

Original Research Article

Appropriate use of stress ulcer prophylaxis in non-critically ill patients in a tertiary academic center: A retrospective study

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Sent for review: 2 August 2024

Revised accepted: 11 June 2025

Abstract

Purpose: To investigate the appropriate use of stress ulcer prophylaxis (SUP) in non-critically ill hospitalized patients.

Methods: This study was a retrospective cohort study that included all non-critically ill adult patients ($n = 369$) admitted to the General Medical Wards of King Abdulaziz Medical City in Riyadh, Saudi Arabia. The patients were administered proton pump inhibitors such as esomeprazole and omeprazole; histamine-2 receptor antagonists such as ranitidine; and cytoprotective agents such as sucralfate in different dosage regimens. Baseline characteristics, risk factors, and acid-suppressive therapy were evaluated based on therapeutic guidelines of the Society for Health-System Pharmacists (ASHP) on stress ulcer prophylaxis.

Results: A total of 369 patients were included in the study with mean age of 61.65 ± 18.83 years. Diabetes mellitus was the most encountered comorbidity 169 (45.8 %). Dual antiplatelet use was the most encountered medication 79 (21.94 %) with only 55 (14.9 %) patients meeting the criteria of the American Society for Health-System Pharmacists (ASHP) Therapeutic Guidelines on stress ulcer prophylaxis. Proton-pump inhibitors were the most used 358 (97.02 %) in acid suppressive therapy.

Conclusion: Inappropriate use of stress ulcer prophylaxis is high in this study leading to increase in medication adverse effects. The findings of this study will help in implementing a comprehensive protocol to closely follow up on all admitted patients who use stress ulcer prophylaxis for certain indications.

Keywords: Stress ulcer prophylaxis, Proton pump inhibitors, Acid suppressive therapy

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INTRODUCTION

Stress ulceration is an aggravation of the mucosal injuries of the stomach and/or duodenum that leads to gastric drainage when

left untreated [1]. Though the exact pathogenesis is unknown, stress ulcer develops in an acidic mucosa with a pH of 6.5. This drop in mucosal pH is caused by increased mucosal ion permeability and a defect in the neutralizing

ability, resulting in a high concentration of luminal hydrogen ions (H^+) [2]. The American Society for Health-System Pharmacists (ASHP) Therapeutic Guidelines on Stress Ulcer Prophylaxis addressed the possibility of using stress ulcer prophylaxis (SUP) in non-critically ill patients with risk factors for bleeding, such as transplantation [3]. Stress ulcer prophylaxis is used to prevent stress-related bleeding from gastric mucosa [3].

Previous randomized controlled trials (RCTs) revealed that bleeding was significantly ($p < 0.001$) less frequent with antacid prophylaxis compared to placebo [3,4]. However, the guidelines focused mainly on high-risk patients in Intensive Care Unit (ICU) settings and approved the use of Stress Ulcer Prophylaxis (SUP) head trauma with Glasgow Coma Score of ≤ 10 or inability to follow simple commands, bleeding disorders (defined as platelet count < 50 per mm^3 , International Normalized Ratio (INR) > 1.5 or Partial Thromboplastin Time (PTT) $\times 2$ baseline), burns affecting > 35 % of total body surface area, partial hepatectomy, liver or kidney transplantation, multiple trauma with injury severity score of ≥ 16 , spinal cord injury, liver failure, history of gastric ulceration or bleeding within one year prior to admission, and presence of at least two of the following including sepsis, ICU length of stay of more than one week, occult or overt bleeding for six days or more, and corticosteroid therapy (hydrocortisone > 250 mg, methylprednisolone > 50 mg, prednisone > 60 mg, or dexamethasone > 10 mg) [3].

Several drugs are used for the management/prevention of stress ulcer, which include Proton Pump Inhibitors (PPIs), histamine-2 receptor antagonists (H_2 RAs), and cytoprotective agents (Sucralfate) [3]. Previous studies showed that there was no significant difference in efficacy between H_2 RAs, cytoprotective agents and some proton pump inhibitors when used as SUP in critically ill patients [5]. However, a systematic review and meta-analysis of 14 trials with 1,720 critically ill patients showed that PPIs are more effective than H_2 receptor antagonists in preventing gastrointestinal (GI) bleeding [6].

There are a few studies that support the utilization of SUP in non-critically ill patients, probably because of the low occurrence of GI bleeding. It is, however, over-prescribed without clear indications in non-critically ill patients, and thus may contribute to numerous unfavorable adverse effects, such as osteoporosis, *Clostridium difficile* infection and pneumonia [7]. A prospective observational study ($n = 285$) conducted in three general medical wards at the

University Malaya Medical Center (UMMC), a Tertiary Teaching Hospital in Malaysia, found that 56 (19.6 %) patients received SUP and most of them (96.4 %) were using SUP inappropriately. Also, 35.7 % of these patients received the wrong SUP regimens; either the wrong dose, the wrong frequency, or the wrong route of administration [8]. Following patients' discharge from the hospital, 28.6 % were discharged with SUP prescription without proper indication, with ranitidine being the most prescribed drug [8].

