Research Article
AMERICAN JOURNAL OF PHARMACY AND HEALTH RESEARCH
www.ajphr.com
2016, Volume 4, Issue 4
ISSN: 2321–3647(online)

A Study on Prescribing Pattern of Proton Pump Inhibitors at A Private Tertiary Care Hospital

Prakriti Neupane[1]*, Puran Giri[1], D Nagalatha[1]
1.Aditya Bangalore institute of pharmacy education and research, Bangalore 560064

ABSTRACT

To study the prescribing pattern of proton pump inhibitors at a private tertiary care hospital. This was a descriptive retrospective as well as prospective study carried out using 220 inpatient prescriptions in internal medicine department at a private tertiary care hospital. Out of 220 prescriptions of PPIs 56% were male patients and remaining were female among them 12.27% were alcoholics and 6.36% were smokers. It was highly prescribed in the age group of 26-35 (23.64%). Highly prescribed proton pump inhibitor was Pantoprazole (72%), IV route was used mostly 80.91% and about 53% of IV prescriptions were switched to oral route after patient being stable. Vomiting (34%) and nausea (28%) were the most common symptoms of ulcer presented. Fever (22.63%) was the most common condition under therapy and antibiotics (20.50%) were highly prescribed drugs concurrently with PPIs. Average cost per day of IV PPIs was Rs.54.69/day and of oral PPIs was Rs.7.8/day. Out of 43 drug interactions found 14 interactions were with iron. Widespread prescriptions of PPIs should be taken into consideration as it is irrationally prescribed for prophylaxis with various medications where only NSAIDs induced ulcer and its treatment is approved by FDA.

Keywords: prescribing pattern, proton pump inhibitors, tertiary care hospital.

*Corresponding Author Email: prakriti13ps@gmail.com
Received 18 March2016, Accepted 25March 2016

Please cite this article as:Neupane P*et al*., A Study on Prescribing Pattern of Proton Pump Inhibitors at A Private Tertiary Care Hospital. American Journal of Pharmacy & Health Research 2016.

INTRODUCTION

Medicines are an integral part of the health care, and modern health care is impossible without the availability of necessary medicines. They not only save lives and promote health, but prevent epidemics and diseases too. Accessibility to medicines is the fundamental right of every person. However, to bring optimal benefit, they should be safe, efficacious, cost-effective and rational.

Prescription pattern monitoring studies (PPMS) are drug utilization studies with the main focus on prescribing, dispensing and administering of drugs. They promote appropriate use of monitored drugs and reduction of abuse or misuse of monitored drugs. PPMS also guide and support prescribers, dispensers and the general public on appropriate use of drugs, collaborate and develop working relationship with other key organizations to achieve a rational use of drugs. Prescription Patterns explain the extent and profile of drug use, trends, quality of drugs, and compliance with regional, state or national guidelines like standard treatment guidelines, usage of drugs from essential medicine list and use of generic drugs. There is increasing importance of PPMS because of a boost in marketing of new drugs, variations in pattern of prescribing and consumption of drugs, growing concern about delayed adverse effects, cost of drugs and volume of prescription.

The aim of PPMS is to facilitate the rational use of drugs in a population. Irrational use of medicines is a major problem worldwide. WHO estimates that more than half of all medicines are prescribed, dispensed or sold inappropriately, and that half of all patients fail to take them correctly. The overuse, underuse or misuse of medicines results in wastage of scarce resources and widespread health hazards. The rational use of medicines (RUM) is defined as "Patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community".

A large number of studies have been conducted to study the prescribing pattern of physicians across the country. The studies conclude the irrational prescribing practices of prescribers and suggest RUM at all levels of health care delivery system. However, no systematic reviews, meta-analyses, or randomized controlled trials are present about the relevance of PPMS in promoting rational use of drugs.[1]

Proton Pump Inhibitors

Proton pump inhibitor (PPIs) represents the most important recent advance in the treatment of acid-related gastrointestinal (GI) diseases. Based on efficacy profiles superior to those of H2-receptor antagonists(H2RA), sucralfate, and cisapride, PPIs are now considered the drugs of

choice in managing patients with peptic ulcer disease(PUD), gatroesophageal reflux disease(GERD), and zollinger-Ellison syndrome(ZES), Currently there are five PPIs available, Omeprazole, lansoprazole, Pantoprazole, dexlansoprazole, Rabeprazole and esomeprazole.[2]

Mechanism of Action

Proton pump inhibitors are prodrugs that require activation in an acid environment. After absorption into the systemic circulation, the prodrug diffuses into the parietal cells of the stomach and accumulates in the acidic secretory canaliculi. Here, it is activated by proton-catalyzed formation of a tetracyclic sulfenamide, trapping the drug so that it cannot diffuse back across the canalicular membrane. Acid secretion resumes only after new pump molecules are synthesized and inserted into the luminal membrane, providing a prolonged(up to 24–48 hour) suppression of acid secretion, despite the much shorter plasma half-lives(0.5–2 hours) of the parent compounds. Because they block the final step in acid production, the proton pump inhibitors are effective in acid suppression regardless of other stimulating factors.[3]

Pharmacokinetics

The pharmacokinetics of each PPI depends, in part, on the drug dose and the route of administration.

The short elimination half-life has little bearing on the duration of the antisecretory effect because of their irreversible binding (which may be somewhat different with Rabeprazole) to the proton pump.

All four PPIs undergo extensive hepatic metabolism and are eliminated as urinary metabolites and in the faeces. All four PPIs partially undergo metabolism by cytochrome (CYP) 2C19, a CYP450 Isoform known to exhibit genetic polymorphism. Based on this genetic polymorphism, a small proportion of the Caucasian and Asian populations are poor metabolizers of PPIs. However, the degree by which genetic control influences PPI metabolism appears to vary among the four agents. The relative contribution of CYP2C19 to PPI disposition is greatest with Omeprazole and least with Rabeprazole. Although metabolizer status can influence PPI drug interactions, the clinical implications of the pharmacokinetic differences among the agents are under debate.

