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TIME TO HALT THE INAPPROPRIATE PRESCRIBING OF PROTON PUMP INHIBITORS- A COHORT STUDY

Medicine

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ABSTRACT

Introduction: With the development of newer though not necessarily better drugs, polypharmacy is becoming more prevalent in this ere. The treatment of different acid-related gastrointestinal disorders has been revolutionized with the advent of proton pump inhibitors (PPI). But with due course of time evidence is mounting that these can cause some serious side effects, however inappropriate prescription of PPI rises continuously every year and also increases total health expenditure. In our study we aim to identify the prevalence , indication and evaluate the appropriateness of PPI use in our hospital by assessing the level of its prescribing against established guidelines1

Method And Material: A cohort study of PPI use in patients admitted in medical ward over a period oftwo weeks in our tertiary care hospital. A simple educational intervention was employed to reduce the inappropriate prescribing of PPIs in the community by physicians.

Result: In our study we found 238 patients were on PPI in medical wards. For 48.32% (n=115) of patients , there was no documentation of valid indication for being on PPIs, 23.11% (n=55) had borderline indications and only 28.57% (n=68) of patients fulfilled the criteria of prescribing PPI as approved by FDA (p value=0.05). We noted that 13% (n=32) of patients were receiving PPI for > 2 years and 18% (n=43) of patients for more than 1 year.

Conclusion: Inappropriate use of PPI remains common in hospital practice. The overuse of these drugs leads to increase healthcare costs and many adverse effects. The risk of using long term PPI must be weighed against the benefits before prescribing.

KEYWORDS

PPIs (Proton Pump Inhibitors) , guidelines, inappropriate use, medical ward, FDA

INTRODUCTION

With the development of newer though not necessarily better drugs, polypharmacy is becoming more prevalent in this ere. The treatment of different acid-related gastrointestinal disorders has been revolutionized with the advent of proton pump inhibitors (PPI). PPI are indicated for the treatment of gastric and duodenal ulcers, NSAIDs induced ulcer, dyspepsia, GERD, eradication of H.Pylori infection and hypersecratory disorder like Zollinger Ellison Syndrome. PPI is a widely prescribed medication as it has low toxicity and high efficacy level[2]. But with due course of time evidence is mounting that these can cause some serious side effects (diarrhea, headache in upto 10%)and also increase risk of community acquired pneumonia[3,4], C. difficile diarrhoea[5,6,7]and Campylobactor jejuni gastroenteritis[8], however inappropriate prescription of PPI rises continuously every year and also increases total health expenditure. PPI also can interect with many drugs[9] and causes serious side reactions like hepatic, renal, skin, anaphylaxsis and bone marrow toxicity[10].

In our study we aim to identify the prevalence , indication and evaluate the appropriateness of PPI use in our hospital by assessing the level of its prescribing against established guidelines[1].

MATERIALAND METHOD

This study was conducted in our tertiary care centre. This study included all the patients who were admitted in medical wards and prescription charts were surveyed to identify patients who were on PPIs, this was carried out for two weeks duration in the month of January 2020. Inclusion criteria was all the patients who were admitted in medical ward. Patients excluded from this study were, all those who were under age of 18 years, patients who were not able to understand regional or English language, patients with learning difficulties , who have mini mental state (below 12 points), and patients who were too ill and not able to talk. We structured pro forma for information documentation. Patient's medical record were reviewed via hospital electronic medical records and also cross checked manually for information like name, dosage, and duration of the PPIs and any endoscopies were done to support the diagnosis. These indications were then cross referenced with those approved by FDA[11](Food and Drug Administration).

Inpatients were divided into three groups, 1) those who fulfill FDA criteria; 2) those who have no clear indication; 3) those who have borderline indications. 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 then FDA such as NICE (National Institute of Health and Clinical Excellence) and ACG (American College of Gastroenterology). This is a retrospective study so no blinding was necessary. Statistical analysis was done by using SPSS software. Result was tabulated in EXCEL word file.

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 oesophagtis	Healing and maintenance
Helicobector pylori	Eradication with appropriate antibiotic regimen
Pathological hypersecratory condition	Zollinger Ellison syndrome
Stress ulcer prophylaxsis	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 yrs • History of peptic ulcer disease or upper gastrointestinal tract bleeding • High dose NSAIDs therapy: or • Concomitant NSAIDs use with an anticoagulant , antiplatelet or glucocorticoid
Oesophageal stricture
Barrett's oesophagus
To improve pancreatic enzyme absorption in cystic fibrosis
Uninvestigated dyspepsia (short-term trial;investigation required, if persistent)

RESULT

Among total 262 patients seen in one month in all medical wards, 50 patients were excluded as per the exclusion criteria and the remaining 238 patients were assessed for the use of PPIs.

