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ORIGINAL ARTICLE

Irrational use of proton pump inhibitors in general practise

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Abstract

Background Proton pump inhibitors (PPI) are widely used among general practitioners (GP) and hospital doctors alike as a first-line agent for the management of various approved conditions. However, PPIs do have an established side-effect profile that can be over looked when prescribing these agents outside of their Food Drug Administration (FDA) indications.

Aims The aim of this audit is to establish that PPIs are often prescribed without any clear documented indication as to why, particularly in the elderly population, despite multiple previous studies conducted which showed an over-use of these medicines.

Methods We conducted a retrospective observational study of the patients admitted to an acute hospital in Ireland in February 2018. A cohort of patient charts were pulled from medical records and reviewed. Medical notes, GP letters, discharge summaries and prescriptions were reviewed in order to establish the primary indication for PPI prescription.

Results One hundred seventy-four ($n = 174$) inpatient records were randomly assessed during the audit. Of these patients, 85 of them were taking PPIs regularly. 54.7% ($n = 46$) were prescribed a PPI without any documented indication. 46.4% ($n = 39$) of these patients were > 75 years of age. 54.7% ($n = 46$) of patients were prescribed esomeprazole. The commonest indication for prescribing PPIs was to reduce the risk of gastric ulceration associated with NSAID use, which was 68.4% ($n = 26$) of those who were prescribed a PPI in accordance with guidelines.

Conclusion Irrational prescribing of PPIs continues both in hospital and in general practise. It is imperative that the side-effects of these medicines are weighed against the benefit and cost effectiveness, especially in the elderly population where polypharmacy remains a substantial concern.

Keywords Approved indication · Food Drug Administration · Inappropriate · Proton pump inhibitors

Introduction

The proton pump inhibitors (PPI) work via binding to hydrogen (H+)/potassium (K+) exchanging ATPase (the proton pump) in gastric parietal cells, which results in a blockage of acid secretion. They are the most potent inhibitors of acid secretion available today [1]. There is no evidence that one agent within the class is superior to another agent [2]. Generally, the PPIs are very well tolerated; however, there are some potential harmful side-effects with prolonged use [3]. The FDA-approved indications (Table 1) for the use of PPIs are:

Despite the well-prescribed indications as listed above (Table 1), the inappropriate prescribing of PPIs continues to rise, increasing concerns surrounding elderly patients at risk of polypharmacy, adverse side-effects related to the drug itself, adverse drug interactions and the negative impact on health economics.

Due to common prescribing of PPIs in general practice, this propagates among clinicians a belief that PPIs are safe to prescribe on a long-term basis when in fact, they are not [3].

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Table 1 FDA-approved indications

1. Healing of erosive oesophagitis (EO)
2. Maintenance of healed EO
3. Treatment of gastro-oesophageal reflux (GORD)
4. Risk reduction for gastric ulceration (GU) associated with non-steroidal anti-inflammatory use (NSAID)
5. *H.Pylori* eradication
6. Pathological hyper-secretory conditions, e.g. Zollinger-Ellison Syndrome
7. Treatment and maintenance of duodenal ulcer (D.U.)

Previous studies undertaken have shown increasing concern regarding the rise of inappropriate PPI prescribing at an alarming rate [4, 5]. Hence, we conducted a medical audit to assess the appropriateness of PPI usage in our local institution.

Method

This audit was carried out in an acute regional hospital. The participants in the audit were selected from medical admissions in February 2018. Their medical notes including admission note, GP letters, discharge summary and prescriptions were reviewed. A pro forma was designed which included the demographic details, agent used, whether or not PPI was continued on discharge from hospital and if the PPI had been prescribed for an FDA-approved indication. For the purpose of our audit, we grouped the patients according to age in the following brackets: aged < 50, aged between 50 and 75 and aged > 75 years old. This enabled us to accurately compare the use of PPIs in an elderly population versus a younger population. We also studied the most common PPIs prescribed and at which dosage they were prescribed in order to establish a link between cost-effectiveness and choice of agent. The study was conducted in adherence with the Declaration of Helsinki and International Committee on Harmonisation good clinical practices.

