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Proton Pump Inhibitors Usage Among Discharged Patients in a Tertiary Care Hospital- An Observational Study

Akhlak Ahmed[1], Benojeer Akter[2], Md. Mahmudun Naby[3], Md. Romanur Rahman[4], Syed Zakir Hossain[5]

Abstract

Background: *Proton pump inhibitors (PPI) have reportedly been used in inappropriate clinical settings, often leading to an increased risk of adverse effects, drug interactions, and costs.*

Aim: *The aim of this study was to evaluate the appropriateness of PPI prescription on discharge of patients in medicine ward of a tertiary care hospital in Bangladesh.*

Methods: *A cross-sectional study was done for 3 months in the department of medicine in a tertiary care hospital to evaluate the indications of PPI use, appropriateness of PPI use and types of PPI prescribed. A total of 107 patients who were prescribed PPI on discharge were enrolled after written informed consent and data were collected in a structured questionnaire.*

Results: *Among the 107 patients discharged, 64 were males and 43 were females. The mean age was 51.3 ±17.6 (SD) years. Among the study population, 49 were appropriately prescribed PPI and 58 were inappropriately prescribed PPI. Regarding indications, 53.1% received PPI for prevention of anti-platelet induced gastric erosion and 18.9% were prescribed PPI for no apparent reason. Age (p=0.199) and gender (p=0.605) was not significantly associated with the appropriate prescription of PPI. Of the various preparations of PPI prescribed, esomeprazole was prescribed in most of the discharged patients (56%).*

Conclusion:*this study demonstrates the existence of an over-prescription of PPI. PPI prescription needs to be improved, thereby reducing drug interactions, adverse effects and unnecessary economical expenses.*

Keywords: *Proton pump inhibitors (PPIs), prescription, overuse, indications*

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Background

Proton pump inhibitors (PPIs) are one of the most widely used pharmacological drug classes in the world to block acid secretion in gastric parietal cells by binding to hydrogen/potassium ATPase or proton pumps.[1]PPIs are the most effective inhibitors of acid secretion available, and there is no evidence to suggest that one agent is superior to another.[2] While PPIs are generally welltolerated, prolonged use can lead to potential harmful side effects.[3] The FDA-approved indications (table 1) for the use of PPIs arehealing and maintenance therapy of erosive esophagitis (EO), treatment of gastroesophageal reflux (GORD), risk reduction for gastric ulceration (GU) associated with nonsteroidal anti-inflammatory use (NSAID), H.Pylori eradication, pathological hypersecretory conditions, e.g.,Zollinger-Ellison Syndrome, treatment and maintenance of duodenal ulcer.[4] Additionally, there are other valid indications for PPI therapy, which include areduction in the risk of gastric ulcers in high-risk patients treated with antiplatelet agents, eosinophilic esophagitis, steatorrhea refractory to enzyme replacement therapy in patients with exocrine pancreatic insufficiency and upper gastrointestinal bleeding in patients with high-risk ulcers (table1).[5,6]

PPIs are among the most widely prescribed drugs in the world, and their increasing accessibility due to generics and over-the-counter availability has contributed to their widespread use. Despite the excellent effectiveness and safety of PPIs, their use has been expanded to inappropriate clinical contexts, including low-risk patients and prolonged usage beyond the indicated durations. Over prescription of PPIs

1. Assistant Professor, Department of Medicine, Shaheed Suhrawardy Medical College Hospital.
2. Assistant Registrar, Department of Medicine, Shaheed Suhrawardy Medical College Hospital.
3. Registrar, Department of Medicine, Shaheed Suhrawardy Medical College Hospital.
4. Indoor Medical Officer, Department of Medicine, Shaheed Suhrawardy Medical College Hospital.
5. Associate Professor, Department of Medicine, Shaheed Suhrawardy Medical College Hospital.

