Original Research Article

How appropriately are adults being prescribed proton pump inhibitors - experience of a tertiary care centre

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Abstract

Background and Objectives: Proton pump inhibitors (PPIs) are one of the commonest medicines prescribed in recent years as they are highly effective and remarkably safe. However, there is a growing concern that PPIs are being overprescribed and used for poorly defined reasons or for conditions where they are not beneficial. This study was conducted to study the type, duration, indication and appropriateness of PPI use.**Methodology:** This prospective observational study was conducted in medicine department of K.M.C.H and LSK Hospital, Kishanganj, Bihar, India over1 year from January 2020 to December 2020 including adults visiting our medicine OPD for the first time who were already on PPI therapy. Data was collected by direct interviewing as well as review of previous prescriptions.**Results:** Total 393 patients were enrolled and assessed for use of PPIs. Mean duration of PPI use was 11.7 ± 6.1 months. More than half (52.7%) had no clear indication, 37.7% had valid indication and 9.7% had a borderline indication. Patients with valid indication were given PPIs for dyspepsia (27.7%), GERD (24.3%), stress ulcer prophylaxis (19.6%) and peptic ulcer (16.2%). Patients without valid indication were given PPIs for anemia (24.6%), NSAIDs (14%) and corticosteroids therapy (12.6%). Similarly, patients with borderline acceptable indication were given PPIs for post endoscopic procedure (39.5%), use of double antiplatelet agents (18.4%) and uninvestigated dyspepsia (18.4%). Only 61.3% were receiving recommended maintenance dose and the rest 38.7% were using high dose. Only 22.9% had undergone upper G.I endoscopy and the rest 77.1% were prescribed long term PPI without a convincing evidence. **Conclusion:** Doctors should be more thoughtful while prescribing PPIs to provide an appropriate, safe and cost effective advice. Prescription should follow evidence based practice as unnecessary and inappropriate prescribing isn't cost effective and potentially harmful too.

Keywords: Proton pump inhibitors, indication, good clinical practice, guidelines, side effects.

Introduction

Over last few years the progress in medical science has led to discovery of novel therapeutic agents that have saved millions of lives. However, the availability of many of these newer agents has also led to an increased practice of polypharmacy in recent times. One such highly effective, remarkably safe and widely used drug is proton pump inhibitor or PPI[1].This drug has revolutionized the treatment of different acid-peptic related gastrointestinal disorders. Common indications of PPI treatment are gastric and duodenal ulcers, NSAIDs induced ulcer, dyspepsia, GERD, eradication of *H. Pylori* infection and hyper secretory disorder like Zollinger Ellison Syndrome[2].PPIs are one of the commonest medicines prescribed in recent years- for both approved and off-label uses. Infact, it was the third most commonly prescribed class of medication in the United States, with $13.6 billion in yearly sales[3].They enjoy reputation of being highly effective and remarkably safe class of drugs. The availability of PPIs has brought a significant therapeutic advance. The most glaring example is that they have transformed the lives of patients with previously intractable symptoms of gastro-esophageal reflux with its associated complications. Short term course of a PPI is also frequently tried for treating a wide range of acid-peptic conditions[4].

PPIs as a class of medication also have a high prevalence of being prescribed for poorly defined reasons or for conditions where PPIs have not been shown to be beneficial[5]. There is a growing concern that PPIs are being overprescribed worldwide in both primary and secondary care setting[6,7].In hospitalized patients in Australia, Ireland and the UK, 63%, 33%, and 67% of patients taking PPIs did not meet their country's criteria for taking the drug. Researchers have estimated that 25% to 70% of patients taking these drugs have no appropriate indication. It is thus not hard to believe that economic implications of such practice is huge. Though slightly inferior in efficacy but far less expensive alternative drugs, such as H2 receptor antagonists are available for decades, prescriptions for PPIs have superseded all other anti-acid medicines. Infact, PPIs now account for over 90% of the drugs used for treating acid-peptic disorders[8]. It should also be remembered that PPIs are not free of adverse effects. An increase in the prevalence of pneumonia and Campylobacter enteritis is reported, as well as a doubling of the risk of infection with Clostridium difficile[9].Acute interstitial nephritis and osteoporosis are unusual but recognized consequences of treatment with proton

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pump inhibitors. Moreover, the various drug interactions of PPIs can't be overlooked.Based on above background and considering the fact that impact of over prescription on drug budgets around the world is a real problem, we intended to conduct this study at our tertiary care level teaching institute to study the prevalence, indication and appropriateness of PPI use.

Aim and Objectives

Aim: To study the appropriateness of PPI use in adults presenting to our hospital.

Objectives: 1. To characterize the patient population prescribed PPI elsewhere.

2. To study the type and duration of PPI therapy in these patients.

3.To study the reason of PPI therapy and to evaluate the appropriateness of such a prescription.

Methodology

Study setting: OPD of deptt of Medicine K.M.C.H and LSK Hospital, Kishanganj, Bihar, India.

Study Duration: 1 year, from January 2020 to December 2020.

Study Design: prospective observational study.

Inclusion criteria: In the present study we included all adult patients visiting medicine OPD of our hospital for the first time who were already on PPI therapy.