Dosage and Administration

All PPIs may be inactivated by exposure to gastric acid and are formulated as either gelatin capsules containing enteric-coated microspheres (Omeprazole and lansoprazole) or enteric-coated tablets (Pantoprazole and Rabeprazole). The preferred administration time is in the morning about 30 minutes before a meal or snack. The oral administration of the crushed

granules or tablet may lead to inactivation by gastric acid. Various methods of administration have been recommended for patients who are unable to swallow the intact capsule or tablet. Omeprazole and lansoprazole granules may be administered via a nasogastric tube by preparing a suspension in 8.4% sodium bicarbonate solution. Omeprazole and lansoprazole granules may be removed from the capsule and administered with orange juice or apple juice orally, via a nasogastric or gastrostomy tube, sprinkled on applesauce. Lansoprazole granules may also be administered with numerous other foods and beverages.

As approved by FDA, Pantoprazole is the only PPI available in an injectable formulation. Unfortunately, no PPI oral liquid formulations are available.

Goals of PPIS Therapy

PPIs usually work very well to reduce stomach acid and to treat the above conditions. They have made a big impact on the quality of life of many people with these conditions since they first became available in the 1980s. They are commonly prescribed.

Goals of PPI therapy are:

Relief of pain

Ulcer healing

Prevention of complications

Prevention of relapse.[4]

Indications

PPIs are commonly used:

- To treat ulcers in the stomach and the part of the gut called the duodenum.
- To reduce acid reflux which may cause heartburn or inflammation of the gullet (oesophagitis). These conditions are sometimes called gastro-esophageal reflux disease (GORD).
- As one part of treatment to get rid of Helicobacter pylori - a germ (bacterium) found in the stomach, which can cause ulcers.
- To help prevent and treat ulcers associated with anti-inflammatory medicines called non-steroidal anti-inflammatory drugs (NSAIDs).
- In a rare condition called Zollinger-Ellison syndrome.
- PPIs are an alternative for H_2 blockers for prophylaxis of aspiration pneumonia.
- In other conditions where it is helpful to reduce acid in the stomach.[6]

Peptic Ulcer Disease [8]

An ulcer is defined as disruption of the mucosal integrity of the stomach and or duodenum leading to a local defect due to active inflammation. Ulcers occur within the stomach and or duodenum and are often chronic in nature. There are generally two types of peptic ulcer disease, those associated with helicobacter pylori and those associated with various drugs.

Gastroesophageal Reflux Disease[6]

GERD is the retrograde movement of gastric contents from the stomach into the esophagus, when esophagus is repeatedly exposed to refluxed material for prolonged period of time, inflammation of the esophagus (reflux esophagitis) occurs and in some cases, it can progress to erosion of the esophagus(erosive esophagitis).

Gastritis [5]

Gastritis or inflammation of gastric mucosa is not a single disease but rather a group of disorders that all induce inflammatory changes in the gastric mucosa.

Acute Gastritis

Onset of H.pylori infection may result in the acute gastritis. There is an increase in gastric acid followed by hypochorhydria for up to one year. Patients have mild epigastric discomfort.

Chronic Gastritis

It is often patchy and irregular in distribution. It involves the superficial and glandular areas of the gastric mucosa and progresses to glandular destruction.

Zollinger-Ellison Syndrome

ZES, a rare disorder, occurs when gastrin-secreting tumors are present, usually in the pancreas. Gastrin stimulates gastric acid secretion by parietal cells, leading to chronic hypersecretion. The massive acid secretion leads to severe peptic ulcer disease, severe esophagitis, duodenojejunitis, mal absorption, diarrhea, and weight loss. Since acid secretion is the cause of virtually all symptoms associated with ZES, anti secretory agents are considered the mainstay of therapy when surgery is not feasible. Control of symptoms by itself is not adequate. Antisecretory therapy must dramatically reduce acid secretion to prevent complications.

LITERATURE REVIEW

Saman Chubineh et al:[7] studied on Proton Pump Inhibitors: The Good, the Bad, and the Unwanted. Absolute indications for PPI use include PUD, chronic NSAID use, treatment of H pylori infection, and EE. Further studies are needed to establish treatment duration after H. pylori clearance for bleeding PUD and for chemoprophylaxis in Barrett esophagus. PPIs are not without significant adverse effects; therefore, their long-term use must be reevaluated periodically and discontinued when appropriate. This specifically applies to patients with NERD or PUD and

patients taking double-dose PPI, from which questionable benefit is obtained. After 20 years of experience with these drugs, many caveats apply to their use.

Vipin Kumar Singh et al:[8] studied on 'Prescribing pattern of acid suppressants in modern clinical practice - An analysis'. The study was carried out in Gastroenterology Department of Sanjay Gandhi post Graduate Institute of Medical Science Lucknow, India. Data collection form was designed for both physicians and patients to know prescribing pattern of proton pump Inhibitors. A Total of 50Physicians and 50 patients were enrolled in the study. Gastro esophageal reflux Disease (GERD) was the commonest indication for prescribing ASDs by Physicians. Step Down therapy was preferred approach for prescribing AS Ds. Majority of Physicians prescribed AS Ds for 1-3months. Omeprazole was the most commonly used PPIs in the treatment of Acid-peptic diseases. Maximum numbers of patients were suffered from Gaseous and bloating followed by abdominal pain and other symptoms. The most common occurrence of side effects with use of PPIs was Bowel change. Timing of PPIs administration and % of relief noticed with use of PPIs were reported. Percentage of cost addition (10%-30%) in the prescription due to acid-suppressants and patients satisfaction about cost of ASDs was also included in this study.

