

The Prescribing Pattern of Proton Pump Inhibitors by Non-gastroenterologists in a Tertiary Teaching Hospital in the Kingdom of Saudi Arabia

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Abstract

Proton pump inhibitors (PPIs) are widely prescribed classes of medications. Their superior acid suppression lead to its use for the treatment of gastroesophageal reflux disease, helicobacter eradication, and other gastrointestinal problems. However, irrational use outside the approved indications is observed in some settings. The objective is to study the prescription pattern of PPI outside the gastroenterology service and whether this conforms to the best practice guidelines. This was a retrospective descriptive cross sectional study in Aseer central hospital, a tertiary teaching hospital in Abha, Saudi Arabia over a 2-month period. The charts of all new patients who were prescribed PPI outside the gastroenterology service were reviewed. Descriptive statistics were used for analysis. The study included 114 (71 females, 94% Saudis) with mean age of 51.8 (SD 22 years. Range: 13 to 96 years.) The frequencies of prescriptions in different disciplines showed that Cardiovascular disorders (acute coronary syndromes, atrial fibrillation and heart failure) had the highest frequency (37 patients) followed by the neurology division (13 patients with stroke.), respiratory disorders: 12 (pneumonia & COPD), and trauma.(12 patients) Co-administered drugs such as aspirin, clopidogrel, and warfarin were observed in over 40 patients.. The IV route was used in 74 out of the 114 (65%), out of whom 46 patients were able to take orally. Outside the gastrointestinal service, PPIs were irrationally used, sometimes without a guideline support. The IV route was unnecessarily used in the majority of patients.Doctors should abide by the guidelines when they prescribe PPIs.

Introduction

Proton pump inhibitors (PPIs) are widely prescribed classes of medications that are used in the treatment of multiple gastrointestinal (GI) disorders. They exert their effect by inhibiting the H⁺/K⁺-adenosine triphosphatase (ATPase), or proton pump, which is located in the highly acidic lumen of parietal cells (H Blume et al., 2006). This highly acidic environment enables the PPI to become protonated to its active metabolite which then

irreversibly inhibits the activity of the proton pump, resulting in an increase of gastric pH. This class of medications has revolutionized the way in which clinicians manage acid-related disorders of the GI tract. They have become the standard treatment of gastroesophageal reflux disease (GERD), peptic ulcer disease (PUD), and helicobacter eradication, the most commonly encountered conditions resulting in upper GI complaints (Malferteiner P et al., 2013). The use of these agents has increased by 456% since the 1990's (Eid, A et al., 2010)

As a result; these drugs have become one of the world's most frequently prescribed medications. Several clinical trials have demonstrated that proton pump inhibitors are both safe and well tolerated when used appropriately (Malfertheiner P et al., 2013). However, PPI's overuse and accompanying misuse increases the likelihood of adverse effects. Because most gastric-acid related disorders require long-term treatment, the risk for clinically significant adverse drug interactions is probable in patients who are receiving other medications in conjunction with a PPI. Several reports have suggested that PPIs are being overused in hospital and ambulatory care settings and that the appropriateness of PPI prescriptions in some hospitals is as low as 19% (M Naunton et al., 2000).

The incidence of improper use of PPIs varies from 40-70% in various studies. Initiation and the continuous use of these drugs without correct indications will result in significant cost to the patient. Proton pump inhibitors should be used more judiciously and awareness should be created among the clinicians in the hospital so that appropriate prescription of PPIs will improve the patient care at low cost (L Pasina et al., 2010), (Nousheen et al., 2014).

The objective of the present study was to explore the use of these drugs outside the GI service and find out whether this conforms to best practice guidelines in a teaching hospital in Abha, Saudi Arabia, since there is presumptive evidence that the PPI are overused by non-gastroenterologists (Joel J et al., 2010)

Methods

This was a retrospective descriptive cross sectional study performed in Aseer central hospital, a 700 bed tertiary teaching hospital in Abha, Saudi Arabia which serves a population of about 500,000. The study was performed over a 2month period as from September 2013. The charts of all new patients who were prescribed PPI outside the gastroenterology service were reviewed by three of the authors (BA, HA, &EA). Core information such as demographic factors, diagnosis, the attending physician, and medications were recorded.

According to the objective of the study, we did not include patients who were already taking PPIs or patients with definite gastrointestinal

diseases like peptic ulcer disease, gastroesophageal reflux disease, gastrointestinal bleeding, and helicobacter associated dyspepsia. In addition, patients with incomplete details were also excluded. Descriptive statistics were used for analysis.

Results and Discussion

The study included 114 patients (71 females,) with mean age of 51.8 (SD 22 years, range: 14 to 96 years.)

