

## Brief Communication

# The Pattern of Intravenous Proton-Pump Inhibitor Utilization at an Academic Medical Center in Riyadh, Saudi Arabia

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## INTRODUCTION

Due to the exceptional efficacy and greater tolerability, the use of proton-pump inhibitor (PPI) has exorbitantly increased and ultimately contributed to their inappropriate and growing overuse.<sup>[1]</sup> The excess use of PPIs is evident from a study that was carried out during 1995–2006 in the United States, wherein PPI treatment (43.9 prescriptions per 1000 visits) greatly outpacing the increase in gastroesophageal reflux disease (GERD) diagnoses (at 16.3 per 1000 visits) during that time period might be due to its availability at over-the-counter.<sup>[2]</sup> Further, the documented use of PPI is doubled between 2002 and 2009, from 30 million to 84 million; however, the absence of documental evidence of gastrointestinal complaints or diagnoses in over 60%

of these visits has developed concerns in the field of health-care sector in the United States.<sup>[3]</sup> In addition to the reports on the excessive use of PPI, several studies have demonstrated its inappropriate use.<sup>[4,5]</sup>

Out of the several formulations of PPI, intravenous (IV) preparations (IV proton-pump inhibitor [IV-PPI]) are most frequently prescribed for hospitalized patients.<sup>[6]</sup> Unnecessary prescribing of PPIs over the parenteral route in hospitalized patients may lead to a greater financial

## ABSTRACT

**Objective:** This study was designed to evaluate the extent of inappropriate utilization of intravenous proton-pump inhibitors (IV-PPIs) and its financial burden in a Middle Eastern tertiary care university hospital. **Methods:** This was an observational, retrospective, cross-sectional study carried out in King Saud University Medical City, Riyadh, Saudi Arabia. During a study period of 6 consecutive weeks, all hospitalized adult patients (age  $\geq 18$ ) who received IV-PPI selected and mapped with their indications. The patient indications analyzed in comparison with the appropriate indications developed based on the evidence from published literature and guidelines. **Findings:** A total of 347 patients were identified, with a mean age of 51.5 years, of which 51.9% were male. Of all the patients who received IV-PPIs, 251 (72.3%), 66 (19%), and 30 (8.7%) received for stress ulcer prophylaxis (SUP), peptic ulcer disease (PUD) or gastroesophageal reflux diseases (GERDs), and upper gastrointestinal bleeding, respectively. Overall, only 110 (31.7%) of the 347 patients received IV-PPIs appropriately. The patients with SUP showed the highest percentage of inappropriate use of IV-PPI (80.59%) compared to PUD/GERD (19%). The total cost of inappropriate prescription of IV-PPI was 585,167 Saudi Riyal (SAR) (156,044 USD). **Conclusion:** There is a high tendency of IV-PPI's inappropriate prescription in our hospital setting. This large-scale inappropriate prescription of IV-PPI in the hospital setting not only may lead to increased financial burden but also expose patients to number of undesired effects.

**KEYWORDS:** *Inappropriate medication usage, intravenous proton-pump inhibitors, prescribing trend*

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burden on hospitals in addition to putting the patient under several medical risks.<sup>[7]</sup> Previous data showed that 25%–75% of hospitalized patients who prescribed IV-PPIs had no appropriate justification, indicating a high rate of inappropriate prescribing of IV-PPIs.<sup>[8]</sup> Kaplan *et al.* reported that IV-PPIs were prescribed appropriately only for 25% of patients with upper gastrointestinal bleeding (UGIB) and for 51% of patients with non-UGIB groups.<sup>[9]</sup> There is dearth of report on the extent of misuse of IV-PPIs across hospitals in Middle Eastern countries. The aim of this study was to evaluate the pattern of IV-PPI utilization in our hospital and assess its financial burden.

## METHODS

This was an observational, cross-sectional study carried out in King Saud University Medical City, a tertiary teaching hospital after obtaining ethical approval (MCST (AU)-COP 1945/RC). Most of the patients treated in this hospital are local citizens but serve as a referral center for the entire country. Medical care in this hospital is monitored by an attending physician under the supervision of clinician at the rank of consultant/specialist with support from medical residents, interns, students, nursing staff, and other health-care professionals.

During a study period of 6 consecutive weeks of March to April of this year, all hospitalized adult patients (age  $\geq 18$ ) who received IV-PPI were screened on a daily basis from the hospital electronic medical records (electronic system for integrated health information). The patients' medication history, demographic data (age and gender), diagnosis, admission and discharge date, PPI regimen and clinical indications, and nothing by mouth status and prescribers' department and specialty were extracted.

