doi.org/10.36721/PJPS.2021.34.6.REG.2253-2255.1

SHORT COMMUNICATION

Inappropriate use of proton pump inhibitor for stress ulcer prophylaxis in a tertiary care hospital in Karachi, Pakistan

Rohama Samar, Syed Ahsan Ali, Victoria Samar, Muhammad Zain Mushtaq and Arsalan Humayun
Department of Medicine, Faculty Office Building, The Aga Khan University Hospital, Karachi, Pakistan

Abstract: The use of proton pump inhibitors (PPI) has been expanded inappropriately. PPI are among the most selling drugs in the world. There is growing evidence that PPI are associated with significant adverse effects along with undue financial burden. Inappropriate prescription of PPI is common in inpatients. The objective is to determine the frequency of inappropriate use of proton pump inhibitors for stress ulcer prophylaxis. This prospective observational study was conducted in the Department of Medicine of The Aga Khan University Hospital Karachi. 151 adult patients admitted in the hospital were included. All those patients who received PPI due to a condition mentioned by American Gastroenterology Association (AGA) as an indication for PPI, were labeled as PPI appropriately indicated. While those patients who received PPI without a condition mentioned by AGA as an indication for PPI, were labeled as PPI inappropriately indicated. Mean age was 57.2±18.2 years. Route of administration was oral in 110 (72.8%) and IV in 41 (27.2%) patients. Out of 151 patients, 100 (66.2%) patients were receiving PPI without any specific indication while 51 (33.8%) patients were receiving PPI with appropriate indications. Our study showed that inappropriate use of PPI is quite common among admitted patients.

Keywords: Proton pump inhibitors, stress ulcer, inappropriate, inpatients.

INTRODUCTION

In critical care patients, stress-related mucosal damage of upper gastrointestinal tract is quite common. This damage can lead to ulceration of upper gastrointestinal tract mucosa which may in turn lead to complications like gastrointestinal bleeding. Stress ulcer prophylaxis is required for these patients to reduce gastrointestinal bleeding (Sattayalertyanyong *et al*., 2020). As compared to histamine-2 receptor antagonists, proton pump inhibitors (PPI) are more potent in decreasing gastric acidity and are now the first line drugs for prophylaxis of stress ulcers. However, due to tremendous effectiveness and safety profile, the use of PPI has been expanded inappropriately including prophylaxis of gastrointestinal bleeding in low-risk patients and usage for longer than indicated. The increased prescription of PPI, increasing accessibility due to the emergence of several new generics and over-the-counter availability, have placed PPI amongst one of the most selling drugs in the world (Gamelas *et al*., 2019). More than 20 million prescriptions were written for omeprazole in 2007 in United States with a sale accounted for about 10 billion dollars. PPIs are thus one of the most misused drugs (Perwaiz *et al*., 2010). Once considered safe drugs, there is growing evidence that PPI are actually associated with significant adverse effects particularly when they are used for long term. These adverse effects include acute interstitial nephritis, gastric polyposis, vitamin B12 and magnesium deficiency, *Clostridium difficile* infection or bacterial overgrowth in cirrhotic patients with an increased risk of spontaneous bacterial peritonitis. On top of this, there are significant drug interactions associated with these drugs. Moreover, overuse of PPI has a financial burden on patients and public health both (Gamelas *et al*., 2019).

Inappropriate prescription of PPI is common in inpatient as well as in outpatient settings (Nallapeta *et al*., 2020, Sattayalertyanyong *et al*., 2020). There are limited studies done in this part of world which have focused on the subject of inappropriate use of PPI in hospitalized patients (Sarwar *et al*., 2017, Sarwar *et al*., 2018, Asim Syed and Abbas Naqvi, 2016). Avoiding inappropriate prescription of PPI can lead to significant cost saving as well as prevention of adverse effects and drug interactions. The objective of our study is to determine the frequency of inappropriate use of proton pump inhibitors for stress ulcer prophylaxis.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Medicine of The Aga Khan University Hospital Karachi. Approval from institutional Ethical Review Committee was obtained before starting the study (2019-1561-3926). The study was conducted from 1st

*Corresponding author: e-mail: syed.ahsan@aku.edu

January 2020 to 29th February 2020. All adult patients of age equal to or more than 18 years and of both genders, admitted in the hospital and received PPI were included in the study. Those patients who were admitted under the care of author of this study were excluded from the study. The sample size was calculated as 151 patients by taking prevalence of 83%, 5% level of significance and 6% (0.06) bound on error of estimation. All those patients who received PPI due to a condition mentioned by American Gastroenterology Association (AGA) (Perwaiz *et al*., 2010) as an indication for PPI, were labeled as PPI appropriately indicated. While those patients who received PPI without a condition mentioned by AGA as an indication for PPI, were labeled as PPI inappropriately indicated. The indications mentioned by AGA are gastroesophageal reflux disease (GERD), erosive esophagitis, Barrett's esophagus, coagulopathy (platelet count less than 50,000/mm^3, or INR more than 1.5, or aPTT more than 2 times control), mechanical ventilation for more than 48 hours, history of gastrointestinal ulceration or bleeding within 1 year before admission, or have at least two of these risk factors namely sepsis, ICU stay longer than 1 week, occult bleeding lasting 6 days or longer, or use of more than 250 mg hydrocortisone or the equivalent. All data were analyzed using Microsoft Excel and SPSS.