Corresponding author: Dr. Akhlak Ahmed, Assistant Professor, Department of Medicine, Shaheed Suhrawardy Medical College Hospital.

in hospitals has been reported at rates ranging from 50-86%, and this trend often continues after discharge.[2,4,7,8] A recent study in Bangladesh found that 87.2% of patients in a tertiary hospital received PPIs at discharge, and 71.5% of these patients had no indications for PPIs.[16] A study in 31 primary care practices in Germany found that nonindicated PPIs were continued by general practitioners in 58% of patients for at least 1 month.[17] An American study found that after discharge, 46–80% of patients were still on PPIs after 3 months, and 50% were still on PPIs after 6 months.[18] Studies have documented potential adverse effects, including acute interstitial nephritis, gastric polyposis, vitamin B12 and magnesium deficiency, *Clostridium difficile* infection or bacterial overgrowth in cirrhotic patients with an increased risk of spontaneous bacterial peritonitis.[9] Furthermore, there has been an expansion of PPI prescriptions to all age groups, including polymedicated elderly patients, increasing the risk of drug interactions.[9]

Frequent prescription of PPIs in general practice has led to a misconception among clinicians that PPIs are safe to use for prolonged periods, when in reality, they are not without risks. It is crucial for healthcare professionals to regularly review the indication and duration of PPI use to prevent overuse and associated adverse outcomes. Additionally, the overuse of PPIs has significant financial implications for patients and public health spending.[10] Despite the growing concern about inappropriate PPI prescribing,[11,12] it is also crucial to note that PPIs are still essential medications when indicated, and their prescription should not be discouraged. Proper education and awareness among healthcare professionals and patients regarding the appropriate use of PPIs can help minimize overuse and associated risks. To address this issue, we conducted a clinical audit to evaluate the appropriateness of PPI prescriptions on the discharge of medical inpatients from a tertiary care hospital in Dhaka, Bangladesh. This study also aimed to identify the factors that are significantly associated with inappropriate PPI prescriptions and the type of PPI commonly prescribed to these patients.

Method

Thiscross-sectional study was conducted in the internal medicine ward at Shaheed Suhrawardy Medical College Hospital for a period of three months (November 2022 to January 2023). The study included all patients who were discharged to go to home with PPI therapy within this time period and excluded those who were receiving palliative or critical care, who died or who were transferred to another ward or hospital. Their medical notes, including admission notes, discharge summaries and prescriptions, were reviewed. A pro forma was designed that included the demographic details, PPI agent used, whether or not PPI was continued on discharge from hospital and if the PPI prescribed at discharge was according to the recommendation of FDA other valid indications (listed in table-1).Discharge letters were consulted to collect data regarding prehospitalization and discharge medication (PPI, antiplatelet drugs, anticoagulants, corticosteroids, nonsteroidal anti-inflammatory drugs [NSAIDs], and selective cyclooxygenase [COX-2] inhibitors, personal history or recent diagnosis that supported the use of PPI. A history of peptic ulcer documented on upper digestive endoscopy was sought in the patient'selectronic record.

The study was conducted in adherence with the Declaration of Helsinki and good clinical practices. Informed written consent was obtained from all study participants, andstatistical analysis was performed using SPSS version 25.

Table 1 *Indications foruse of PPIs according to the Food and Drug Administration (FDA) and National Institute for Clinical Excellence (NICE) and other valid indications.*[5,6,13-15]

Indications for use of PPIs
FDA and NICE
• Erosive esophagitis – healing and maintenance therapy
• GERD and its clinical manifestations (including nonerosive disease, symptomatic control*, esophageal strictures, Barrett's esophagus
• HP eradication in combination with antibiotics
• Short-term treatment of HP-negative peptic ulcers and maintenance Therapy.
• Treatment of gastric ulcers associated with NSAIDs
• NSAID-induced dyspepsia
• Reduction of risk of gastric ulcers in NSAID users with a high risk** of gastrointestinal complications or COX-2 inhibitor users with previous history of upper gastrointestinal bleeding
• Gastric pathological hypersecretion (Zollinger-Ellison disease)
• Critically ill patients, under prolonged mechanical ventilation
• Short-term treatment* of patients with functional dyspepsia
Other valid indications for PPI therapy
• Reduction of risk of gastric ulcers in high-risk patients** treated with antiplatelet agents
• Eosinophilic esophagitis
• Steatorrhea refractory to enzyme replacement therapy in patients with exocrine pancreatic insufficiency
• Prior to upper gastrointestinal endoscopy for upper gastrointestinal bleeding and following endoscopic therapy in patients with high-risk ulcers***