A prospective observational ($n = 255$) study conducted in the General Surgery Department of the University Hospital of Lausanne, a Tertiary Teaching Hospital in Switzerland, discovered the abuse of PPIs for SUP in non-critically ill general surgery patients, in which 53 (79 %) received SUP without risk factors, 138 (54 %) received PPI, while 129 patients (94 %) continued esomeprazole as a SUP medication, even after discharge [9]. Another retrospective cohort study ($n = 545$) conducted among non-critically ill patients who were admitted to the Internal Medicine Teaching Service at Morristown Memorial Hospital in New Jersey, found that 32.1 % to 54.9 % received SUP without proper indication based on the criteria they applied [10]. A continuous evaluation of SUP in non-critically ill patients is thus necessary to lower risk and promote rational drug use. This study investigated the appropriate use of stress ulcer prophylaxis (SUP) in non-critically ill hospitalized patients.

METHODS

Study design and setting

This was a retrospective cohort study conducted at King Abdulaziz Medical City-Central Region (KAMC-CR), a Tertiary Care Hospital with more than 1500 beds located in Riyadh, Saudi Arabia. It provides health care to patients in different specialties such as internal medicine, surgery, pediatrics, obstetrics and gynecology, critical care, oncology/hematology, cardiology, emergency medicine, psychiatry, genetics and precision medicine, and dental services. Data was collected from January 2017 to January 2018. Ethical approval was obtained from the Institutional Review Board of King Abdullah International Medical Research Center (approval no. IRBC/0289/19).

Inclusion criteria

All non-critically ill patients admitted to the general medical wards > 18 years old and on

PPIs such as esomeprazole and omeprazole; H₂RAs such as ranitidine; or cytoprotective agents such as Sucralfate in different dosage forms and frequency were enrolled in the study.

Exclusion criteria

Patients on SUP for Zollinger-Ellison syndrome, acute upper GI bleeding, erosive esophagitis, *Helicobacter pylori* infections, gastric or duodenal ulceration, gastroesophageal reflux disorders (GERD), regularly scheduled use of SUP prior to admission, patients admitted in the ICU or transferred from the ICU to the general medical wards, and pregnant women were excluded from the study.

The evaluation was based on the American Society for Health-System Pharmacists (ASHP) therapeutic guidelines on stress ulcer prophylaxis [3].

Sample size

All patients who were admitted to King Abdulaziz Medical City-Central Region (KAMC-CR) and met the inclusion criteria from January 2017 to January 2018 constituted the sample size.

Statistical analysis

Data was analyzed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA). Categorical variables were presented in frequency and percentages. Continuous variables were presented as mean $\pm$ standard deviation (SD).

RESULTS

Baseline characteristics

A total of 369 patients with a mean age of 61 $\pm$ 18 years (56.91 % females, 43.09 % males), who received SUP, were enrolled. Diabetes mellitus was the most frequent comorbidity, 169 (45.80 %), dual anti-platelet use of aspirin and clopidogrel was mostly prescribed, 79 (21.94%; Table 1.

Acid suppressive therapy (AST)

The most used SUP was PPIs (96.21 %). A total of 306 patients (82.93 %) received esomeprazole and 49 patients (13.28 %) received omeprazole (Table 2).

Table 1: Baseline characteristics

Characteristic	N (%)
Gender	
Male	210 (56.91%)
Female	159 (43.09%)
Age (years; mean $\pm$ SD)	61.65 $\pm$ 18.83
Comorbidities	
Diabetes (DM)	169 (45.80%)
Dyslipidemia (DLP)	84 (22.76%)
Hypertension (HTN)	154 (41.73%)
Heart Failure (HF)	45 (12.20%)
Myocardial Infarction (MI)	20 (5.42%)
Coronary Artery Disease (CAD)	92 (24.93%)
Coronary Artery Stenosis (CAS)	11 (2.98%)
Deep Vein Thrombosis (DVT)	3 (0.81%)
Pulmonary Embolism (PE)	10 (2.71%)
Atrial Fibrillation (A. fib)	33 (8.94%)
Chronic Kidney Disease (CKD)	39 (10.57%)
Hemodialysis (HD)	21 (5.69%)
Stroke	32 (8.67%)
Systemic Lupus Erythematosus (SLE)	6 (1.63%)
Medications	
Anticoagulation use	45 (12.20%)
Non-steroidal anti-inflammatory (NSAIDs) use	17 (4.61%)
Antiplatelet use	77 (21.27%)
Aspirin	69 (19.06%)
Clopidogrel	13 (3.59%)
Ticagrelor	1 (0.28%)
Dual antiplatelet use	
Aspirin and Clopidogrel	79 (21.94%)
Anticoagulants and antiplatelets use	16 (4.44%)

