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Review of drug indications for proton pump inhibitors among hospitalized patients in King Fahd Hospital, Alkobar, Saudi Arabia

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Abstract

Proton pump inhibitors (PPIs) are among the most commonly prescribed medications worldwide. Irrational use of PPIs is a common practice among hospitalized patients. The major objective of this study was to determine the appropriateness of indications of PPIs among hospitalized patients in King Fahd Hospital, Al Khobar, Saudi Arabia. A cross-sectional study was conducted at King Fahd Hospital, during December 2018 to March 2019. All adult patients admitted to the Medical and Surgical Departments were eligible. Data was collected from each patient's medical record using a structured - data collection form. Assessment of the appropriateness of PPIs indications was performed based on standardized criteria. Descriptive statistics were used to describe all variables. Regression models were performed to identify the determinants of inappropriateness of PPIs indication. A p-value less than 0.05 was considered as statistically significant. Overall, a total of 181 patients was included, of them 96 (53%) were males. Patients aged > 65 years were 47 (26%). Out of all patients PPIs was prescribed as prophylactic therapy for 163 (90.1%) and for 18 (9.9%) as treatment. For 128 (70.7%) patients PPIs was inappropriately indicated. Multiple logistic regression analysis showed that, age more than 65 years [AOR 8.36 (3.82 - 18.3), ($P < 0.001$)] was significantly associated with appropriate indication of PPIs. PPIs indications was irrational as it was inappropriately prescribed for a considerable number of patients. Urgent interventions are needed to improve the quality of prescribing of this important class of drugs.

Keywords: Drug; Indications; Proton pump inhibitors

1. Introduction

Acid suppressive therapy (AST) includes Proton Pump Inhibitors (PPIs) and Histamine H₂ receptors Antagonist (H₂RA). AST is indicated to treat several gastrointestinal disorders associated with increased secretion of acid, like upper gastrointestinal bleeding, different types of esophageal reflux disease (GERD), beside other indications [1]. Due to their high level of efficacy and low rate of toxicity, PPIs are among the most commonly prescribed medication worldwide [2]. The use of PPIs is linked with the risk of hip, spine, and any-site fracture [3], with increased risk of intestinal infections with *C. difficile* [4] and *Candida* infections [5]. Also, the use of PPIs is associated with potentially life-threatening hypomagnesaemia [6].

The use of AST among hospitalized patients has been the subject of many studies conducted around the world. Irrational use during hospital admission and after discharge was documented [7,8]. Non-adherence to international guidelines for stress ulcer prophylaxis and the inappropriate use of these agents among non-critically hospitalized patients were reported [9]. Overutilization of PPI in the medical department was inappropriately linked to stress ulcer prophylaxis as a main indication [10]. Discharge on acid suppressive medication indicated for stress ulcer prophylaxis is one of the manifestations of irrational use documented in literature [11]. Another example of malpractice is the prescribing of

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PPIs for elderly patients without documented indication [12]. Beside the health impact, the economic burden of unjustified use of these agents is huge in terms of money spent on drugs [13].

In Saudi Arabia few studies explored the use of PPIs among hospitalized patients. For example, one study identified inappropriate use of intravenous PPIs in critically and non-critically ill patients [14]. Another study documented the inappropriate use of AST for stress ulcer prophylaxis for non-critically ill patients lacking the risk factors for GI bleeding [15]. The major objective of this study was to determine the appropriateness of indications of PPIs among hospitalized patients in King Fahd Hospital. In addition, the research aimed to identify the factors associated with the appropriate use of PPIs and the predictors of the use of PPIs via parenteral route.

2. Patients and methods

2.1. Study design and setting

A cross-sectional study was conducted at The Medical and Surgery Departments in King Fahd Hospital, Al Khobar, Saudi Arabia, during December 2018 to March 2019.

2.2. Inclusion criteria

The study included All adult patients (18 years and above) hospitalized during the study period and for whom PPIs was prescribed.

2.3. Exclusion criteria

- Pediatric patients
- Patients with incomplete medical records
- Severely ill patients (terminal illness and malignancy)

2.4. Sample size and sampling technique

A convenient method of sampling was adopted and a total of 181 patients was included.

2.5. Data collection

Data was collected from each patient medical record using a structured- data collection form.

The data collection form composed of the following sections:

Basic and demographic data (age, gender), comorbidities, primary reason of admission and date of admission, and Intensive Care Unit (ICU) stay.

