

Use and inappropriate use of proton pump inhibitors in hospitalized patients

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ABSTRACT

Background: The discovery of *Helicobacter pylori* infection in etiology of peptic ulcer disease and proton pump inhibitors (PPI) in management of upper gastrointestinal diseases had been the milestones in medical science. PPI are currently being both overused and misused. In countries like India, where over 500 branded formulations of PPI are available, probability of misuse and abuse increases exponentially. The aim of the study was to find out inappropriate use of PPI, among hospitalized patients.

Methods: In order to find answer to the research question a cross sectional study was conducted in indoor patient of a tertiary care private hospital at Jaipur, Rajasthan. Patients of either sex, aged 18 years or above belonging to rural and urban communities were participating in study. The sample size was 500.

Results: It was noted that Inappropriate PPI use was observed in most of the hospital admitted patients (78%). Most common diagnosis among inappropriate PPI use was dengue fever (due to increased number of dengue cases during study period), followed by cerebrovascular accidents and urinary tract infection. Most common indication for appropriate PPI use was stress ulcer prophylaxis, again in dengue case (due to cardinal manifestation of thrombocytopenia).

Conclusions: Almost all patients were once prescribed PPI after admission and discharged on PPI (99.2%). Thus, we recommend evidence-based prescription of PPI, to reduce side effects and excess cost.

Keywords: PPI, Gastrointestinal diseases, Hospitalized patients, Dengue fever

INTRODUCTION

The discovery of *Helicobacter pylori* infection in etiology of peptic ulcer disease (PUD) and proton pump inhibitors (PPI) in management of upper gastrointestinal diseases had been the milestones in medical science.

After the introduction of PPIs more than two decades ago, many studies have documented their beneficial effect in inhibiting gastric acid production.¹⁻⁵ PPIs are now the drugs of choice for treating gastroesophageal reflux disease (GERD), which occurs in 42% of Westerners on a monthly basis, as well as for treating

PUD, *Helicobacter pylori* infection, and Zollinger-Ellison syndrome.⁶⁻⁹ Their treatment effects have been well described and PPIs are now among the most prescribed drugs in the world.¹⁰⁻¹⁵

As PPIs are considered generally safe drugs to use, a large percentage of patients are prescribed PPIs without a proper medical indication.^{16,17} However, some observational database studies have suggested an increased risk of adverse events associated with PPI use, including cancer, osteoporosis, fractures, diarrhea, cardiovascular events, and pneumonia.¹⁸⁻²⁴

PPI are currently being both overused and misused. In countries like India, where over 500 branded formulations of PPI are available, probability of misuse and abuse increases exponentially. Although safe and very effective class of pharmaceutical agents, PPI should be used only when there is documented evidence of GI disorder that cannot be treated with H2 receptor antagonist and where a PPI use is clinically justified. Increased clinician awareness on appropriate PPI prescription will lead to better patient outcome at low cost.^{25,26}

It was observed that whether indicated or not almost all patients admitted in the hospital and even on discharge have the prescription of either of the PPI. In our society

where food taboos are more, we need to justify their increasing use. However, it was realized that these drugs have been inadvertently used, which apart from increasing the risk of side effects, will also increase health care cost. Although, there have been some reports on this aspect in the literature, we hardly found any such report from our country. This led us to study the appropriate use of PPI in a hospital setup.

Objectives

The objective of the present study was to find out inappropriate use of proton pump inhibitors among hospitalized patients.

METHODS

A cross sectional study was conducted in indoor patient at Santokba Durlabji Memorial Hospital (SDMH), Jaipur, Rajasthan. Patients of either sex, aged 18 years or above belonging to rural and urban communities were participating in study. The sample size was 500.

Only adult indoor patients of SDMH on PPI were included in the study, while intensive care unit (ICU) patients were excluded.

