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Research Paper

Utilization of intravenous proton pump inhibitors in non-critically ill patients and the impact of pharmacist-led interventions in a private tertiary hospital in Metro Manila, Philippines

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ABSTRACT

Objectives: The study aims to evaluate the impact of pharmacist-led interventions on the utilization of intravenous proton pump inhibitors (IV PPIs). Methods: A two-phase study with quasi-experimental design compared outcomes relevant to inappropriate IV-PPI utilization before and after implementation of pharmacist-led interventions through retrospective review of dispensing records of 508 patients admitted to different wards of a private tertiary hospital in the Philippines. Pharmacist-led interventions include creation of institution-specific guidelines on appropriate IV PPI therapy and educational interventions for prescribers. Results: The interventions contributed to 4.4% decrease in prescribed IV PPI, 28.5% decrease in inappropriate IV PPI orders and 23.7% and 25.3% decrease in the cost of inappropriate use of Omeprazole and Pantoprazole, respectively. Conclusion: Reductions in the prescribing rate of IV PPI, inappropriate IV PPI orders and cost of inappropriate therapy after implementing pharmacist interventions, supported the need for continuous education of physicians on appropriate IV PPI therapy.

Key words: Proton pump inhibitors, pharmacists, Omeprazole, Pantoprazole

1. Introduction

Proton Pump Inhibitors (PPIs) are effective in treating many acid-related disorders; however, they are often overutilized and inappropriately prescribed in 30–60% patients hence resulting in increased risk of adverse effects and unnecessary hospital costs. (Abukhalil et al., 2023; Davis et al., 2017; Juneja et al., 2023) The two main reasons why IV PPIs were administered to non-critically ill patients are non-adherence to stress ulcer prophylaxis (SUP) guidelines and because of their documented safety and tolerability profile. However, in 2012, the U.S. Food and Drug Administration (FDA) issued an advisory that PPI use may be associated with an increased risk of *C. difficile*-associated diarrhea (CDAD).

The 1999 American Society of Health System (ASHP) guidelines, which remains the gold standard and basis of all other international guidelines, do not recommend SUP for adult non-ICU patients with less than two risk factors for clinically important bleeding. This was supported by a study done by Herzig et al., which proved that stress-induced GI bleeding outside of the ICU setting is a rare occurrence (0.27%) (Herzig, 2012). Additionally, recent studies by Cook and Guyatt (2018), confirmed that the incidence of clinically important bleeding is "approximately 0.2% among heterogeneous patients in medical and surgical units". Therefore, the recommendation on the 1999 ASHP SUP guidelines remains accurate and relevant.

Numerous studies demonstrated the effectiveness of pharmacist-led interventions such as physician education, medication use review and implementation of institution-specific SUP guidelines in reducing inappropriate use of oral and injectable PPIs (Bazan et al., 2021; Belfield et al., 2017; Hong et al., 2020; Luo et al., 2018). A systematic review by Haastrup et al. (2014) reported successful PPI stewardship program in several studies, with discontinuation rates of 14%

to 64%, while Wahking et al. (2018) and Masood et al. (2018) reported 4–14% success rates in deprescribing strategies. This study aimed to implement pharmacist-led interventions to promote appropriate IV PPI use in non-critically ill patients.

2. Methods

A. Utilization of IV PPIs

2.1. Research design and Sampling Population

The study utilized a quasi-experimental design to compare the utilization of injectable esomeprazole, omeprazole and pantoprazole before and after implementation of pharmacist-led interventions. A retrospective review of dispensing records of patients who received IV PPIs and were admitted to the non-ICU ward of a private tertiary hospital in Metro Manila for the pre-intervention phase (June 1, 2019, to February 29, 2020) and post-intervention phase (February 23, 2022, to May 23, 2022) was conducted. Patients who received IV PPIs during admission to the Intensive Care Unit (ICU) were excluded from the study.

Using Daniel's formula, the pre-intervention sample size of 339 patients, selected through systematic random sampling, provided a precise estimate of the population prevalence (Naing et al., 2006). The post-intervention cohort comprised of 169 patients who received IV PPIs during the three (3)-month study period following the interventions.

2.2. Data collection

The following information were collected by the investigator to establish appropriateness of IV PPI use: final diagnosis, or diagnoses, and relevant concurrent medications (oral steroids, oral nonsteroidal anti-inflammatory drugs, antiplatelet agents, anticoagulants, and antibiotics). The cost of inappropriate IV PPI therapy was computed by the number of IV PPI vials inappropriately given per patient multiplied by the drug acquisition cost.