Table 2: Acid suppressive therapy

Medication	N (%)
Proton Pump Inhibitors (PPIs)	358 (97.02%)
Esomeprazole	306 (82.93%)
Omeprazole	52 (14.09%)
Dose/Frequency	
20 mg orally once daily	69 (18.70%)
40 mg orally once daily	247 (66.94%)
20 mg intravenous once daily	2 (0.54%)
40 mg intravenous once daily	36 (9.76%)
80 mg intravenous once daily	3 (0.81%)
Others	1 (0.27%)
Ranitidine	9 (2.72%)
Dose/Frequency	
150 mg orally twice daily	6 (1.63%)
Intermittent bolus or infusion: 50 mg every 6 to 8 h (maximum of 400 mg/day)	2 (0.54%)
Others	1 (0.27%)

Table 3: Risk factors for developing stress ulcer

Risk factor	N (%)
History of gastric ulceration or bleeding during the year before admission	6 (1.63%)
Occult or overt bleeding for ≥ 6 days	7 (1.897%)
Coagulopathy	15 (4.1%)
Brain trauma (head injury with Glasgow coma score of ≤ 10 or inability to obey simple commands, Multiple traumas with Injury Severity Score of ≥ 16)	4 (1.08%)
Hepatic failure	19 (5.15%)
Hepatic/Renal transplant	10 (2.7%)
Steroid use (Hydrocortisone > 250 mg, Methylprednisolone > 50 mg, Prednisone > 60 mg, Dexamethasone > 10 mg)	4 (1.1%)
Sepsis	6 (1.63%)
Met ASHP guideline criteria (less than two risk factors, Strength of evidence = B, patients with two or more risk factors, strength of evidence = D)	55 (14.9%)
1 risk factor	39 (10.6%)
2 risk factors or more	16 (4.3%)

Risk factors for developing stress ulcers

The most commonly documented risk factor for developing stress ulcer was coagulopathy (3.84 %), and only 55 (14.9 %) received SUP appropriately and met the ASHP therapeutic guidelines on SUP, while 314 patients (85.1 %) received SUP inappropriately (Table 3).

DISCUSSION

Inappropriate use of SUP has been revealed in previous studies [8-10]. This has led to higher risk incidence, adverse effects, and poor rational drug use. This study investigated the appropriate use of stress ulcer prophylaxis (SUP) in non-critically ill hospitalized patients at King Abdulaziz Medical City-Central Region (KAMC-CR) in Riyadh, Saudi Arabia. The results revealed inappropriate use of PPIs as SUP in 85.1 % of patients. However, only 14.9 % met the criteria of the ASHP therapeutic guidelines on stress ulcer prophylaxis, while the most frequent PPI used was esomeprazole. These results were similar to previous findings at Dayton Veteran Affairs Medical Center (DVAMC) which found that SUP was documented in 32 % of patients, but only 10 % met the criteria of the American Society for

Health-System Pharmacists (ASHP) therapeutic guidelines on stress ulcer prophylaxis while the most frequently prescribed PPI regimen was pantoprazole 40 mg once daily [11].

A similar study conducted among 157 patients revealed the overuse of AST without proper indication (72.2 %) and no indication (52.1 %), while the most frequent AST prescribed were proton pump inhibitors [12]. Overuse of AST was also found in 226 patients admitted to the General Medical Nursing Unit of an Urban Community Teaching Hospital at the Hospital of Saint Raphael, New Haven, Connecticut, USA [13]. Furthermore, at a Lebanese Health Care Center, 67 % received SUP without appropriate indication [15]. These findings posit that inappropriate use of SUP is becoming increasingly prevalent among prescribers.

Although prescribed, inappropriate use has been documented in patients with extremely low risk for gastrointestinal bleeding [16]. As a result, there has been a concerted effort to address the irrational use of SUP in non-critically ill patients. In a previous study, the rate of inappropriate SUP use reduced significantly from 85 to 50 % in patients admitted to the Internal Medicine ward

after interventions and discussions with the medical residents about the inappropriate use of SUP [17]. Thus, health policymakers may find this efficient in combating the inappropriate use of SUP in Saudi Arabia.

Limitations of the study

This study has some limitations, which include, small sample size, single center, and the retrospective nature of the study design.

CONCLUSION

Inappropriate use of stress ulcer prophylaxis is high in this study leading to high medication cost and adverse effects. The findings of this study could help in implementing a comprehensive protocol to closely follow up on all admitted patients who use stress ulcer prophylaxis for certain indications.

DECLARATIONS

Acknowledgment/Funding

None.

Ethical approval

The Institutional Review Board of King Abdullah International Medical Research Center approved this study (approval no. IRBC/0289/19).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them. AIMolaiki and Mohammed Alessa contributed equally to this study.

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