Validity and Execution of Stress Ulcer Prophylaxis in Surgical Patients: A Single-Center, Retrospective Cohort Analysis in Islamabad, Pakistan

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KEYWORDS
stress ulcer prophylaxis; proton pump inhibitors; PPI; NSAID; surgical prophylaxis; real-world study; Pakistan.

ABSTRACT
Introduction: Stress ulcer prophylaxis (SUP) is recommended in critically ill patients to prevent stress-related mucosal damage, however, there is inconsistent adherence to established standards and guidelines for those who receive SUP medications outside of this patient group. The present study aimed to evaluate the appropriateness of SUP medications for surgical patients at the tertiary care hospital in Islamabad, Pakistan.
Methodology: A 1-year, retrospective cohort study was conducted, using a convenience sampling approach, involving patients undergoing surgical procedures at the Surgical Wards of a tertiary care hospital located in Islamabad. Data collection was performed using a pre-designed checklist, with main areas including demographic characteristics, data on their presenting complaint, SUP medications (dosage, route of administration and duration) and presence of stress ulcer risk factors.
Results: n=418 patient records were assessed: the majority of the patients were female (62.6%; n=262), with a mean age was 53.6±11.7 years, treated at the General Surgery department (81.8%; n=342). All patients managed for SUP were prescribed PPIs; the most commonly used PPI was omeprazole, both orally (37.7%; n=158) and parenterally (39.7%; n=166). The majority of patients (72.2%; n=302) were prescribed SUP for an appropriate indication or an associated risk. 46.1% (n=193) received SUP as a discharge medication with no records showing a follow-up, and there was no clear evidence that suggested that SUP had been stopped.
Conclusions: This study highlights the irrational prescribing of PPIs in non-critical patients and the improper continuing of PPI prescriptions after discharge in a real-world setting, indicating the need to address suggested protocols for rationalizing the use of SUP and limiting the use of PPIs for appropriate purposes.

1. Introduction

Patients undergoing surgery are susceptible to stress ulcers (SU), which have the potential to result in clinically significant gastro-intestinal (GI) bleeding (CIB) [1]. SUs may affect individuals who have had severe stressful events – such as multiple traumas, sepsis, major surgeries, multiple organ failure (MOF) or severe heatstroke – in their past medical history [2]. Although the pathogenesis of SU is not fully understood, patients may be more susceptible to SU and disruption of the gastric mucosal barrier in case of splanchnic hypoperfusion, reduced microcirculation, and a general pro-inflammatory state [3]. On the other hand, stress-related mucosal disease (SRMD) is most frequently occurring in intensive care unit (ICU) patients. During surgical procedures, inpatients who become anxious due to trauma, pain, or starvation are more likely to encounter SRMD or subsequent GI hemorrhage. Generally, proton pump inhibitors (PPIs; such as pantoprazole, omeprazole, esomeprazole) and histamine-2 receptor antagonists (H2RAs; such as famotidine and ranitidine) are used in stress ulcer prevention (SUP) [4, 5]. The baseline risk for GI bleeding and adverse pharmacological events may have an impact on the ratio of SUP's benefits to risks (6). In patients at >4% risk for CIB, a recent guideline conditionally recommended using SUP (ideally in conjunction with a PPI); however, it did not support SUP usage in patients at ≤4% risk [7].

There is inconsistent adherence to established standards and guidelines for those who receive SUP medications. The widely recognized guidelines for SUP have been issued by the American Society of Health-System Pharmacists (ASHP) (8); according to those recommendations, patients who are critically ill having a higher risk of GI bleeding, and therefore should receive SUP. An ICU stay of ≥7 days, sepsis, occult GI bleeding, and use of glucocorticoids are considered minor risk factors for GI bleeding; on the other hand, coagulopathy, history

of GI ulcerations, mechanical ventilation for ≥48 hours, spinal cord injury, burn injuries or traumatic brain injuries are considered major risk factors for GI bleeding [8-10]. The benefits of SUP, outside of these recommended critical care situations, are not well supported by currently available evidence and research. There are hazards associated with the inappropriate prescribing of SUP medicines; the prevention of GI bleeding routinely in non-critical patients is often unnecessary and inappropriate, considering the higher chances of adverse drug events such as cardiac ischemia and nosocomial infections, as well as potential impacts on death in the critical patients [11].

While the misuse of SUP medications is prevalent in Pakistan, limited epidemiological information exists regarding the prescribing practices of SUP medications for surgical inpatients and the factors influencing their prescription. Consequently, it is imperative to investigate the current state of SUP prescription patterns aiming to establish a foundation for local guidelines, and future SUP stewardship in Pakistan. Hence, the current study aimed to evaluate the appropriateness of SUP medications for patients undergoing surgical procedures in a tertiary care hospital in Pakistan. Our initial hypothesis was to suggest a substantial prevalence of inappropriate SUP prescribing patterns among surgical patients.