2.3. Instrumentation

The appropriateness of IV PPI in terms of indication, dosage and duration was determined using the scoring system of the Medication Appropriateness Index by Somers et al. wherein a score equal to or greater than '3' indicated an inappropriate medication. (Fitzgerald et al., 1997; Somers et al., 2012) The frequencies and percentages were calculated for each of the demographic and clinical profiles of the pre- and post-intervention cohorts. The Chi-square test was used to determine whether there is an association between the demographic variables and use of IV-PPI. The student's t-test was used to determine if means were statistically different between age groups. A resulting p-value of less than 0.05 was considered statistically significant.

2.4. Ethical Considerations

In compliance with the Data Privacy Act of 2012 and its 2016 IRR, the investigator complied with the institution's policies on handling patient information. Data collection was only started upon approval of UP Manila Research Ethics Board (UPMREB) and the hospital Administration Committee. Only the investigator had access to the database of all the information throughout the implementation of the study. The investigator secured certification on Good Research Practice to be able to manage and handle possible study-related risks that may be encountered.

B. Pharmacist-led interventions

1. Proposed guidelines on appropriate IV PPI therapy were submitted to the Pharmacy and Therapeutics Committee (PTC) in May 2022.

2. Educational interventions for physicians, which entailed a 15-minute Zoom presentation on January 28, 2022, and academic detailing and distribution of information education materials from February 9–16, 2022, were implemented by the investigator. The educational materials provided include information regarding the rate of IV PPI use in the medical wards, adverse drug effects, review of the 1999 ASHP guidelines on SUP, 2012 Philippine Consensus Statements on the Management of Non-Variceal Upper Gastrointestinal Bleeding and a deprescribing proton pump inhibitors algorithm published by the Bruyere Research Institute (Farrell et al., 2017).

3. Results

3.1. Pre-intervention phase

The prescribing rate of IV PPIs was 18.8% (1,241 out of 6,590 patients) with inappropriate IV PPI use found higher in male patients and in the age groups 19–39 years old. Sex and age group were not statistically significantly associated with IV PPI use. High prevalence of inappropriate use of IV PPI was observed in all medical ward patients, with differences being statistically significant (p-value = 0.004). Sixty percent (60%) of SUP patients who were mainly admitted due to cardiovascular diseases (CVDs) and infectious diseases, were inappropriately prescribed IV PPIs, presumably to prevent gastrointestinal bleeding.

The total quantity utilized during admission (Table 1) was 3.59 ± 4.01 vials of IV-PPI. For Pantoprazole, the average quantity was higher for inappropriate (6.25 ± 5.71) than appropriate prescriptions (4 ± 4.2), with the difference being statistically significant (p-value = 0.0134).

3.2. Post-intervention phase

The prescribing rate of IV PPIs in non-critically ill patients was 14.4% (169 out of 1,171 patients). Lower rates of inappropriate IV PPI use were reported for both sexes. Sex, age groups and ward admission were not statistically significantly associated with IV-PPI use. Post-intervention rate of inappropriate IV PPI use was 31.4%; higher among patients with infectious diseases, AGE and CVD (Table 2).

Table 1. Pre-intervention utilization of IV PPIs from June 1, 2019, to February 29, 2020.

