Appropriateness of proton pump inhibitor use in patients admitted under the General Medical Unit

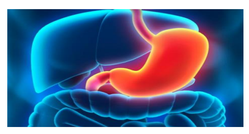
Yap M[1,2], Madden A[1,2], Yip G[3], D'Intini V[3], Tong E[1,2]

1. Pharmacy Department, Alfred Health, Melbourne, Victoria 2. Faculty of Pharmacy and Pharmaceutical Sciences, Monash University, Melbourne, Victoria 3. General Medicine Unit, Alfred Health, Melbourne, Victoria

Background and Aim

Proton pump inhibitors (PPIs) are among the most widely prescribed medication classes in Australia[1]. Indications for use include gastro-oesophageal reflux disease (GORD), peptic ulcer disease (PUD), dyspepsia, Zollinger-Ellison syndrome, Scleroderma oesophagus, *Helicobacter pylori* eradication, prevention and/or treatment of gastrointestinal (GI) adverse effects of non-steroidal anti-inflammatory drugs (NSAIDs) and stress ulcer prophylaxis[2].

Although PPIs are considered to be well tolerated, there is expanding evidence demonstrating association with long-term adverse effects. Meta-analyses report that PPIs increase risk of hypomagnesemia by 40%, *Clostridium difficile* infection by 74%, community-acquired pneumonia by 34% and fracture by 33%. Many studies also show that PPIs are often inappropriately initiated or maintained[3].



The aim was to identify the proportion of General Medical Unit (GMU) inpatients receiving PPIs on admission, and evaluate the appropriateness of use.

Methods

This prospective observational study was conducted between June and July 2016 at The Alfred Hospital, a tertiary referral hospital in Melbourne. The study was approved by the Alfred Human Research Ethics Committee.

Participants: Consecutive patients prescribed a PPI prior to admission were identified during initial medication reconciliation. Recruitment continued until approximately 200 patients were identified.

Data collection: Clinical pharmacists recorded the purported clinical indication, dose and duration of PPI use admission. Appropriateness of PPI use was evaluated in two ways:

1) Concordance with Australian Therapeutic Guidelines, and the National Prescribing Service (NPS) Guidelines on PPI use in GORD;
2) Assessment of indication, dose and treatment duration by a multidisciplinary panel of two general physicians and a senior clinical pharmacist.

Outcomes: The primary outcome was the proportion of patients with inappropriate use of PPIs on admission. Secondary outcomes included the proportion of patients on PPI on admission, reasons for and duration of use.

Results

Among 442 patients admitted to GMU during the study period, two were excluded due to incomplete data. Of the 440 in the final sample, 198 patients (45.0%) were taking PPIs on admission.

Table 1: Patient demographics and clinical characteristics

Variable, n (%)	PPI users	PPI non-users	p-value
Number of patients	198	242	
Age years, mean ± SD	78 ± 12.8	72 ± 19.8	**<0.001**
Male	83 (41.9)	112 (46.3)	0.386
Potential GI irritating medications			
None	69 (34.8)	114 (47.1)	**0.011**
Aspirin	77 (38.9)	73 (30.2)	0.068
Anticoagulants	46 (23.2)	37 (15.3)	**0.037**
Steroids	24 (12.1)	6 (2.5)	**<0.001**
Anti-platelets	21 (10.6)	19 (7.9)	0.323
NSAIDs	6 (3.0)	6 (2.5)	0.775
Relevant documented current and past co-morbidities			
Osteoporosis or past history of fracture	85 (42.9)	63 (26.0)	**<0.001**
Community acquired pneumonia	29 (14.6)	39 (16.1)	0.693
Hypomagnesaemia	21 (10.6)	8 (3.3)	**0.003**
B12 deficiency	16 (8.1)	10 (4.1)	0.109
Type of PPI			
Esomeprazole	80 (40.4)		
Pantoprazole	79 (39.9)		
Omeprazole	20 (10.1)		
Rabeprazole	16 (8.1)		
Lansoprazole	3 (1.5)		

SD: Standard deviation; NSAIDs: non-steroidal anti-inflammatory drugs

Results

Primary outcome: PPI use was deemed to be inappropriate in 66.2% of patients (n=131) receiving PPIs on admission, according to consensus.