Results

During the study period, February 2018, 174 medical patient files were reviewed. Data assessed included demographic details, choice of agent, discharge summaries, discharge prescriptions and indication for prescribing of PPI. In our patient cohort, 77 (44.2%) were male and 97 (55.8%) were female (Table 2). Out of 174 patients, 85 (48.8%) of them were taking PPIs (Table 2). Thirty-nine females (45.9%) were taking PPIs, as were 46 (54.1%) males (Table 2). In the younger age group (< 50 years old), only 8 patients (9.4%) were taking a PPI (Table 2). In the next age category (50–75 years old), 38 patients (44.7%) were taking PPIs (Table 2). In the group of patients aged 75 and over, 39 of them (45.9%) were on a PPI (Table 2).

Table 2 Demographic details and brief summary of results

Number of patients (*n*)	174
Gender	
Male *(n)*	77 (44.2%)
Female *(n)*	97 (55.8%)
Patients on PPI (*n*)	85
Female pts. on PPI *(n)*	39 (45.9%)
Male pts. on PPI *(n)*	46 (54.1%)
Age	
< 50	8 (9.4%)
50–75	38 (44.7%)
> 75	39 (45.9%)
PPI prescribed	
Esomaprazole 40 mg	42 (49.4%)
Esomaprazole 20 mg	4 (4.7%)
Omeprazole 40 mg	0
Omeprazole 20 mg	3 (3.5%)
Pantoprazole 40 mg	14 (20%)
Pantoprazole 20 mg	2 (2.3%)
Lansoprazole 30 mg	16 (18.8%)
Lansoprazole 15 mg	1 (1.1%)
Patients discharged on PPI	79 (93%)
Patients with PPI discontinued	6 (7%)
FDA-approved indication	38 (44.7%)
Healing of erosive oesophagitis	0
Maintenance of healed EO	1 (2.6%)
Treatment of GORD	11 (29%)
Risk reduction for gastric ulceration associated with NSAIDS	26 (68.4%)
H. Pylori eradication	0
Pathological hyper-secretory conditions	0
Treatment and maintenance of duodenal ulceration	0

Of the available choices of agent, esomeprazole 40 mg daily was the most widely used, with 42 patients (49.4%) taking this drug, followed by pantoprazole 40 mg daily, taken by 14 (20%) of patients (Table 2). Lanzoprazole 30 mg once daily was consumed by 16 (18.8%) patients [Table 2]. Esomeprazole at a dosage of 20 mg daily was taken by 4.7% of patients ($n = 4$) (Table 2). Omeprazole 20 mg was taken by 3.5% ($n = 3$) patients, pantoprazole 20 mg and lansoprazole 15 mg were consumed by 2 (2.3%) and 1(1.1%) of patients, respectively (Table 2). Omeprazole at a dose of 40 mg once daily was not prescribed to any patient in our cohort (Table 2).

Thirty-eight of our patients (44.7%) were taking a PPI in accordance with the FDA-approved indications for the drug, conversely, 54.1% of patients ($n = 46$) that were on a PPI did not have a documented FDA-approved indication for taking

the drug (Table 2). Of the FDA-approved indications, the one most commonly encountered in our cohort was to reduce the risk of gastric ulceration associated with NSAID/aspirin use; with 26 patients (68.4%) using a PPI for this reason (Table 2). The second most commonly encountered indication for PPI prescribing was the treatment of GORD; 11 patients, (29%) (Table 2). Only one patient (2.6%) was taking a PPI for the maintenance of healed erosive oesophagitis (Table 2).

On discharge, 93% ($n = 79$) of patients that had been taking a PPI on admission, remained on a PPI (Table 2). Only 7% of patients ($n = 6$) had their PPIs discontinued on their discharge prescription. Forty (50.6%) of our cohort were discharged on a PPI despite there being no documented FDA-indication for being so (Table 2).