A precise list of indications considered appropriate for IV-PPI prescribing was predefined based on an available literature and guidelines. We defined appropriate prescribing (evidence based) for IV-PPIs if a patient received one or more dose/s of IV-PPI for (a) prevention of stress-related mucosal disease bleeding in critically ill and/or mechanically ventilated patients (ASHP guidelines for stress ulcer prophylaxis [SUP]), (b) treatment of active UGIB, and (c) treatment of peptic ulcer diseases (PUDs) or GERD.<sup>[10-14]</sup>

Descriptive statistics (mean with standard deviation [SD], median with interquartile range, frequencies, and percentages) were used to describe quantitative and categorical variables as appropriate.

## RESULTS

A total of 347 patients were identified who received IV-PPI upon hospitalization [Table 1]. The mean age of the patients was 51.5 years (SD  $\pm 19$ ), of which 51.9% were male.

Of all the patients who received IV-PPIs, 251 (72.3%) received it for SUP, 66 (19%) were administered for either PUD or GERDs, and 30 (8.7%) were given for UGIB.

Out of the 251 patients who received IV-PPI for SUP, 157 (62.5%) had indications for PPI (either orally or through IV); only 60 (23.90%) of them were in nil per os (NPO) (nothing by mouth) category and hence deemed fit for IV-PPI appropriately [Table 2]; the other 97 (38.64%) patients were concurrently receiving all other medications orally but received PPI by IV route. The remaining 94 (37.45%) patients out of 251 of this group were administered IV-PPI without its appropriate indication [Table 2]. Therefore, 191 (76%) of the 251 patients in SUP category received inappropriate IV-PPI therapy [Table 3].

In the category of patients (66) who received IV-PPP for PUD or GERD, only 20 (30.3%) of them received IV-PPI appropriately; the remaining 46 (66.7%) patients

**Table 1: Baseline characteristics of the studied patients (n=347)**

n	Variable	Value
1	Age in years	52 $\pm$ 19
2	Gender	
	Female	167 (48%)
	Male	180 (52%)
3	Hospital care	
	ICUs	108 (31.12)
	Non-ICU	239 (68.88)
4	Duration of IV-PPI use in days	8.2 $\pm$ 13.1
5	Length of stay in days	24.6 $\pm$ 2.9

Values are expressed in mean $\pm$ SD, or number (%). SD=Standard deviation, ICU=Intensive care unit, IV-PPI=Intravenous proton-pump inhibitor

**Table 2: Appropriate and inappropriate indications of proton-pump inhibitor**

Patient category (n)	Frequency (%)	
	Appropriate PPI indications	Inappropriate PPI use
SUP (251)	157 (62.5)	94 (37.45)
PUD/GERD (66)	66 (100)	-
UGIB (30)	30 (100)	-
Overall PPI indications (347)	253 (72.91)	94 (27.08)

SUP=Stress ulcer prophylaxis, PUD=Peptic ulcer disease, GERD=Gastroesophageal reflux disease, UGIB=Upper gastrointestinal bleeding

**Table 3: Appropriate and inappropriate use of intravenous proton-pump inhibitor**

Patient category (n)	Frequency (%)	
	Appropriate IV-PPI indications	Inappropriate IV-PPI use
SUP (251)	60 (23.90)	191 (76.09)
PUD/GERD (66)	20 (30.3)	46 (66.7)
UGIB (30)	30 (100)	-
Overall IV-PPI use (347)	110 (31.70)	237 (68.29)

SUP=Stress ulcer prophylaxis, PUD=Peptic ulcer disease, GERD=Gastroesophageal reflux disease, UGIB=Upper gastrointestinal bleeding, IV-PPI=Intravenous proton-pump inhibitor

were concurrently receiving all other medications orally but received PPI intravenously. However, in the third category of patients with UGIB, all 30 patients received IV-PPI therapy appropriately [Table 3].

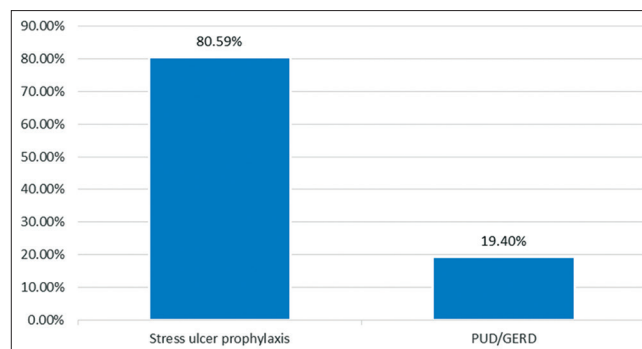
Overall, a total of 110 (31.7%) of the 347 patients received IV-PPIs appropriately [Table 3]. Most of the inappropriate use of IV-PPI was found in patients with SUP category (80.59%) compared to PUD/GERD (19%) [Figure 1]. No inappropriate use of IV-PPI was noted in patients with UGIB.