Exclusion criteria: all those who were under 18 years of age, patients who were not able to understand regional or English language, patients with learning difficulties and those with mini mental state score below 15 points were excluded.

Study technique

After obtaining written informed consent, we enrolled participants in the present study. Information regarding baseline characteristics was collected and entered in a structured proforma. Review of prescription of all patients who were on PPI therapy from elsewhere was carried out. Data regarding dosage, duration of PPI used and indication of such a use was specifically surveyed. Reasons for PPI use was then cross referenced with those approved by US FDA (Food and Drug Administration)to divide all such prescriptions into three groups: 1) those who fulfilled FDA criteria; 2) those who had no clear indication; 3) those who had borderline indications (table 1 and 2). Borderline indications is defined as indications not approved by FDA but deemed acceptable on the basis of general expert consensus, or based on guidelines other than FDA such as NICE (National Institute of Health and Clinical Excellence) and ACG (American College of Gastroenterology)[10]

Statistical analysis: Data so collected was recorded, tabulated and entered in Microsoft excel sheet, and then analyzed by using statistical software "SPSS ver.20®. Variables were expressed as mean, standard deviation, proportions and percentiles as appropriate. Dichotomous variables were compared using Chi-square test whereas continuous variables were compared using Student t-test. P-value <0.05 was taken as significant.

Table 1:Food And Drug Administration accepted indications for the use of PPIs

Indications	Approved use
Peptic ulcer disease	Treatment of duodenal ulcer/gastric ulcer
Erosive esophagitis	Healing and maintenance
Helicobacter pylori infection	Eradication with appropriate antibiotic regimen
Pathological hyper secretory condition	Zollinger Ellison syndrome
Stress ulcer prophylaxis	In critically ill patients

Table 2:Other accepted/off-label Indications for the use of PPIs

Risk reduction of NSAIDs associated peptic ulcer, in patients on NSAIDs with > 2 of the following risk factors: ➢ Age > 65 years ➢ History of peptic ulcer disease or upper gastrointestinal tract bleeding ➢ High dose NSAIDs therapy: or ➢ Concomitant NSAIDs use with an anticoagulant , antiplatelet or glucocorticoid
Esophageal stricture
Barrett's esophagus
To improve pancreatic enzyme absorption in cystic fibrosis
Uninvestigated dyspepsia (short-term trial; investigation required if persistent)

Observation and Results

Over the study period, we assessed 532 patients for eligibility. After exclusion of 139 patients, total 393 patients were enrolled in our study and were assessed for the use of PPIs. Mean age of the study population was 39.6 ± 10.1 years. Mean weight of the study population was 58.1 ± 13.7 kg. Males outnumbered females with a male: female ratio of 1.6:1. Mean duration of PPI use was 11.7 ± 6.1 months.We were surprised to find that more than half of such patients(n=207, 52.7%) on PPIs had no clear indication. While 148(37.7%) patients had an acceptable indication, 38 (9.7%) still had a borderline indication for such use. Most common medically approved reason for PPI use was found to be dyspepsia (n= 41, 27.7%), followed by GERD (n=36, 24.3%), stress ulcer prophylaxis (n= 29,19.6%), peptic ulcer (n= 24,16.2%) and others (n= 18, 12.2%) as shown in table 3. Among the patients who were advised PPI without a valid indication, the most common primary disease was anemia (n=51, 24.6%) followed by NSAIDs (n= 29, 14%) and corticosteroids therapy (n= 26, 12.6%) as shown in table 4. Similarly, the most common reason of prescription for borderline acceptable indication was post endoscopic procedure (n= 15, 39.5%) followed by use of double antiplatelet agents (n= 7, 18.4%) and uninvestigated dyspepsia (n= 7, 18.4%) as shown in table 5.

Table 3: Patients with a valid indication For PPI prescription as per medical Record (n= 148)

Indication/condition	Number	Percentage
Dyspepsia	41	27.7%
GERD	36	24.3%
Stress ulcer prophylaxis	29	19.6%
Peptic ulcer treatment	24	16.2%
Others	18	12.2%
Total	148	100%

Table 4:Patients without a valid indication For PPI prescription as per medical Record (n= 207)

Indication/condition	Number	Percentage
Anemia	51	24.6%
NSAID therapy	29	14.0%
Corticosteroid therapy	26	12.6%
Chest pain (musculoskeletal)	23	11.1%
Warfarin therapy	18	8.7%
Bone fracture	17	8.2%
Malignancy	15	7.2%
No clear cause identified	28	13.5%
Total	207	100%

Table 5:Patients with a borderline valid indication For PPI prescription as per medical Record (n= 38)

Indication/condition	Number	Percentage
Post endoscopic procedure	15	39.5%
Therapy of double antiplatelet agents	7	18.4%
Anemia(clinically unstable / with possible history of G.I bleeding)	4	10.5%
Uninvestigated dyspepsia	7	18.4%
G.I adverse effect risk of NSAIDs in presence of risk factors	5	13.2%
Total	38	100%

