Research Article

Cost Saving of Stress Ulcer Prophylaxis Used in Non-Intensive Care Unit (ICU) Inpatients

Hening Pratiwi, Laksmi Maharani, dan Ika Mustikaningtias

Pharmacy Department, Faculty of Health Sciences, Jenderal Soedirman University, Purwokerto, Indonesia

Correspondence: Hening Pratiwi
Email: hening.pratiwi@ymail.com

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ABSTRACT: *Stress ulcer prophylaxis (SUP) is largely prescribed to ICU and non-ICU patients. SUP, an acid-suppressive drug, is overused in hospital settings mainly due to inadequate prescriptions in low-risk patients. In this context, the appropriate administration of SUP needs to be analyzed, and the potentially saved money from reducing excessive use can thereby be quantified. This study was intended to calculate potential cost savings in inappropriate SUP therapy in non-ICU inpatients. With a non-experimental retrospective design, it analyzed medical records and details obtained from the financial department of "X" hospital in Purwokerto, Indonesia. The data were collected from 80 non-ICU inpatients in May 2015, which were selected by purposive sampling. We calculated potential cost savings by referring to the American Society of Health-System Pharmacists (ASHP) guidelines that had been modified by Zeitoun (2011) for stress ulcer prophylaxis in non-ICU inpatients. The results showed that inappropriate indications and doses were found in 32.5% and 18% of selected patients, respectively. Before the cost-saving calculation, patients had to spend USD 2,411. However, after the analysis eliminated unnecessary SUP use, this number was proven to be potentially decreased by USD 512 to only USD 1,899. Based on the Wilcoxon Sign Rank Test result (p = 0.000 (≤ 0.05)), there was a significant difference between the total cost before and after the application of modified ASHP guidelines for appropriateness. After a thorough assessment, we concluded that the treatment cost could be reduced by identifying and excluding inappropriateness in SUP therapy.*

Keywords: *stress ulcer prophylaxis; non-ICU; potential cost saving*

1. Introduction

The cost of health services, especially pharmaceutical spending, increases every year. It appears to be inevitable as the population grows and patterns of diseases and treatments constantly change. The large size of the patient population is likely to increase drug use, including new drugs traded at a high price, and affect courses of medication [1]. Drug use can be rational if patients receive therapy fitting to their clinical needs and appropriate doses at the lowest possible cost. Also, therapy must respect the choices that patients have made. A component of the principles of rational drug use is considering the drug cost. Most importantly, health care providers are obligated to be able to choose cost-effective drugs for patients.

More than 50% of drugs are reportedly administered with inappropriate indications and doses, indicating ubiquitous cases of irrational drug use. The most common types of irrational drug use are polypharmacy and non-compliance with the guidelines. Moreover, 14.7% of 102 geriatric patients exhibit side effects of drug use that lead to hospitalization. There have been several studies highlighting many stress ulcer prophylaxis (SUP) prescribed, especially in Indonesia. Ninety-three percent of ICU patients diagnosed with stroke receive SUP, especially ranitidine [2].

Stress ulcers are single or multiple gastroduodenal mucosal defects that cause a broad range of clinical manifestations from superficial mucosal erosions or mild-severe ulceration to life-threatening bleeding. The pathophysiology of stress ulcers is related to a reduction in mucosal blood flow or a breakdown in other normal mucosal defense mechanisms in conjunction with the injurious effects of acid and pepsin on the gastroduodenal mucosa. Since acid does appear to be involved in the pathogenesis of these lesions, acid-suppressive regimens have the potential to prevent stress ulcers [3]. Stress ulcer prophylaxis is commonly used to decrease gastrointestinal bleeding in critically ill patients. However, SUP is commonly used in non-critically ill patients despite little evidence to support it [4].

Stress ulcers are managed by acid-suppressive drugs, such as Histamine-2 blockers (H2 blockers) and Proton Pump Inhibitor (PPI). The most commonly used H2 blockers are cimetidine and ranitidine [5]. PPI is more potent, such as omeprazole, lansoprazole, and pantoprazole. Several consensus guidelines for SUP have been published. The most recent guidelines available were published by The American Society of Health-System Pharmacists (ASHP) in 1999. These guidelines provide evidence-based recommendations for non-critically ill medical and surgical patients, critically ill patients, and ICU pediatric populations. Zeitoun (2011) has also modified these for non-critically ill patients [3].