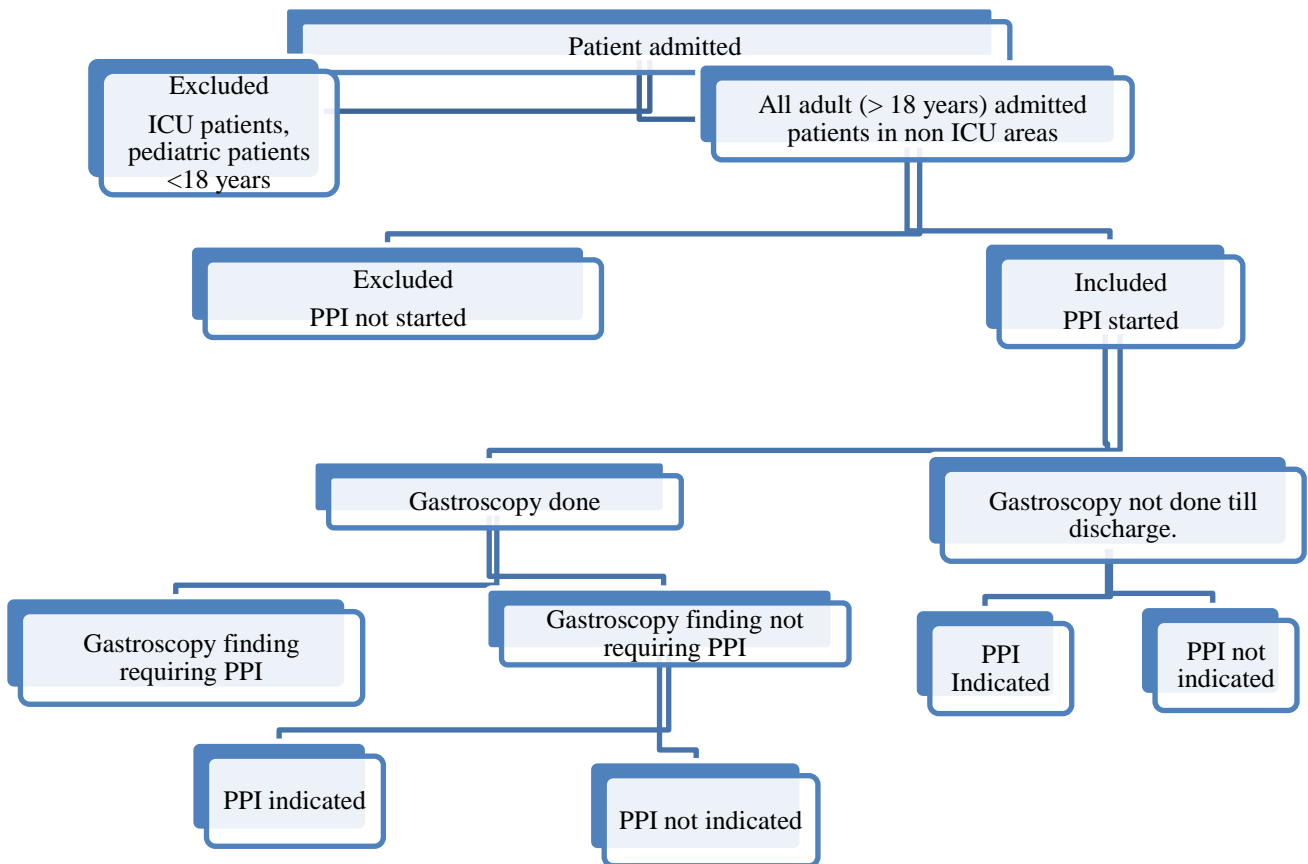


Figure 1: Admission criteria of the patients.

Procedure

In-depth interview was taken by investigator himself and data was recorded on a pre-designed pro-forma, which served as a study tool. All patients during the study period were divided as following (Figure 1).

Group A where gastroscopy was done. Among these Gastroscopy findings requiring PPI were erosive esophagitis, GERD, *H. pylori* infection, gastric ulcers, duodenal ulcers and gastritis. Gastroscopy findings not requiring PPI were further divided into two- PPI indicated as symptomatic GERD, functional dyspepsia, suspected upper GI Bleeding, gastrointestinal ulcer bleeding prophylaxis non-steroidal anti-inflammatory drug {NSAIDs and age >70 year, NSAIDs and corticosteroids, NSAIDs and warfarin/coumadin, NSAIDs and h/o ulcer/GI bleed, aspirin and corticosteroids, aspirin and warfarin / coumadin, aspirin and NSAID and high dose NSAID), stress ulcer prophylaxis (platelets <50000, INR >1.5, activated partial thromboplastin time (aPTT) >2 times control, h/o GI ulcer or bleed within 1 year of admission, atleast 2 sepsis, ICU>1 week, occult bleeding lasting 6 or more days, >250 mg hydrocortisone or equivalent, severe head injury and burn patient) and PPI not indicated as portal hypertension and celiac disease.

