

# Assessment of Stress Ulcer Prophylaxis Pattern in the Intensive Care Unit Patients

Mahshid ARAMESH<sup>1</sup>, Mohammad Amin Valizade HASANLOIE<sup>2</sup>, Siamak AGHLMAND<sup>3</sup>, Hamdollah SHARIFI<sup>2,4</sup>

<sup>1</sup>Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran

<sup>2</sup>Clinical Research Development Unit of Imam Khomeini Hospital, Urmia University of Medical Sciences, Urmia, Iran

<sup>3</sup>Department of Public Health, Urmia University of Medical Sciences, Urmia, Iran

<sup>4</sup>Faculty of Pharmacy, Urmia University of Medical Sciences, Urmia, Iran

**Cite this article as:** Aramesh M, Hasanloei MAV, Aghlmand S, Sharifi H. Assessment of Stress Ulcer Prophylaxis Pattern in the Intensive Care Unit Patients

**Corresponding Author:** Hamdollah Sharifi  
**E mail:** sharifi.h@umsu.ac.ir

©Copyright 2021 by Society of Turkish Intensivist - Available online at [www.dcyogunbakim.org](http://www.dcyogunbakim.org)

**Received:** Oct 09, 2021

**Accepted:** Oct 22, 2021

**Available online:** Dec 24, 2021



Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

## ABSTRACT

**Aim:** Stress ulcer prophylaxis (SUP) is often overused in the intensive care unit. Evaluation of the rate of unsuitable stress ulcer prophylaxis upon ICU admission and determine the frequency of overutilization or underutilization of SUP.

**Study design:** This study was performed in Imam Khomeini Hospital of Urmia University of Medical Sciences in Iran. The risk of stress ulcer development was assessed using American Society of Health-System Pharmacists (ASHP) guideline.

**Materials and Methods:** Patients with at least one major or two minor risk factors had an indication of receiving prophylactic stress ulcer. Stress ulcer prophylaxis was considered as appropriate if patients were in one of these two groups and receiving medication.

**Results:** In total of 200 patients included in this study, 55.5% were male, mean hospitalization in ICU was 17.9±8.7 days. The mean age of patients was 56.1 ±17.4 years. Thirty two percent of patients had at least one major and 47.5% had at least two minor risk factors. The most common major risk factor was coagulopathy and the most minor risk factor was using heparin with therapeutic dose. Seventy-nine and a half percent of patients received stress ulcer prophylaxis based on guideline and forty-one (20.5%) had not any indication for stress ulcer prophylaxis and they received drugs inappropriately. The most commonly, used drug class in the prevention of stress ulcer was H2 blockers.

**Conclusions:** Physicians are familiar with risk factors, but they are not familiar with the importance of rational prescription, and overuse of stress ulcer prophylaxis. So, we are far from ideal conditions.

**Key words:** Stress ulcer Prophylaxis, Intensive Care Unit, ASHP, Gastrointestinal bleeding

## Introduction

Stress-related mucosal disease (SRMD) is a gastric mucosal inflammatory lesion triggered by abnormally elevated physiological demand in stressful situations (1,2). Coagulopathy, artificial ventilation for more than 48 hours, a history of gastrointestinal (GI) ulceration or GI bleeding in the past year, head trauma, more than 35% of the total body surface burning, sepsis, organ failure, and a history of use of non-steroidal anti-inflammatory drugs (NSAIDs) for less than three months are all potential risk factors for this phenomenon(3,4). Stress ulcer is a significant factor for morbidity and mortality in the intensive care unit (ICU) (5). If stress ulcer prophylaxis is not given to the patients, 15–50% of critically ill patients experience occult bleeding and 5–25% of the patients experience noticeable bleeding (6).

ICU patients are at the highest risk of bleeding which may cause hemodynamic instability or requires red blood cell transfusion. Rather than stress ulcer treatment and bleeding, it seems that interventions should rationally concentrate on preventing them (7,8). Stress ulcer prophylaxis (SUP) is a common strategy for hospitalized patients, especially in the ICU, to prevent upper gastrointestinal bleeding (UGIB), but it is sometimes overused. Therefore, the starting of SUP usage in the ICU but is continued after transfer and discharge, resulting in health care costs, side effects, and drug /food interactions (9–11). Physicians can identify patients at the highest risk of bleeding using the established guidelines for SUP administration in critically ill patients. A strategy like this may help to reduce stress ulcer complications and improve outcomes (12). The American Society of Health-System Pharmacists (ASHP) guideline for physicians and pharmacists

is one of these guidelines based on risk categories (7,13). In the ICU, inadequate stress ulcer prophylaxis has been found, for both underutilization and overutilization, despite availability of guidance (14-18). On the other hand, there is insufficient knowledge about prescription based on guideline during an ICU stay. As a result, the aim of this study was to prospectively assess the incidence of inappropriate SUP administration and determine the prevalence of overuse or underuse of SUP administration in ICU patients.