Variables	Use of IV-PPI			χ^2/t	p-value
	Total	Appropriate (n=136)	Inappropriate (n=203)		
	n (%)	n (%)	n (%)		
Sex				0.2815	0.5960
Female	191 (56.3)	79 (41.4)	112 (58.6)		
Male	148 (43.7)	57 (38.5)	91 (61.5)		
Age group				7.5658	0.1040
19–29	46 (13.6)	12 (26.1)	34 (73.9)		
30–49	84 (24.8)	29 (34.5)	55 (65.5)		
50–69	124 (36.6)	57 (46)	67 (54)		
70–89	77 (22.7)	35 (45.5)	42 (54.5)		
90 and above	8 (2.4)	3 (37.5)	5 (62.5)		
IV PPI				5.9688	0.0520
Esomeprazole	37 (10.9)	10 (27)	27 (73)		
Omeprazole	178 (52.5)	67 (37.6)	111 (62.4)		
Pantoprazole	124 (36.6)	59 (47.6)	65 (52.4)		
Total quantity by admission (mean ± SD)[+]	3.59 ± 4.0	3.44 ± 3.9	3.68 ± 4.1	–0.5471[+]	0.5847
Esomeprazole	2.51 ± 1.8	2.8 ± 2.3	2.41 ± 1.6	0.5074[+]	0.6207
Omeprazole	2.7 ± 2.9	3.04 ± 3.7	2.49 ± 2.4	1.0786[+]	0.2833
Pantoprazole	5.18 ± 5.2	4 ± 4.2	6.25 ± 5.7	–2.5100[+]	0.0134*
Room Number				16.6176	0.0040*
Medical I	86 (25.4)	29 (33.7)	57 (66.3)		
Medical II	81 (23.9)	34 (42)	47 (58)		
Medical Mission	2 (0.6)	–	2 (100)		
MSU	81 (23.9)	24 (29.6)	57 (70.4)		
Obstetrics	2 (0.6)	2 (100)	0 (0)		
Surgical	87 (25.7)	47 (54)	40 (46)		
Diagnosis					
Treatment	30 (8.8)	30 (100)	–		
Surgery	43 (12.7)	43 (100)	–		
Stress Ulcer Prophylaxis (SUP)					
CVD	69 (20.4)	32 (46.4)	37 (53.6)		
Infectious disease	61 (18)	8 (13.1)	53 (86.9)		
Dengue	26 (7.7)	2 (7.7)	24 (92.3)		
AGE	23 (6.8)	2 (8.7)	21 (91.3)		
Others	17 (5)	1 (5.9)	16 (94.1)		
Cancer	15 (4.4)	1 (6.7)	14 (93.3)		
Respiratory disease	9 (2.7)	3 (33.3)	6 (66.7)		
Viral infection	8 (2.4)	1 (12.5)	7 (87.5)		
Pleural effusion	5 (1.5)	–	5 (100)		
Sepsis	4 (1.2)	2 (50)	2 (50)		
Kidney failure	4 (1.2)	2 (50)	2 (50)		
Colonoscopy	3 (0.9)	–	3 (100)		
Liver failure	3 (0.9)	3 (100)	–		
LGIB	3 (0.9)	–	3 (100)		
Pancreatitis	3 (0.9)	–	3 (100)		
Accident	2 (0.6)	1 (50)	1 (50)		
GI disease	2 (0.6)	–	2 (100)		
Endocrine disease	2 (0.6)	–	2 (100)		
Poisoning	2 (0.6)	–	2 (100)		
Gout	1 (0.3)	1 (100)	–		
Coagulopathy	1 (0.3)	1 (100)	–		
Dyspepsia	1 (0.3)	1 (100)	–		
Shock	1 (0.3)	1 (100)	–		
BPPV	1 (0.3)	1 (100)	–		

[+]Using t-test for equality of means
*p-value ≤ 0.05

Table 2. Post-intervention utilization of IV PPIs from February 23, 2022, to May 23, 2022.

Variables	Total	Use of IV-PPI		χ^2/t	p-value
		Appropriate (n=116)	Inappropriate (n=53)		
	n (%)	n (%)	n (%)		
Sex				2.2783	0.1310
Female	91 (53.8)	67 (73.6)	24 (26.4)		
Male	78 (46.2)	49 (62.8)	29 (37.2)		
Age group				4.9274	0.2780
18–29	16 (9.5)	9 (56.3)	7 (43.8)		
30–49	50 (29.6)	33 (66)	17 (34)		
50–69	60 (35.5)	39 (65)	21 (35)		
70–89	38 (22.5)	31 (81.6)	7 (18.4)		
90 and above	5(3)	4 (80)	1 (20)		
IV PPI				0.465	0.4950
Omeprazole	67 (39.6)	48 (71.6)	19 (28.4)		
Pantoprazole	102 (60.4)	68 (66.7)	34 (33.3)		
Total quantity by admission (mean ± SD)[+]	4.34 ± 6.1	4.81 ± 6.9	3.30 ± 3.2	1.5058[+]	0.1340
Omeprazole	3.57 ± 3.7	3.5 ± 3.5	3.74 ± 4.4	–0.2326[+]	0.8168
Pantoprazole	4.84 ± 7.2	5.73 ± 8.5	3.06 ± 2.4	1.7961[+]	0.0755
Room Number				9.3005	0.0930
Annex	1 (0.6)	1 (100)	–		
Medical I	31 (18.3)	20 (64.5)	11 (35.5)		
Medical II	57 (33.7)	42 (73.7)	15 (26.3)		
MSU	34 (20.1)	17 (50)	17 (50)		
Obstetrics	2 (1.2)	2 (100)	–		
Surgical	44 (26)	34 (77.3)	10 (22.7)		
Diagnosis					
Treatment	32 (18.9)	32 (100)	–		
Surgery	31 (18.3)	30 (96.8)	1 (3.2)		
Stress Ulcer Prophylaxis (SUP)					
CVD	28 (16.6)	18 (64.3)	10 (35.7)		
Infectious disease	24 (14.2)	10 (41.7)	14 (58.3)		
Cancer	10 (5.9)	8 (80)	2 (20)		
Others	8 (4.7)	1 (12.5)	7 (87.5)		
GI disease	8 (4.7)	4 (50)	4 (50)		
AGE	5 (3)	–	5 (100)		
Accident	4 (2.4)	1 (25)	3 (75)		
Sepsis	4 (2.4)	4 (100)	–		
Pleural Effusion	2 (1.2)	2 (100)	–		
Anemia	2 (1.2)	–	2 (100)		
Liver failure	2 (1.2)	2 (100)	–		
Dengue	2 (1.2)	–	2 (100)		
Kidney failure	2 (1.2)	2 (100)	–		
Pancreatitis	1 (0.6)	1 (100)	–		
Renal disease	1 (0.6)	–	1 (100)		
Endocrine disease	1 (0.6)	–	1 (100)		
Respiratory disease	1 (0.6)	1 (100)	–		
LGIB	1 (0.6)	–	1 (100)		

