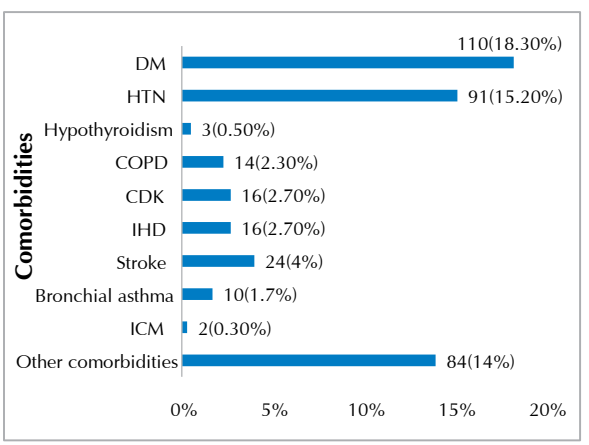

Figure-2: Bar diagram showing the individual co-morbidity of the study patients (N=600)

Table-III showed that among patients who were given PPIs for an appropriate indication, the appropriate dose was followed mostly in the gastroenterology department (83.1%), followed by the medicine department (47.3%). Whereas in the surgery department, only 35% of patients were given PPIs with an appropriate dose and the difference in the usage of the appropriate doses of PPIs among the three departments is significant with a p-value <0.001 (Table-III).

Table-III: Distribution of the study patients by department basis usage of appropriate dose of PPIs (N=255)

Appropriate Dose	Gastroenterology (n=59)	Medicine (n=93)	Surgery (n=103)	p-value
Yes	49(83.1%)	44(47.3%)	36(35.0%)	<0.001[s]
No	10(16.9%)	49(52.7%)	67(65.0%)	

Chi-squared Test (χ^2) was done to analyze the data**.**
s=significant

Discussion:

In this study, most of the patients belonged to the age group 41-60 years (267, 44.5%), 258 (43%) patients were of age between 21-40 years, 69 (11.5%) patients were of age between 61-80 years and only 6(1%) patients were of age ≤20 years. The mean age of my study population was 44.8±13.5 years. Similar results were reported by Airee et al,[8] where they found most of the patients (47%) were in the age group 40-60 years and 10% of patients were in the age group >60 years. Another study by Nousheen, Tadvi, and Shareef[3] showed similar results, where 41% of patients were middle-aged between 41-60 years age group and 15% of patients were aged >60 years. Considering the department basis distribution of study patients, we found that the majority of patients were from the surgery department (241; 40.2%) followed by the medicine (220; 36.6%) and the gastroenterology department (139; 23.2%). In a study conducted by Mathew et al[11] majority of the patients (42.34%) were from the general medicine department, whereas 20.47% of patients were from the general surgery department. They also included patients from the ICU and orthopedic departments. No study could be found that included patients from the gastroenterology department. In this study, out of 600 patients, 521 (86.8%) patients were prescribed PPIs, whereas only 79 (13.2%) patients were not given PPIs. A similar result was found by Haroon, et al,[12] where out of 205 consecutive medical inpatients 162 patients (79%) were prescribed PPIs. In this study, a total of 521 patients were prescribed PPI which included 440 (84.5%) omeprazole, 70 (13.4%) esomeprazole, 6 (1.2%) pantoprazole, 4 (0.8%) rabeprazole and 1 (0.2%) lansoprazole, when generic name of PPIs was considered. Similar results were shown by Akram, et al,[13] where omeprazole was given in 87.5% of prescriptions, but the study by Kunwar, et al.[14] reported majority (98.7%) of PPIs prescription with pantoprazole. Concerning the co-morbidities, 255 (42.5%) patients had different co-morbidities, whereas 345 (57.5%) patients had single disease conditions. The co-morbidity disease pattern of our study population ranged from 2 to 7 diseases. Unlike this study, Mathew, et al[11] found 68.58% of patients with co-morbidities, whereas 31.42% of patients had single disease conditions and they reported, that the co-morbidity disease pattern ranged from 2 to 4 diseases. The maximum number of disease co-morbidity in this study was observed in one patient who had seven diseases i.e. Chronic pancreatitis, Liver abscess, Cholangitis, Hemolytic anemia, Biliary ascariasis, Oesophageal candidiasis, Gastric erosion. Regarding the frequency of co-morbidities among the study patients, diabetes mellitus marked the highest frequency (110 patients), followed by hypertension (HTN) (91 patients) and stroke (24 patients). In this study, out of 255 patients, who were prescribed PPIs for an appropriate indication, 129 (50.6%) patients were given PPIs in an appropriate dose, whereas the dose was inappropriate in 126 (49.4%) patients. A significant difference (p<0.001) in the usage of appropriate doses of PPIs among the three departments was observed. The present study showed that among patients who were given PPIs for an appropriate indication, the appropriate dose was followed mostly in the gastroenterology department (83.1%), followed by the medicine department (47.3%). Whereas in the surgery department, only 35% of patients were given PPIs with an appropriate dose. The benefits of PPI therapy for appropriate indications need to be considered, along with the likelihood of the proposed risks. Patients with a proven indication for a PPI should continue to receive it at the lowest effective dose.[15]

Limitations:
The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

Conclusion:
This study estimates that only 50.6% of the 255 patients received the appropriate PPI dosage. The gastroenterology department had the highest adherence to appropriate dosing (83.1%), while the medicine and surgery departments had lower adherence rates (47.3% and 35%, respectively), with significant differences between departments. Diabetes was the most common comorbidity among patients (18.3%), followed by hypertension (15.2%) and stroke. These results highlighted the need for improved adherence to PPI dosing guidelines across departments to enhance therapy effectiveness.

Recommendation:
To improve the effectiveness of PPI therapy, it is recommended to implement standardized dosing guidelines across all departments, with a focus on increasing adherence in the medicine and surgery departments. Additionally, targeted education for healthcare professionals on appropriate PPI dosing and regular audits could help ensure that patients receive the correct dosage, especially considering common comorbid conditions like diabetes and hypertension.

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