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Research Article

Appropriateness and Cost of Prophylaxis Stress Ulcer for Inpatient in the Internal Medicine Department in a Government Hospital: A Cross-Sectional Study

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Abstract

Guidelines from the American Society of Health-System Pharmacists (ASHP) 1999 prohibit acid-suppressing therapy for stress ulcer prophylaxis (SUP) in patients who are not critically ill. Stress ulcer prophylaxis is not recommended in non-ICU patients with <2 risk factors. Inappropriate use of SUP can increase costs for patients. This study aims to evaluate the use and the cost of SUP. This research was a non-experimental observational study with a cross-sectional approach. Data was collected retrospectively using the consecutive sampling method with a random sampling technique on the medical records of inpatients in the internal medicine ward of Sleman Regional Public Hospital from January to December 2020, totaling 340 samples. The results showed that proton pump inhibitors were the most widely used acid-suppressing drugs, with 45.8%. Furthermore, the histamine-2 receptor antagonist was 42.6%, the sucralfate group was 7.4%, and the antacid group was 4.2%. Of 340 patients, 57 (16.8%) were in the proper indication based on the guidelines, and 283 (83.2%) were under the wrong indication for SUP. They were using SUP with the proper indication so that the therapy could save treatment costs by Rp. 19,933,582. There was a high prevalence of inappropriate SUP prescriptions among inpatients in the internal medicine department; if these drugs were given with the appropriate indications, they could save more on the prophylaxis cost. Clinician pharmacists should develop an effective intervention strategy to reduce inappropriate SUP drugs.

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INTRODUCTION

Stress ulcer prophylaxis (SUP) is generally given to critically ill patients and treated in the intensive care unit (ICU)[1]. Appropriate use of SUP is defined when proton pump inhibitors (PPIs) and histamine-2 receptor antagonists (H2RAs) are administered to patients with at least one risk factor (coagulopathy, mechanical ventilation ≥48 hours, and gastrointestinal bleeding or ulceration within a year) before hospitalization) or with some minor risk factors (sepsis, multiple organ failure, liver failure, renal insufficiency, inpatient ICU ≥7 days, hypotension or shock, organ transplant, multiple trauma, burns of more than 25-30% of body surface area, major surgery, hidden gastrointestinal bleeding ≥6 days, and use of anticoagulants, corticosteroids, or nonsteroidal anti-inflammatory drugs (NSAIDs))[2]. The American Society of Health-System (ASHP) in 1999 published guidelines for the use of SUP in medical, surgical, respiratory and pediatric patients in the ICU[3]. Research related to inappropriate prescribing of acid-suppressing therapy due to a low-risk factor for bleeding in the use of SUP based

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on the stress ulcer-related gastrointestinal bleeding (SURGIB) criteria was developed by Herzig *et al*.[4] of 88.5% and an estimated cost savings of inpatient medication hospitalization of $114,622 (approximately Rp. 1,396,095,960) in the 253 studied patients[5].

Long-term use of acid-suppressing therapy is of particular concern as complications (*Clostridium difficile*: diarrhea, osteoporosis, and pneumonia) are associated, mainly when PPIs are used for long durations at high doses[6]. Several studies[7,8] reported that *C. difficile* infection increased three times from prolonged use of SUP. If SUP is not used based on the indications of the disease in the patient, it will lead to unexpected side effects such as diarrhea due to *C. difficile*, the incidence of pneumonia, and increased unnecessary costs[9]. Therefore, evaluating SUP can be an evaluation for health workers in providing therapy to patients and obtaining optimal therapeutic effectiveness. The researcher is interested in conducting a study regarding the utilization of SUP in patients hospitalized in the internal medicine ward of Sleman Regional Public Hospital due to the completeness of medical record documentation reaching 85% out of 100% based on the patient safety and quality improvement program.