Group B where gastroscopy was not done. Among these in some cases PPI was indicated as symptomatic GERD, dyspepsia acid peptic diseases (APD) type, suspected upper GI bleeding, gastrointestinal ulcer bleeding prophylaxis (NSAIDs and age >70 year, NSAIDs and corticosteroids, NSAIDs and warfarin/Coumadin, NSAIDs+h/o ulcer/GI bleed, aspirin and corticosteroids, aspirin and warfarin/Coumadin, aspirin and NSAID, high dose NASID), stress ulcer prophylaxis (platelets <50000, INR >1.5, a PTT >2 times control, h/o GI ulcer or bleed within 1 year of admission, atleast 2- sepsis, ICU >1 week, occult bleeding lasting 6 or more days, >250 mg hydrocortisone or equivalent, severe head injury and burn patient) and chest pain with negative cardiac and pulmonary workup, suspected due to GERD or dyspepsia. And in some cases PPI was not indicated as dyspepsia (dysmotility type), acute gastro enteritis, anemia, ulcer porphylaxis with clopidogrel and low dose aspirin and all admitted patients except those with pneumonia, liver abscess and UTI. All patients belonging to PPI not indicated group were considered as inappropriate PPI use and rest all as appropriate use of PPI. Diagnosis by the treating doctor was considered the final diagnosis.

Data analysis

Continuous variables were summarized as mean and standard deviation, whereas nominal or categorical variables were summarized as proportions (%). Categorical or nominal data was analyzed by using χ^2 test. Risk assessment was done by using non-adjusted

odds ratio including 95% CI. P<0.05 was taken as significant. Med calc 14.0.0 version software was used for all statistical analysis.

RESULTS

Out of 500 patients, PPI was not indicated in 390 (78%) (Figure 1) and only 110 of patients it was indicated. Most common indication among appropriate use was, stress ulcer prophylaxis (78 patients) (Table 1).

Table 1: Distribution of subjects according to PPI indication.

Indication of PPI	No.	%
Unindicated	390	77
Erosive esophagitis	1	0.2
Dyspepsia (APD type)	1	0.2
Gastro esophageal reflux disease	1	0.2
Helicobacter pylori infection	1	0.2
Duodenal ulcers	1	0.2
Gastric ulcers	2	0.4
Zollinger-Ellison syndrome		
Gastritis	4	0.8
Suspected upper GI bleeding	3	0.6
NSAID+age >70 years	7	1.4
NSAID+corticosteroids	7	1.4
NSAID+warfarin/Coumadin	1	0.2
Asprin+NSAID	3	0.6
Platelets <50000, INR>1.5, aPTT>2 times control	70	14
H/O GI ulcer or bleed within 1 year of admission	4	0.8
Atleast 2-sepsis, ICU>1wk, occult bleeding lasting 6 or more days, >250 mg hydrocortisone/equivalent	2	0.4
Severe head injury	1	0.2
Burn patient	1	0.2
Total	500	100.00

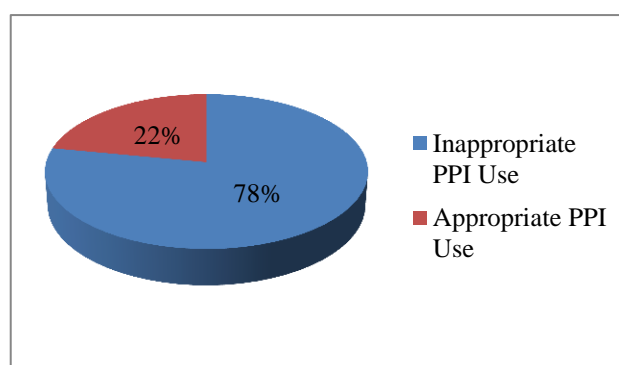


Figure 2: Inappropriate PPI use among total subjects.

Out of 390 patients, in which PPI was not indicated. Most common diagnosis was dengue fever (33), followed by

CVA (25), UTI (17) and pancreatitis (15) (Table 2). Out of 110, appropriate PPI use, 59 patients were of dengue, followed by 8 CVA and others.

Out of 500 study subjects, 494 were discharged on PPI. And out of 390 inappropriate PPI use, 386 were discharged on PPI (Table 3). Odds ratio for PPI on discharge was 1.787 (95% CI: 0.323 to 9.888).

Table 2: Distribution of subjects according to inappropriate use.