Secondary outcomes: see Figures 1 and Table 2

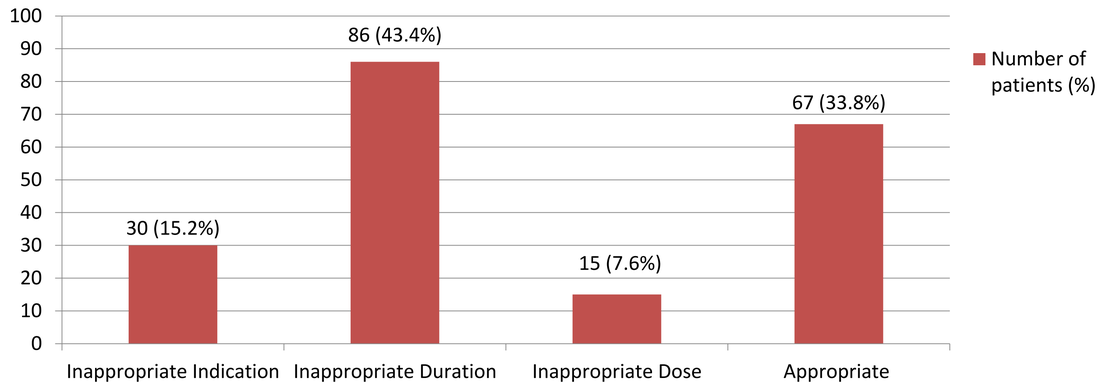


Figure 1: Appropriateness and reasons for inappropriateness of PPI use

Table 2: Factors associated with PPI use

Variable	No. pts	Inappropriate n (%)	OR* (CI 95%)
GI irritating medications			
None	69	48 (69.6%)	
Aspirin	77	55 (71.4%)	0.68 (0.36-1.25)
Anticoagulants	46	24 (52.2%)	2.18 (1.11-4.28)
Anti-platelets	21	14 (66.7%)	0.98 (0.37-2.54)
Steroids	24	11 (45.8%)	2.63 (1.11-6.24)
NSAIDs	6	2 (33.3%)	4.10 (0.73-22.96)
Indication for PPI use			
GORD	135	88 (65.2%)	0.87 (0.46-1.65)
Gastroprotection	15	8 (53.3%)	1.79 (0.62-5.18)
PUD	14	2 (14.3%)	14.07 (3.05-64.98)
Barrett's oesophagus	3	0 (0%)	
Gastritis on endoscopy	8	2 (25.0%)	6.34 (1.24-32.35)
H. pylori	2	0 (0.0%)	
Dyspepsia	9	9 (100%)	0.10 (0.01-1.67)
Other	22	15 (68.2%)	0.90 (0.35-2.33)
Unknown	17	15 (83.3%)	0.36 (0.10-1.30)
Duration of PPI use			
< 1 month	6	3 (50.0%)	1.66 (0.39-10.2)
1-6 months	12	6 (50.0%)	1.43 (0.80-2.57)
6-12 months	15	10 (66.7%)	0.98 (0.32-2.98)
1-2 years	39	28 (71.8%)	0.72 (0.33-1.56)
> 2 years	126	84 (66.7%)	0.94 (0.51-1.73)

* OR: Odds Ratio for the stated variable being appropriate vs inappropriate

For patients prescribed PPIs for GORD (n=135), use was deemed inappropriate in 65.2% of cases. Evaluation of co-morbidities associated with long-term PPI use, between PPI-users compared to non-users, demonstrated that PPI-users had higher prevalence of osteoporosis and/or history of fracture (42.9 vs 27.2%, p<0.001), hypomagnesaemia (10.6 vs 3.4%, p=0.003) and vitamin B12 deficiency (8.1 vs 4.3%, p=0.109).

Discussion

Almost half of all GMU inpatients were taking a PPI on admission. The high rates of inappropriate use (66%) are consistent with rates reported in recent international studies (52-80%).[4,5,6]

The most frequent indication for PPI use was GORD (68.2%), where use was deemed inappropriate in 65.2% of cases. The highest rate of inappropriate use was inappropriate duration. Current practices recommend a 4-8 week treatment duration in GORD, dyspepsia and peptic ulcers with stepdown therapy; 19.7%, and 63.6% of PPI users were on a PPI for one-two years or more than two years, respectively. Whilst the odds of the duration being inappropriate was not statistically significant, the extended duration of treatment is concerning in the clinical setting.

Conclusion

Inappropriate PPI use occurs frequently among GMU patients. Given the potential for side effects, unnecessary health expenditure and pill burden, clinicians should implement closer evaluation of the underlying clinical conditions and consider de-prescribing in situations where continued use may no longer be warranted. Pharmacists are well placed to have an integral role in implementing change in this area of practice.

References

1. Al-Sohaily S. *Aust Prescriber.* 2008; 31:5-7.
2. AMH Australian Medicines Handbook. Adelaide (SA); 2016.
3. Schoenfeld A, et al. *JAMA Intern Med 2016;* 176(2):172-4.
4. Lodato F, Poluzzi E, et al. *Eur J Intern Med*. 2016;30:31-6
5. Ramirez E, et al. *Curr Clin Pharmacol*. 2010;5(4)288-97
6. Ahrens D, et al. Intern J Clin Prac. 2012;66(8):767-773.