Prescription parameters: current indication of PPIs, drug prescribed, dose, frequency, duration, route of administration. Information about the use of anti-platelet, anti-coagulant, Non-steroidal Anti-inflammatory Drugs (NSAIDs) and corticosteroids drugs were also collected.

2.6. Definitions

Use of acid suppressive therapy was defined as "any prescription of PPIs medication regardless of dosage regimen in which the patient received at least one dose during the hospitalization".

2.7. Appropriateness of indications of PPIs

Indication was considered appropriate if it was complying with the indications stated by Scarpignato et al [1]. For the purpose of this research the following indications were considered appropriate:

- Long-term Management both gastroesophageal reflux disease (GERD) and non-erosive esophageal reflux disease (NERD)
- Extra-digestive GERD
- Uninvestigated Dyspepsia in Patients younger than 45 yrs.

- Peptic Ulcer (PU) Bleeding
- Use of steroid therapy in combination with NSAIDs.
- Use of anti-platelet therapy in patient at gastrointestinal (GI) risk.
- Use of anti-coagulant therapy in combination with antiplatelet therapy.
- Otherwise, all other indications were considered as inappropriate.

2.8. Data analysis

Descriptive statistics was used to describe demographic and clinical characteristics of the patients. Percentages and frequencies were used for the categorical variables. Regression models were used to identify factors; such as gender, patient's age presence of comorbid condition/s, the primary reason of admission and ICU stay (independent) that affect prescription appropriateness and using PPIs via parenteral route (dependent). A p-value less than 0.05 was considered as statistically significant.

2.9. Ethical approval

The study was approved by The Institutional Review Board in Imam Abdulrahman bin Faisal University for Ethical Clearance.

3. Results and discussion

3.1. Background characteristics

Overall, a total of 181 patients was included, of them 96 (53%) were males and 85 (47.0%) were females. Patients aged ≥ 65 years were 47 (26%). Patients with other comorbid chronic diseases were 148 (81.8%), of them 128 (86.5%) had cardiovascular diseases. Table (1) showed patients' background characteristics.

Table 1 Patients' background characteristics

Background characteristic		n (%)
Gender	Male	96 (53%)
	Female	85 (47%)
Age	<65 years	134 (74%)
	65 years or above	47 (26%)
Admission specialty	Medical	109 (60.2%)
	Surgical	72 (39.8%)
ICU stay	Yes	22 (12.2%)
	No	159 (87.8%)
Comorbidity	Present	148 (81.8%)
	Absent	33 (18.2%)
History of peptic ulcer or gastro bleeding	Yes	8 (4.4%)
	No	173 (95.6%)
Prior use of PPIs or H2RA	Yes	58 (32%)
	No	123 (68%)
Total		181(100%)

3.2. Prescribing Patterns of PPIs

Out of all patients PPIs was prescribed as prophylactic therapy for 163 (90.1%) and for 18 (9.9%) of them indicated for treatment. For nearly half of the patients PPIs was prescribed for stress ulcer prophylaxis, other indications were shown in table (2).

Table 2 Indications for PPIs

Indication	Frequency (%)
Stress Ulcer Prophylaxis	85 (47%)
Prevention of gastro-duodenal lesions and events	78 (43.1%)
Bleeding	2 (1.1%)
Long-term Management (both GERD and NERD)	1 (0.6%)
Extra-digestive GERD	1 (0.6%)
Uninvestigated Dyspepsia in Patients younger than 45 yrs	1 (0.6%)
Acute pancreatitis	1 (0.6%)
Others	12 (6.6%)

PU= peptic ulcer; GERD= Gastroesophageal reflux disease; NERD= non-erosive esophageal reflux disease

Table 3 showed the drugs names, doses, frequencies and durations of PPIs.

The results showed that 42 (79.2%) of the patients received NSAIDs and 24 (45.3%) used anticoagulants, 26 (14.4%) were on antiplatelet and 14 (7.7%) had steroid drugs.

Out of all patients 59 (32.60%) were discharged on PPIs, 96 (35%) discharged without PPIs, while 26 (14.40%) were still hospitalized.

Table 3 Drug names, routes of administration, doses, frequencies and durations

Variable	Frequency (%)
Drug name	
Pantoprazole	180 (99.4%)
Esomeprazole	1(0.6%)
Route of administration	
Oral	89 (49.2%)
Intravenous	92 (50.8%)
Dose	
20 mg	2 (1.1%)
40 mg	179 (98.9%)
Frequency of administration	
Once	173 (95.6%)
Twice	8 (4.4%)
Duration of use	
Up to 7 days	59 (32.6%)
8-30 days	75 (41.4%)
>30 days	47 (26.0%)

3.3. Appropriateness of indication of PPIs and its determinants

For 128 (70.7%) of all the included patients, PPIs was inappropriately indicated. Initially, univariable analysis showed that advanced age > 65 years ($P < 0.001$) and presence of other comorbidities conditions ($P = 0.005$) were significantly associated with appropriateness of indication of PPIs. However, multiple logistic regression analysis showed that age more than 65 years was the only predictor of appropriateness of PPIs use ($P < 0.001$), as shown in table (4).