Stress ulcer prophylaxis is largely prescribed in ICU and non-ICU patients. Scagliarini et al. (2005) have found that SUP is frequently overused in hospital settings because of inadequate prescriptions in low-risk patients. Inappropriate use of SUP will expose patients to potential adverse effects, such as Clostridium difficile-associated diarrhea, community-acquired pneumonia, malabsorption, osteoporosis, and hip fracture. Previous studies have shown that 56% to 75% of general medicine patients begin inappropriate use of SUP in the hospital [6]. A retrospective chart review of medical and surgical ICU patients shows that 80% of patients transferred from the ICU continued to receive SUP (60% is inappropriate SUP), and 24.4% of those patients are discharged from the hospital with SUP and no appropriate indication [7].

SUP may lead to adverse drug interactions (e.g., clopidogrel) and increase the risk of re-hospitalization and additional health care costs [6]. The ICU-based study performed in a tertiary-care teaching hospital in Vancouver, British Columbia, Canada has concluded that after the introduction of a guideline for SUP administration, appropriateness of therapy increases from 75.8% to 91.1%, and medication costs decrease from $2.50/day to $1.30/day without any statistically

significant difference in clinical outcomes. As for this study, it focuses on analyzing the appropriate use of acid-suppressive drugs, namely SUP, and calculate the potential cost savings from its inappropriate use. It is very useful to know the potential cost saving from inappropriate or unnecessary stress ulcer prophylaxis (SUP) therapy in non-ICU inpatients.

2. Methods

2.1. Design and setting

This non-experimental study was performed on medical records and details acquired from the financial department of "X" hospital in Purwokerto, Indonesia. Using a retrospective design and hospital perspective, we collected data from non-ICU inpatients in May 2015. From a population of 316 patients during this month, a minimum of 80 patients was selected by purposive sampling according to the predefined inclusion and exclusion criteria. This sample size was determined using the Slovin's formula with a confidence level of 90.

Patients were included in data collection if they used SUP, such as H2 blockers, proton pump inhibitor (PPI), sucralfate, and antacids. Meanwhile, they were excluded from data collection if they had gastric disorders (i.e., peptic ulcer disease, nephrolithiasis phosphate, dyspepsia, gastroesophageal reflux disease (GERD), gastritis, duodenal ulcers, mucositis or stomatitis).

We referred to ASHP guidelines for safe use of SUP (1999) that had been modified by Zeitoun (2011) for non-ICU inpatients [3], and then we calculated potential cost savings from inappropriate drug use. ASHP guidelines exhaustively include both independent and non-independent risk factors (Table 1). Indications are categorized as appropriate if patients have one of the independent risk factors: (1) Patients with coagulopathy

Table 1. Risk factors associated with stress ulcers

Types	Risk factors
Independent	1. Coagulopathy (including medication-induced coagulopathy): platelet count < 50,000/mm^3, INR > 1.5, or PTT > 2× control value
	2. Respiratory failure: mechanical ventilation ≥ 48 hours
Others	1. Spinal cord injuries
	2. Multiple trauma: trauma sustained to more than one body regions
	3. Hepatic failure: total bilirubin level > 5 mg/dL, AST > 150 U/L (3× ULN), or ALT > 150 U/L (3× ULN)
	4. Thermal injuries > 35% of body surface area
	5. Partial hepatectomy
	6. Head injury with Glasgow coma score of ≤ 10 or inability to obey simple commands
	7. Hepatic or renal transplantation
	8. History of gastric ulceration or bleeding during a year before admission
	9. Sepsis/septic shock: vasopressor support and/or positive microbiologic cultures/suspected infection
	10. Intensive care unit stay for > 1 week
	11. Occult or overt bleeding for > 6 days

INR: International Normalized Ratio

Adapted from: ASHP Therapeutic Guidelines on Stress Ulcer Prophylaxis. Am J Health-Syst Pharm 1999; 56:347–79.

