El Ouweini A, Slevaraju K, Olaitan VO, Levien T, Malaeb D. Assessment of proton pump inhibitors utilization in intensive care units patients of a tertiary care hospital in the United Arab Emirates. Pharmacy Practice 2024 Jul-Sep;22(3):2978.
https://doi.org/10.18549/PharmPract.2024.3.2978

Original Research

Assessment of proton pump inhibitors utilization in intensive care units patients of a tertiary care hospital in the United Arab Emirates

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Received (first version): 21-Sep-2023 Accepted: 21-Oct-2023 Published online: 04-Jul-2024

Abstract

Background: PPI prescriptions have consistently increased in hospitals and ambulatory care facilities. Because PPIs are widely used, readily available, highly effective, and heavily marketed, they are susceptible to over-prescription and misuse. This study aims to assess the PPI utilization pattern and prescribing appropriateness in terms of indication, dose, and route of administration in the ICU setting. **Methods:** A retrospective, cohort study performed from October 2020 - October 2022 in a tertiary care hospital in the UAE. All patients received a proton pump inhibitor in the ICU. **Results:** Only 20.3% had an appropriate indication for prophylaxis and matched either of the 1 major criteria of SUP or at least 2 minor criteria. The highest percentage of patients (66.2%) were receiving inappropriate prophylaxis therapy. Pantoprazole was the most commonly prescribed PPI followed by Esomeprazole and Lansoprazole. PPI dose was appropriate in 66.9% of the patients and PPI route of administration was appropriate in 87.8% of the patients. Total PPI appropriateness was achieved in only 17.6% of the patients. Patients with moderate GI bleeding risk and who are non-smokers are more likely to have total PPI inappropriateness. **Conclusion:** This study identified a significant number of inappropriate prescriptions of PPIs for critically ill patients, not in accordance with clinical guidelines. These findings underscore the necessity for educational interventions aimed at physicians to promote more rational prescribing practices.

Keywords: proton pump inhibitors; intensive care unit; stress ulcer prophylaxis; utilization; safety

INTRODUCTION

Proton-pump inhibitors (PPIs) are commonly prescribed medications that treats several acid-related disorders, including dyspepsia, gastro-oesophageal reflux disease (GERD), peptic ulcer disease, and upper gastrointestinal bleeding.[1] Moreover, they are also used as a prophylactic medicine for patients who take non-steroidal anti-inflammatory drugs (NSAIDs) and for stress ulcer prophylaxis (SUP).[1] Examples of PPIs approved by the US Food and Drug Administration include omeprazole, esomeprazole, lansoprazole, rabeprazole, and pantoprazole. While PPIs are an essential part of treating and preventing gastric acid-related disorders, they are associated with increased risk of side effects, drug-drug interactions, and increased healthcare costs.[1] The most common side effects of PPIs include constipation, headache, abdominal pain, flatulence, and diarrhea, which are mild and usually resolve on their own. However, prolonged use of PPIs may increase the risk of hip fractures, community-acquired pneumonia, Clostridium difficile infection, gastric carcinoids, and hypomagnesemia.[2,3] Proton pump inhibitors are commonly prescribed in medical practice and their use has grown worldwide.[4,5] A previous study indicated that in 2009, over 113 million PPIs were prescribed globally, and this number is predicted to have risen since then.[4] Over the past few years, PPI prescriptions have consistently increased in hospitals and ambulatory care facilities.[1] Because PPIs are widely used, readily available, highly effective, and heavily marketed, they are susceptible to over-prescription and misuse.[6] Many drug usage investigations have found that PPIs are often used inappropriately, which can lead to severe and unfavorable health consequences.[7-10] As a member of a multidisciplinary management team, pharmacists utiliza their clinical expertise to perform an important role in the care of intensive care unit (ICU) patients. Prior research on prescription patterns indicated that approximately 75% of patients were given stress ulcer prophylaxis while in the ICU, and within that group, 14.4-42% had no apparent risk of stress ulcers.[11,12] While it has been demonstrated that SUP can effectively reduce the occurrence of gastrointestinal bleeding, it also results in greater occurrences of myocardial ischemia, infections caused by Clostridium difficile, hospital-acquired pneumonia, longer hospital stays, and higher prescription expenses and