Table 4 Predictors of appropriateness of PPIs indications

Variable	% appropriateness	AOR (95% CI)	p-value
Age in years			
< 65	16.4	Reference	
More than 65	66.0	8.36 (3.82,18.3)	< 0.001
Other Comorbidity conditions			
Absent	9.1	Reference	0.201
Present	33.8	2.32 (0.64, 8.4)	

3.4. Determinants of route of administration

Multiple logistic regression analysis showed that admission specialty ($P=0.019$) and indication of PPIs ($P=0.005$) were significantly associated the use of PPIs via the parenteral route, as shown in table (5)

Table 5 Predictors of using PPIs via intravenous route

Variable	% used PPIs via IV	AOR (95% CI)	p-value
Admission specialty			
Medical	43.1	Reference	
Surgical	58.3	2.12 (1.13, 3.97)	0.019
Indications for PPI			
Prophylaxis	46.0	Reference	0.005
Therapy	77.8	5.54 (1.67, 18.36)	

4. Discussion

The irrational use of medicines is a big problem that face the healthcare systems with huge impact on both health outcomes and wastage of resources [16]. Drug utilization review in hospitals is important for improving the services provided to the patient, as it identifies the malpractices, which will be the focus of future interventions [17].

Analysis of the demographic and clinical characteristics of the included patients revealed that above quarter of them were aged above 65 years old. The use of medicines at this age range should deserve special attention as this subset of the population at increased risk of adverse drug reactions due to polypharmacy and the presence of multiple comorbidities [18]. From a clinical point of view the advanced age is considered as a risk factor of GI bleeding for those who use aspirin-based antiplatelet therapy without the routine PPIs use [19] and patients using complex antithrombotic therapy [20].

Few patients had a history of peptic ulcer or GI bleeding. Quantification of this factor is important, as duodenal ulcer disease was found to be the most common risk for nosocomial bleeding that occur after a prolong hospital stay [21].

The current study attempted to identify the appropriateness of PPIs indications among hospitalized patients. The majority (90.1%) of the patients had PPIs as prophylactic therapy. The two main indications for the use of PPIs as prophylactic therapy were stress ulcer prophylaxis and prevention of gastro-duodenal lesions and events. For the first indication, stress ulcer prophylaxis, the international guidelines justify the use of prophylaxis in critically ill patients admitted to the ICU based on standardized criteria, but not for those admitted to the ward [22]. Likewise, in the case of using of PPIs for prevention of gastro-duodenal lesions and events [1]. Generally, the use PPIs for prevention of gastro-duodenal lesions and events can be easily explained by the fact that a considerable number of patients had cardiovascular diseases for which they used treatment or prevention with ulcerogenic agents like, antiplatelets and anticoagulants. However, as observed in this study the healthcare providers ignore the criteria of when to use these drugs in such situations. For example, PPIs was prescribed almost for every patient who was using an antiplatelet agent

without the presence of gastro-duodenal risk factor for bleeding, like advanced age. This finding emphasizing the need for in-service education to raise the awareness of the physicians with the evidenced-based guidelines regarding the proper use of PPIs.

The results showed that for all patients included approximately 70% PPIs was inappropriately indicated. In agreement with the results obtained from another study conducted in South Africa, a high percent of the hospitalized patients (73%) had acid suppressive therapy, which was prescribed irrationally [23].

The only predictor of appropriateness of indication documented in our study was the age ≥ 65 years. Likewise, younger age together with female gender were found to be the most significant determinants for the inappropriateness [24]. The appropriateness of PPIs indications among elderly patients may be attributed to their use of ulcerogenic agents either as single or combined as in the case of using anti-coagulant therapy with antiplatelet agents.

The results showed that nearly 12% of the patients who were already admitted to the ICU continue using PPIs after discharged to the ward. The same malpractice was documented in another study, whereby more than 50% of the patients who were discharged from ICU continue inappropriately prescribed AST [25]. Here, there should be a system in place to evaluate the appropriateness of the continuation of the drug when the patient transferred to the wards.