[+]Using t-test for equality of means

The total quantity of IV omeprazole and Pantoprazole utilized by patients was an average of 4.34 ± 6.1 vials per admission; no Esomeprazole was dispensed in 2022. Appropriately prescribed IV-PPI had a mean of 4.81 ± 6.9, higher than inappropriately prescribed IV-PPI (3.3 ± 3.2), with the difference being non-statistically significant.

3.3. Impact of Pharmacist Interventions

In Table 3, there was a 4.4% decrease in the percentage of IV-PPI orders and a 28.5% decrease in the percentage of inappropriate IV PPI orders after implementation of pharmacist-led interventions and both association being statistically significant (p-value < 0.0001). The cost of

Table 3. Impact of Pharmacist interventions.

Outcome Measures	Pre-intervention	Post-intervention	Difference	χ^2/t	p-value
Percentage (%) of IV-PPI orders	18.8	14.4	–4.4	12.9448	<0.0001*
Percentage (%) of inappropriate IV-PPI orders	59.9	31.4	–28.5	36.6979	<0.0001*
Inappropriate IV-PPI acquisition cost[+], Php (mean ± SD)	110,451.4 ± 20,487.1	75,602.5 ± 13,005.8	–31.6[a]	1.7264	0.0854
Esomeprazole	10,997.8 ± 832.9	–			
Omeprazole	36,107.3 ± 7,030.3	27,551.1 ± 4,717.6	–23.7[a]	0.3218	0.07481
Pantoprazole	67,929.6 ± 4,374.6	50,737.9 ± 3,830.6	–25.3[a]	3.5592	<0.001*

[+] monthly average
* p-value ≤ 0.05
[a] percent change

inappropriate IV-PPI post-intervention showed a 23.7% reduction for Omeprazole and 25.3% for Pantoprazole, which is statistically significant.

4. Discussion

4.1. Pre-intervention and post-intervention utilization of IV PPIs

The pre-intervention prescribing rate of 18.8% was similarly observed by Torres-Bondia et al. (2022). On the other hand, several studies revealed higher prescribing rates of 20.4% to 37.2%. (Fah et al., 2019; Luo et al., 2018; Masoompour et al., 2017) The majority of the patients who received IV PPIs were females (56.3%); several studies likewise reported more female patients being prescribed IV PPIs (Bez et al., 2013; Elmubarak et al., 2021; Guda et al., 2004; Michal et al., 2016; Sudhakar et al., 2019). Additionally, a higher number of patients (73.7%) who received IV PPIs were from the medical wards; similar trends were reported by Alhujilan et al., 2023; Ching et al., 2019; Churi and Jogani, 2014 and Nasser et al., 2010.

Moreover, a higher percentage of older patients (aged 50–69 at 36.6%) received IV PPIs; similar observations were documented by Abukhalil et al. (2023); Moradi et al. (2016); Lai et al., (2014); Torres-Bondia et al. (2022); Nasser et al. (2010) and Guda et al. (2004). According to Alsultan et al. (2010), physicians considered elderly patients with multiple chronic diseases and patients on medications, such as, NSAIDs, aspirin, corticosteroids and chemotherapeutic drugs, to be at high risk in developing stress ulcers. Paradoxically, physicians have not realized that older people are also more susceptible to the adverse effects of PPIs, such as, bone deficiency, fractures and risk of pneumonia and CDAD, not to mention the burden of healthcare costs (Sohrevardi et al., 2015).