Discussion

Although efficacious and well-tolerated, there remain few indications for their long-term use today. Many clinicians continue to over-prescribe these agents at worryingly high rates without observing the approved indications for these drugs [4, 5]. In our institution, no previous audit had been undertaken to assess the prescribing of PPIs among the general adult population and so we conducted a retrospective study to ascertain whether or not clinicians were adhering to approved indications for PPI prescribing.

From our collected data, we can clearly see that more than 50% of the patients are consuming PPIs without any clearly documented indication (54.1%) and 45.9% of these patients are elderly individuals, where polypharmacy and over-use of medication is already a significant burden. This population are at a vastly increased risk of developing side-effects from any medicine, including PPIs [3]. Recently, the risk of nosocomial *clostridium difficile* associated diarrhoea has been noted in association with the use of PPIs [6, 7]. In a large trial published in the Journal of the American Medical Association in 2016 demonstrated a significant risk of developing chronic kidney disease (CKD) with long-term use of PPIs. The risk of developing CKD was 20–50% higher in those taking long-term PPIs [8]. Another problem arising from the over-use of PPIs is drug interactions between the PPIs and other medicines the patient may already be taking [9].

All PPIs are considered to have been created equal in efficacy; however, the cost varies significantly between agents [1]. This problem has been described in the literature dating back to 2005, when a study published in the Irish Medical Journal showed that substituting omeprazole, at that time the most expensive PPI for pantoprazole, could produce annual savings of up to five million euros [10]. In our audit, 49.4% of our patients were found to be on esomeprazole 40 mg, which is one of the most expensive PPIs in Ireland. A study published in the USA demonstrated that switching to esomeprazole, either 20 mg or 40 mg, resulted in an addition cost of 10,000 dollars per quality-adjusted life year (QALY) gained by the patient [11].

In our audit, we found that the most common indication for PPI prescribing was to reduce the risk of gastric ulceration associated with the use of NSAIDs and aspirin (Table 2). We consider this to be related to the fact that the prevalence of coronary artery disease and subsequently primary percutaneous intervention (PCI) has risen significantly among the general population in recent times [12]. In 2013, there was more than seven times the number of PCIs when compared with two decades earlier, in 1993 [12]. As demonstrated by a study conducted in the United Kingdom (UK), between 1991 and 2014, the number of prescriptions for diseases related to the circulatory system increased by around 243 million [12]. GORD is prevalent worldwide, and the disease burden is increasing [13]. We also found among our data that the second most common reason for PPI prescribing was the treatment of GORD (Table 2). While we unfortunately were unable to comment on the duration of PPI therapy taken by the patients in our audit as this information was unobtainable from the medical records due to poor documentation by clinicians, another locally published study suggested that one third of their cohort were taking PPIs for longer than 2 years, which is far beyond the recommended duration of therapy [4]. We strongly feel that in order to improve our PPI prescribing practises, we need to improve upon the documentation of the indication for these drugs, the duration of therapy and we must ensure that these medicines are appropriately rationalised upon the patients discharge from hospital.

Conclusion

To conclude, we have clearly shown that more than half of our cohort was taking PPIs for inappropriate reasons. As with all medicines, the risks of long-term PPI use must be weighed against the benefits of these medicines in the general population. Furthermore, it is imperative that documentation practises among both clinicians and general practitioners in the primary care setting are improved. There must be a clear indication for commencing therapy, and a clear indication for long-term continuation; if one exists. Moreover, if there is any doubt as to the rationale for PPI therapy, secondary/tertiary care physicians should take the initiative and discontinue the PPI if appropriate in order to avoid adverse long-term outcomes.

Finally, further auditing would be required in future in order to ensure that we continue to improve our prescribing practises and to increase the awareness of the existing guidelines for PPI prescribing among clinicians.

Compliance with ethical standards

Ethical approval was sought and granted by the institutional ethics committee at Our Lady's Hospital, Navan.

Conflict of interest The authors declare that they have no conflicts of interest.

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