We also assessed the appropriateness of dose and duration of such therapy. We were shocked to find that >90% of patients were prescribed the same "high" dose for both healing and maintenance therapy of peptic ulcer. Overall, only 241 (61.3%) patients were on prescribed recommended maintenance dose and the rest 152 (38.7%) still were using long term high dose of PPIs. Less than one-fourth (n=90, 22.9%) had undergone an upper gastro endoscopy for confirmation and justification of being on PPI and the rest 203 (77.1%) were prescribed long term PPI without a convincing evidence. We found that the most common PPI prescribed was Pantoprazole (n=162, 41.2%) followed by Rabeprazole (n= 97, 24.7%), Omeprazole (n= 86, 21.9%), Lansoprazole (n= 26, 6.6%) and Esomeprazole (n= 22, 5.6 %). Mean duration of PPI use was 11.7 ± 6.1 months (mean ± S.D). While the majority of patients (n=187, 47.6%) were using it for short term (<6 months), we also had patients who were using it for 6-12 months (n=109, 27.7%), 1-2 years (n= 59, 15%), 2-3 years (n= 30, 7.6%) and >3 years (n= 8, 2%). Most of these chronic PPI users had no clear indication of use.

Discussion

In the present study we intended to study pattern and determinants of PPI use in patients presenting to the Medical OPD of our Hospital for the first time. Our study shows that less than two-fifths of patients (37.7%) receiving PPI had a valid indication for PPI therapy as per FDA approved criteria. Whereas, more than half of all PPIs prescriptions (52.7%) were found to have no clear indication for their use.This has been flagged in many studies mostly from developed countries that have shown that PPI are over utilized and used indiscriminately in many cases without valid indications[11]. Despite being a poor country, India is witnessing a similar trend of overprescription of PPIs over recent years[12,13]. In their study, Verma et al found that among 600 outpatients, 80.33% patients were prescribed gastric acidity-reducing drugs[14]. However, it was reassuring that only 27% patients were prescribed PPI that constituted 33.6% of the acid-suppressant drugs prescribed. The most common approved indication of PPI therapy in present study was found to be dyspepsia (n= 41, 27.7%), followed by GERD (n=36, 24.3%), stress ulcer prophylaxis (n= 29, 19.6%) and peptic ulcer (n= 24, 16.2%). This is comparable to the findings of Nidhi et al at a tertiary care hospital in Jaipur who found that dyspepsia (29.41%), followed by GERD (25%) and prophylaxis (20.59%) and peptic ulcer treatment (17.65%) were the common indications of PPI therapy[15]. Guidelines recommend that PPIs should be prescribed with NSAIDs/aspirin in only those patients who have risk factors. But in our study PPI were prescribed in nearly all patients receiving such therapy and majority of them (29 out of 34 i.e. 85.3%) were for routine primary prophylaxis and there were other documented risk factors. This highlights that it is totally irrational to prescribe PPI to all patients receiving NSAIDs.In our study we found that less than one-fourth (n=90, 22.9%) had undergone an upper G.I endoscopy for confirmation and justification of being on PPI and the rest 203 (77.1%) were prescribed long term PPI without a convincing evidence. Similar to our findings, Haroon et al demonstrated that only 12% of patients underwent upper GI endoscopy prior to prescription of PPI[16]. Such rampant misuse of PPI in patients with dyspepsia without a convincing evidence has a potential to delay the diagnosis of gastric cancer. Axon et al have recommended referral to an endoscopy unit for high-risk group of patients aged over 45 years with new onset of dyspepsia[17].In our study we found that more than half (52.3%) patients were on chronic PPI therapy (>6 months). This finding is a cause of concern on the pattern of PPI usage in the community as there is evidence based guidelines regarding long-term therapy for few indications only: 1) patients who are on NSAIDs induced ulcer and must unavoidably continue NSAIDs therapy 2) Gastroesophageal reflux disease. However in the present study, majority of patients were inappropriately given long term PPI therapy and that too at a higher than required dosage. There is emerging evidence that use of PPI in hospitalized patients increases the risk of developing pneumonia[18]. Moreover studies suggest that the use of PPI for more than 1 year increases risk of hip fracture and other osteoporotic fractures, which has strong dose and duration-response relationship [19,20]. This could have been brought down to lower maintenance doses or could have been withdrawn totally. When indicated, PPI should be prescribed at lowest effective dose and that too for the shortest possible duration.

Conclusion

Doctors should be more thoughtful while prescribing PPIs to their patients to provide an appropriate, safe and cost effective prescript-tion. Prescription of every PPI should follow evidence based practice as unnecessary and inappropriate prescribing of these drugs is a sheer wastage of valuable resources and such a practice is potentially harmful too. Regular monitoring and re-evaluation by the physician regarding the continued requirement and dose of PPI remains vital. As with any other disease, patients should be educated about their disease in detail and a care plan devised at the onset.

Limitations

There are a few limitations to our study. First, ours is a single centre study and so our findings may not be reflective of PPI usage pattern of the entire community. Second limitation is the relatively short duration of our study. Third, it is possible that documentation of indication in medical record and/or communication of the indication

of PPI therapy to the patient was missing in some cases which could have led to underestimation of patients who had actual indications.

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