(platelet count < 50,000 per mm^3, International Normalized Ratio (INR) > 1.5 or PTT > 2x control value or drugs that affect coagulation, (2) using a ventilator for more than 48 hours, and (3) history of gastrointestinal bleeding or ulceration before entering the hospital, and if patients have at least two non-independent risk factors: (1) sepsis, (2) in the ICU for more than one week, (3) bleeding for 6 days or more, (4) taking high-dose corticosteroids (> 250 mg/day) [8].

2.2. Data analysis

From the datasheet, we classified patients into several groups based on (1) demographic characteristics, such as gender, (2) SUP regimen that included use, dose, and duration, and (3) appropriateness according to ASHP/Zeitoun guidelines. The data were classified into either appropriate or inappropriate indications of stress ulcer, and then for inappropriate indications, we calculated the potential of cost-saving. Data on pharmaceutical spending, especially before and after the calculation of cost-saving, were analyzed in SPSS 20 program. The analysis also included the Kolmogorov Smirnov normality test and the Wilcoxon Sign Rank test to identify any differences between before and after the calculation of potential cost saving

3. Results and discussion

Based on gender, 56.25% of the selected 80 patients were males, and 43.75% of them were females (Table 2). This gender distribution is similar to Zeitoun et al. (2011), in which the share of male patients is larger than their female counterparts [3]. Kerama et al. (2014) also show that in a hospital ICU in Kenya, 57.5% of SUP users were male [7]. Furthermore, according to Chu et al. (2010), male patients have a higher risk of gastrointestinal bleeding (57.5%) than female patients (42.5%).

The majority of the sampled patients (91%) underwent monotherapy, whereas only a few of them (9%) took combination therapy. Of the 91% of patients with monotherapy, 69% of them received ranitidine, and the remaining 17% took omeprazole as stress ulcer prophylaxis. As for the combination therapy, more than half of the patients in this category (56%) took ranitidine IV combined with omeprazole PO. The non-ICU patients in "X" hospital in Purwokerto mostly used Histamine-2 blockers (H2RA) as SUP. H2RA inhibits histamine-stimulated acid secretion by reversible, competitive inhibition of H2 receptors on parietal cells. Among the available H2RA, cimetidine is the least potent, ranitidine is in the middle, and famotidine is the most potent [7]. In a meta-analysis by Cook et al. various prophylactic therapies, including antacids, sucralfate, and H2-RAs, have been found to reduce the incidence of clinically significant bleeding compared with no prophylaxis. However, antacids are no longer considered a viable therapeutic option because of the labor-intensive dosing frequency and potential side effects. According to the ASHP guidelines, SUP is not recommended for general medical and surgical patients in non-ICU settings with fewer than two risk factors for clinically significant bleeding or patients with two or more risk factors. A retrospective case-control study conducted by Qadeer et al. at an American tertiary care center (n =17707 patients) demonstrates that hospital-acquired bleeding is uncommon in non-critically ill patients; therefore, routine prophylaxis is unnecessary in most hospitalized patients [9]. Various agents that protect the gastric mucosa from acid have been used for SUP. Antacids such as aluminum and magnesium hydroxide were historically used because of their ability to buffer stomach acid. Sucralfate does not neutralize acid but forms a protective barrier over the gastric mucosa. Histamine-2 receptor antagonists (H2RAs) and proton pump inhibitors (PPIs) both inhibit gastric acid secretion. The non-ICU of "X" hospital in Purwokerto mostly used Histamine-2 blockers (H2RA).

Appropriate indication of stress ulcers in non-ICU settings according to ASHP guidelines must

Table 2. General characteristics of the samples (n =80)

Patient characteristics	n (%)
Gender	
Male	45 (56.25)
Female	35 (43.75)
Therapy	
Monotherapy	73 (91)
Combination therapy	7 (9)
Acid-suppressive drugs mono-therapy	56 (69)
Ranitidine	8 (10)
Lansoprazole	14 (17)
Omeprazole	1 (1)
Antacid	2 (3)
Sucralfate	
Combination therapy	
Ranitidine iv + pantoprazole iv	1 (11)
Ranitidine iv + omeprazole iv	3 (33)
Ranitidine iv + omeprazole po	5 (56)

