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Research Article

USE OF PROTON PUMP INHIBITORS IN GENERAL PRACTICE, ITS EFFICACY, DOSE AND FREQUENCY¹Dr. Faraz Saif, ²Dr. Saad Ijaz, ³Dr. Muhammad Aamir¹Ayub Teaching Hospital, Abbottabad²Ayub Teaching Hospital, Abbottabad³Ayub Teaching Hospital, Abbottabad

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Abstract:

The frequency of PPI abuse varies between 40% and 70% in various studies. Starting and continuing to use these drugs without the correct indications will cost the patient considerably. This study was planned to explore the rational use of PPI in tertiary hospital patients.

Purpose: To evaluate the indications for the use of PPI with dose, frequency, treatment rationality, safety and efficacy.

Place and Duration: In the Surgical and Medical departments of Ayub teaching Hospital, Abbottabad for six months duration from January 2019 to June 2019.

Methods: A prospective observational study on the drug use of PPI was conducted in patients hospitalized in General Medicine and Surgery services. The size of the study sample was (n = 100). Patient case sheets were reviewed for PPI prescription and relevant data were collected. An approved reflux disease diagnostic questionnaire (RDQ) with 12 items and a five-point Likert scale were used to evaluate the symptom score to evaluate the effectiveness of PPIs.

Results: A total of 46.72% inpatients were on proton pump inhibitors, in surgery (47.52%) and medicine wards (46.01%). The indications for PPIs therapy were acute gastritis (4%), Gastro Esophageal reflux disease (5%), Duodenal ulcer (1%), co-administration with Non-Steroidal Anti-Inflammatory Drugs (32%). PPIs were prescribed irrationally in 58% of patients without any valid indication. The incidence of polypharmacy was high, average number of drugs per prescription was 4.93. Antimicrobials were the most common drugs used in (71%).

Conclusion: Proton pump inhibitors should be used more rationally and awareness should be increased among hospital physicians in order for PPIs to be properly prescribed to improve patient care at a low cost.

Key Words: Proton pump inhibitors, General practice, Rationale.

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INTRODUCTION:

Proton pump inhibitors (PPI) are a group of drugs that cause a significant and permanent decrease in stomach acid production¹⁻². They are the most potent stomach acid suppressors currently in clinical use. PPIs irreversibly inhibit the stomach pump $H^+ - K^+ ATPase$, also known as the proton pump, and reduce both basal and stimulated gastric output³⁻⁴. Currently, PPIs found in Pakistan are omeprazole, esomeprazole, pantoprazole, rabeprazole and lansoprazole. PPIs are used therapeutically in active ulcers, in Zollinger-Ellison syndrome, together with antibiotics for gastroesophageal reflux disease (GERD), gastrointestinal bleeding, and NSAID dyspepsia and helicobacter pylori⁵⁻⁶. Proton pump inhibitors have been shown to be safe and well-tolerated medicinal products, but short-term adverse effects such as headaches, dizziness, and diarrhea have been reported. Fatigue, skin rashes and abdominal pain in 5%. Patients taking proton pump inhibitors⁷. Treatment of chronic PPI carries an increased risk of bacterial enteritis due to gastric acidity that allows colonization of digested pathogens as well as Clostridium difficile infection. Despite concerns about PPIs, it has become one of the most frequently prescribed drugs worldwide. Some reports show that up to 60% of patients with dyspepsia take drugs such as PPI without proper indication. PPIs take longer to relieve symptoms than H₂ blockers or antacids. For sporadic dyspepsia, emergency relieving agents other than PPI will provide greater patient satisfaction and better clinical outcomes⁸⁻⁹. PPI prescription have been increasing in recent years. Many drug use studies have reported that PPIs are widely used and are out of current prescription guidelines. The frequency of PPI abuse varies from 40% to 70% in various studies. Starting and continuing to use these drugs without the correct indications will cost the patient considerably. WHO definition, rational use of drugs, stating that the rational use of drugs requires patients to take medications that meet their clinical needs at the lowest cost for a suitable period of time¹⁰.