2. Materials and Methods

2.1. Study design, study setting

A retrospective cohort study was conducted, using a convenience sampling approach, at the tertairy care hospital in Islamabad, Pakistan. The study spanned over a 12-month period (2022.01.01-2022.12.31).

2.2. Inclusion and exclusion criteria, data collection

Data collection was carried out at Surgical Wards (i.e. general surgery, orthopedic surgery, plastic surgery, the ear, nose and throat (ENT) department and gynecological surgery) of the tertiary-care hospital. Patients aged ≥18 years, admitted to the Surgical Wards of the hospital for more than 2 days during the study period were included in the data analysis. The exclusion criteria were the following: patients diagnosed with active GI bleeding, gastric ulcer, active peptic or duodenal ulcer at the time of admission or during their hospital stay, and the patients who received acid-suppressing therapy as treatment.

A pre-designed checklist was used for the data collection, which included four main sections; the first section included inquiries for the demographic characteristics of the pa-tients, i.e. their gender, age, and duration of hospital stay. The second section collected data on the presenting complaint or disease state of the patient. The third section collected data on the medications utilized, dosage, route of administration, and duration of the SUP regimen, to allow for the appropriateness of the SUP to be determined. Finally, the fourth section collected data on the presence of stress ulcer risk factors.

2.3. Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki (and its later amendments), and national and institutional ethical standards. The ethical approval (IRB#0160-23) for the study was received from the Institutional Review Board of Shifa International Hospital and the GSRMC (Graduate Studies and Research Management Council) of Shifa-Tameer-e-Millat University.

2.4. Sample size determination, statistical analysis

Sample size determination was carried out considering a 50% prevalence of SUP in Pakistan, as there is a lack of prior research in the area under investigation [12]. By con-sidering a margin of error of 5% at a 95% confidence level, the required sample size for this research was set at n=385. However, during the data collection, additional data became available, therefore an adjustment was made to the required sample size. Hence, a total of n=418 patient records were assessed retrospectively, from which, data was extracted for the purposes of the study.

During descriptive statistics of the respondents' initial characteristics, all continuous variables were expressed as means and standard deviations (means±SD), whereas cate-gorical variables were expressed as frequencies (n) and percentages (%). Data analysis was performed using SPSS for Windows version 24.0 (IBM Inc., Chicago, IL, USA).

3. Results

During the 12-month retrospective cohort analysis, a total of n=418 patient records were assessed; the demographic characteristics, medical history and data related to their hospitalization is summarized in Table 1. The majority of the patients were female (62.6%; n=262), with a mean age was 53.6±11.7 years. Among the patients who received SUP after admission to the Surgical Ward, 47.6% (n=199) patients ended up staying in the surgical ward for less than 3 days. SUPs were most commonly prescribed in general surgery (81.8%; n=342). The major indications for surgical intervention were acute injuries (19.3%; n=81) or other chronic conditions (33.4%; n=140). Data indicates that all the patients managed for SUP were prescribed PPIs; the most commonly used PPI was omeprazole, both orally (37.7%; n=158) and parenterally (39.7%; n=166) (Table 2).

Table 1. Demographic characteristics of patients admitted at the Surgical Wards of the tertiary care hospital (n=418)

Patients' characteristics		n (%)	Mean ± SD
Gender	Male	156 (37.3)	
	Female	262 (62.6)	
Age			53.6±11.7
Length of Hospital Stay	< 3 days	199 (47.6)	
	>3 days	83 (19.8)	
	3 days	136 (32.5)	
Specialty of the Surgical Ward	General surgery	342 (81.8)	
	Orthopedic surgery	12 (2.8)	
	ENT Surgery	48 (11.4)	
	Plastic Surgery	0 (0.0)	
	Gynecological Surgery	16 (3.8)	
Medications taken by patients at the time of admission	NSAIDs	11 (2.6)	
	Glucocorticoids	6 (1.4)	
	SSRI	19 (4.5)	
	Anticoagulants	41 (9.8)	

ENT: ear, nose and throat; NSAID: non-steroid anti-inflammatory drugs; SSRI: selective serotonin reuptake inhibitor

Table 2. Drugs administered for stress ulcer prevention (SUP), their dosage forms and doses used

	SUP	Dosage form	Dose	n (%)
PPIs	Omeprazole	Capsule	40 mg	158 (37.7)
	Omeprazole	Injection	40 mg	166 (39.7)
	Esomeprazole	Tablet	20 mg	42 (10.0)
	Pantoprazole	Tablet	40 mg	31 (7.4)
	Dexlansoprazole	Capsule	30 mg	19 (4.5)
	Lansoprazole	Capsule	30 mg	2 (0.4)

PPI: proton pump inhibitor

Table 3 illustrates the appropriateness and route of administration of the SUP regimen. The majority of the patients (60.2%; n=252) received SUP orally. The majority of patients (72.2%; n=302) were prescribed SUP for an appropriate indication or an associated risk. As the study was conducted in patients treated at the surgical ward and non-critically ill patients, the major indications observed for SUP were prolonged hospital stay (27.4%; n=83), patients who had major surgery (18.8%; n=57) and renal dysfunction (16.2%; n=49). Among the patients, 46.1% (n=193) received SUP as a discharge medication with no records showing a follow-up, and there was no clear evidence that suggested that SUP had been stopped.