Cheryl Durand et al:[9] studied on Proton Pump Inhibitor use in Hospitalized Patients: Is Overutilization Becoming a Problem? Proton pump inhibitors (PPIs) are among the most common classes of medications prescribed. Though they were previously thought of as safe, recent literature has shown risks associated with their use including increased risk for Clostridium difficult infection, pneumonia, and fractures. Due to these risks, it is important to determine if PPIs are being used appropriately. This review evaluates seven studies in hospitalized patients. Additionally, this review evaluates literature pertaining to recently discovered adverse reactions; all studies found PPIs are being over utilized. Findings highlight the importance of evaluating appropriate therapy with these agents and recommending discontinuation if a proper indication does not exist.

Shobha et al:[10] studied on Assessment of Prescribing Pattern of Intravenous Proton Pump Inhibitors .Prospective assessment involved 611 patients over a 1-month period. For prophylaxis (stress ulcer, pre-operative and postoperative prophylaxis) and treatment, IV PPIs were prescribed inappropriately to 289 (89.2%) internal medicine and 97 (34.04%) surgery ward patients. Prolonged therapy was found in patients who received IV PPIs for stress ulcer prophylaxis. This study revealed significant inappropriateness of PPI administration with particular reference to indication to use, duration of therapy, and changeover of therapy in an Indian tertiary-care teaching hospital.

Objective of the Study

- To conduct a retrospective and prospective study on prescribing pattern of proton pump inhibitor in the department of general medicine.
- To evaluate the rational use of proton pump inhibitors by analysing the appropriateness of prescription with special reference to :
    - Selection of proton pump inhibiter in various clinical conditions
    - Concomitant drugs used
    - Dosage
    - Cost effectiveness
    - Route of administration
    - Drug interactions

MATERIALS AND METHOD

Duration of Study

The study was conducted for a period of 6 month.

Site of the Study

Study was conducted at private tertiary care hospital.

Study Design

A hospital based retrospective and prospective cross sectional study.

Sources of Data and Materials

- Patient case sheet
- Medication/treatment chart
- Suitable design documentation form
- Laboratory data report

Study Criteria

Inclusion Criteria

- Patients receiving PPIs drug treatment for peptic ulcer, gastritis, GERD.
- Patient receiving prophylactic PPI therapy during NSAID, antibiotics, steroids, etc

Exclusion Criteria

- Pregnancy women and children

Method of Data Collection

- Data collection form

Study procedure

A retrospective and prospective hospital based observational study was carried out in the patients satisfying the inclusion criteria. The clinical pharmacist will reviewed the patient case notes, medication chart, laboratory data and other prevalent data.

A suitable designed data collection was used to record all the necessary data including patient demographic details, patient medication history, and reason for admission, any allergic reaction, medication details and lab investigation.