The frequencies of prescriptions in different disciplines were as follows: (Table 1):

- Cardiovascular disorders: 37 (acute coronary syndromes, atrial fibrillation and heart failure).
- Neurological problems: 13 patients with stroke.
- Respiratory disorders: 12 (pneumonia & COPD),
- Trauma: 12,
- Rheumatology: 10 (Rheumatoid arthritis and , SLE),
- ICU: 10 (critically ill patients),
- General surgery 10 patients,
- Others: DM, 4 (DKA). Infectious diseases: 4 (sepsis), renal diseases: 2 (renal failure).

Table 1: Proton Pump Inhibitors Prescriptions by different disciplines

Discipline	Number	%
Cardiovascular	37	32
Neurology	13	11.3
Pulmonary	12	10.5
Trauma	12	10.5
ICU	10	9
Rheumatology	10	9
General Surgery	10	9
Endocrine	4	3.5
Infectious diseases	4	3.5
Renal	2	1.7

Co-administered drugs: 39 patients were given aspirin with or without clopidogrel, while 29 patients were using warfarin. The overall rate of inappropriate use was 72%. The main reason for this was the lack of a valid indication. Others reasons for inappropriateness included the failure to indicate the right dose and duration of therapy. The IV route was used in 74 out of the 114 (65%), out of whom 46 patients were able to take orally. Pantoprazole was the commonest prescribed PPI through the IV route. Others

included omeprazole (18 patients), and esomeprazole for 8 patients.

This study showed that, outside the gastrointestinal service, there was a high rate of inappropriate use of PPIs, particularly so in the cardiovascular discipline. The possible interactions between antithrombotic drugs and proton pump inhibitors resulting in reduced antithrombotic effect and increased cardiovascular risk for patients receiving combination therapy has been suggested in previous studies (Mette Charlot et al., 2011). Particular attention has been given to the interaction between clopidogrel and proton pump inhibitors, but an interaction between aspirin and proton pump inhibitors has also been proposed (Heidelbaugh JJ, 2010) (Bhatt DL, 2012). Another area of inappropriate use was observed in patients admitted with pneumonia who received a PPI. A previous meta-analysis study demonstrated that the PPIs use was associated with increased prevalence of community acquired pneumonia, thus such patients should not receive PPIs without a solid indication (Giuliano C, 2012). Also, the present study documented prophylactic use of PPIs in the ICU and trauma units to prevent stress and NSAIDS induced gastritis based upon guideline recommendations that stressed that ulcer prophylaxis should be administered to all critically ill patients who are at high risk for gastrointestinal (GI) bleeding, although disagreement about which clinical characteristics define high risk exists. Moreover, the Surviving Sepsis Campaign guidelines recommend the use of PPIs rather than H2RBs for stress ulcer prophylaxis citing level 2C evidence (Dellinger RP, 2013) (Alhazzani W, 2013) Furthermore, the post-operative use of PPIs is generally not recommended unless there is a clear indication. As well, using PPIs for diabetic patients with complications such as ketoacidosis is not justified without a clear indication.

This study also revealed that the IV route was in judiciously used in most patients, the majority of whom were able to take by mouth. Approved indications of intravenous (IV.) proton pump inhibition (PPI) are limited to acute gastrointestinal bleeding, treatment of reflux oesophagitis, in patients unable to tolerate oral medications, and for patients with pathologic hypersecretory states.¹⁴ Furthermore, such inappropriate use of the IV

route will increase the total estimated direct cost (drug acquisition cost) as shown in a study from Saudi Arabia which revealed that the cost of IV PPI was very high and that inappropriate IV PPI utilization was predominant in non-ICU patients, mostly for stress ulcer prophylaxis that leads to a waste of resources (Alsultan MS 2010).

Overall, PPIs are considered over utilised when prescribed without an appropriate indication and when patients are left on them 'indefinitely' (Bhatt DL, 2012). Moreover, further studies found that inappropriate prescribing of PPIs without documented valid indications to be prevalent among elderly patients in Singapore, providing further evidence that shows a similar trend to PPI prescribing data from Western countries (Farooq A, 2016).

Thus, multiple variables should be taken into account before prescribing a proton pump inhibitor including: dosages, duration of therapy and clinical reasons for the use of a PPI, accompanied by an assessment of the appropriateness of the treatment (Boparai V, 2008).

Also, the economic impact of overprescribing PPIs should be taken in consideration. A previous study showed that between 25% and 70% of patients who took these drugs long term did not have an appropriate indication (Forgacs I, 2008).

Another retrospective review of 946 patients conducted in an ambulatory care setting found only 35% of the patients were given PPIs for an appropriately documented upper gastrointestinal tract diagnosis, whereas the remaining patients were given PPIs for either extraesophageal symptoms, unclear gastroprotection, or no documented appropriate indication (Heidelbaugh JJ, 2010).