RESULTS

According to our sample size we included 151 admitted patients in our study. Out of these, 72 (47.7%) were males. Mean age was 57.27±18.22 years. Among the PPI formulations esomeprazole, omeprazole and dexlansoprazole were used by 108 (71.52%), 41 (27.15%) and 2 (1.32%) patients, respectively. The route of administration was oral in 110 (72.84%) and IV in 41 (27.2%) patients. The dose used by patients using omeprazole and esomeprazole was 40 mg in 146 (96.7%) patients. The dose used by patients using dexlansoprazole was 30mg in only 2 (1.32%) patient. There were 4 (2.64%) patients who were on omeprazole continuous infusion at the rate of 8 mg per hour. The frequency of PPI was once daily in 134 (88.74%), twice daily in 13 (8.60%) and continuous infusion in 4 (2.64%) patients. Out of 151 patients, 100 (66.2%) patients were receiving PPI without any specific indication while 51 (33.8%) patients were receiving PPI with appropriate indications (fig. 1). The indications of using PPI in patients who were receiving PPI appropriately are given in table 1.

STATISTICAL ANALYSIS

All data were analyzed using Microsoft Excel (version 2019) and SPSS (version 22.0).

DISCUSSION

Our study has clearly shown that in admitted patients significant majority are receiving PPI without any appropriate indications. This inappropriate prescription of PPI in admitted patients is common in other parts of world as well and our results are in agreement with similar studies carried out elsewhere (Pappas *et al*., 2016, Kelly *et al*., 2015, Perwaiz *et al*., 2010). Perwaiz *et al* have shown that intravenous omeprazole was inappropriately prescribed in two thirds of the patients without any specific indication in a hospital based in New York USA (Perwaiz *et al*., 2010). A study conducted at an Irish hospital showed that around one fourth of admitted patients received PPI without any indication with two thirds of the patients received higher than recommended dose (Kelly *et al*., 2015). Apart from these western studies, our local data has also shown the same results. Sarwar *et al* has shown in his study, done in Punjab province of Pakistan, that the most commonly prescribed drug for inpatients was omeprazole (Sarwar *et al*., 2017). Sarwar *et al* in another of his study from Lahore, the second most populous city of Pakistan, has shown that among the potentially inappropriate medication prescription during hospital stay, the second most common drug prescribed was omeprazole (Sarwar *et al*., 2018). As opposed to several studies mentioned above which either focused only on frequency of intravenous PPI (Kelly *et al*., 2015, Perwaiz *et al*., 2010) or did not give any details about route of administration of PPI (Sarwar *et al*., 2017, Sarwar *et al*., 2018), we have mentioned the frequency of route of PPI administration with oral being more common than intravenous route.

Table 1: Frequency of indications of appropriate use of PPI (n=51)

	Indications of PPI	Frequency (Percentage)
1.	Use of glucocorticoids	13 (25)
2.	Gastrointestinal bleeding	13 (25)
3.	Deranged Coagulation	11 (21)
4.	Thrombocytopenia	10 (19)
5.	Sepsis	7 (14)
6.	Mechanical Ventilation	4 (8)
7.	More than 1 causes	10 (19)

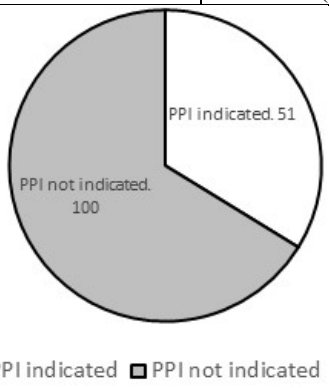

Fig. 1: Frequency of PPI use with and without indications.

The unwarranted use of PPI is not only a source of undue financial burden on individual patient as well as the healthcare system but it can also lead to some untoward adverse effects within the hospital. Papas *et al* has shown that PPI are associated with increased mortality in admitted patients. Additionally, inappropriate continuation of PPI, which the patient was taking at home before admission, is also a major issue and is also associated with increased mortality (Pappas *et al*., 2016). While a patient is in hospital, physicians should take this opportunity to discontinue PPI in patients who chronically take PPIs but are not at high risk of upper gastrointestinal bleed. Interestingly, Gamelas *et al* has shown that many patients are being discharged home from hospital without PPI prescription when PPI were actually required (Gamelas *et al*., 2019).