RESULTS AND DISCUSSION

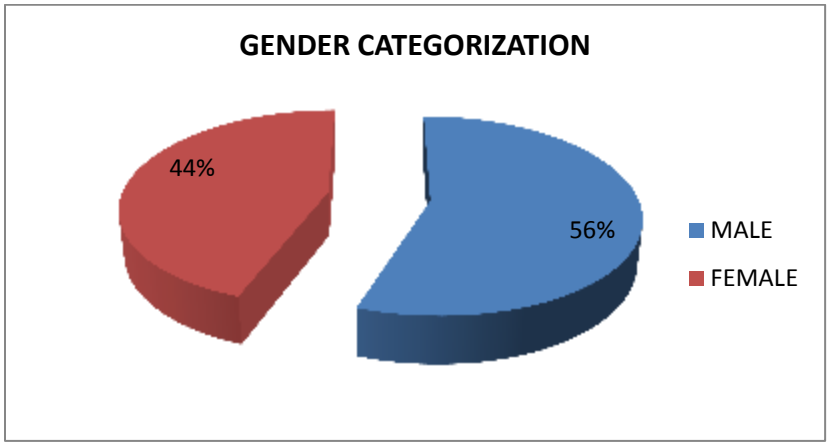

Figure 1: Gender Categorization

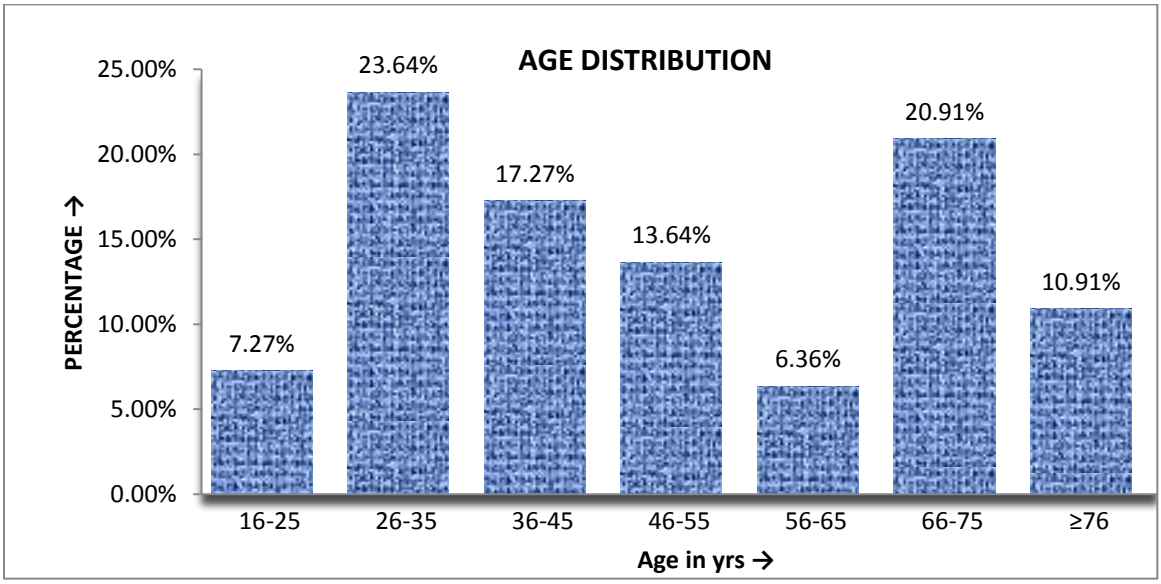

Figure 2: Age Distribution

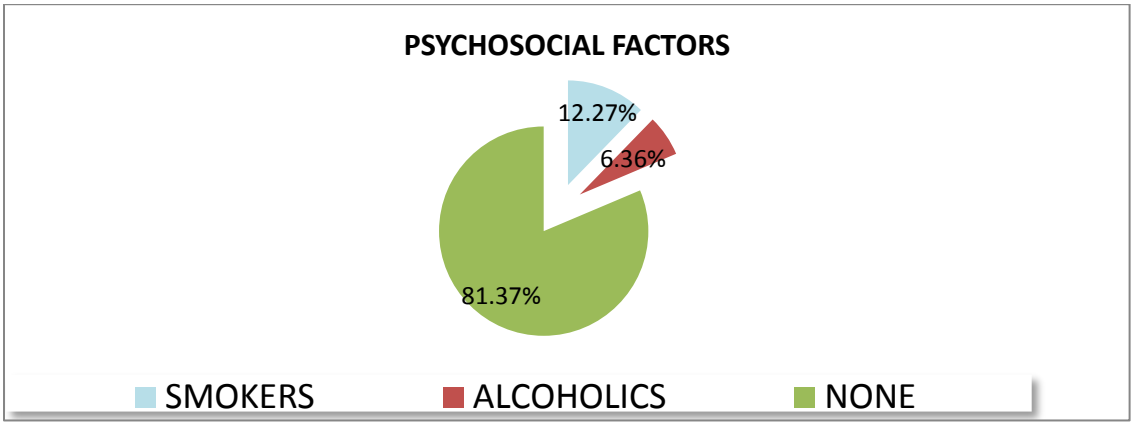

Figure 3: Psychosocial Factors

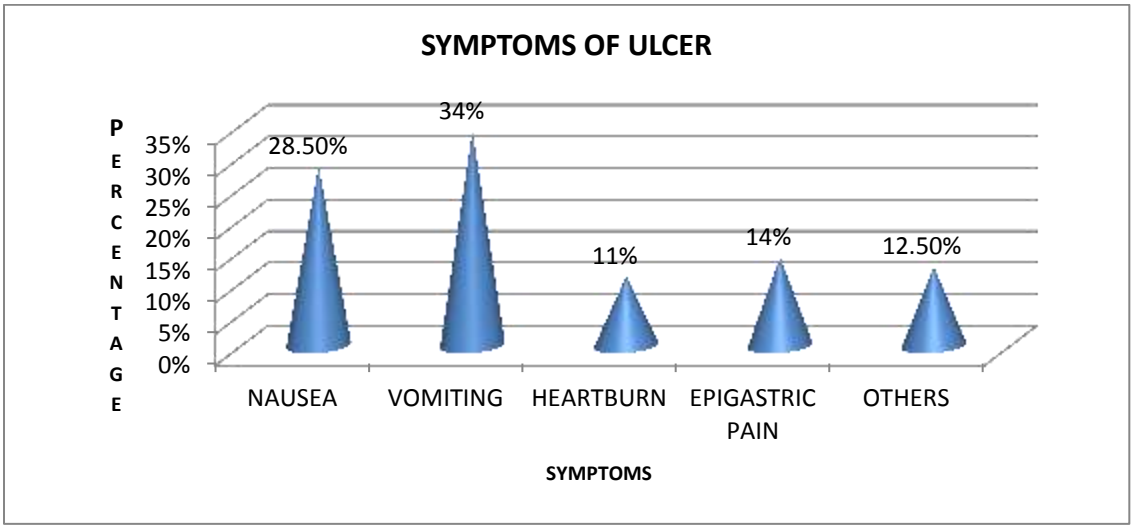

Figure 4: Symptoms of Ulcer

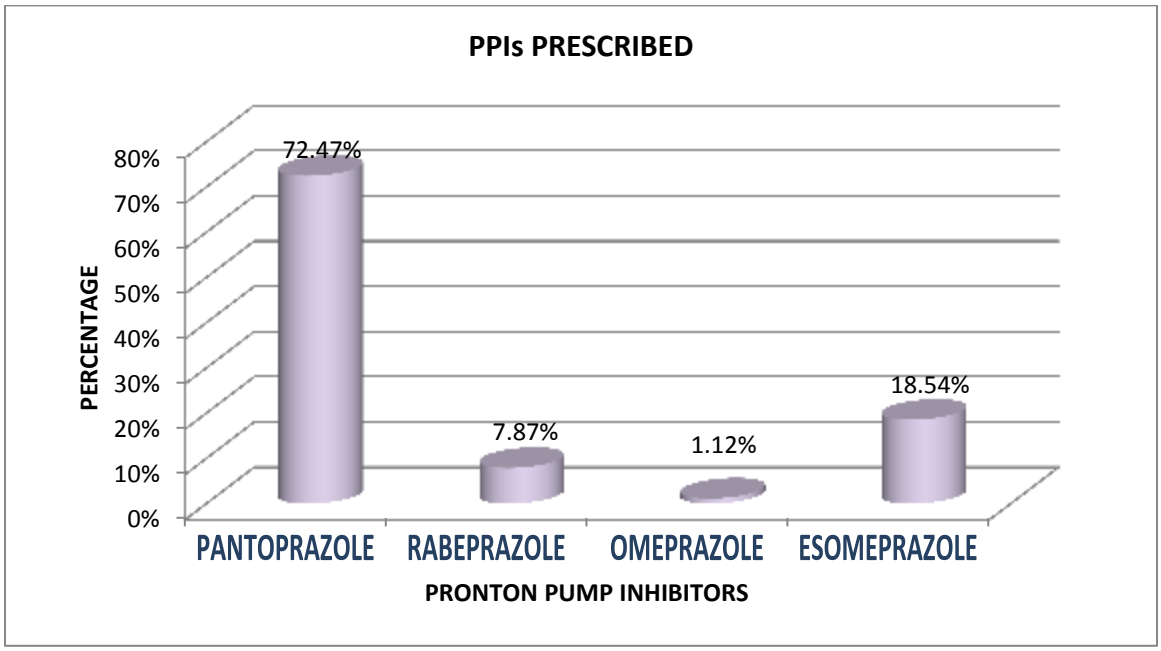

Figure 5: Proton Pump Inhibitors Prescribed

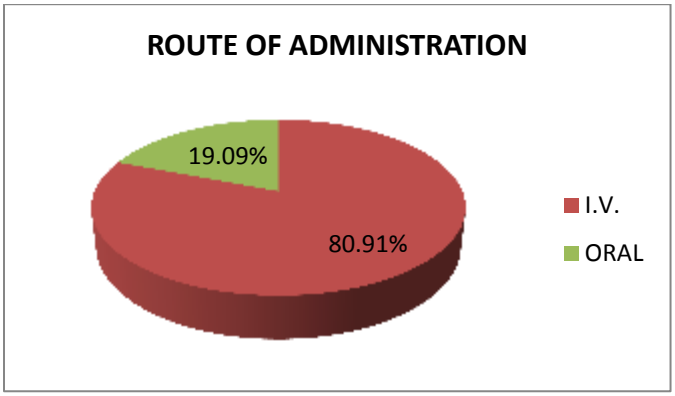

Figure6 : Route of Administration

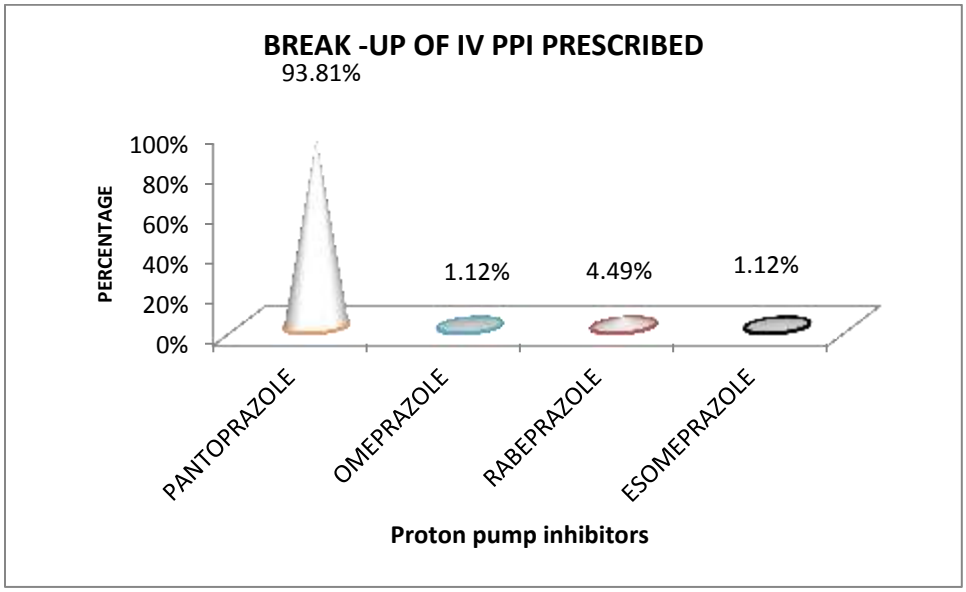

Figure7: Break Up of IV Therapy

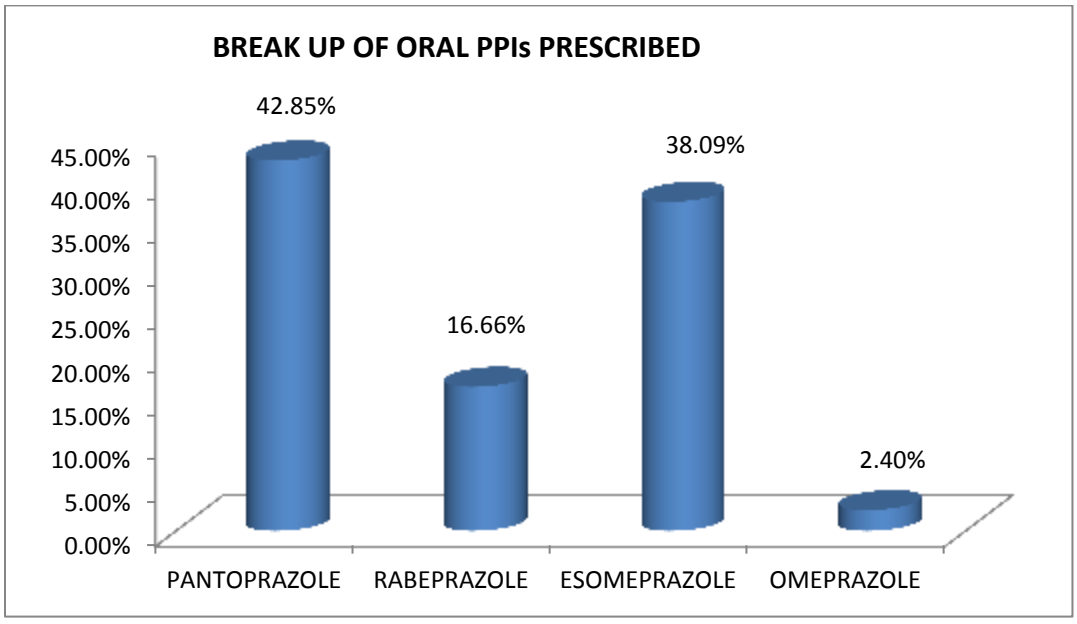

Figure 8: Break-Up of Oral PPIs Therapy

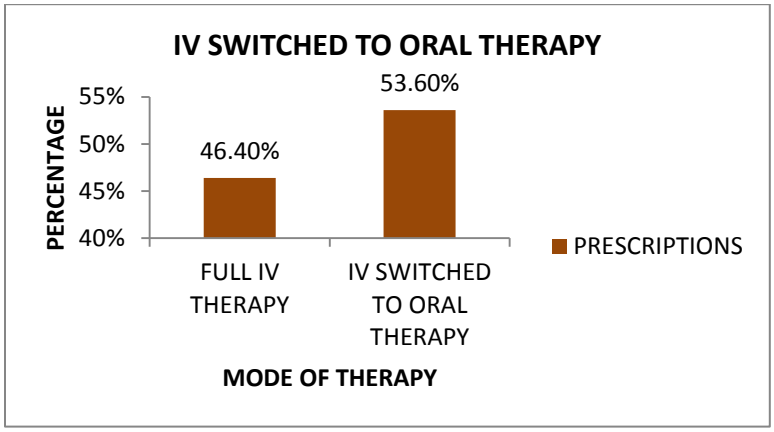

Figure 7:PPIs switched to oral from IV therapy

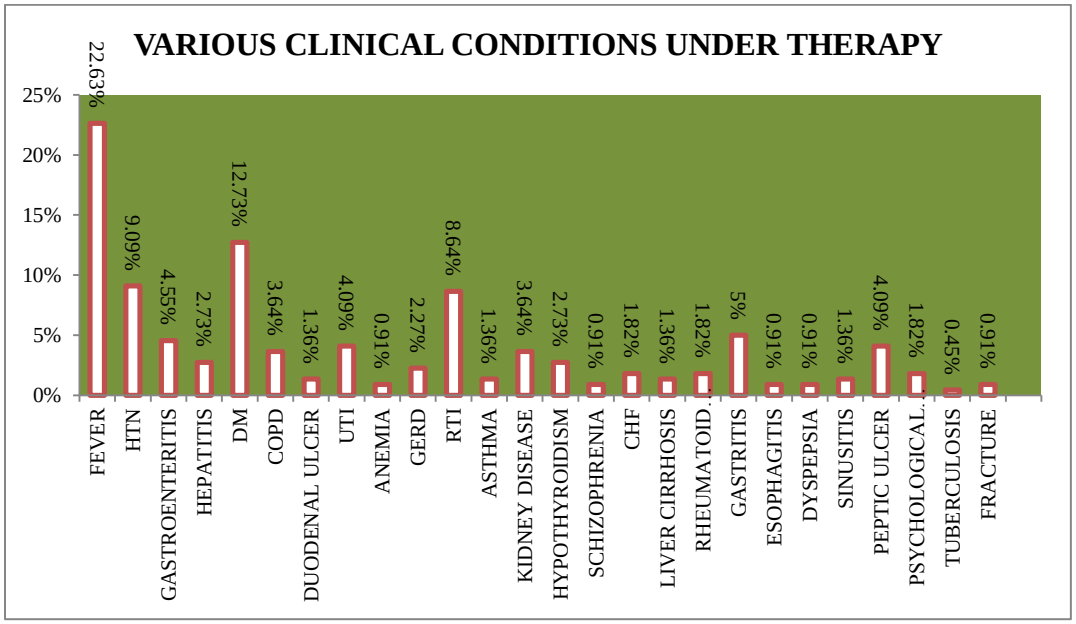

Figure 10: Various Conditions under Therapy

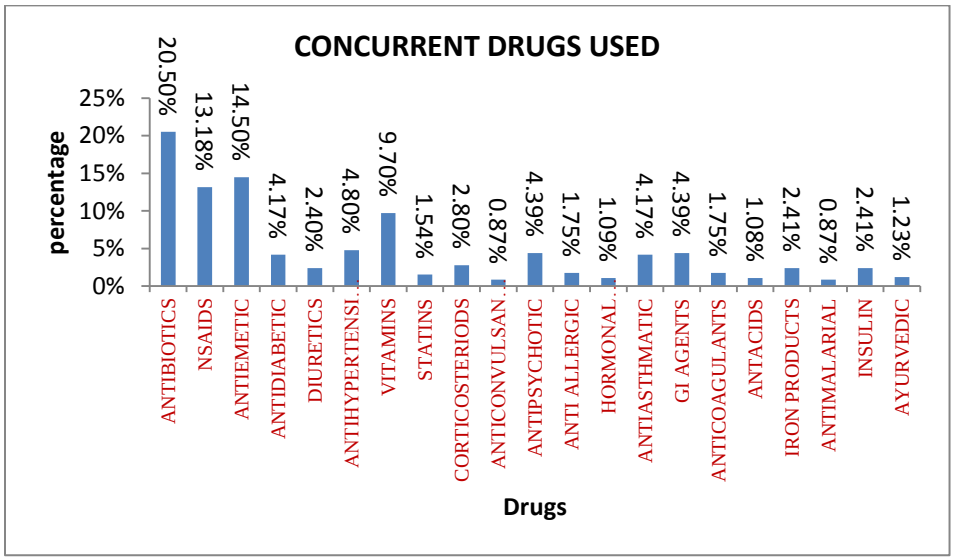

Figure11: Concurrent Drug Prescribed

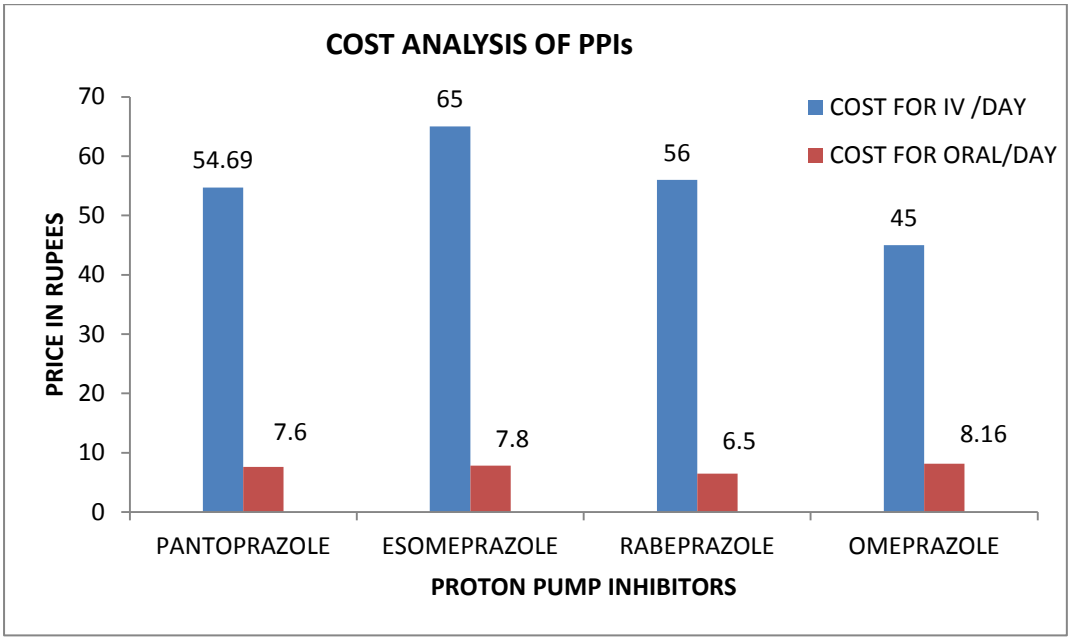

Figure 12: Cost Analysis of PPIs

Gender Categorization

In the study population of 220 patients males were found to be more (56%) than the females (44%).

Age Distribution