METHODOLOGY:

The study was conducted at hospital departments of general medicine and general surgery in Ayub

Teaching Hospital in cooperation with the Department of Pharmacology after obtaining the consent of the Institute of Institutional Ethics. It was a prospective observational study conducted from January 2019 to June 2019. Included were patients of both sexes of aged 20-70 years. All patients received informed consent. Patients who refused to consent were excluded from the study. The sample size for the study was (n = 100). Demographic and detailed patient history of past, present, family, personal and drug history was retrieved. Other details have also been recorded, such as the current diagnosis, the reason for the current admission, any examinations carried out to confirm the diagnosis, such as endoscopy, etc. The number of drugs, dosage form, frequency and duration of the medications on which the patient is being taken were also taken. Patients were asked to improve symptoms or any adverse drug reactions during their current stay. To assess symptom scoring, a five-point Likert scale was used to assess PPI efficacy with an approved gastro-reflux disease (RDQ) 20 questionnaire containing 12 items. This questionnaire was completed during a personal conversation with the patient regarding his inclusion in the examination and discharge from the hospital. The questionnaire had a maximum score of 40 and a minimum of 12 depending on the severity of the symptoms, such as epigastric pain, bloating, vomiting, nausea, burning heart, belching, anorexia, etc. 21 Inquiry or adverse reaction questions from PPI patients survey. The PPI cost analysis was performed taking into account the PPIs available in the hospital and used in the study. The prescription's rationality was assessed according to the criteria listed in previous studies.

RESULTS:

A total of 214 files were examined, 101 from the surgery department and 113 from the medicine department.

Of these 214 cases, 100 (46.72%) concerned proton pump inhibitors. 47.52% of patients hospitalized in surgical wards and 46.01% of patients hospitalized in therapeutic wards were treated with proton pump inhibitors as shown in Table 1.

Table1: Department wise distribution of patients on Proton pump inhibitors

Department	No. of patients on PPIs	No. of case sheets reviewed	patients on PPIs (%)
Surgery	48	101	47.52
Medicine	52	113	46.01
Total	100	214	46.72

$Z = 0.442$, hence there is no significant difference in rewriting PPI between Departments (test for the difference between two proportions). Of the 100 patients receiving proton pump inhibitors, most of them 41% were middle-aged between 41 and 60 years old, 61% were men and 39% were shown in Table 2 and Table 3.

Table 2: Age wise distribution of patients on proton pump inhibitors

Age	% of Patients
20-40	44
41-60	41
60 and above	15

Table 3: Gender Distribution of patients on proton pump inhibitors

Gender	% of patients
Male	61
Female	39

$Z = 4.5081$, Hence significant difference in the prescription of PPIs between males and females

Table 4: Indications for prescribing PPIs

S.No	Indication	% of patients
1.	Acute Gastritis	4
2.	Duodenal ulcer	1
3.	With NSAIDS	32
4.	GERD	05
5.	Others	58

4% of patients with acute gastritis, 5% of patients with gastroesophageal reflux disease (GERD), 1% duodenal ulcer, 32% of patients along with NSAIDs and 58% of patients received PPI for other reasons and were not on NSAIDs or not had no symptoms associated with GERD or acid digestive disease as shown in Table 4. Oral PPI therapy was recommended in 70% of patients and intravenous PPI in 30% of patients. Intravenous PPI used in all these patients is pantoprazole 40 mg administered once a day early in the morning. Most patients were prescribed PPI once a day. 97% only in 3% of patients. Was administered twice a day. As shown in Table 5 and Table 6.

Table 5: Route of administration of PPI

Route	% of patients
Oral	70
Intravenous	30

Table 6: frequency of administration of PPIs

Frequency	% of patients
Once daily	97
Twice daily	03

The incidence of polypharmacy was high, all patients in the study received many medications. The average number of prescription drugs was 4.93. Antimicrobials were the most common drugs used in (71%) patients followed by non-steroidal anti-inflammatory drugs and multivitamin preparations in 32% of patients, as shown in Table 7.

Table 7: Concomitant drugs used along with Proton pump inhibitors

S.No	Drugs used	patients %
1.	Antimicrobials	71
2.	NSAIDs	32
3.	Multivitamin preparations	32
4.	Calcium and vitamin D	07
5.	Antihypertensives	09
6.	Vitamin C	10
7.	Antidiabetics	03
8.	Antiemetics	13
9.	Antiplatelets	03
10.	Purgatives /laxatives	02
11.	Corticosteroids	01
12.	Diuretics	03
13.	Antiepileptics	01
14.	Antacids	03
15.	Antimalarial	04
16.	Oral Iron therapy	05
17.	Hypolipidemics	03
18.	Tramadol	22

Majority of the patients 88% were having a low Likert score of < 20, prior to start of therapy only 12 % of the patients were having significant symptoms (Likert score above 21) related to Acid peptic disease or GERD as shown in Table 9.