Pre-intervention results revealed that 78.5% of patients were assumed to have been given IV PPIs for SUP; 59.9% of SUP cohorts received IV PPIs inappropriately and mostly those admitted with diagnoses not related to acid -related disorders (CVD, infectious diseases, dengue, AGE and cancer). This result is greater than those reported by three researchers, 72.3% (Mohzari et al., 2020), 46% (Fah et al., 2019) and 54% (Hwang et al., 2007) for patients receiving IV PPIs as prophylaxis for stress-related GI bleeding.

To summarize, in all those cases where the indications do not meet SUP criteria, dosage and duration of treatment were considered inappropriate and overutilized. Luo et al. (2018) reasoned that the overutilization of PPIs was due to "lack of knowledge by physicians of the infrequent adverse drug events (ADEs) and their lack of attention to the serious ADEs, especially when considering the short course of PPI administration." Moreover, physicians prescribed PPIs out of fear of being sued in cases where patients developed gastric ulcers under their supervision (Ching et al., 2019; Hussain et al., 2010; Lai et al., 2014).

The post-intervention cohorts (Table 2) shared the same demographic and clinical profiles as the pre-intervention cohorts, with more female patients belonging to the elderly population (age groups 50–69) and admitted to the medical wards. Comparing pre- and post-intervention results in terms of indication of SUP, the top two (2) diagnoses were CVD (20.4% vs. 16.6%) and infectious diseases (18% vs. 14.2%); physicians generally prescribed IV PPIs concomitantly with either anticoagulants or antibiotics to prevent GI adverse effects associated with medications, even with no risk factors of stress-related GIB.

4.2. Impact of Pharmacist Interventions

A slight decrease (4.4%) in IV-PPI orders was also reported by Freedberg et al. (2015) and Luo et al. (2018). However, the decrease in the prescribing rate of IV PPIs cannot be directly attributed to the pharmacist's interventions. A decreasing trend in IV PPI prescribing rate (21.2% to 7.3%) has been observed in China due to the nationwide campaign on rational use of PPIs and with the emergence of the COVID-19 (Zeng et al., 2023) In his editorial, Sebastián Domingo (2021) cited four studies which confirmed that the regular use of PPI is associated with COVID-19 especially in the elderly population with comorbidities and that the current users of PPIs have a higher risk of severe COVID-19 symptoms or complications, which could have made physicians cautious in prescribing PPIs.

The effect of the pharmacist-led interventions resulted in a 28.5% reduction in inappropriate IV PPI orders; the positive impact of one-time educational interventions was also

demonstrated in two (2) studies, Agee et al. (2015) and Jain et al. (2013). On the other hand, a substantial reduction in inappropriate IV PPI use was demonstrated in other international studies which employed multiple strategies. (Bazan et al., 2021; Belfield et al., 2017; Hong et al., 2020; Hughes et al., 2011; Jain et al, 2013; Luo et al., 2018; Tasaka et al., 2014; Vazin et al., 2018; Wan et al., 2018).

The post-intervention cost for inappropriate IV-PPI showed a reduction of 23.7% for Omeprazole and 25.3% for Pantoprazole; however, Hong et al. (2020) and Masood et al. (2018) reported a much greater cost reduction in inappropriate PPI therapy. No post-intervention consumption data on IV esomeprazole was collected; hospital pharmacy records showed the last usage of esomeprazole was November 13, 2021.

Pharmacists play a vital role in strengthening the capability of the Pharmacy & Therapeutics Committee (PTC) in its role in drug formulary selection as well as in treatment guideline development. The extensive knowledge of pharmacists in terms of pharmacokinetic and pharmacodynamic studies can support evidence-based decisions in drug formulary selection. Moreover, implementation of these guidelines can be efficiently carried out by concerted efforts of the PTC and the institution's Patient Safety department. The active involvement of the Patient Safety department is imperative to ensure medication and patient safety.

5. Scope and Delimitations

The limitation of this study includes the small sample size in a single hospital setting for a limited period of time. Review of patients' dietary requirements was not allowed during the pandemic and may have underestimated the rate of inappropriate IV PPI use. Additionally, since this type of study involves "before-after" design, it has its intrinsic limitations such as no control group and no randomization in post-intervention cohort, which may affect the robustness of the research.

The pharmacist-led interventions were conducted by the investigator only on one occasion during the duration of the study, which limited the observation of further change in IV drug use. Furthermore, there was no direct and active participation of the investigator in terms of pharmacotherapeutic recommendations or decisions in changing drug therapy.

The impact of pharmacist-led interventions was measured in terms of reductions in IV PPI orders and/ or inappropriate IV PPI orders, cost of inappropriate IV PPI therapy without observation of clinical outcomes such as the presence or absence of clinically important bleeding.