MATERIALS AND METHODS

Materials

The research instruments included medical records of patients hospitalized in the internal medicine ward of Sleman Regional Public Hospital, Special Region of Yogyakarta, Indonesia, in 2020. ASHP Therapeutic Guidelines on Stress Ulcer Prophylaxis 1999[3] and Stress Ulcer Prophylaxis Clinical Guidelines from Stanford Hospital and Clinics 2015[10] were used as therapeutic references. Sample recording was adjusted according to the inclusion criteria such as gender, patient age, length of hospitalization, drug name, drug class, drug dose, rules of use, and duration of drug use. This research has obtained research ethics approval from the Health Research Ethics Committee, Sleman Regional Public Hospital with number 180/4126.

Methods

Research design and participants

The study took medical record data of inpatients at the Sleman Regional Public Hospital and the costs of using SUP from January to December 2020. Patient characteristics and therapy data were obtained from medical records, while therapy costs were obtained from the hospital's finance department. The sample in this study was all inpatients in the internal medicine ward who used SUP and met the inclusion criteria at the Sleman Regional Public Hospital for January to December 2020. The inclusion criteria were that patients hospitalized in the internal medicine ward were given SUP during treatment with data, and the medical records were complete and legible. The exclusion criteria were patients who entered and experienced bleeding in the gastrointestinal tract, which was marked by the occurrence of hematemesis, melena, and blackish-red NG fluid; Patients with a diagnosis of gastrointestinal disorders; and a history of peptic ulcers or gastrointestinal bleeding within one year before admission.

Sample size calculation

The sample was calculated using the proportion estimation formula as shown in **Equation 1**, taking the following assumptions: the proportion of appropriate use of SUP = 0.5, a margin of error = 5%, and a 95% confidence interval[11]. The correction formula was used since the population was less than 10,000 (total patient population in a year (N) = 3000), which could represent the study sample. The corrected number of samples was then calculated, as shown in **Equation 2**. Then, 340 samples were selected with a random sampling technique.

$$n = \frac{Z_{\alpha/2}^2 P(1-P)}{d^2} = \frac{(1.96)^2\ 0.5(1-0.5)}{(0.05)^2} = 384 \quad [1]$$

$$n = \frac{N \times n}{N + n} = \frac{3000 \times 384}{3000 + 384} = 340 \quad [2]$$

Criteria establishment

Based on published evidence-based guidelines and previous literature on SUP clinical practices, we established the criteria to evaluate the appropriateness of SUP medication. Stress ulcer prophylaxis medication was considered appropriate if an inpatient in the internal medicine department had one major or at least two minor risk factors[3,10] in **Table I**.

Table I. Risk factor for stress ulcer.

The presence of of one major risk factor from the following:
1. Respiratory failure: mechanical ventilation >48 hours
2. Coagulopathy: platelet count <50,000/mm^3 (50 × 10^9/L), international normalized ratio >1.5, or partial thromboplastin time >2.0 times the control value
The presence of at least two minor risk factors of the following:
1. Head injury with a Glasgow Coma Score of ≤10 or an inability to obey simple commands
2. Thermal injury involving >35% of the body surface area
3. Partial hepatectomy
4. Hepatic or renal transplantation
5. Multiple traumas with the Injury Severity Score of ≥16
6. Acute renal failure or hepatic failure
7. Traumatic brain injury or spinal cord injury
8. Insufficiency renal
9. Sepsis
10. Occult or overt bleeding for ≥6 days
11. Length of stay >7 days
12. Corticosteroid therapy (>250 mg/day hydrocortisone or equivalent daily)
13. Using antiplatelet

Outcome measurement

Our primary outcome variable was the appropriateness evaluation of SUP prescribing patterns for inpatients in the Internal Medicine Department and the cost of using SUP, both the total cost and average cost per patient of appropriate and inappropriate indicated prophylactic use.

Data analysis

Data analysis in this study was in the form of descriptive analysis to describe the characteristics of patients based on gender, age, length of hospitalization, and risk factors to determine the profile of SUP used by inpatients in the internal medicine ward of Sleman Regional Public Hospital based on the class of drugs used, to determine the accuracy and inaccuracy of the indications for the use of SUP for inpatients in the internal medicine ward, as well as identifying the costs calculated by multiplying the total number of appropriate and inappropriate therapeutic doses given during hospitalization with the price of the drug used.