Most common indication for its use was found dyspepsia (29.41%), followed by GERD (25%), prophylaxis (20.59%), peptic ulcer (17.65%) and others **(Table 3).** Among these patients who were taking PPIs, most common indication was anemia followed by NSAIDs **(Table 4).** Most common indication for borderline use was after endoscopic procedure followed by antiplatelet agents **(Table 5).**

Total patients on PPIs – 262
Patients excluded – 50
Patients on PPIs- 238
Patients on PPIs with no clear indication – 115(48.32%)
Patients on PPIs with borderline indication – 55(23.11%)
Patients on PPIs with proper indication-68 (28.57%)

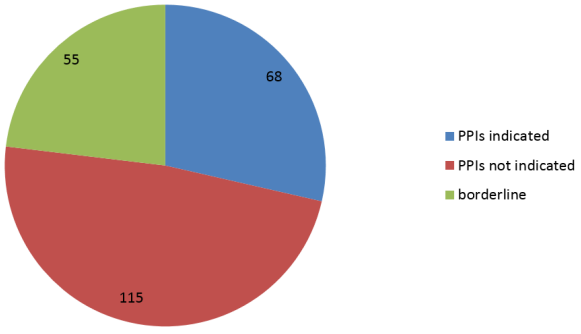

Figure 1:- Distribution Of Patients On PPIs

Table 3:- Indication For PPIs As Per Medical Record (n=68)

Indication	Number	Percentage (%)
Prophylaxis (NSAIDs/ Aspirin)	14	20.59
Dyspepsia	20	29.41
GERD	17	25
Peptic ulcer	12	17.65
Others	5	7.35

Table 4:- Patients With No Clear Indication For The Use Of PPIs (n=115)

Indication	Number	Percentage (%)
Anemia	32	27.83
Aspirin/NSAIDS	18	15.65
Corticosteroids	12	10.43
Warfarin	10	8.70
Malignancy	10	8.70
Bone fracture	5	4.35
No clear indication(as shown in EMR)	15	13.04
Others (nasopharngeal tube, musculoskeletal chest pain, post tonsillectomy)	13	11.30

Table 5:- Patients With Borderline Indication For The Use Of PPIs (n=55)

Indication	Number	Percentage (%)
Endoscopy	22	40
Double antiplatelet agent	7	12.72
Anemia(clinical unstable / with possible history of gastrointestinal bleeding)	6	10.91
Double antiplatelet+anaemia	5	9.1
Uninvestigated dyspepsia	6	10.91
Others*	9	16.36

*patients requiring post critical care, such as ICU/ CCU or those on steroids due to advanced malignancy

Table 6:- PPI Prescribed

PPIs	Number	Percentage (%)
Esomprezole	36	15
Pantoprazole	130	55
Lansopraole	7	3
Omeprazole	48	20
rabeprazole	17	7

Table 7:- Duration Of Therapy

DURATION	NUMBER	%
>3 years	21	9
2-3 years	32	13
1-2years	43	18
6-12 months	52	22
< 6 months	90	38

Duration of therapy= Mean$\pm$SD= 47.6$\pm$26.40, CI=44.229-50.971

SD=standard Deviation

CI= coefficient Index

We found that dose of PPI used either for healing or maintenance purpose. Only 13% (32 out of 238) patients were on prescribed recommended maintenance dose and vast majority of patients were using long term high dose of PPIs. Overall pantoprazole was used by 55% of patients and least used PPI is lansoprazole(3%) (**Table 6**). We noted that 90.83% were using PPI. We found that 38% of patients were taking PPI for less than 6 months and 9% of them are using for more than 3 years(**Table 7**).

Only 13% patients had their upper gastro endoscopy done for confirmation and justification of being on PPI. p value of this study is < 0.05.