## Materials and Methods

### Study design and subjects

This study was conducted in the general intensive care unit (GICU) of Imam Khomeini Hospital of Urmia University of Medical Sciences in Iran after approval by the University Research Council and obtaining permission from the research ethics committee at Imam Khomeini Hospital of Urmia University of Medical Sciences in Iran.rec.1396.36. The study was conducted from October 1 to December 30, 2018 to assess appropriateness of SUP use for patients admitted to the GICU of Imam Khomeini Hospital of Urmia University of Medical Sciences in Iran.

*Inclusion criteria* were: hospitalization in the intensive care unit for at least 72 hours and patients receiving prophylactic stress ulcers.

*Exclusion criteria* include: patients diagnosed with gastrointestinal bleeding, hemorrhage in the first 24 hours of hospitalization and under 18 years old.

The sample size was calculated using a single population proportion formula based on the following assumptions:

proportion of appropriate SUP use = 0.5, margin of error = 5%, and 95% confidence interval

$$n = \frac{Z \alpha/2^2 p(1-p)}{d^2} = \frac{(1.96)^2 0.5(1-0.5)}{(0.05)^2} = 384$$

Correction formula was applied as the source population was less than 10,000 (total population of patients in 3 months [(N) = 415]

$$\text{Corrected sample size} = n = \frac{N * 384}{415 + 384} = 199.45 \approx 200$$

Finally, 200 patients were selected by simple random sampling technique.

### Data collection and management

Patient's demographic information such as age, sex, diagnosis, type of medication received for prophylaxis, and length of stay in the GICU were included in a pre-prepared form. The ASHP guideline was used to measure the risk of developing a stress ulcer. Patients with at least one major risk factor or at least two minor risk factors, according to the ASHP guideline, have an indication for receiving prophylaxis of stress ulcer.

Thereafter patients were assessed in the first day of admission for associated risk factors of stress ulcer and administration of SUP medication. The number of patients with at least one major or two minor risk factors was determined. As a result, patients with indications for receiving prophylactic stress ulcer were reported.

SUP use was considered appropriate if patients were in one of these two groups and receiving medication. The data were collected by an intern who had been educated in data collection procedures. A clinical pharmacologist tested the completeness and accuracy of the collected data on daily basis.

### Statistical analysis

The mean SD and frequency (percentage) were used to define quantitative and qualitative data, respectively. SPSS version 21 was used for all statistical analysis.

## Results

In a total of 200 patients included in this study, 111 (55.5%), were male, mean hospitalization in ICU was 17.9±8.7 day. The mean age of study subjects was 56.1 ±17.4 years. 121 (60.5%) of patients had surgical indication, 51(25.5%) were medical patients and 28(14%) were hospitalized with trauma indication. A brief overview of the characteristics of study participants is given in Table 1.

**Table 1.** The detailed description of characteristics of study participants

Mean Age	56.1±17.4	
Sex	Male	55.5%
	Female	45.5%
Mean Length of ICU stay	17.9±8.7	
	Surgical	60.5%
Medical diagnosis	Medical	25.5%
	Trauma	14%

Sixty-four (32%) patients had at least one significant risk factor (11 patients had more than one major risk factor), and received stress ulcer prophylaxis that the most common of them were coagulopathy (49.3%), followed by mechanical ventilation for more than 48 hours (28%) and peptic ulcer history in the past year (22.7%). Also 95 (47.5%) patients had at least two minor risk factors and received stress ulcer prophylaxis. The minor risk factors include: using heparin with therapeutic dose, ICU admission lasting >1 week, glucocorticoid therapy (>250 mg hydrocortisone or the equivalent), heart failure, head trauma or spinal cord injury. Details are given in Table 2.

Overall, 159 patients (79.5%) received stress ulcer prophylaxis based on guideline and 20.5% had not any indication of stress ulcer prophylaxis, they received drugs inappropriately.

H2 blockers were the most widely used drug class in the prevention of stress ulcer. (61.5% of patients who were on SUP). Drugs used for SUP is shown in Table 3.