RESULTS AND DISCUSSION

Based on the data obtained from 340 samples in **Table II**, there are more male (55%) than female patients (45%). Patient characteristics by gender are dominated by males, with a higher prevalence of male smokers (62.9%). Based on Indonesian Basic Health Research 2018 (*Riset Kesehatan Dasar*, Riskesdas)[12], regularly consuming coffee could increase the risk of stress ulcers. Coffee containing caffeine can stimulate the hormone gastrin, which stimulates and accelerates the production of stomach acid, resulting in gastric ulceration[13]. In addition, regularly drinking coffee can increase the risk of 3.57 times experiencing gastritis. If left untreated, it will worsen, and the stomach acid can cause ulcers[14].

Inpatients in the internal medicine ward who receive SUP are given at >65 years old who have entered older people. The increasing age can cause a decrease in gastric mucosal function, reduced secretory function, and loss of nutritional factors in the gastric mucosa, so the stomach is prone to bleeding[15]. Age does not affect the incidence of stress ulcers as it is not included as a risk factor for gastrointestinal bleeding. However, a study revealed that older age becomes one factor in the administration of excessive gastric acid-suppressing drugs[9].

Furthermore, the maximum length of hospitalization was <7 days with a percentage of 93.24% and >7 days with a percentage of 6.76%. Farsaei *et al*.[9] explained that patients who required longer hospitalization and more medical services could unconsciously encourage doctors to provide SUP, preventing more gastrointestinal bleeding complications. Elderly

patients and longer hospitalization were shown to be significant overuse predictors of SUP. In addition, Issa *et al*.[16] have similarly identified factors contributing to the overuse of SUP. They revealed that the length of hospitalization is one of the factors in which SUP is frequently used.

In this study, the major risk factor was the incidence of coagulopathy (12.35%), in which most patients were dengue fever patients. Therefore, according to Huang *et al*.[17], it is necessary to give anti-ulcer to prevent stress ulcers. Meanwhile, the minor risk factor is the use of antiplatelets (10.59%), which can inhibit the production of prostaglandins by the gastric mucosa associated with gastric epithelial damage[18]. Our previous study[19] revealed that there were 52 patients receiving antiplatelets, where the use of antiplatelets significantly affected the incidence of bleeding.

Table II. Patients characteristics.

Parameter	Number of patients (n (%))
Gender	
Female	153 (45)
Male	187 (55)
Age (years old)	
5-11	4 (1.2)
12-16	9 (2.6)
17-25	28 (8.2)
26-35	28 (8.2)
36-45	42 (12.4)
46-55	74 (21.8)
56-65	57 (19.7)
>65	88 (25.9)
Length of Hospitalization (days)	
≤7	317 (93.24)
>7	23 (6.76)
Risk factors	
Coagulopathy	40 (12.35)
Antiplatelet use	38 (10.59)
Corticosteroid use	29 (8.53)
Congestive heart failure	26 (7.94)
Kidney insufficiency	13 (3.82)
Sepsis	12 (3.53)
Head injury	3 (0.88)

The profile of SUP in inpatients in the internal medicine ward at the Sleman Regional Public Hospital in 2020 was primarily the PPIs group of 45.8% (**Table III**). Acid suppressive therapy (AST), including PPIs and H2RAs as SUP, is one of the most common medical practices in inpatients[5]. The PPIs are more potent in increasing gastric pH than H2RAs and maintain gastric pH between 3.5 and 5.0, which can minimize the risk of gastric mucosal injury. Of the four meta-analyses comparing PPIs with H2RAs, three suggested that PPIs are superior to H2RAs[20].

Table III. Stress ulcer prophylaxis use profile.