6. Conclusion

There is overutilization of IV PPIs for SUP in non-critically ill inpatients with low or no risk factors of GIB. Post-intervention reduction in the percentages of inappropriate use of IV PPIs and cost of inappropriate IV PPI therapy confirmed an improvement in IV PPI prescribing, which can be attributed to the effectiveness of the pharmacist interventions. However, the decrease in IV PPI prescribing rate may not be fully attributed to the pharmacist's interventions; a decreasing trend in IV PPI prescriptions due to the association of COVID-19 and PPI use might have caused doctors to be cautious in prescribing PPIs.

References

Abukhalil A, Ali O, Saad A, Falana H, Al-Shami N, Naseef H, et al. Evaluation of Proton Pump Inhibitors Prescribing Among Hospitalized Patients: A Cross-Sectional Study. Int J Gen Med. 2023; 16: 141-150.

Agee C, Coulter L and Hudson J. Effects of pharmacy resident-led education on resident physician prescribing habits associated with stress ulcer prophylaxis in non-intensive care unit patients. Am J Health Syst Pharm. 2015; 72(11 Suppl 1): S48-S52. doi: 10.2146/sp150013

Alhujilan, S, Saeed M and Alalwan A. Assessment of adherence to the national stress ulcer prophylaxis guidelines: A cross-sectional analysis. Saudi Pharm J. 2023; 31: 101754. doi: 10.1016/j.jsps.2023.101754

Alsultan M, Mayet A, Malhani A and Alshaikh M. Pattern of Intravenous Proton Pump Inhibitors Use in ICU and Non-ICU Setting: A Prospective Observational Study. Saudi J Gastroenterol. 2010; 16(4): 275-279. doi: 10.4103/1319-3767.70614

American Society of Health-System Pharmacists. Therapeutic guidelines on stress ulcer prophylaxis. Am J Health-Syst Pharm. 1999; 56(4): 347-379. doi: 10.1093/ajhp/56.4.347

Bazan N, Farid S and Baines D. Impact of clinical pharmacists on adherence to stress ulcer prophylaxis protocol in critically ill Egyptian patients: a comparative study. Drugs Ther Perspect. 2021; 37: 35-43. doi: 10.1007/s40267-020-00786-y

Belfield K, Kuyumjian A, Teran R, Amadi M, Blatt M and Bicking K. Impact of a collaborative strategy to reduce the inappropriate use of acid-suppressive therapy in non-intensive care unit Patients. Ann Pharmacother. 2017; 51(7): 577-583. doi: 10.1177/1060028017698797

Bez C, Perrottet N, Zingg T, Leung Ki EL, Demartines N and Pannatier A. Stress ulcer prophylaxis in non-critically ill patients: a prospective evaluation of current practice in a general surgery department. J Eval Clin Pract. 2013; 19(2): 374-378. doi: 10.1111/j.1365-2753.2012.01838.x

Ching SL and Sukumaran LD. Appropriateness of Intravenous Proton Pump Inhibitor Use in Labuan Hospital, Federal Territory of Labuan. Ministry of Health Malaysia. Pharmacy Research Reports 2019; 2.

Churi S and Jogani A. Prospective Assessment of Prescribing Pattern of Intravenous Proton Pump Inhibitors in an Indian Tertiary Care Teaching Hospital. Indian Journal of Pharmacy Practice. 2014; 7(4): 2-7. doi: 10.5530/ijopp.7.4.2

Cook D and Guyatt G. Prophylaxis against Upper Gastrointestinal Bleeding in Hospitalized Patients. N Engl J Med 2018; 378: 2506-2516. doi: 10.1056/NEJMra1605507

Davis KW, Hanners RE and Lockwood SM. Implementation of a proton pump inhibitor stewardship program. Am J Health Syst Pharm. 2017; 74(12): 932-937. doi: 10.2146/ajhp160670

Domingo S. Los inhibidores de la bomba de protones en la pandemia por la COVID-19. Gastroenterol Hepatol. 2021; 44: 611-613.

Elmubarak A, Badi S and Yousef BA. Adherence to Stress Ulcer Prophylaxis Guideline in Medicine Unit at Soba University Hospital: A Descriptive Retrospective Study. Dr. Sulaiman Al Habib Med J. 2021; 3: 125-130.

Fah T, Yi Jun T, Yan P and JinYu C. Appropriateness of Proton Pump Inhibitors Prescription in Patients Admitted to a Malaysian Tertiary Hospital. International Journal of Public Health Research. 2019; 9(1): 1043-1050.