iv: intravenous, po: per oral

Table 3. Stress ulcer prophylaxis use with appropriate indications

SUP variables	(%)
Risk factors (appropriate indications)	
Coagulopathy	88
Coagulopathy + sepsis	8
Coagulopathy + corticosteroids high dose	4
Dose	
Appropriate	18
Inappropriate	9

have at least one of the independent risk factors or two/more non-independent risk factors. Zink et al. reviewed 814 general adult medicine admissions in a community hospital setting, of which 324 were given SUP (40% of total). They noted that 40% of patients receiving SUP were actually given acid-suppressive drugs for an appropriate medical indication (therefore not SUP), while 60% were not [10]. Our study showed that of 80 patients who received SUP, 67.50% had inappropriate stress ulcer indications and 32.50% had appropriate indications. In 2010, Reid and colleagues conducted a retrospective review of the use of PPIs in 9875 patients in a university-affiliated public safety-net hospital and 6,520,100 patients in the University Health System Consortium. Of the nearly 1 million patients who received PPIs between 2008 and 2009, 73% did not have a valid indication for acid-suppressive therapy. SUP was cited as the reason for inappropriate prescribing in 56% of cases. Duration of SUP use in our study varied from 1 to 16 days, and the largest dose of SUP use was for 5 days. Long-term use of acid-suppressive medications was associated with an increase in unnecessary expenses, and, most importantly, with an elevated risk of pneumonia, hip fracture, and Clostridium difficile colitis.

After the data were classified into either appropriate or inappropriate indications, then we calculated the potential cost saving from inappropriate indications. This cost-saving refers to the cost reduction of SUP use and drug administration kits (i.e., syringe and alcohol swab use) in patients with inappropriate indications. Data on pharmaceutical costs, especially before and after the application of ASHP guidelines, were analyzed in SPSS 20 program. The analysis also included the Kolmogorov Smirnov Normality test and the Wilcoxon Sign Rank Test to identify any differences between before and after the detection of inappropriateness based on ASHP guidelines. The results showed p = 0.000 (≤ 0.05), which indicates that a significant difference between the total cost before and after the application of ASHP guidelines for the identification of inappropriateness.

The overuse of SUP can have a substantial economic impact on both patients and the health care system. The study by Heidelbaugh and colleagues, which included 1769 general

Table 4. The potential cost savings from inappropriate indications

Before ASHP	After ASHP	Potential Cost Saving
USD 2,411	USD 1,899	USD 512

USD 1 = IDR 13,164 (based on Bank Indonesia, exchange rate on January 31, 2018)

medicine patients at a major university hospital, found that the inappropriate use of SUP increased annual inpatient costs by USD 44,096 and outpatient costs by USD 67,695, for a total of USD 111,791 [11]. In a large managed care organization, in which 68% of 29,348 patients were prescribed a PPI inappropriately at hospital discharge, inappropriate continuation for just 30 days after discharge was associated with a cost of more than $3 million over 4 years. Neither of these studies took into account the costs incurred from complications of SUP therapy [12]. Another ICU-based study performed in a tertiary-care teaching hospital in Vancouver, British Columbia, Canada concluded that after the introduction of a guideline for SUP administration, appropriateness of therapy increased from 75.8% to 91.1%, and medication costs decreased from USD 2.50/day to USD 1.30/day without any statistically significant difference in clinical outcomes. In our study, the cost-saving refers to the cost reduction of SUP use and drug administration kits (i.e., syringe and alcohol swab use) in patients with inappropriate indications. The total cost potentially saved due to inappropriate indications was IDR 6,739,498 or equal to USD 512. The data were examined using the Wilcoxon Sign Rank Test, and the results showed p = 0.000 (≤ 0.05), indicating a significant difference between the total cost before and after the cost-saving calculation.

4. Conclusion

The percentages of inappropriate indications and doses are 32.5% and 18%, respectively. After the introduction of ASHP guidelines for appropriateness, the total cost decreases from USD 2,411 to USD 1,899. In other terms, the potential cost-saving from inappropriate indications is USD 512. Based on the Wilcoxon Sign Rank Test results (p = 0.000 (≤0.005)), there is a significant difference between the total cost before and after the introduction of ASHP guidelines for appropriateness.

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