Nearly one third of the patients had a history of using AST prior to admission, we observed from the retrieval of the patients' records that prior use was associated with recent previous hospitalization as these patients discharge on these drugs after hospitalization.

Nearly half of the patients (48.6%) received PPIs in an injectable form. Excessive use of injections among hospitalized patients associated with multiple risk like, bloodstream infections, catheter-related bloodstream infections. In addition, it is a well-known risk factor for other side effects such as infiltration, extravasation, phlebitis and pain [26]. Furthermore, the use of injections from economical point of view is expensive compared to the oral formulation and time consuming for the staff taking care of the patients. Here a system should be in place to assess the patient edibility for conversion from intravenous route to oral one, if the indication is appropriate.

Admission in surgical units was significantly associated with using PPIs in an injectable form. The irrational use of intravenous PPIs in patients admitted to surgical department was found to be 3 times more inappropriately used as injections in another study [27].

One third of the patients were discharged on PPIs for different durations of use, in some patients, the durations was six months. Here the pharmacist can play a major role to identify the rationality of indication, if a proper system of medication reconciliation is in place. Comparatively, in another study the quantification of the amount of appropriateness of PPIs use after discharge showed that nearly 60% of the patients were discharged on the drug without documented indication [28].

The study had some limitations, it was a cross-sectional, so the obtained results cannot be generalized to all hospitals in the country. For the patients who had prior history of AST use we didn't know exactly what the indication was, but as mentioned above it was strongly linked to recent hospitalization.

5. Conclusion

Overall PPIs utilization was irrational as it was inappropriately indicated for nearly 70% of the patients and there was a high rate of using the drugs in an injectable form. A qualitative study must be conducted to explore the reasons of why the healthcare providers use PPIs to identify the gaps in their knowledge.

The proposed interventions to improve the situation can be in a form of developing a stewardship program [29]. Prescriber feedback and developing clinical guidelines or a pathway to unify the prescribing patterns are interventions of value. In addition, providing an ongoing in-service education is important to upgrade the physicians' knowledge about the use of this important class of drugs.

Compliance with ethical standards

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Disclosure of conflict of interest

None to be declared.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans subjects by any of the authors'

References

- [1] Scarpignato C, Gatta L, Zullo A, Blandizzi C; SIF-AIGO-FIMMG Group; Italian Society of Pharmacology, the Italian Association of Hospital Gastroenterologists, and the Italian Federation of General Practitioners. (2016). Effective and safe proton pump inhibitor therapy in acid-related diseases - A position paper addressing benefits and potential harms of acid suppression. *BMC Med*, 14, 179.
- [2] Forgacs I and Loganayagam A. (2008). Overprescribing proton pump inhibitors. *BMJ*, 336 (7634), 2–3.
- [3] Zhou B, Huang Y, Li H, Sun W and Liu J. (2016). Proton-pump inhibitors and risk of fractures: an update meta-analysis. *Osteoporos Int*, 27(1), 339-47.
- [4] Trifan A, Stanciu C, Girleanu I, Stoica OC, Singeap AM, Maxim R, et al. (2017). Proton pump inhibitors therapy and risk of *Clostridium difficile* infection: Systematic review and meta-analysis. *World J Gastroenterol*, 23(35), 6500-6515.
- [5] Daniell HW. (2016). Acid suppressing therapy as a risk factor for *Candida* esophagitis. *Dis Esophagus*, 29(5), 479-83.
- [6] Cheungpasitporn W, Thongprayoon C, Kittanamongkolchai W, Srivali N, Edmonds PJ, Ungprasert P, et al. (2015). Proton pump inhibitors linked to hypomagnesemia: a systematic review and metaanalysis of observational studies. *Ren Fail*, 37(7), 1237-41.
- [7] Bez C, Perrottet N, Zingg T, Leung Ki EL, Demartines N and Pannatier A. (2013). Stress ulcer prophylaxis in non-critically ill patients: a prospective evaluation of current practice in a general surgery department. *J Eval Clin Pract*, 19(2), 374-8.
- [8] Nardino RJ, Vender RJ and Herbert PN. (2000). Overuse of acid-suppressive therapy in hospitalized patients. *Am J Gastroenterol*, 95(11), 3118-22.
- [9] Masoompour SM, Kasaee R and Mahdaviazad H. (2017). Evaluation of Adherence to American Society of Health-System Pharmacists Guidelines: Stress Ulcer Prophylaxis in Shiraz, Iran. *Gastroenterol Nurs*, 40(6), 491-495.
- [10] Alqudah MA, Al-Azzam S, Alzoubi K, Alkhatatbeh M and Rawashdeh N. (2016). Overuse of proton pump inhibitors for stress ulcer prophylaxis in Jordan. *Int J Clin Pharmacol Ther*, 54(8), 597-602.
- [11] Ali O, Poole R, Okon M, Maunick S and Troy E. (2019). Irrational use of proton pump inhibitors in general practise. *Ir J Med Sci*, 188(2), 541-544.
- [12] Heidelbaugh JJ and Inadomi JM. (2006). Magnitude and economic impact of inappropriate use of stress ulcer prophylaxis in non-ICU hospitalized patients. *Am J Gastroenterol*, 101(10), 2200-5.
- [13] Haroon M, Yasin F, Gardezi SK, Adeeb F and Walker F. (2013). Inappropriate use of proton pump inhibitors among medical inpatients: a questionnaire-based observational study. *JRSM Short Rep*, 4(8).
- [14] Alsultan MS, Mayet AY, Malhani AA and Alshaikh MK. (2010). Pattern of intravenous proton pump inhibitors use in ICU and Non-ICU setting: a prospective observational study. *Saudi J Gastroenterol*, 16(4), 275-9.
- [15] Malhis A, Alghamdi T, Alfandi R, AlHaj Issa Z, Alanazi H, Alfintoukh H, et al. (2019). Appropriateness of acid-suppressing agents for stress ulcer prophylaxis in non-intensive care unit setting in Saudi Arabia. *J Pharm Bioallied Sci*, 11(1), 96-101.

