**Analysis of the use and cost of stress ulcer prophylaxis for surgical inpatients (maximum 50 words)**

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**Abstract**

**Background:** A concise abstract is required (± 250 words). this section provides context to the brief information including problem statement, rationale or limitation of the previous studies, and the aim of study.

**Methods:** this section consist the brief essential material and methods or procedures used in research study.

**Results:** this section consist the summary of the most important results that obtained from study. The information need to be clear and straightforward.

**Conclusion:** this section contained explanation about the experimental results and/or the results fit into bigger picture.

**Keywords:** stress ulcer prophylaxis, overuse, stress ulcer, drug costs.

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**Introduction**

Stress ulcer is damage to the gastric mucosa in critically ill patients or patients with severe trauma, which is characterized by acute bleeding or perforation of the upper gastrointestinal tract [1]. The damage is in the form of lesions that can cause complications in the form of massive bleeding in patients [2]. The bleeding can increase the morbidity and mortality of patients.

Stress ulcer prophylaxis (SUP) is given to prevent mucosal bleeding in the upper gastrointestinal tract associated with stress[3]. Pharmacological drugs such as the proton-pump inhibitor (PPI) group, histamine 2-receptor antagonist (H2RA), and protective gastric mucosa drugs such as sucralfate can be used for therapy purposes as SUP [4].

Overuse of SUP has some risks of adverse drug reactions(ADRs) such as nosocomial pneumonia and *Clostridium difficile* infection [6]. For the use of SUP, guidelines are needed to prevent overuse of SUP drugs that may cause ADRs. The American Society of Health-Systems Pharmacists (ASHP) in 1999 formulated guidelines related to the use of SUP. Those guidelinesare based on evidence of base medicines that are systematically obtained and used in large quantities in reference to other SUP guidelines. The ASHP guidelines contain a clear description of the criteria for patients at risk for stress ulcers, drug choice, and duration of taking SUP [7].

Dr. Soetomo General Hospital is the major referral hospital in the eastern part of Indonesia. Patients who undergo surgical procedures are at risk of experiencing stress ulcers due to anxiety, stress, and trauma;therefore, they need stress ulcer therapy that is appropriate and not excessive [11]. Excessive prescription of SUP drugs will certainly burden patient costs during hospitalization. Therefore, SUP medicines must be given according to ASHP criteria in order to reduce patient care costs.However, there are no studies that analyze the use of SUP drugs based on the ASHP criteria and drug costs of the overuse of SUP drugs among surgical inpatients of Dr.Soetomo General Hospital. Therefore, it is important to analyze the use of SUP drugs based on ASHP criteria and analyze the cost of the overuse of SUP drugs. This research was conducted to calculate the excess costs caused by overuse of SUP in Dr. Soetomo General Hospital, which may best representing the general condition in Indonesia.

**Materials and Methods**

This study was designed to comply the criteria for ethical conduct and was approved by the Health Research Ethics Committee of Dr. Soetomo General Hospital, with reference number 1121/KEPK/IV/2019. This research was conducted using a prospective observational method from mid of April 24 to mid of May 2019 in the surgical ward of Dr. Soetomo General Hospital. This study involved medical observations on the use of ulcer drugs by surgical patients who had been given prescriptions by doctors.

The use of SUP is assessed based on ASHP criteria. Briefly, the use of SUP is declared appropriate and not excessive if it has 1 absolute indication or ≥ 2 relative indications. Absolute indications include patients with coagulopathy and/or using mechanical ventilation> 48 hours. Relative indications include Glasgow Coma Scale (GCS) head injury of patients ≤ 10, burns> 35%, partial hepatectomy, liver or kidney transplantation, multiple trauma Injury Severity Score (ISS) ≥ 16, spinal cord injury, impaired liver function, history of gastric ulcer or gastrointestinal bleeding < 1 year before hospitalization, sepsis, ICU stay> 1 week, bleeding ≥ 6 days, use of high-dose corticosteroids, and kidney disorders (creatinine clearance <40 mL/min or creatinine> 2.8 mg/dL). An assessment of the accuracy of indications and route of drug administration was performed.

**Results**

Demographic data include gender, age, length of stay at the Surgical Inpatient Installation, and the reason for patient discharge. Male patients were more dominant than female ones, with the percentage being 55.26%. Of the sample of patients,52.63% hadages from 40-64 years, while patients of ages <40 years and ≥ 65 years amounted to 34.21% and 13.16% of the total sample, respectively. Patients treated for> 7 days amounted to 55.26%, and the rest were treated ≤ 7 days (Table 1).