Farrell B, Pottie K, Thompson W, Boghossian T, Pizzola L, Rashid FJ, et al. Deprescribing proton pump inhibitors: Evidence-based clinical practice guideline. Canadian family physician Medecin de famille canadien. 2017; 63(5): 354-364.

Fitzgerald L, Hanlon J, Shelton P, Landsman P, Schmader K, Pulliam C, et al. Reliability of a Modified Medication Appropriateness Index in Ambulatory Older Persons. Ann Pharmacother. 1997; 31: 543-547.

Freedberg D, Salmasian H, Abrams JA and Green RA. Orders for intravenous proton pump inhibitors after implementation of an electronic alert. JAMA Intern Med. 2015; 175(3): 452-454. doi: 10.1001/jamainternmed.2014.6680

Guda NM, Noonan M, Kreiner MJ, Partington S and Vakil N. Use of intravenous proton pump inhibitors in community practice: an explanation for the shortage? Am J Gastroenterol. 2004; 99(7): 1233-1237. doi: 10.1111/j.1572-0241.2004.30894.x

Haastrup P, Paulsen MS, Begtrup LM, Hansen JM and Jarbøl DE. Strategies for discontinuation of proton pump inhibitors: a systematic review. Fam Pract. 2014; 31(6): 625-630. doi: 10.1093/fampra/cmu050

Herzig S, Rothberg M, Feinbloom D, Howell M, Ho K, Ngo L, et al. Risk Factors for Nosocomial Gastrointestinal Bleeding and Use of Acid-suppressive Medication in Non-critically Ill Patients. J Gen Intern Med. 2012; 28(5):683-690. doi: 10.1007/s11606-012-2296-x

Hong Y, Ye Z, Gao Z and Rao Y. Continuous improvement on the rationality of prophylactic injectable PPIs usage by a clinical pharmacist-led guidance team at a Chinese tertiary teaching hospital. J Int Med Res. 2020; 48(10): 300060520954729. doi: 10.1177/0300060520954729

Hughes GJ, Belgeri MT and Perry HM. The impact of pharmacist interventions on the inappropriate use of acid-suppression therapy. Consult Pharm. 2011; 26(7): 485-490. doi: 10.4140/TCP.n.2011.485

Hussain S, Stefan M, Visintainer P and Rothberg M. Why do physicians prescribe stress ulcer prophylaxis to general medicine patients? South Med J. 2010; 103(11): 1103-1110. doi: 10.1097/SMJ.0b013e3181f6539d

Hwang KO, Kolarov S, Cheng L and Griffith RA. Stress ulcer prophylaxis for non-critically ill patients on a teaching service. J Eval Clin Pract. 2007; 13(5): 716-721. doi: 10.1111/j.1365-2753.2006.00742.x

Jain G, Jabeen S and Vallurupalli S. Efforts to reduce stress ulcer prophylaxis use in non-critically ill hospitalized patients by internal medicine residents: A single-institution experience. Journal of clinical outcomes management: JCOM, 2013; 20(1): 13-19.

Juneja S, Rana P, Manoj S, Kalia R and Singh RP. Appropriateness of Proton Pump Inhibitor Use in Hospitalized Patients: A Cross Sectional Study in a Tertiary Care Hospital in North India. J Pharm Care. 2023; 11(2): 61-65.

Lai PS, Wong YY, Low YC, Lau HL, Chin KF and Mahadeva S. Unexplained abdominal pain as a driver for inappropriate therapeutics: an audit on the use of intravenous proton pump inhibitors. PeerJ. 2014; 2: e451. doi: 10.7717/peerj.451

Luo H, Fan Q, Xiao S and Chen K. Changes in proton pump inhibitor prescribing trend over the past decade and pharmacists' effect on prescribing practice at a tertiary hospital. BMC Health Serv Res. 2018; 18, 537. doi: 10.1186/s12913-018-3358-5

Mahmoud H and Matar R. Oral PPI vs IV PPI in Hospitalized Patient. Research Article J Gastro & Digestive Systems. 2018; 2(2): 1.

Masood U, Sharma A, Bhatti Z, Carroll J, Bhardwaj A, Sivalingam D, et al. A successful pharmacist-based quality initiative to reduce inappropriate stress ulcer prophylaxis use in an academic medical intensive care unit. Inquiry. 2018; 55: 46958018759116. doi: 10.1177/0046958018759116

Masoompour S, Kasaee R and Mahdaviazad H. Evaluation of adherence to American Society of health-system pharmacists' guidelines. Gastroenterol Nurs. 2017; 40(6): 491-495.