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hospitalization costs.[13-15] A local study in the United Arab Emirates (UAE) that addressed the utilisation appropriateness of PPI, found that out of 172 patients admitted to the internal medicine ward, 103 (60%) had inapporpriate PPI prescription. Of these inappropriate prescriptions, 22 patients had no clear indication for PPI use and for 16 patients; PPIs were used for stress ulcer prophylaxis in the low-risk category.[16] However, there are no studies addressing the PPI use among ICU patients in UAE. Therefore, this study aims to assess the PPI utilization pattern and prescribing appropriateness in terms of indication, dose, and route of administration in the ICU setting.

MATERIALS AND METHODS

Study Design

Retrospective, cohort study performed from October 2020 - October 2022 in a tertiary care hospital in the UAE. This study was approved by the Institutional Review Board. Eligible patient medical charts were reviewed from the ICU-admitted patients, and information was collected using a data collection sheet. Eligibility criteria included patients aged 18 and above who are admitted to the ICU and had received any PPI whether oral or IV. Patients who did not meet these criteria were excluded.

Sample size calculation

Using the G-power software, a minimum sample of 365 was deemed necessary, based on a R^2 deviation of 5%, an alpha error of 5%, a power of 80% and a maximum of 23 variables to be entered in the final model.

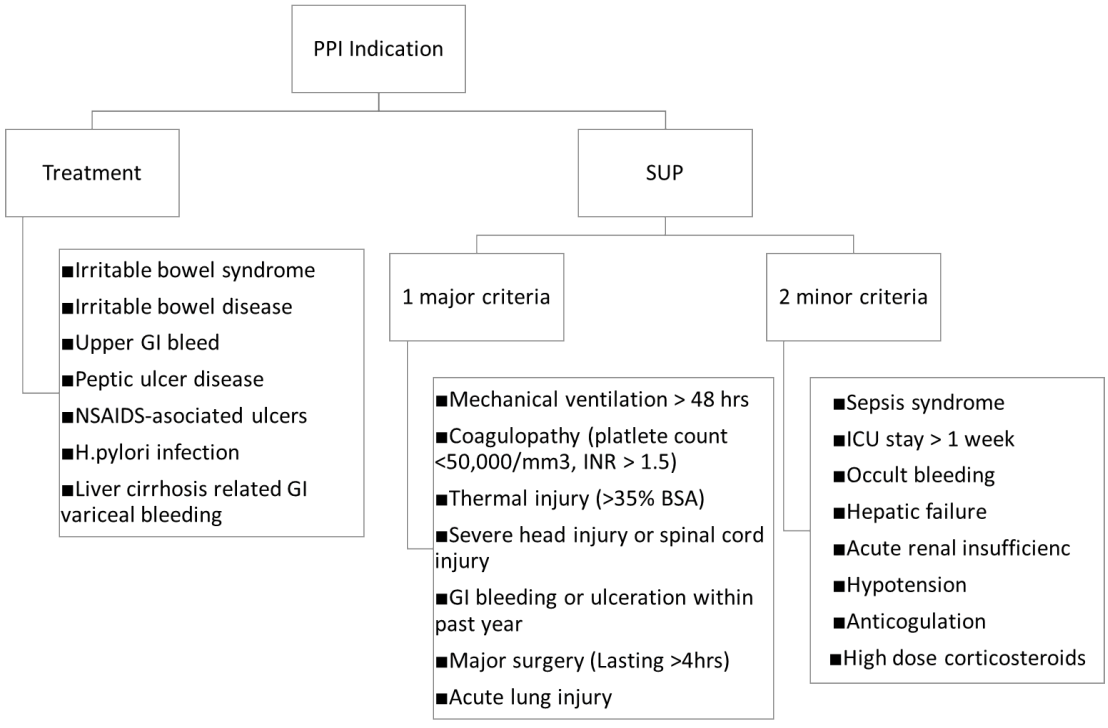
Data collection and variables

A data collection sheet was created to study the variables that were important to assess the appropriate use of PPIs in the ICU. The data collection sheet was content-validated by a panel of experts including PharmD professors. Data collection was performed by a registered clinical pharmacist and last year pharmD students. A report was extracted from the hospital's electronic medical record for all patients admitted to the ICU and received oral or IV PPI in the specified period. The data collection sheet included several sections: patient demographic characteristics, data about PPI name, route, dose, duration, and indications. An algorithm was developed to decide the appropriateness of PPI utilization. PPI's duration of therapy, dose, and route were all assessed for appropriateness as well. Moreover, the timely switch of PPI from IV to oral route was evaluated. Total PPI appropriateness was calculated based on the appropriateness of the following variables combined: appropriate PPI indication, route of administration, dosing regimen, and IV to PO shift.

Algorithm 1.[17]

Statistical analysis

IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, N.Y., USA) was used to perform the data analysis. Dichotomous and categorical variables were presented as percentages, and the continuous variables were displayed as mean±standard deviation (SD). Mean values, standard deviations, and frequencies were computed to illustrate current prescribing practices of PPI in the adult intensive care unit in



Algorithm 1.[17]

www.pharmacypractice.org (eISSN: 1886-3655 ISSN: 1885-642X)

this tertiary care hospital. All factors that showed significance in the bivariate analysis were entered as independent variable. P <0.05 was deemed statistically significant in the final model.

RESULTS

A total of 148 patients were enrolled in this study. Table 1 provides a summary of the patients' demographic statistics, including age, smoker and alcohol intake status, chronic diseases, and baseline total GI bleeding risk.

Table 1.Sociodemographic Characteristics of Enrolled Patients

Age, years, mean (±SD)	45.26 (±14.74)
Gender, no. (%)	
• Male	97 (65.5)
• Female	51 (34.5)
Smoker, no. (%)	
• Yes	18 (12.2)
• No	130 (87.8)
Alcohol intake, no. (%)	
• Yes	4 (2.7)
• No	144 (97.3)
Chronic Diseases (Past Medical History), no. (%)	
CVD	21 (14.2)
GI	21 (14.2)
Osteoarthritis	3 (2)
Others	75 (50.7)
Chronic GI Diseases (Past GI Diseases), no. (%)	
GERD	15 (10.1)
PUD	6 (4.1)
Upper GI Bleeding	10 (6.8)
Total GI Bleeding Risk, no. (%)	
High GI Risk (3 or more risk factors)	28 (18.9)
Moderate GI Risk (1-2 risk factors)	81 (54.7)
Low GI Risk (No risk factors)	39 (26.4)

Most of the study participants were non-smokers and non-alcohol users accounting for 87.8% and 97.3% of the study participants respectively. Cardiovascular diseases (14.2%) and Gastrointestinal (GI) disorders (14.2%) were the most common comorbidities.

PPI utilization patterns were analysed. 13.5% of all patients had indications for treatment, such as GERD, upper GI bleed or peptic ulcer disease (PUD). On the other hand, 20.3% had an appropriate indication for prophylaxis and macthed either of the 1 major criteria of SUP or at least 2 minor criteria (described in the Algorithm 1). The highest percentage of patients (66.2%) were receiving inappropriate prophylaxis therapy. Pantoprazole was the most commonly prescribed PPI followed by Esomeprazole and Lansoprazole. Around two-thirds of patients were on intravenous PPI. The mean duration of PPI use in the ICU was around 6 days. PPI dose was appropriate in 66.9% of the patients and PPI route of administration was appropriate in 87.8% of the patients. Among the 105 patients receiving IV PPI, 93 of them had justifiable reason to be shifted from IV to PO, and from those 93, only 25 patients were shifted to PO therapy, and among 25, the shift was timely in only 15 out of the 25 patients. SUP was appropriate in only 20.3% of the patients who were prescribed PPI for SUP purposes. Total PPI appropriateness was achieved in only 17.6% of the patients.