In this study, the number of drugs refers to dispensed unit doses, where 1 unit dose of ranitidine injection is the use of a 50 mg/2 mL ranitidine ampoule, 1 unit dose of ranitidine tablet is the use of a 50 mg ranitidine tablet, 1 unit dose of omeprazole injection is the use of a 40 mg/10 mL omeprazole vial, and 1 unit dose of sucralfate syrup is the use of 500 mg/5 mL of sucralfate syrup. With a percentage of 80.26%, ranitidine injection is the most widely used ulcer drug followed by sucralfate syrup at 10.19%. Omeprazole injection and ranitidine tablets have small usage proportions, being 5.99% and 3.56% respectively. Regarding the assessment of accuracy of indications, ranitidine with inappropriate indication was found for 605 unit doses and appropriate indication was for 522 unit doses. Appropriate indications of sucralfate syrup doses totaled 136 units, while 7 units were inappropriate indications. Appropriate indication for the use of omeprazole injection was greater than the inappropriate indication, being 60 unit doses compared to 24 unit doses. Meanwhile, in comparing appropriate indications and inappropriate indications for ranitidine tablets, the number of inappropriate unit dose indications is greater than appropriate indications, being 38 to 12 (Table 2).

The intended use of drugs has an indication of either SUP or non-SUP. The use of an ulcer drug is appropriate if indicated as SUP or non-SUP. The use of an ulcer drug is inappropriate if it has no indication of use as SUP or non-SUP. Usage of ulcer drugs that is inappropriate is considered as excessive use. Excessive use was found for 48% of ulcer drugs that were declared for inappropriate indications. Appropriate assessment of ulcer drug indications was stated for more non-SUP indications than SUP indications, being 36.4% compared to 15.95% (Figure 1).

**Discussion**

There is an increase in the use of stomach acid suppressants for both stress ulcer prophylaxis (SUP) and non-SUPindications. A study shows an increase in the use of ulcer drugs from 2011 to 2013 with indications of use for both SUP and non-SUP therapy [12]. This study was conducted to analyze the use and cost of SUP medicine for inpatient surgery in Dr.Soetomo General Hospital.

In this study, 152 patients were examined for their use of ulcer drugs, with the male patients having a greater proportion than female patients. This is similar to a research conducted in 2016 on the use of PPIs in hospitals, where the proportion of male patients is higher than females, because in the hospital where the study was conducted, the population of male patients was more dominant than females [13]. The number of patients treated over a span of> 7 days is greater than patients treated ≤ 7 days. The length of time for a surgical patient may be caused by the long waiting period for an operation that is affected by the unavailability of equipment and comorbid patients [14]. Greater lengths of stay in a hospitalfor patients results in a greater risk of patients experiencing nosocomial infections and an increased burden of patient care costs.

The use of ulcer drugs is considered excessive if they are not indicated as SUP or non-SUPfor patients. SUP is indicated if the patient has 1 absolute indication or more than 1 relative indication. The non-SUP indication is therapy for GI disorders and ulcer prophylaxis due to the use of NSAIDs. In this study, prophylactic pulmonary aspiration and premedication hypersensitivity reaction (HSR) are included for non-SUP indications. This is in accordance with recommendations from the 2017 American Society of Anesthesiologists (ASA), which state that ulcer drugs are needed to reduce the risk of pulmonary aspiration [16]. Premedication hypersensitivity reaction (HSR) was included for non-SUP indications because H2RA drugs are needed to prevent hypersensitivity reactions from the use of chemotherapy drugs [17]. In this study, it was found that the percentage of ulcer drug usage for appropriateindicationswas greater than for inappropriate indications. A research conducted by Taha*et al.* (2012) also showed similar results, where the appropriateusage for drugs was greater than inappropriate drug usage, being 66.2% compared to 33.8% [18].

In this research, ulcer drugs without SUP or non-SUP indication contributedthe most into overuse assessment. This is because patients do not show the use of ulcer drugs without clear indications, such as in the research conducted by Abdikarim*et al*. (2017),where it is stated that 26% of patients use ulcer drugs without proper indications [23]. Ulcer drugs are also consideredto be inappropriately indicated if only 1 relative indication is found. This is not in accordance with ASHP guidelines. In a study conducted by Cook and Guyat (2018), among 1,769 patients,it was found that SUP was prescribedfor 54% of patients who did not meet the suitability criteria of SUP usage [24]. In addition to increasing the burden of drug costs, the use of ulcer drugs without proper indications will result in ADRs, including pneumonia and *C. difficile*infections, and increased patient mortality related to sepsis. This is due to an increase in the growth of pathogenic bacteria due tothe suppression of gastric acid as a defense against the immune system [25].

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**Figure 1:** Percentages of ulcer drugs with appropriate and inappropriate indications. The indications were evaluated based on ASHP criteria. (Note: Please also submit Figure separately from text in JPEG/JPG format)

**Table 1:** Demographic data sample of ulcer drug users, as the inpatients of Dr. Soetomo General Hospital

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| --- | --- | --- | --- |
| Demographic data | Category | n | Percentage (%) |
| Gender | Male | 84 | 55.26 |
| Female | 68 | 44.74 |
| Age (years) | < 40  | 52 | 34.21 |
| 40 - 64  | 80 | 52.63 |
| ≥ 65  | 20 | 13.16 |
| Length of Stay (days)  | ≤ 7 | 68 | 44.74 |
| > 7 | 84 | 55.26 |