DISCUSSION

We found that 90.83% of medical inpatients were on PPIs. The findings emerged as a cause of concern on the pattern of PPI usage in the hospital. The guidelines recommend, long-term therapy for few indications only such as 1) patients who are on NSAIDs induced ulcer and must unavoidably continue NSAIDs therapy 2) Gastro esophageal reflux disease. However in our study majority of them were using long term high dose of PPIs which can be brought down to lower maintenance doses or could have been withdrawn from the therapy. The guidelines recommend that prescribing PPI with NSAIDs/aspirin in only those patients who have risk factors but in our study PPI were prescribed in 20.59%of patients and majority of them (10 out of 14 i.e. 71%) were for routine primary prophylaxsis and there were no risk factor documented. This highlights that actions should be taken to minimize expenses on prophylaxsis.

In contrast to previous studies[12,13,14,15,16,17,18] pantoprazole and esomprezole accounted for 70% of total prescription and omeprazole was used in only 20% of prescription. This is however reassuring as omeprazole is the PPI which has highest ingredient cost under the community drug scheme in 2002. However we noted that least expensive PPI (rabeprazole) is prescribed in only 7% of cases. It was alarming that upper gastro endoscopy was done in only 13% of patients and majority of patients were prescribed long term PPI without adequate investigation. This is a matter of concern as potent action of PPI can suppress the features of gastric cancer and result in delay of its diagnosis.

Our study shows that only 29% of PPIs prescribed to our indoor patients were indicated , based on FDA approved criteria and the common inappropriate indication was anaemia (27.83%) followed by aspirin/NSAIDs drugs(15.65%). Nearly half of all PPIs prescriptions (48.32%) were found to have no clear indication for their use. This finding is in accordance to other western studies which support the notion that PPIs are the most overprescribed medicine[19,20,21,22,23,24,25,26]. Such inappropriate use can lead to adverse effects like pneumonia, gastrointestinal tract infection and bone fracture[27,28,29,30,31,32,33].

According to a study[34] patients who are hospitalized and received PPI have a 30% risk of developing pneumonia. Moreover studies suggest that the use of PPI for more than 1 year has increases risk of hip fracture and other osteoporotic fractures, which has strong dose and duration-response relationship[35,36,37,38,39]. Two studies also shows the development of clostridium difficile in PPI usage due to acid suppression[40,41]. There is a growing evidene of loss of beneficial effect of clopidogrel when used with PPI and causes adverse cardiovascular outcomes and gastrointestinal bleeding[42,43]. There is a risk of developing acid hyper secretion after stopping PPI which may causes drug dependence[44].

There are some limitations to our study, first this study was carried in one tertiary centre and it may not be possible to generalize our result to entire region population. So inclusion of other multicenter may have better represented the prevalence of PPI use, second this study duration was short and third that it is possible that documentation of indication for PPI use in some electronic medical record were not comprehensive in our study. Insufficient documentation could have resulted in an underestimation of patients who have actual indications and by categorizing them in non-indicated patients instead. So efforts were made to manually check all the records of those patients who have o indications in their electronic medical records.

CONCLUSION

The steps which are required to curb and to reduce inappropriate

prescribing of PPIs include:-

1) Recognition of problem
2) Use of alternative approaches to manage conditions currently treated "by default" with proton pump inhibitors.
3) Education regarding indication and duration of their use.
4) Enhance drug stewardship akin to that employed widely for antimicrobials, mandating better documentations for PPIs prescription and its regular review.

Dyspepsia is one of the most frequent reason for long term PPI use. This condition can be ameliorated by lifestyle modification and medications rationalization. Drugs which causes dyspepsia are NSAIDs, calcium channel blockers, theophylline, nitrates, bisphosphonates and antiplatelts. A review should be considered that whether these are still indicated or could be substituted. Lowest effective dose of PPI should be prescribed and for shortest possible duration.

Patient should be reviewed annually who are on long term therapy. Substitution of PPIs with antacids or H_2- receptor antagonists or alginate therapy can be considered. Measures should be put in place to educate prescribes on appropriate indications and duration of PPI use, facilitate long term users to de-escalating therapy and provide a degree of stewardship.

Our observation from this study shows that more thought is needed when PPIs are prescribed both in hospital and community to ensure appropriate, safe and cost conscious prescription. Prescribing of PPIs should follow evidence based practice as unnecessary and inappropriate prescribing of these drugs causes wastage of valuable resources and are harmful also. Regular monitoring and re-evaluation by the physician, regarding the need of PI remain vital. Patient should be educated about their disease and a care plan at the onset before commencing any medication is critical in clinical practice.

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