Bivariate analysis

Having inappropriate SUP indication is significantly associated with higher total PPI appropriateness. Additionally, patients with moderate GI bleeding risk and who are non-smokers are more likely to have total PPI inappropriateness. On the other hand, patients taking NSAIDs are likely to have a significant association with higher total PPI appropriateness. Among the antiplatelets used, clopidogrel intake was more significanlty associated with inappropriate total PPI utilization. Similarly, taking anticoagulants was more significanlty associated with inappropriate total PPI utilization. Finally, having a previous GI disease is significantly associated with inappropriate total PPI utilization.

DISCUSSION

Currently, there is a scarcity of information in the literature describing the utilization pattern of PPIs in patients admitted to the intensive care units of hospitals within the UAE. Most of the study participants were non-smokers and non-alcoholic users. As it is scientifically proven, smoking and alcohol intake are significant risk factors for GI bleeding.[17] Cardiovascular diseases were among the most common chronic comorbidities present in the study population. Significant portion of these patients were also on antiplatelets and/or anticoagulants (Tables 2-4), both which significantly increases the risk of GI bleeding. 13.5% of all patients had proper PPI indications for treatment, such as GERD, upper GI bleeding, or PUD. These patients were either taking PPI before coming to the hospital or they were started on it in the hospital. In both cases, it was important to continue PPI use in such patients. In this study, pantoprazole and esomeprazole were the most commonly prescribed PPIs in the ICU, with the former having a significantly higher prescription frequency than the latter. The frequent

Table 2.Concomitant inpatient medications

Medication	**No. (%)**	**Duration of use, days, mean (±SD)**
NSAIDs	40 (27)	5.87 (±3.11)
• Ketoprofen	18 (12.2)	
• Diclofenac	20 (13.5)	
• Ibuprofen	2 (1.4)	
Corticosteroid	16 (10.8)	8 (±14.46)
• Methylprednisolone	3 (2)	
• Hydrocortisone	3 (2)	
• Prednisolone	7 (4.7)	
• Dexamethasone	3 (2)	
Anticoagulant	42 (28.4)	N/A
• Low Molecular Weight Heparin	39 (26.4)	
• Apixaban	2 (1.4)	
• Warfarin	1 (0.7)	
Antiplatelet	41 (27.7)	N/A
• Aspirin	34 (23)	
• Clopidogrel	19 (12.8)	
• Ticagrelor	23 (15.5)	

Table 3. PPI Utilization and Appropriateness Pattern

	No. (%)
PPI Indication	
Treatment	20 (13.5)
Appropriate SUP prophylaxis	30 (20.3)
Inappropriate SUP Prophylaxis	98 (66.2)
PPI Indication for Treatment	
GERD	8 (5.4)
Upper GI Bleeding	10 (6.8)
PUD	5 (3.4)
PPI Indication for Prophylaxis	
SUP due to Major Criteria (At least 1)	27 (18.2)
SUP due to Minor Criteria (At least 2)	4 (2.7)
PPI received in the ICU	
Pantoprazole	109 (73.6)
Esomeprazole	23 (15.5)
Lansoprazole	16 (10.8)
Route of PPI administration	
• IV	105 (70.9)
• PO	56 (37.8)
Dosing Regimen	
• 30 mg once daily	16 (10.8)
• 40 mg once daily	103 (69.6)
• 40 mg twice daily	29 (19.6)
Duration of PPI Use in the ICU, days, mean (±SD)	5.79 (±6.04)
Appropriate Dose	99 (66.9)
Appropriate Route of Administration	99 (87.8)
IV to PO shift justifiable	93 (62.8)
IV to PO shift done	25 (16.9)
IV to PO shift done timely	15 (10.1)
SUP Appropriate?	
• No	98 (66.2)
• Yes	30 (20.3)
Total PPI Appropriateness	
• No	122 (82.4)
• Yes	26 (17.6)