Most of the patients treated with PPIs were in age group between 26-35 years (23.64%) as the food habits of youngster is not managed well, followed by age group 66-75 years (20.91%) old patients whom tendency of disease is more as the metabolic system as well as other systems are decreasing their function, Patients in older age group ≥76 were 10.91% were treated with PPIs and remaining other age group are 38.18%.

Psychosocial Factors

Of the population studied, 6.36% were alcoholics and 12.27% of smokers were found to be under PPIs therapy and 81.37% were non smokers and non alcoholics.

Symptoms of Ulcer

The major ulcer symptoms treated with PPI include vomiting 34% patients, nausea 28.50% patients, epigastric pain in 14% patients, heartburn 11% and others 12.5%.

Proton Pump Inhibitors Prescribed

Major prescriptions of PPIs include Pantoprazole 72.47%, followed by Esomeprazole 18.54%. Least prescribed PPIs were Omeprazole 1.12% and remaining was Rabeprazole 7.87%.

Route of Administration

Among the PPIs prescribed 80.91% was I.V and remaining 19.09% were prescribed oral form.

Break Up of IV Therapy

Among the I.V PPIs prescribed Pantoprazole was the highest 93.81%, least prescribed were Omeprazole and Esomeprazole 1.12% and remaining was Rabeprazole 4.49%.

Break-up of oral PPIs Therapy

Among the oral PPIs prescribed Pantoprazole was highest 42.85%, followed by Esomeprazole 38.09%. The least prescribed PPIs were Omeprazole 2.40% and remaing was Rabeprazole 16.66%.

PPIs switched to oral from IV therapy

Among the IV prescriptions 53.60% were switched to oral therapy after patient being stable and 46.40% were continued as I.V therapy. According to the studies IV prescription of PPIs should be switched to oral therapy after 72 hrs.

Various Conditions under Therapy

Various conditions like gastritis 5%, gastroenteritis 4.55%, GERD 2.27%, duodenal ulcer 1.36%, esophagitis 0.91% and dyspepsia 0.91% were treated with PPIs as the first line treatment and other cases 89.5% were treated with PPIs as prophylaxis. PPIs should be initiated as the 1st line therapy only for severe GERD, ZES and PUD. PPI should be used only when there is documented evidence of a GI disorder that cannot be treated with an H2-receptor antagonist and where a PPI use is clinically justified. Thus PPI are often used unnecessarily in patients who do not require total suppression of acid production. PPI is not only less effective in mild and acute conditions and symptom relief, it also has adverse effects such as it triples the risk of dangerous clostridium difficile diarrhoea, increases susceptility to GI infections, delays diagnosis of gastric cancer and sudden withdrawal causes hyper secretion of acid.

Concurrent Drug Prescribed

Major prescriptions of PPIs were with antibiotics 20.5%, antiemetics 14.5% and NSAIDs 13.18%. Other concurrent prescriptions were with vitamins 9.70%, antihypertensive 4.80%, anti psychotic 4.39%, gastro-intestinal agents 4.39%, antidiabetics 4.17%, corticosteroids 2.80%, iron products 2.41%, diuretics 2.40%, anti allergic 1.75%, anticoagulants 1.75%, statins 1.54%, hormonal products 1.09%, anticonvulsants 0.87%, antacids 1.08%, antimalarial 0.87% and ayurvedic drugs 1.23%, where FDA approves the prophylactic use of PPI in NSAID ulcer and treatment of it.