Diagnosis	Inappropriate use (n=390)	
	N	%
Acute appendicitis	2	0.51
Acute enteritis	7	1.79
Acute vertiginous syndrome	1	0.26
Acute appendicitis	1	0.26
Acute cholecystitis	2	0.51
Adult polycystic kidney disease	1	0.26
Atrial fibrillation	1	0.26
Acute kidney injury	2	0.51
Alcoholic liver disease	1	0.26
Anxiety neurosis	2	0.51
Anemia	6	1.54
Ascites	1	0.26
Aspergillosis	1	0.26
Benign paroxysmal positional vertigo	4	1.03
Cancer	6	1.54
Congestive heart failure	3	0.77
Chikungunya fever	1	0.26
Chronic Constipation	2	0.51
Chronic kidney disease	8	2.05
Chronic liver disease	1	0.26
Cluster Headache	1	0.26
Chronic obstructive lung disease	14	3.59
Chronic suppurative otitis media	1	0.26
CVA	26	6.76
Dilated cardiomyopathy	2	0.51
Dengue fever	33	8.46
Diabetic ketoacidosis	1	0.26
Diabetes mellitus type 2	3	0.77
Dysfunctional uterine bleeding	1	0.26
Deep vein thrombosis	3	0.77
Enteric fever	5	1.28
Epistaxis	3	0.77
Esophageal ulcers	1	0.26
Fibroid uterus	1	0.26
Fibromyalgia	2	0.51
Full term normal delivery	6	1.54
Gastritis	1	0.26
Guillain-Barre syndrome	6	1.54
Hansen's disease	1	0.26
Hepatitis	4	1.03
Hypertension	7	1.79
Hypoglycemia	1	0.26
Hyponatremia	5	1.28
Hypothyroidism	1	0.26
Interstitial lung disease	3	0.77
Liver abscess	14	3.59
Lower segment caesarean section	1	0.26

Continued.

Diagnosis	Inappropriate use (n=390)	
	N	%
Lumbar canal stenosis	1	0.26
Lower urinary tract obstruction	1	0.26
Malaria	6	1.54
Mixed connective tissue disorder	1	0.26
Meningitis	6	1.54
Myocardial infarction	2	0.51
Micturition syncope	1	0.26
Migraine	1	0.26
Mitral regurgitation	1	0.26
Nephrotic syndrome	1	0.26
Normal pressure hydrocephalus	1	0.26
Obstructive sleep apnea	1	0.26
Pulmonary artery hypertension	1	0.26
Pancreatitis	15	3.85
Prolapsed inter vertebral disc	1	0.26
Pleural effusion	4	1.03
Pneumonitis	9	2.31
Pneumothorax	2	0.51
Psychogenic vomiting	2	0.51
Pyrexia of unknown origin	1	0.26
Rheumatoid arthritis	7	1.79
RBBB	1	0.26
Renal calculi	1	0.26
Rheumatic heart disease	2	0.51
Subacute intestinal obstruction	10	2.56
Scrub typhus	11	2.82
Seizure	6	1.54
Sepsis	1	0.26
Septicemia	1	0.26
Status lower anterior resection with ileostomy	1	0.26
Transient ischemic attack	2	0.51
Transverse myelopathy	1	0.26
Transverse myelitis	1	0.26
Ulcerative colitis	1	0.26
Ulcers	1	0.26
Ureteric calculus	1	0.26
Urinary tract infection	17	4.36
Vertigo	1	0.26
Viral fever	4	1.03
Viral hepatitis	1	0.26
Wilson's disease	1	0.26
Ulcer	1	0.26
Gall stone disease	12	3.08
Carcinoma lung	1	0.26
Cholangitis	2	0.51
Tuberculosis	12	3.12
Myositis	1	0.26
Ac gastroenteritis	11	2.82
Candida esophagitis	1	0.26
Myopathy	1	0.26
Encephalopathy	1	0.26
Space-occupying lesion of the brain	1	0.26
HIV	1	0.26

Continued.

Diagnosis	Inappropriate use (n=390)	
	N	%
Seizure	2	0.51
Coronary artery disease	2	0.51
Asthma	4	1.03
Abscess	2	0.51
Hemorrhoids	1	0.26
Mesentric ischemia	1	0.26
Cellulitis	1	0.26
Benign prostatic hypertrophy	1	0.26
Mitral stenosis	1	0.26

Table 3: Comparison of status of PPI on discharge.

PPI on discharge	Inappropriate use		Appropriate use		Total	
	No.	%	No.	%	No.	%
No	4	66.67	2	33.33	6	100.00
Yes	386	78.14	108	21.86	494	100.00
Total	390	78.00	110	22.00	500	100.00

Chi-square=0.032 with 1 degree of freedom; p= 0.858; Odds ratio=1.787 (95% confidence interval: 0.323 to 9.888).