The total cost of drug acquisition of IV-PPI (pantoprazole) in this hospital was 33 SAR/vial. The mean duration of IV-PPI used for each patient was 8.2 days out of 40 days of duration of the study. The number of patients who received IV-PPI inappropriately during this period was 237. Assuming a similar pattern of prescription of IV-PPI to be continued throughout the year, the extrapolated cost per year will reach approximately 585,167 SAR (156,044 USD). The cost of inappropriate prescription of IV-PPI was significantly higher than the cost of appropriate IV-PPI use.

## DISCUSSION

The result of this retrospective study describes a high trend of inappropriate prescription of PPIs through parenteral route in Riyadh hospital. Patients with SUP were found with an excessively high percentage of inappropriate prescription, whereas all patients with UGIB had appropriate indications for the prescription of IV-PPI as all of them were in NPO category.

The use of PPIs has to be regulated based on ASHP guidelines that prohibit routine prescription of this class of agent to avoid both health-related adverse impact and increased treatment cost. The guidelines permit the use of IV-PPI in SUP only in critically ill patients with specific risk factors, however, despite stringent regulations, several studies have shown large-scale inappropriate prescription of IV-PPIs even in patients



**Figure 1:** Distribution of inappropriate use of intravenous proton-pump inhibitors based on patient category

who were not critically ill,<sup>[9]</sup> while there are also studies that documented a decline in the use of PPIs after the introduction of SUP criteria from 100% to 38% in some of the hospitals.<sup>[15]</sup> Retrospective data obtained from the medical record in this study showed that 80.59% of patients who received inappropriate prescription were in SUP category. Our outcomes are congruent with another study carried out in Riyadh few years back.<sup>[16]</sup>

UGIB is potentially a life-threatening condition that warrants the use of medications that can elicit pharmacological effects promptly. A meta-analysis of randomized controlled trials reported favorably for the use of IV-PPI in alleviating the rate of rebleeding and surgical intervention compared to histamine 2 receptor antagonist and placebo in Asian trials.<sup>[17]</sup> Hence, the use of PPI by IV route is recommended,<sup>[18]</sup> and all patients in this study who were categorized in the UGIB group received PPI-IV and considered their use as “appropriate.”

One of the interesting observations of this study was that the inappropriate prescription of IV-PPI was not limited to one specialty. Almost a similar number of inappropriate prescriptions of IV-PPIs were written by cardiologist, nephrologist, rheumatologist, and oncologist. There is no documented reason for the prescription of IV-PPI given by a physician in the medical record. It is speculated that the cardiologist would have written to obviate the aspirin-induced gastric irritation (rare at antiplatelet dose) or to prevent gastrointestinal bleeding in oral anticoagulant prophylactic therapy.<sup>[12]</sup> Nephrologist may usually write to ameliorate the gastric upset induced by dialyzing fluid in patients under dialysis, while rheumatologist to overcome the gastric ulcer due to chronic nonsteroidal anti-inflammatory drug therapy and oncologist may write to prevent blood dyscrasia from chemotherapy. Although a physician would have added the PPIs in the prescription as a prophylactic measure for their patients with the right intent, it was written without evaluation of

the extent of risk. Therefore, the inappropriate addition of IV-PPIs has not only caused an increased risk of infections and other adverse effects of PPIs but also has resulted in increased financial burden on the hospital without producing any benefit to the patient.

The rightful utilization of resources is essential for promoting rational prescribing. Hence, it is proposed to improve the prescribing habits of the physician by developing standard criteria at the level of hospital with active participation of prescribers. An active health-care team will not only reduce the unnecessary financial burden on the hospital but also provide the best health-care services to the patients.

### AUTHORS' CONTRIBUTION

Yahya Ali Mohzari and Ahmed Alsaegh were responsible for gathering data and developing initial draft of the manuscript. Sulafah N. Al Shanawani participated in data curation, analysis, and interpretation. Amani A. Albraiki was tasked to screen the data and filter data with missing information, while Syed Mohammed Basheeruddin Asdaq was responsible for conceptualization, designing, analyzing, and interpreting the results as well as final review of manuscript.

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### Conflicts of interest

There are no conflicts of interest.

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