* 4–8 weeks of treatment, followed by minimum effective dose or use on demand, if symptoms persist.
** Age >65 years or concomitant use of corticosteroids, antiplatelet agents, or anticoagulants or previous history of peptic ulcer disease.
***Forrest classification Ia, Ib, IIa, and IIb.

Result

During the study period, a total of 107 PPI-prescribed patient discharge certificates were collected. The mean age of the patients was 51.3 ±17.6 years, and most of them were in the age group 61-70 years (28%). Among the 107 PPI users, 64 were male and 43 were female. A total of 16.8% were taking NSAIDs, and 6.5% were taking steroids. Histories of CKD, COPD and hypercalcemia were reported by 24.3%, 6.5% and 2.8% of patients, respectively. Among the clinical features, 28% had dyspepsia, and 21.5% had a heart-burning sensation (table 2).

Table 2 .*Characteristics of the study population (n=107).*

Variable	n	%
Age (years)		
<20	3	2.8
20-30	17	15.9
31-40	12	11.2
41-50	13	12.1
51-60	24	22.4
61-70	30	28
>70	8	7.5
Mean ±SD(years)	51.3 ±17.6	
Gender		
Male	64	59.8
Female	43	40.2
Clinical features		
Dyspepsia	30	28
Heart burning sensation	23	21.5
H/O of smoking	26	24.3
H/O steroid intake	7	6.5
H/O NSAIDS	18	16.8
H/O COPD	7	6.5
H/O of CKD	26	24.3
H/O of Hypercalcemia	3	2.8

Abbreviations: COPD-chronic obstructive pulmonary disease, CKD-chronic kidney disease, NSAIDS-nonsteroidal anti-inflammatory drugs

Among the 107 PPI users, 49 (45.8%) were appropriately prescribed PPIs for treatment as defined by the FDA and NICE, and 58 (54.2%) were inappropriately prescribed PPIs for treatment (figure-1). Regarding indications, 53.1% received PPIs for the prevention of antiplatelet-induced gastric erosion, 16.3% for the prevention of NSAIDS-induced ulcers and 16.3% for the prevention of steroid-induced gastric erosion.Of the 58 patients prescribed PPIs inappropriately, 24.1% were prescribed for infections, 15.5% for cardiovascular disease and 10.3% for CKD. A total of 18.9% were prescribed PPIs for no apparent reason (table-3).

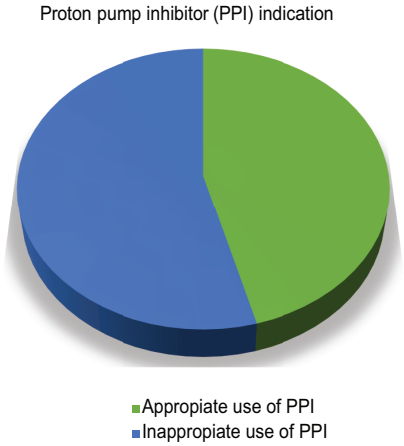

Figure 1 *Distribution of appropriate and inappropriate PPI indications among respondents (n=107)*

Table 3 *Proton pump inhibitor (PPI) indications in the appropriate PPI prescription group and the inappropriate PPI prescription group (n=107)*

Variable	n	%
Appropriate use of PPI (n=49)		
Esophagitis	2	4.1
Nonerosive reflux disease	0	0
Peptic ulcer disease	5	10.2
Zollinger-Ellison syndrome	0	0
Part of triple therapy	0	0
Prevention of NSAIDS induced ulcer	8	16.3
Prevention of steroid induced gastric erosion	8	16.3
Prevention of antiplatelet induced gastric erosion	26	53.1
Inappropriate use of PPI (n=58)		
COPD and bronchial asthma	3	5.2
CKD	6	10.3
Anxiety disorder	1	1.7
CVD	9	15.5
CLD	2	3.4
Infections	14	24.1
Malignancy	1	1.7
Insecticide poisoning	1	1.7
Bleeding disorder	3	5.2
Viral fever	1	1.7
AKI	2	3.4
Renal cyst	1	1.7
others	3	5.2
No clear reason for PPI use found	11	18.9