## Discussion

In this study, 20.5% of prophylaxis for stress ulcer was without indication. Horsa et al. in a study conducted in Ethiopia, reported the use of SUP without indication was 63.5% of hospitalized patients in medical wards (7) Santos, et al. reported 56% and Rafinazari et al. reported 44.4% SUP without indication in ICU patients (6,19). In the present study, SUP was lower and more rational compared with mentioned studies, however, we are far from ideal conditions. The findings of this study are, in agreement with the study of Vazin et al. who found that 23.8% of SUP was inappropriate (20).

**Table 2.** Major and minor risk factors for stress-related bleeding according to American Society of Health-System

Type of Risk Factors	Indications for stress ulcer prophylaxis	Frequency	%
Major	Coagulopathy defined as a platelet count lower than 50,000 or INR higher than 1.5 or a PTT higher than two times the control value	37	49.3
	Respiratory failure requiring mechanical ventilation for longer than 48 h	21	28
	History of GI ulceration or GI bleeding during past year	17	22.7
	Head trauma or spinal cord injury	30	8.2
	Burn >35% BSA	2	0.54
	Sepsis	24	6.6
	ICU admission lasting >1 week	68	18.7
	Occult GI bleeding lasting >6 days	-	-
	Renal insufficiency	21	5.8
	Minor	Hepatic failure	1
Heart failure		40	11
Use of warfarin		7	1.9
Multiple trauma		25	6.9
History of use of NSAID >3 months		4	1.09
Prolonged NPO status lasting >5 days with GI pathology or after major surgery		8	2.2
Glucocorticoid therapy (>250 mg hydrocortisone or the equivalent)		59	16.2
Use of heparin with therapeutic dose		75	20.6

INR: International Normalized Ratio, PTT: partial thromboplastin time, GI: Gastrointestinal, BSA: Body Surface Area, ICU: Intensive Care Unit, NSAID: Non- Steroid Antiinflammatory Drug, NPO: Non Per Oral

**Table 3.** Drugs used for stress ulcer prophylaxis.

Drug Class	No. of Patients	% of Population
H2 Blockers	123	61.5
PPIs	77	38.5
<b>Route of Administration</b>		
Intravenous	166	83
Oral	34	17
<b>Rationality</b>		
Guideline Based	159	79.5
Without Indication	41	20.5

Our results have shown the most major risk factor to stress ulcer prophylaxis was coagulopathy (49.3%), followed by mechanical ventilation for more than 48 hours (28%) and history of GI ulceration or GI bleeding during past year (22.7%). These findings were in line with the results of studies conducted by Horsa et al. (7), Rafinazari et al. (6), Farsaei et al. (11) and Foroughinia et al. (21) In other studies, mechanical ventilation for more than 48 hours was the primary major risk factor for SUP (5,20,22). SUP was the third symptom in all of the studies examined for a history of GI ulceration or GI bleeding in the previous year.

According to minor risk factors, in the present study, using heparin with therapeutic dose, ICU admission lasting >1 week and glucocorticoid therapy were the most indications for SUP (20.6%,18.7% and 16.2% respectively). These results were, in agreement with Farsaei et al. (1), Vazin et al. (20) and Foroughinia et al. (21) findings. Given that the methodology, applied guideline, and the setting of the studies were almost similar in, all of, these investigations and the difference in the priority of risk factors is small, it seems that physicians are familiar with risk factors. However, they are not familiar with the importance of rational prescription, and overuse of SUP is a universal problem. Overutilization of SUP medications shows that physicians may not

fully aware of the side effects of drugs, or the risks of GI bleeding have been instrumental in their decision for prophylaxis (6).

In this study, drug selection for SUP was determined by the H2RA class and the PPI class was the second choice, which is consistent with survey findings among Canadian (2) and United States (23) prescribers. In contrast, results of the studies by Vazin et al. (20) and Shahbazi et al. (24) in Iran, by Horsa et al. (7) in Ethiopia and by Chen et al. (25) in the United States, revealed that intravenous pantoprazole was the most prescribed drug for SUP. The use of H2RAs versus PPIs is a point of contention on SUP. While PPIs have more potent acid suppression and recent meta-analyses indicate that PPIs may be superior to H2RAs for SUP (26-28), no well-designed randomized trial has independently demonstrated this. Moreover, low association between H2RA use, *C. difficile* infection, and nosocomial pneumonia, as well as the lower cost, it seems that the choice of H2RAs is rational (29,30). Accordingly, the choice of drug type in the present study seems logical.