Undue prescription of PPI is not only an issue for admitted patients but this practice is also prevalent in outpatient clinics (Nallapeta *et al*., 2020, Lassalle *et al*., 2020, Boster *et al*., 2020). Apart from undue prescription of PPI, there is an issue of long-term use of these medications without any specific indications (Lassalle *et al*., 2020). Studies have shown that timely intervention can lead to dramatic improvement in unwanted prescriptions of PPI (Nallapeta *et al*., 2020, Helgadottir and Bjornsson, 2019, Buckley *et al*., 2015). This 'deprescribing' strategy can lead to reduction in healthcare cost, adverse effects and drug interactions (Buckley *et al*., 2015).

Our study is not without limitations. The relatively small sample size, a limited period of time and study being done in a single hospital unit, limit the extrapolation of data to other institutions or longer periods of time. Moreover, we did not collect data regarding the 'inappropriate' indications being considered by physicians to prescribe PPI for admitted patients in hospital. This data might help in focusing health authorities towards the actual etiology of inappropriate prescription of PPI.

CONCLUSION

Inappropriate use of PPI is quite common among admitted patients. Evidence based medicine teaching, implementation of institutional protocols and frequent review of treatment regimen are required to limit inappropriate PPI administration.

ACKNOWLEDGMENT

We acknowledge the statistical support by our research faculty Dr. Bilal Ahmed.

REFERENCES

Asim Syed IA and Abbas Naqvi SH (2016). Proton pump inhibitors use; beware of side-effects. *J. Pak. Med. Assoc.,* **66**(10): 1314-1318.

Boster J, Lowry LE, Bezzant ML, Kuiper B and Surry L (2020). Reducing the inappropriate use of proton pump inhibitors in an internal medicine residency clinic. *Cureus,* **12**(1): e6609.

Buckley MS, Park AS, Anderson CS, Barletta JF, Bikin DS, Gerkin RD, O'malley CW, Wicks LM, Garcia-Orr R and Kane-Gill SL (2015). Impact of a clinical pharmacist stress ulcer prophylaxis management program on inappropriate use in hospitalized patients. *Am. J. Med.,* **128**(8): 905-13.

Gamelas V, Salvado V and Dias L (2019). Prescription pattern of proton pump inhibitors at hospital admission and discharge. *GE. Port J. Gastroenterol,* **26**(2): 114-120.

Helgadottir H and Bjornsson ES (2019). Problems associated with deprescribing of proton pump inhibitors. *Int. J. Mol. Sci.,* **20**(21): 5469.

Kelly OB, Dillane C, Patchett SE, Harewood GC and Murray FE (2015). The inappropriate prescription of oral proton pump inhibitors in the hospital setting: a prospective cross-sectional study. *Dig. Dis. Sci.,* **60**(8): 2280-2286.

Lassalle M, Le Tri T, Bardou M, Biour M, Kirchgesner J, Rouby F, Dumarcet N, Zureik M and Dray-Spira R (2020). Use of proton pump inhibitors in adults in France: A nationwide drug utilization study. *Eur J Clin Pharmacol.,* **76**(3): 449-457.

Nallapeta N, Reynolds JL and Bakhai S (2020). Deprescribing proton pump inhibitors in an academic, primary care clinic: quality improvement project. *J. Clin. Gastroenterol*., **54**(10): 864-70.

Pappas M, Jolly S and Vijan S (2016). Defining appropriate use of proton-pump inhibitors among medical inpatients. *J. Gen. Intern. Med.,* **31**(4): 364-71.

Perwaiz MK, Posner G, Hammoudeh F, Schmidt F, Neupane N, Enriquez D and Gulati N (2010). Inappropriate use of intravenous ppi for stress ulcer prophylaxis in an inner city community hospital. *J. Clin. Med. Res.,* **2**(5): 215-219.

Sarwar MR, Atif M, Scahill S, Saqib A, Qamar-Uz-Zaman M and Babar Z (2017). Drug utilization patterns among elderly hospitalized patients on poly-pharmacy in Punjab, Pakistan. *J. Pharm. Policy Pract.,* **10**(1): 23.

Sarwar MR, Dar AR, Mahar SY, Riaz T, Danish U and Iftikhar S (2018). Assessment of prescribing potentially inappropriate medications listed in Beers criteria and its association with the unplanned hospitalization: A cross-sectional study in Lahore, Pakistan. *Clin. Interv. Aging.,* **13**(8): 1485-1495.

Sattayalertyanyong O, Thitilertdecha P and Auesomwang C (2020). The inappropriate use of proton pump inhibitors during admission and after discharge: A prospective cross-sectional study. *Int. J. Clin. Pharm.,* **42**(1): 174-183.

doi.org/10.36721/PJPS.2021.34.6.REG.2253-2255.1