Agent	Type	Number	%
PPIs	Lansoprazole injection	66	14
	Lansoprazole capsules	36	7.6
	Pantoprazole injection	84	17.6
	Esomeprazole injection	4	0.8
	Esomeprazole tablets	2	0.4
	Omeprazole injection	3	6
	Omeprazole tablets	21	4.4
H2RAs	Ranitidine injection	187	39.6
	Ranitidine tablets	14	3
Sucralfate	Sucralfate syrup	18	3.8
	Sucralfate tablets	17	3.6
Antacid	Antacid syrup	4	0.8
	Antacid tablets	16	3.4
Total		**472**	**100**

Evaluation of the use of SUP revealed that patients prescribed acid-suppressing drugs were 40 patients or 11.76%. One indication had a major risk factor; 17 patients, or 5%, had at least two or more indications of a minor risk factor as SUP, and 283 patients, or 83.24%, received acid-suppressing drugs without appropriate indications (**Table IV**). This is similar to several studies conducted abroad regarding the high prescription of gastric acid suppressant drugs that are not appropriate to treatment guidelines[5,21-23]. In recent years, SUP has become commonplace in patients with general treatment and little or no supporting evidence[24]. Inappropriate use of indications for SUP can increase the incidence of unexpected drug reactions, drug interactions, problems in polypharmacy, and unnecessary drug costs[25].

Table IV. The use of SUP.

Stress ulcer prophylaxis	n (%)
Correct indication	
1 major risk factor	40 (11.76)
≥2 minor risk factors	17 (5)
Incorrect indication	283 (83.24)
Total	**340**

A cost analysis was performed to assess the economic impact of SUP during therapy without incorrect indications. The cost of prophylaxis is calculated based on the total oral administration or injection of acid-suppressing drugs given during hospitalization, looking at the smallest unit of drug price from the hospital. The biggest expenditure on SUP was the inappropriate of the drug, which was Rp. 19,933,582 (**Table V**). It indicated that the hospital could save on that cost if the drug is not used Rp. 19,933,582. Moreover, there were limitations in identifying the patient's direct costs, so the cost calculation is only from the drug's price.

Table V. Drug expenses for the use of SUP.

Indication	Number of patients	Total drug cost (Rp)	Average cost (Rp)
Appropriate	57	6,240,384	109,480
Inappropriate	283	19,933,582	70,436

Researchers have not been able to explain the factors that influence the high prevalence of inappropriate prescribing, but there is a similar study that observed the factors that influence the inappropriate prescribing of prophylactic stress ulcers; a study stated that the reasons why clinicians prescribed SUP inappropriately were multifactorial. First, the fear of the development of SUP in non-ICU patients who were not on SUP therapy. Second, Due to the tense relationship between doctors and patients in China, doctors had to prescribe SUP therapy for low-risk inpatients to protect themselves from litigation. Third, the incidence of an adverse reaction related to acid suppression medicines has not been high. For this reason, doctors have believed PPIs to be safe[26]. One study[27] reported that several adverse effects (specified in *C. difficile* infections, respiratory infections, hypomagnesemia, adverse skeletal muscle effects, and psychiatric symptoms) after reducing inappropriate proton pump inhibitor use for SUP decreased significantly (35% control group versus 8% intervention group)[28]. The inappropriate use of SUP therapy can also have economic implications for patients and the healthcare system. Associated with those factors, the researcher indicated that clinicians needed to provide more information about the rationality and efficiency of their prescribing practices. Clinical pharmacists should execute effective intervention strategies to reduce improper SUP medication. The ASHP Therapeutic Guidelines on Stress Ulcer Prophylaxis 1999[3] and Stress Ulcer Prophylaxis Clinical Guidelines from Stanford Hospital and Clinics 2015[10] can be implemented in clinical practice to prevent unnecessary acid-suppressing therapy in patients due to the low risk of stress ulcer bleeding. Computerized ordering systems can reduce unnecessary use of acid suppression therapy, lower patient prescribing costs, and limit side effects[25,28].

CONCLUSION

The profile of the use of SUP drugs in patients hospitalized in the internal medicine ward at Sleman Regional Public Hospital in 2020 included PPIs of 45.8%, H2RAs of 42.6%, sucralfate of 7.4%, and antacid of 4.2%. The use of SUP in the patients described 57 patients (16.8%) with correct indications and 283 patients (83.2%) with incorrect indications. Expenditure on

the use of SUP drugs in a correct indication was Rp 6,240,384 with an average of Rp 109,480 for 57 patients and Rp 19,933,582 for an incorrect indication with an average of Rp 70,436 for 283 patients.

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AUTHORS' CONTRIBUTION

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Visualization: -
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DATA AVAILABILITY

None.

CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

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