- [16] Ofori-Asenso R and Agyeman AA. (2016). Irrational Use of Medicines-A Summary of Key Concepts. *Pharmacy (Basel)*, 4(4), 35.
- [17] Robert N. (2008). *Managed Care Pharmacy Practice*. 2nd edition. USA: Jones & Bartlett Learning.
- [18] Jose J. (2012). Promoting drug safety in elderly--needs a proactive approach. *Indian J Med Res*, 136 (3), 362-4.
- [19] Li L, Geraghty OC, Mehta Z, Rothwell PM; Oxford Vascular Study. (2017). Age-specific risks, severity, time course, and outcome of bleeding on long-term antiplatelet treatment after vascular events: a population-based cohort study. *Lancet*, 390 (10093), 490-499.
- [20] Abraham SA, Hartman C, Richardson P, Castillo D, Street Jr RL and Naik AD. (2013). Risk of lower and upper gastrointestinal bleeding, transfusions, and hospitalizations with complex antithrombotic therapy in elderly patients. *Circulation*, 128(17), 1869-77.
- [21] Terdiman JP and Ostroff JW. (1998). Gastrointestinal bleeding in the hospitalized patient: a case-control study to assess risk factors, causes, and outcome. *Am J Med*, 104(4), 349-54.
- [22] ASHP Therapeutic Guidelines on Stress Ulcer Prophylaxis. (1999). ASHP Commission on Therapeutics and approved by the ASHP Board of Directors on November 14, 1998. *Am J Health Syst Pharm*, 56(4), 347-79.
- [23] Gupta R, Garg P, Kottoor R, Munoz JC, Jamal MM, Lambiase LR, et al. (2010). Overuse of acid suppression therapy in hospitalized patients. *South Med J*, 103 (3), 207-11.
- [24] Singh A, Bodukam V, Saigal K, Bahl J, Wang Y, Hanlon A, et al. (2016). Identifying risk factors associated with inappropriate use of acid suppressive therapy at a community hospital. *Gastroenterol Res Pract*.
- [25] Mohebbi L and Hesch K. (2009). Stress ulcer prophylaxis in the intensive care unit. *Proc Bayl Univ Med Cent*, 22(4), 73–376.
- [26] Hugill K. (2017). Preventing bloodstream infection in IV therapy. *Br J Nurs*, 26(14), S4-S10.
- [27] Craig DG, Thimappa R, Anand V and Sebastian S. (2010). Inappropriate utilization of intravenous proton pump inhibitors in hospital practice—a prospective study of the extent of the problem and predictive factors. *QJM*, 103(5), 327-35.
- [28] Ahrens D, Behrens G, Himmel W, Kochen MM and Chenot JF. (2012). Appropriateness of proton pump inhibitor recommendations at hospital discharge and continuation in primary care. *Int J Clin Pract*, 66 (8), 767-773.
- [29] Davis KW, Hanners RE and Lockwood SM. (2017). Implementation of a proton pump inhibitor stewardship program. *Am J Health Syst Pharm*, 74 (12), 932-937.

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