Michal J, Henry T and Street C. Impact of a pharmacist-driven protocol to decrease proton pump inhibitor use in non-intensive care hospitalized adults. Am J Health Syst Pharm. 2016; 73(17 Suppl 4): S126-S132. doi: 10.2146/ajhp150519

Mohzari YA, Alsaegh A, Basheeruddin Asdaq SM, Al Shanawani SN, Albraiki AA and Bagalb A. The Pattern of Intravenous Proton-Pump Inhibitor Utilization at an Academic Medical Center in Riyadh, Saudi Arabia. J Res Pharm Pract. 2020; 9(3): 151-154. doi: 10.4103/jrpp.JRPP_20_62

Moradi M, Raeesi S and Sepheri Z. Audit of IV Pantoprazole: pattern of administration and compliance with guidelines in a teaching hospital. Springer Plus. 2016; 5: 1749.

Naing L, Winn T and Rusli BN. Practical issues in calculating the sample size for prevalence studies. Medical Statistics. Archives of Orofacial Sciences. 2006; 1: 9-14. Retrieved from: https://www.scribd.com/doc/63105077/How-to-Calculate Sample-Size

Nasser SC, Nassif JG and Dimassi HI. Clinical and cost impact of intravenous proton pump inhibitor use in non-ICU patients. World J Gastroenterol. 2010; 16(8): 982-986. doi: 10.3748/wjg.v16.i8.982

Philippine Society of Gastroenterology. Philippine consensus statements on the management of non-variceal upper gastrointestinal bleeding: Compendium of Philippine medicine. 16th ed, 2012.

Sohrevardi SM, Vahidi A, Mosadegh MH, Dehghani Tafti A and Dadollahi A. Evaluation of prescriptions and use of intravenous pantoprazole in general wards and intensive care unit of Shahid Sadoughi Hospital in Yazd. J Pharm Care. 2015; 3(1-2): 7-10.

Somers A, Mallet L, van der Cammen T, Robays H and Petrovic M. Applicability of an adapted medication appropriateness index for detection of drug-related problems in geriatric inpatients. Am J Geriatr Pharmacother. 2012; 10(2): 101-109. doi: 10.1016/j.amjopharm.2012.01.003

Sudhakar R, Saju D, Jose M, Arulmoorthy M, Selvaraj H and Sherief SH. Drug use evaluation of Proton pump inhibitors in a Tertiary care hospital. World Journal of Pharmaceutical and Medical Research. 2019; 5(12): 134-139.

Tasaka CL, Burg C, VanOsdol SJ, Bekeart L, Anglemyer A, Tsourounis C, et al. An interprofessional approach to reducing the overutilization of stress ulcer prophylaxis in adult medical and surgical intensive care units. Ann Pharmacother. 2014; 48(4): 462-469. doi: 10.1177/1060028013517088

Torres-Bondia F, de Batlle J, Galván, L, Buti M, Barbé F and Piñol-Ripoll G. Evolution of the consumption trend of proton pump inhibitors in the Lleida Health Region between 2002 and 2015. BMC Public Health. 2022; 22(818): 818. doi: 10.1186/s12889-022-13217-6

U.S. Department of Health and Human Services. U.S. Food and Drug Administration. FDA Drug Safety Communication: Clostridium difficile-Associated Diarrhea Can Be Associated with Stomach Acid Drugs Known as Proton Pump Inhibitors. 2012; Retrieved September 2021. http:/www.fda.gov/Drugs/DrugSafety/DrugSafetyPodcasts/ucm291058.htm

Vazin A, Karimzadeh I, Karamikhah R, Oveisi Z, Mohseni S, Keykhaee M, et al. Clinical and economic impacts of guideline implementation by the pharmaceutical care unit for high-cost medications in a referral teaching hospital. BMC Health Serv Res. 2018; 18: 815. doi: 10.1186/s12913-018-3627-3

Wahking RA, Steele RL, Hanners RE, Lockwood SM and Davis KW. Outcomes From a Pharmacist - led Proton Pump Inhibitor Stewardship Program at a Single Institution. Hosp Pharm. 2018; 53(1): 59-67. doi: 10.1177/0018578717747192

Wan A, Halpape K, Talkhi SC, Dixon C, Dossa H, Tabamo J, et al. Evaluation of Prescribing Appropriateness and Initiatives to Improve Prescribing of Proton Pump Inhibitors at Vancouver General Hospital. Can J Hosp Pharm. 2018; 71(5): 308-315.

Zeng M, Li Y, Chen T, et al. Evolution of proton pump inhibitor prescribing from 2017 to 2021 at 14 secondary and tertiary hospitals in China: a multicenter cross-sectional study. BMJ Open. 2023; 13(7): e072793. doi: 10.1136/bmjopen-2023-072793