Cost Analysis of PPIs

Among the IV PPIs prescribed Esomeprazole was of highest price Rs.65/day, next was Rabeprazole with Rs. 56/day, Pantoprazole with Rs.54.69/day and Omeprazole was Rs. 45/day.

Among the oral PPIs prescribed Omeprazole was of highest price Rs.8.16/day, next was Esomeprazole Rs.7.8/day, Pantoprazole was Rs.7.6/day and Rabeprazole was Rs.6.5/day.

Drug Interaction

The major interactions were with iron (14), Clopidogrel (7), Cyanocobalamine (8) and Atorvastatin (4). Other drug interactions were Fluconazole (1), Dexamethasone (2),Phenytoin (2), Cefodoxime (1) and Fosphenytoin (1). Out of 220 prescriptions, 43 had drug interaction.

CONCLUSION

Irrationality was found in selection of PPIs, concomitant drug use, route of administration, cost effectiveness of drug. As such wide spread prescription of proton pump inhibitors should be taken into consideration. With the present scenario we can say that PPIs are being use for un-recommended prophylaxis more than the indicated use to overcome pharmacists should intervene with the physicians in selection of right anti ulcer drug therapy and pharmacist should educate the patients regarding the danger of self medication with PPIs which improves the quality of life of patients.

REFERENCES

1. Shipra Jain, Prerna Upadhyaya, Jaswant Goyal, Abhijit Kumar, Pushpawati Jain, Vikas Seth, and Vijay V Moghe “A systematic review of prescription pattern monitoring studies and their effectiveness in promoting rational use of medicines”
2. Protonpumpinhibitors.http.://www.clevandclinicmeded.com/medical_info/pharmacy/july august20
3. Laurence L. Brunton, Keith L. Parker,editors. Goodman and Gilman’s manual of pharmacology and therapeutics. McGraw Hills Company. 2008
4. Margaret A. Hamburg, M.D. Commissioner Food and Drug Administration Department of Health and Human Services August 23, 2011 www.citizen.org
5. patient.info/health/proton-pump-inhibitors © EMIS Group plc
6. Dipiro JT, Robert LT, Gary CY, Gary RM, Barbara GW, Micheal PC. Pharmacotherapy: A pathophysiologic Approach. 7th edition: New York: McGraw-Hill
7. SamanChubineh et al; Proton Pump Inhibitors: The Good, the Bad, and the Unwanted, Department of Gastroenterology, University of Connecticut,AM041,MC1845, Farmington, CT 06030.
8. James N R Bashford et al; Why are patients prescribed proton pump inhibitors? Retrospective analysis of link between morbidity and prescribing in the General Practice

Research Database BMJ VOLUME 317 15 AUGUST 1998

9. Vipinkumarsingh et al; prescribing pattern of acid suppressants in modern clinical practice - An analysis. Pelagia Research Library Der Pharmacia Sinica, 2011, 2 (3): 67-73
10. Durand et al; Proton Pump Inhibitor use in Hospitalized Patients: Is Overutilization Becoming a Problem?; Clinical Medicine Insights: Gastroenterology 2012:5; doi: 10.4137/CGast.S9588
11. ShobhaChuri, Arun Jogani, Prospective Assessment of Prescribing Pattern of Intravenous Proton Pump Inhibitors in an Indian Tertiary-Care Teaching Hospital, Indian Journal of Pharmacy Practice, Vol 7, Issue 4, Oct-Dec, 2014
12. Lynda S et al: Evaluation of Omeprazole, Lansoprazole, Pantoprazole, and Rabeprazole in the treatment of Acid related diseases. J Am Pharm Assoc 2000:40(1):5
13. Bernard Wathen et al., Context- sensitive medicine as an approach to rationalizing proton pump inhibitor prescribing in primary care. The Pharmaceutical Journal 2000 Jun 24; 264 (7102): 959-960
14. Karen Kaye et al; NSW Therapeutic Assessment GroupJuly 2001
15. Chakrapani Cheekavolu et al Evaluation of Drug Utilization Patterns during Initial Treatment in the Emergency Room: A Retroprospective Pharmacoepidemiological Study, International Scholarly Research Network ISRN Pharmacology Volume 2011, Article ID 261585, 3 pages
16. Marta Illueca et al : Proton Pump Inhibitor Prescribing Patterns in Newborns and Infants J Pediatr Pharmacol Ther 2014;19(4):283–287
17. Benjamin Lazarus et al : Proton Pump Inhibitor Use and the Risk of Chronic Kidney Disease JAMA InternMed2016;176(2):238246.doi:10.1001/jamainternmed.2015.7193.
18. JJ Heidelbaugh, AH Kim et al. Overutilization of proton-pump inhibitors: what the clinician needs to know TherAdvGastroenterol(2012) 5(4) 219–232
19. Joel J. Heidelbaugh Proton pump inhibitors and risk of vitamin and mineral deficiency: evidence and clinical implications TherAdv Drug Saf(2013) 4(3) 125–133
20. A. S. RAGHUNATH et al. the long-term use of proton-pump inhibitors Aliment Pharmacol Ther 2005; 22 (Suppl. 1): 55–63.
21. Tamuno & FadareDrug Prescription Pattern in a Nigerian Tertiary Hospital Trop J Pharm Res, February2012;11 (1): 147

22. Daniel Sifrim and Frank Zerbib Diagnosis and management of patients with reflux symptoms refractory to proton pump inhibitors Gut 2012 61: 1340-1354 originally published online June 8, 2012

23. NirajanKunwar et al A study on proton pump inhibitors in general medicine unit of tertiary care teaching hospital, World Journal of Pharmaceutical Research, Volume 4, Issue 6, 1519-1534.