Abbreviations:CVD-cardiovascular disease,CLD-chronic liver disease,CKD-chronic kidney disease,AKI-acute kidney injury, COPD-chronic obstructive pulmonary disease

Table 4. *Proton pump inhibitor (PPI) use and appropriateness at discharge (n=107)*

Variable	Total PPI users n	PPI prescribed with an indication n=49 n(%)	Inappropriate PPI use n=58n(%)	p value*
Age (years)				0.199
<20	3	1(33.3)	2(66.7)	
20-30	17	5(29.4)	12(70.6)	
31-40	12	4(33.3)	8(66.7)	
41-50	13	4(45.8)	9(69.2)	
51-60	24	11(45.8)	13(54.2)	
61-70	30	19(63.3)	11(36.7)	
>70	8	5(62.5)	3(37.5)	
Gender				0.605
Male	64	28(43.8)	36(48.8)	
Female	43	21(48.8)	22(51.2)	

*p value obtained by chi-square test

Table 4 demonstrates PPI consumption and appropriate use of PPIs. PPI consumption increased with age, and 75 patients aged >40 years were prescribed PPIs, of whom 36 were inappropriately prescribed PPIs and 39 were prescribed PPIs with indications. However, the difference was not significant (p=0.199). Total inappropriate prescriptions by gender was not statistically significant (p=0.605), although there was a trend toward more inappropriate prescriptions among females (51.2%) compared to males (48.8%).

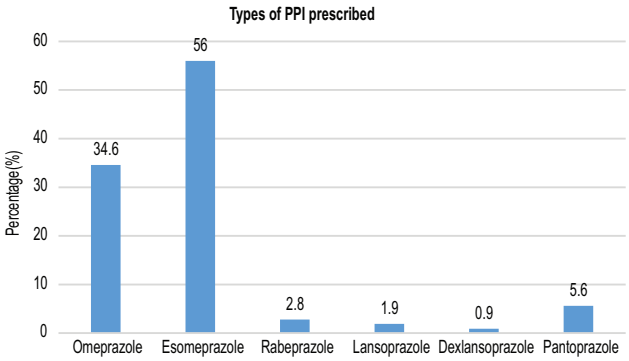

Figure 2: *Types of proton pump inhibitors (PPIs) prescribed to the study population (n=107)*

Among the various preparations of PPIs prescribed, esomeprazole was prescribed in most of the discharged patients (56%); 34.6% were prescribed omeprazole, 5.6% were prescribed pantoprazole, and 2.8% and 1.9% were prescribed rabeprazole and lansoprazole, respectively.

Discussion

Although proton pump inhibitors (PPIs) are effective and have minimal side effects, there are only a limited number of situations where they are recommended for long-term use. However, many healthcare providers are still prescribing these drugs at alarming rates, often without following approved indications.[11,12] In our institution, we had not previously assessed how PPIs were being prescribed to the general adult population, so we conducted a cross-sectional study to determine whether clinicians were adhering to approved indications for PPI prescription.From our collected data, it was observed that more than half of the patients were consuming PPIs without any clearly documented indication (54%), which was comparable to the 54.1% reported in the study by Osama et al.[2]Our study results were in line with those of the aforementioned studies that demonstrate PPI overuse and inappropriate prescriptions among different studies, countries, and healthcare systems.