Table 3. Route of administration of stress ulcer prevention (SUP) regimen and their appropriateness

Route of administration for the SUP regimen	
	n (%)
Oral	252 (60.2)
Parenteral	166 (39.7)
Appropriateness of prescribing SUP, according to indication and the risk factors the patients presented with	
Appropriate	302 (72.2)
Non-appropriate	116 (27.7)
Indications for SUP	
High doses of corticosteroid treatment	34 (11.2)

History of GI ulceration or bleeding	46 (15.2)
Renal dysfunction	49 (16.2)
Prolonged hospital stay	83 (27.4)
Major surgery	57 (18.8)
Sepsis or septic shock	22 (7.2)
Chronic use of NSAIDs	11 (3.6)

SUP: stress ulcer prevention; NSAIDs: non-steroid anti-inflammatory drugs

4. Discussion

The outcomes of the present study evaluated the details and rationality of using SUP medications for patients undergoing surgical procedures in a tertiary-care hospital. SUP should not be commonly suggested in non-critically ill surgical and medical patients; in-stead, it should be limited to patients exhibiting a higher chance of bleeding [12]. Despite the available guideline, more than 22%–88% of those admitted outside the ICU continue to receive SUP without being at risk of SRMD or consequent GI bleeding, depicting the pattern of the inappropriate use of PPIs [13]. In the present study, more than 70% of patients were prescribed SUP for appropriate indications or associated risks. A previous study re-ported that around 48% of SUP usage was not appropriate – according to the ASHP crite-ria – and was considered medicine overuse [14]. Previous studies have shown that more than 60% of inpatients in the surgical department were found to have had inappropriate PPI prescriptions for SUP [15, 16]. Preceding research has shown that inappropriate SUP medication is more frequently observed in patients referred to surgical wards, with ortho-pedic and general surgeons prescribing the majority of PPIs [15]. A similar trend of pre-scribing SUPs was observed in the present study in which, more than 80% of PPIs were prescribed in general surgery. In the current study, the majority of the patients received SUP orally. In the study of Liu et al., 62% of the patients had unnecessary intravenous treatment, where it would have been more appropriate to use oral formulations [2]. Wijaya et al. showed that the rate of omeprazole given by inappropriate methods was extremely high (96.7%) [15], which was at a far greater rate than what we found in the current sam-ple. Oral PPIs are equally effective as injectable forms at comparable doses, but are addi-tionally less expensive and associated with fewer complications due to intravenous ad-ministration. This emphasizes the way skilled pharmacists must step in and recommend the most appropriate strategies for inpatients to administer medications [17].

In the current study, all the patients managed by SUP were prescribed PPIs; while the most commonly used PPI among the rest was omeprazole. In their report, Liu et al. noted that 94% of patients received esomeprazole, with the most frequent dosage at 40 mg, once daily [2]. PPIs are now among the most frequently prescribed medications, and their use has been rising globally in recent years [18]. There is unquestionable data that hospital-ized patients are overusing PPIs [17]; it is reported that approximately 25% to 70% of hos-pitalized patients are prescribed PPIs without a valid medical reason [19]. This indicates that every year, over £2 billion is spent needlessly on PPIs worldwide putting additional financial burdens on both individuals and healthcare systems [20]. Inappropriate PPI use may raise the risk of adverse effects; they have been reported to raise the risk of hospi-tal-acquired pneumonia and community-acquired pneumonia by making it easier for bacteria to infect the upper GI tract; furthermore, the GI tract's capacity for absorption may also be impacted by acid suppression. Long-term PPI use has been linked to Vitamin B12, iron, calcium and magnesium malabsorption [21]. In the present study, it was observed that longer hospital stays were associated with a higher risk of improper SUP prescrip-tions for inpatients. According to Liu et al, the length of hospital stay may be a major con-tributing factor to SUP usage. However, research has also indicated that - in contrast to the present study's findings - the percentage of appropriately using SUPs has increased while the percentage of using SUP improperly has declined in extended hospital stays [2].

The present study possesses some limitations: firstly, the data was collected from a single hospital in Islamabad, Pakistan, which limits the generalizability of the findings to other clinical settings. Secondly, this study is conducted retrospectively and the sample was not randomly selected. Variables that affect the choice of PPI and H2RAs were not addressed in full, and not all confounding variables could be controlled for properly, be-cause of insufficient data on patients prescribed SUP.

5. Conclusions

This study highlights the irrational prescribing of PPIs in non-critical patients and the improper continuing of PPI prescriptions after discharge in a real-world setting, indi-cating the need to address suggested protocols for rationalizing the use of SUP and limit-ing the use of PPIs for appropriate purposes. Furthermore, there is a need

for the develop-ment of guidelines both locally and internationally to ensure safe prescribing patterns of SUP in both critical and non-critical patients.

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