Table 4. Bivariate Analysis of factors associated with PPI appropriateness

Variables	Total PPI Appropriateness No. (%)		P- value
	No	Yes	
SUP Appropriateness			
No	98 (100)	0 (0)	**< 0.001**
Yes	14 (46.7)	16 (53.3)	
Total GI Bleeding Risk			
High GI Risk (3 or more risk factors)	14 (50)	14 (50)	**< 0.001**
Moderate GI Risk (1-2 risk factors)	80 (98.8)	1 (1.2)	
Low GI Risk (No risk factors)	28 (71.8)	11 (28.2)	
Gender			
Male	43 (84.4)	8 (15.7)	0.821
Female	78 (81.3)	18 (18.8)	
Smoker			
Yes	10 (55.6)	8 (44.4)	**0.004**
No	112 (86.2)	18 (13.8)	
Alcohol intake			
Yes	3 (75)	1 (25)	0.542
No	119 (82.6)	25 (17.4)	
Taking NSAID?			
No	83 (76.9)	25 (23.1)	**0.003**
Yes	39 (97.5)	1 (2.5)	
Which NSAID?			
Ketoprofen	17 (94.4)	1 (5.6)	0.534
Diclofenac	20 (100)	0 (0)	
Ibuprofen	2 (100)	0 (0)	
Is the patient taking antiplatelets?			
No	92 (86)	15 (14)	0.090
Yes	30 (73.2)	11 (26.8)	
Which Antiplatelet?			
Aspirin	8 (30.8)	26 (21.3)	0.311
Clopidogrel	7 (26.9)	12 (9.8)	**0.046**
Ticagrelor	19 (15.6)	4 (15.4)	1.000
Is the patient taking anticoagulants?			
No	92 (86.8)	14 (13.2)	**0.033**
Yes	30 (71.4)	12 (28.6)	
Anticoagulant Used			
LMWH	29 (74.4)	10 (25.6)	0.062
Apixaban	0 (0)	2 (100)	
Warfarin	1 (100)	0 (0)	
Is the patient taking corticosteroids?			
No	108 (81.8)	24 (18.2)	0.739
Yes	14 (87.5)	2 (12.5)	
Corticosteroids Used			
Methylprednisolone	3 (100)	0 (0)	0.558
Hydrocortisone	2 (66.7)	1 (33.3)	
Prednisolone	6 (85.7)	1 (14.3)	
Dexamethasone	3 (100)	0 (0)	
Dosing Regimen			
40 mg once daily	87 (71.3)	19 (73.1)	0.374
40 mg twice daily	20 (16.4)	6 (23.1)	
30 mg once daily	15 (12.3)	1 (3.8)	
Route of PPI administration			
IV	91 (86.7)	14 (13.3)	0.055
PO	43 (76.8)	13 (23.2)	0.185
Chronic Diseases (Past Medical History)			
CVD	14 (66.7)	7 (33.3)	0.06
GI	11 (52.4)	10 (47.6)	**0.001**
Osteoarthritis	2 (66.7)	1 (33.3)	0.442
Others	60 (80)	15 (20)	0.519

Numbers in bold indicate significant *p* values

utilization of these two PPIs in the current study could be indicative of prescribers' sound understanding of pantoprazole and esomeprazole and the wide prevalence and accessibility of both drugs in this hospital's drugs formulary. Despite the prevalent recommendations for oral administration of PPIs in the hospital whenever possible, this study showed that around 70% of patients were administered PPIs intravenously. Similar findings were reported in a retrospective cohort study conducted at a teaching hospital in the United States indicating a percentage of 71% of patients receiving pantoprazole intravenously.[19] While there is no widespread consensus among most gastroenterology associations, some randomized controlled trials have supported the clinical advantages of intravenous PPI administration to treat cases of acute acid-related disorders or as a justifiable indication for SUP.[20] In this study, PPI route of administration was appropriate in 87.8% of the patients. In this study, 20.3% had an appropriate indication