Conclusion

The strong evidence supporting PPI efficacy and a favorable safety profile may have contributed to significant overprescription. Physicians should abide by the published practice guidelines (Such as the Saudi drug formulary, the Saudi gastroenterology association guidelines, and other international guidelines) when prescribing PPIs so as to avoid patient harm and wasting of resources (Forgacs I, 2008), (Heidelbaugh J, 2012).

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Obviously our study has some limitations, mainly the retrospective nature of the study and the fact that it was conducted only among inpatients users.

References

- Blume H, Donath F, Warnke A and Schug B. Pharmacokinetic drug interaction profiles of proton pump inhibitors. *Drug Safety*. 2006; 29: 769-780.
- Chiba T, Malfertheiner P and Satoh H. *Proton Pump Inhibitors: A Balanced View*. Karger publisher. 2013
- Eid A, Boueiz S, Paranjy C, Mativo R, Landis M and Abougergi. Patterns and predictors of proton pump inhibitor overuse among academic and non-academic hospitalists. *Internal Med* 2010; 49: 2561-2568.
- Naunton M, Peterson G and Bleasel M. Overuse of proton pump inhibitors. *J Clin Pharm Ther*. 2000;25:333-338.
- Pasina L, Nobili A, Tettamanti M, Salerno F, Corrao S and Marengoni A et al. Prevalence and appropriateness of drug prescriptions for peptic ulcer and gastroesophageal reflux disease in a cohort of hospitalized elderly. *Am J Managed Care* 2010;16:228-234.
- Nousheen, Tadvil NA and Shareef SM. Use of proton pump inhibitors in general practice: Is it rationale. *Int J Med Res Health Sci* 2014;3(1):37-42
- Joel J, Heidelbaugh, Kathleen L, Goldberg and John MI. Magnitude and economic effect of overuse of antisecretory therapy in the ambulatory care setting. *Curr Clin Pharmacol* 2010;5:288-297.
- Mette C, Erik LG, Peter RH, Jonas BO, Ole Ahlehoff, Christian S et al. Proton pump inhibitor use and risk of adverse cardiovascular events in aspirin treated patients with first time myocardial infarction: nationwide propensity score matched study. *British Med J* 2011; 342:2690
- Bhatt DL, Cryer BL, Contant CF, Cohen M, Lanos A, Schnitzer TJ, et al. Clopidogrel with or without omeprazole in coronary artery disease. *N Engl J Med* 2010;363:1909-1917.
- Heidelbaugh JJ, Metz DC and Yang YX. Proton pump inhibitors: are they overutilised in clinical practice and do they pose significant risk? *Int J Clin Pract* 2012; 66(6):582-91.
- Giuliano C, Wilhelm SM and Kale-Pradhan PB. Are proton pump inhibitors associated with the development of community-acquired pneumonia? A meta-analysis. *Expert Rev Clin Pharmacol* 2012; 5(3):337-44
- Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, Sevransky JE, Sprung CL and Douglas IS. Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup: Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med* 2013;41:580-637
- Alhazzani W, Alenezi F, Jaeschke RZ, Moayyedi P and Cook DJ. Proton pump inhibitors versus histamine 2 receptor antagonists for stress ulcer prophylaxis in critically ill patients: a systematic review and meta-analysis. *Crit Care Med* 2013;41:693-705.
- Law JK, Andrews CN and Enns R. Intravenous proton pump inhibition utilization and prescribing patterns escalation: a comparison between early and current trends in use. *Gastrointest Endosc*. 2009;69(1):3-9.
- Alsultan MS, Mayet AY, Malhani AA and Alshaikh MK. Pattern of intravenous proton pump inhibitors use in ICU and Non-ICU setting: A prospective observational study. *Saudi J Gastroenterol* 2010;16:275-9
- Farooq A, Yufang H, Valencia L, Paul JH and Reshma AM. Proton pump inhibitors: Are we still prescribing them without valid indications? *Australia Med J*. 2014;7(11):465-470.
- Boparai V, Rajagopalan J and Triadafilopoulos G. Guide to the use of proton pump inhibitors in adult patients. *Drugs* 2008;68:925-947.

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Forgacs I. Overprescribing proton pump inhibitors. *British Med J* 2008;336:2-3.

Heidelbaugh JJ, Goldberg KL and Inadomi JM. Magnitude and economic effect of overuse of antisecretory therapy in the ambulatory care setting. *Am J Manag Care* 2010;16:e228- e234.

Forgacs I and Loganayagam A. Overprescribing proton pump inhibitors is expensive and not evidence based. *British Med J* 2008;336:2-3

Heidelbaugh J, Kim A, Chang R and Walker P. Overutilization of proton-pump inhibitors: what the clinician needs to know. *Therap Adv Gastroenterol* 2012;5:219-32.