Table 8: Categorization based on likert scale

Likert scale score	% of patients at onset of therapy	% of patients at discharge
12	47	73
13-20	41	22
21-30	07	05
Above 30	05	00

Table 9: Likert Score of patients at start of therapy with PPIs and at discharge (Mean \pm SD)

	Likert score (Mean \pm SD)
At start of therapy	15.15 \pm 5.28
At discharge	12.98 \pm 1.90

Pantoprazole was most commonly prescribed PPI in 82% of patients followed by omeprazole in 11% and esomeprazole in 7 % as shown in Table 10. Omeprazole and esomeprazole were cheaper in comparison to pantoprazole

Table 10: Proton pump inhibitors used in the study

PPI	% of patients
Pantoprazole	82
Omeprazole	11
Esomeprazole	07

Table 11: Cost analysis of Proton pump inhibitors used in the study

Drug	Formulation	Dose	Frequency	Cost per day
Pantoprazole	Oral	40 mg	OD	6.5 Rs
Pantoprazole	IV	40 mg	OD	60 RS
Omeprazole	Oral	20 mg	OD	3 RS
Esomeprazole	Oral	20 mg	OD	3 RS

DISCUSSION:

Prescriptions for proton pump inhibitors are growing rapidly in Pakistan, as well as around the world, and PPI has become one of the most commonly prescribed drugs. This study shows that a total of 46.72% of hospitalized patients used proton pump inhibitors during the study period. This is in line with the previous study by Ramirez E. et al. Who found PPI to be between 28.65% and 82.65%, and Sandozi T who reported 45%¹¹. There was no significant difference in the prescription of the proton pump inhibitor between the surgical and medical departments ($Z = 0.442$). PPI was significantly higher in men than in women $Z = 4.5081$. This is in line with the previous Mayet AY study. Only 42% of patients received PPI according to rationality criteria. 58% of the PPI recommendations were unfounded. This is consistent with the Sandozi T study (55%), but more than with the Mayet AY study (43%)¹²⁻¹³. Naunton M et al (39.6%), the frequency of PPI administration was once a day in 97% of cases, PPI doses are recommended as once a day, but they can be administered twice a day also for fast action because steady state is fast achieved. The most common drugs used simultaneously with PPI were antimicrobials, this is a serious problem because 58% of PPI prescriptions were unjustified and it is well known that patients taking proton pump inhibitors are also susceptible to colonization of pathogens, which can lead to bacterial gastroenteritis, and also their greater risk of developing *Clostridium difficile* infection (antibiotic-related diarrhea). Although many symptom scales and quality of life instruments have been used in clinical trials, not all have been fully validated¹⁴. We used the Reflux Disease Diagnostic Questionnaire (RDQ) because it is specific for GERD and indigestion. The validity, reliability and responsiveness of this test have been well demonstrated. In our study, 47% of patients had an RDQ score of 12, indicating that the majority of patients had no GERD symptoms because this was the minimum possible score, and only 12% of the patients had significant symptoms, as shown by an RDQ score greater than 20. Significant improvement in score RDQ of patients showing PPI effectiveness ($Z = 3.86$). We cannot comment much on the effectiveness because our study was not interventionist and the duration of PPI treatment varied among patients¹⁵. The study

design was not appropriate to assess our performance goal for IPP. Randomized prospective clinical trials are better in this respect. The most commonly used proton pump inhibitor was pantoprazole in 82% of patients followed by omeprazole (11%) and esomeprazole (7%). At least one adverse effect was seen in 14% of patients. The most common adverse reaction was headache observed in 5% of patients. No serious or life-threatening adverse reaction was seen in patients receiving proton pump inhibitors. Cost analysis showed that pantoprazole was twice as expensive as omeprazole and esomeprazole preparations available in a hospital pharmacy.

CONCLUSION:

Fifty-eight percent of the patients in our study received Proton pump inhibitors incorrectly due to unwarranted indications. Awareness should be increased among hospital clinicians so that proper PPI prescription improves patient care at a low cost. Although we found PPI to be effective in our study, the design of the study was not appropriate for assessing efficacy. In the future, more drug use and pharmaco-economic research should be conducted to compare the rationality of using proton pump inhibitors and other anti-secretory drugs such as H2 blockers to find out the exact scenario and plan countermeasures.

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