for SUP and matched either of the 1 major criteria of SUP or at least 2 minor criteria (described in the Algorithm 1).[17]Hence, around 80% of these critically ill patients had inappropriate indication for SUP other than those recommended by the guidelines. These findings are consistent with those of previous studies reported by Akram et al.[21] and Madi et al.[22] Furthermore, this study showed that from 93 patients who received IV PPI, only 25 patients were shifted to PO route of administration, and among these 25, the shift was timely in only 15 out of the 25 patients. In a pharmacoeconomic study, using IV instead of PO PPI therapy would cost an incremental $708,735 per year to gain one additional Quality-Adjusted Life Year in high-risk ulcer hemorrhage patients.[23] These findings underscore the need for ICU prescribers to practice more vigilant timely IV to PO shifts in PPI. Total PPI appropriateness was achieved in only 17.6% of the patients which was mainly due to inappropriate SUP indication. The improper PPI prescriptions indicate a requirement for clinicians to follow official monographs and guidelines more diligently to ensure the rational and safe use of PPIs in the UAE. Additionally, patients with moderate GI bleeding risk and who are non-smokers were more likely to have total PPI inappropriateness. This demonstrates the perception of clinicians that having one or more GI bleeding risk factors is enough to prescribe PPI for SUP. This study represents the first study to delineate the prescription trends of PPIs at the ICU of tertiary care hospitals in the UAE. Our results underscore the importance of physicians following the present guidelines when prescribing PPIs to mitigate the rise in drug-related complications. To regulate the utilization of PPIs in hospital settings, especially the ICUs, it is advisable to introduce an educational initiative focusing on the appropriate usage and long-term side effects of these drugs. Additionally, the establishment of a prescribing protocol for ICU-admitted patients and the engagement of medication safety officers in overseeing PPI prescription patterns should be put into action.

Limitations

This research has a number of limitations. To begin with, the small sample size could diminish the significance of the findings. Another drawback involves the data collection being limited to just one hospital, which constrains the generalizability of the findings to other hospitals in other emirates. Furthermore, the retrospective study design posed a limitation by restricting prospective interactions with patients and raising the rate of missing data and accuracy of collected data. Since it is a retrospective study, this study did not assess PPI continuation after transfer to the general ward and/or home discharge with no clear indication. This occurs because numerous physicians persist in continuing PPIs, perceiving them as benign and devoid of any serious risk, without evaluating the potential side effects associated with their prolonged treatment. Hence, investigating this practice opens the door for future research. Additionally, the study team lacked access to this data because it was a retrospective study, and not all the necessary information had been documented.

CONCLUSION

In conclusion, this research reveals that PPIs were often prescribed without clear indications. The findings highlight the importance of introducing educational interventions for physicians to promote rational prescription practices and encourage adherence to the guidelines outlined in official monographs for the appropriate use of PPIs.

DECLARATIONS

Ethical statement

The study was approved by the Institutional Review Board of Gulf Medical University (Ref: IRB-COP-STD-60-APRIL-2023).

DATA AVAILABILITY STATEMENT

The database cannot be shared publicly but is available upon a reasonable request from the corresponding author.

DECLARATION OF INTERESTS

The authors declare no conflict of interest.

FUNDING

This research received no external funding.

AUTHOR CONTRIBUTIONS

Conceptualization: AEO; Methodology: AEO; Validation: AEO, DM and TL; Formal analysis: AEO, DM and TL; Investigation: AEO, DM; Resources: TL; Data curation: AEO, KS, VO; Writing—original draft preparation: AEO, KS, VO; Writing—review and editing: DM,TL; Visualization: AEO, DM; Supervision: DM; Project administration: AEO, DM and TL; Funding acquisition. All authors have read and agreed to the published version of the manuscript.

ACKNOWLEDGMENTS

None.

ABBREVIATIONS

PPI: Proton pump inhibitor

GERD: Gastro-Esophageal Reflux Disease

NSAIDs: Non-Steroidal Anti-Inflammatory Drugs

SUP: Stress Ulcer Prophylaxis

ICU: Intensive Care Unit

UAE: United Arab Emirates

SD: Standard Deviation

GI: Gastrointestinal

CVD: Cardiovascular Diseases

PUD: Peptic Ulcer Disease

LMWH: Low Molecular Weight Heparin

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