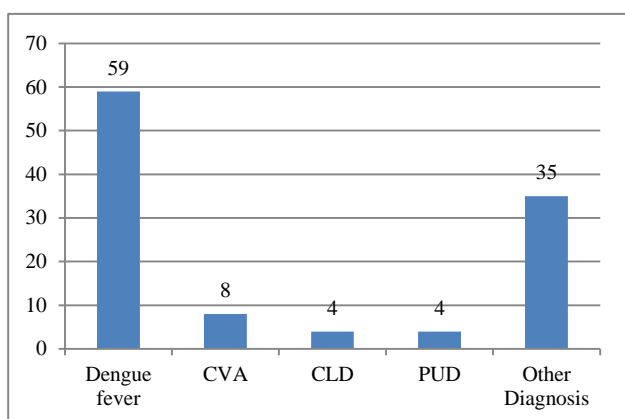


Figure 3: Common diagnosis among appropriate PPI use.

DISCUSSION

PPIs are potent gastric acid suppressing agents that are extensively used in the treatment of multiple gastrointestinal disorders. Because of physician's perception of the safety of this medication, lack of knowledge about practice parameters or a component of defensive medicine, PPI have become one of the world's most frequently prescribed medications with annual sales worldwide surpassing US \$25 billion.^{27,28}

Recent literature has attributed a growing number of side effects to these drugs (4-8, 16). So more rationale and judicious use will not only have positive outcome on patient safety but definitely prevent unnecessary health care expenditure.

In our study, 78% of the PPI use was inappropriate. This is in accord with other studies.

Gingold et al, studied indications and frequency of PPI use in hospitalized patients of a large teaching hospital. It was observed that, 92% of the patients had no evidence-based indication for using PPI and most common indication of PPI was to prevent GI bleeding.²⁹

In our study, most common diagnosis among the inappropriate use was found to be dengue fever. Out of 500 patients, 92 were diagnosed as dengue fever. Out of these 92 patients, 33 were inappropriately prescribed and 59 were appropriately prescribed PPI. The possible reason for this could be, firstly, because of increased number of dengue cases during the study period. Secondly, most of the dengue patients are admitted with thrombocytopenia, which might be responsible for increased prescriptions of PPI for stress ulcer prophylaxis. As platelet count <50,000, is an indication for stress ulcer prophylaxis but it was prescribed even when platelets were >50,000. After dengue fever, CVA followed by UTI, pancreatitis, liver abscess and chronic obstructive pulmonary disease were the common diagnosis, among inappropriate use of PPI. Possible reason for this could be, most of CVA patients are on anti-platelet therapy and are elderly, so to prevent gastrointestinal bleeding, PPI is started. Secondly, for patients complaining of pain abdomen, PPI is generally started first and later evaluated for the cause.

Simultaneously, dengue cases had impact on appropriate use also. Out of 110 appropriate PPI use, 59 patients were of dengue. Out of these 59, we cannot say how many were knowingly given PPI for some indication or was started as a routine practice. This could have further increased the number of inappropriate PPI use. But this shows that, gastrointestinal bleeding prophylaxis was the most common indication for both appropriate and inappropriate use of PPI. However, in literature, we could not find this alarming association with dengue fever.

Almost all patients, who were given PPI during hospitalization, were discharged on PPI (99.2%). This is much higher than the study done by Ahrens et al, in which 54.5% of PPI on discharge had no justified recommendations and 12.7% indications were uncertain.³⁰ This may lead to unnecessarily increasing polypharmacy and risk of adverse events as well as burdening the public health budget. Possible reason for this could be, as ours is a large teaching hospital where residents making discharge letters are still in training and are not fully aware of evidence based practices.

Therefore, interventions aimed at improving residents education will help prevent inappropriate long term use. Hospitals should critically review their practice of recommending PPIs in their discharge letters and clearly document the reason for continued PPI use after discharge.

CONCLUSION

It was noted that inappropriate PPI use was observed in most of the hospital admitted patients (78%). Most common diagnosis among inappropriate PPI use was dengue fever (due to increased number of dengue cases during study period), followed by CVA and UTI. Most common indication for appropriate PPI use was stress ulcer prophylaxis, again in dengue case (due to cardinal manifestation of thrombocytopenia). Almost all patients were once prescribed PPI after admission and discharged on PPI (99.2%). Thus, we recommend evidence-based prescription of PPI, to reduce side effects and excess cost.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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