The indications for appropriate PPI use considered in this analysis include both a group of well-accepted indications (FDA and NICE) and others considered valid by experts but not yet covered by current recommendations.[6,19]Even though other indications are emerging, scientific evidence is still lacking, and therefore, further research is needed.The reasons that PPIs are overprescribed in hospitals are neither well studied nor well understood. Physicians may have inaccurate or insufficient understanding about the risk of ulcer development during hospitalization, and they prescribe PPIs with good intent to prevent ulcer development even though

they are not in compliance with existing PPI guidelines. Some physicians routinely continue PPIs considering them safe, long-term medications without assessing the risks and benefits of long-term therapy.[11] Other recent studies have shown that physicians do not review and document PPI indications in a large number of cases, which often results in their long-term or indefinite continuation.[20,21]Another possible explanation for inappropriate use of PPIs includes trust in the judgment of the physician who initially prescribed PPIs and a failure to reassess indications for PPI since it was a part of the patient's normal medication prior to admission. Inappropriate prescription of PPIs is an important issue for several reasons. First, the administration of unnecessary medication leads to polypharmacy, resulting in side effects and pharmacological interactions. Second, PPI use is found to be significantly associated with community-acquired pneumonia[22] and *Clostridium difficile*-associated diarrhea.[23] Moreover, long-term PPI therapy is suspected to be associated with an increased risk of hip fracture.[24]A large trial published in the Journal of the American Medical Association in 2016 demonstrated a significant risk of developing chronic kidney disease (CKD) with long-term use of PPIs. The risk of developing CKD was 20–50% higher in those taking long-term PPIs.[25] Another problem arising from the overuse of PPIs is drug interactions between the PPIs and other medicines the patient may already be taking.[26]

In our study, the most common indication for appropriate PPI prescription was prevention of antiplatelet-induced gastric ulcers in high-risk patients (53.1%). It is important to highlight that using PPIs for ulcer prophylaxis from antiplatelets can be considered either appropriate or inappropriate depending on individual patient characteristics. Patients receiving antiplatelets with one of the risk factors (e.g., age > 60 years, co-prescription with antiplatelets/anticoagulants/NSAIDs/corticosteroids, and present symptoms of dyspepsia or GERD) were defined as "high-risk patients" who are suitable for PPI prescription. In contrast, patients taking antiplatelets without those risk factors were defined as "low-risk patients" who were unsuitable for PPI prescription. In addition, patient monitoring is also sensible to periodically evaluate the necessity of using PPIs. If the drug required for prophylaxis is discontinued, the PPI prescription should also be discontinued. Additionally, the unnecessary prescription of any drugs unnecessarily exhausts resources either from private individuals, public healthcare systems, or insurance companies/funds/schemes.[7] PPI consumption increased with age, and 75 patients aged >40 years were prescribed PPIs, of whom 48% were inappropriately prescribed PPIs and 52% were prescribed PPIs with indications; however, this difference was not significant (p=0.199). It is known that older age is associated with an increased prevalence of chronic diseases and a higher risk of polypharmacy and inappropriate prescriptions,[27]making them exposed to an increased risk of developing sideeffects from any medicine, including PPIs. Among the various preparations of PPIs prescribed, esomeprazole and omeprazole were shown to be the most prescribed PPIs at hospital discharge. On the other hand, pantoprazole, lansoprazole and rabeprazole were used rarely; nevertheless, it should be noted that rabeprazole and pantoprazole, due to their lower dependence on cytochrome CYP2C19 metabolism, may be preferable in an elderly and polymedicated population, as it would decrease the likelihood of drug interactions. We strongly feel that to improve our PPI prescribing practices, we need to improve upon the documentation of the indication for these drugsand we must ensure that these medicines are appropriately rationalized upon patient discharge from the hospital.

Conclusion

In summary, we have demonstrated that more than 50% of our study group were taking PPIs for inappropriate reasons.Taking proactive measures to enhance the utilization of PPIs while adhering to approved and recognized indications, as well as regularly reevaluating the necessity of their prescription, is crucial for promoting responsible prescribing practices. Therefore, it is imperative to take decisive actions aimed at enhancing the usage of PPIs, which in turn can help minimize potential drug interactions, adverse effects, and avoidable economic costs. Moreover audits will be necessary to ensure ongoing improvement of our prescription practices and to raise awareness among clinicians of the current guidelines for PPI prescribing.

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