The limitations of this study are worth noting: first, since residents more than attending physicians determine whether, or not prescribe SUP in academic center, extrapolation of the result of our academic center to other hospitals was difficult. Second, our study was limited to the ICU and cannot be generalized to other wards.

## Conclusion

Physicians are familiar with risk factors, but they are not familiar with the importance of rational prescription, and overuse of SUP. So, we are far from ideal conditions.

## Acknowledgment

The authors would like to express their gratitude to the Clinical Research Development Unit of Imam Khomeini Hospital, Urmia University of Medical Sciences, for English editing.

**AUTHOR CONTRIBUTIONS:**

**Concept:** HS; **Design:** HAV; **Supervision:** HS; **Data Collection and/or Processing:** MA; **Analysis and/or Interpretation:** SA; **Literature Search:** MA; **Writing Manuscript:** SA, MV; **Critical Review:** HS.

**Ethics Committee Approval:** Approved by the research ethics committee of Urmia University of Medical Sciences, Iran. ir.umsu.rec.1396.36.

**Informed Consent:** No. Because our data collected from Patients\records and we had no intervention.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** Authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**References**

- Farsaei Sh, Ghorbani S, Adibi P. Variables Associated with Adherence to Stress Ulcer Prophylaxis in Patients Admitted to the General Hospital Wards: A Prospective Study. *Adv Pharm Bull*, 2017, 7(1), 73-80.
- Shears M, Alhazzani W, Marshall JC, Muscedere J, Hall R, English S.W. et al. Stress ulcer prophylaxis in critical illness: a Canadian survey *Traitement prophylactique de l'ulcère de stress en cas de maladie grave: un sondage canadien. Can J Anesth*, 2016, 63:718–24.
- Malhis A, Alghamdi T, Alfandi R, Issa ZA, Alanazi H, Alfintoukh H, et al. Appropriateness of acid-suppressing agents for stress ulcer prophylaxis in non-intensive care unit setting in Saudi Arabia. *J Pharm Bioall Sci* 2019;11: 96-101.
- Madsen KR, Lorentzen K, Clausen N, Oberg E, Kirkegaard PR, Maymann-Holler N et al. Guideline for stress ulcer prophylaxis in the intensive care unit. *Dan Med J*, 2014; 61(3): C4811.
- Masood U, Sharma A, Bhatti Z, Carroll J, Bhardwaj A, Sivalingam D, et al. A Successful Pharmacist-Based Quality Initiative to Reduce Inappropriate Stress Ulcer Prophylaxis Use in an Academic Medical Intensive Care Unit. *The Journal of Health Care Organization, Provision, and Financing*, 2018; 55: 1–5.
- Rafinazari N, Abbasi S, Farsaei S, Mansourian M, Adibi. Adherence to stress-related mucosal damage prophylaxis guideline in patients admitted to the Intensive Care Unit. *J Res Pharm Pract*. 2016;5(3):186-92.
- Horsa BA, Ayele Y, Ayalew MB, Assessment of pharmacologic prophylaxis use against stress ulcer in the medical wards of University of Gondar Hospital. *SAGE Open Medicine*.2019; 7: 1–7.
- Eisa N, Bazerbachi F, Alraiyes AH, et al. Q: do all hospitalized patients need stress ulcer prophylaxis? *Cleve Clin J Med* 2014; 81(1): 23–25.
- Barletta JF, Bruno JJ, Buckley MS, Cook DJ. Stress ulcer prophylaxis. *Crit Care Med*. 2016;44(7):1395-405.
- Lin CC, Hsu YL, Chung CH, Lee TH, Stress ulcer prophylaxis in patients being weaned from the ventilator in a respiratory care center: A randomized control trial. *Journal of the Formosan Medical Association* 2016; 115: 19-24.
- Huang HB, Jiang W, Wang CY, Qin HY, Du B, Stress ulcer prophylaxis in intensive care unit patients receiving enteral nutrition: a systematic review and meta-analysis. *Critical Care* 2018; 22:20:9 Pages.
- Farrell CP, Mercogliano G, Kuntz CL. Overuse of stress ulcer prophylaxis in the critical care setting and beyond. *J Crit Care*. 2010;25: 214-20.
- Mahmoudi L, Mohammadi R, Niknam R. Economic impact of pharmacist interventions on correction of stress-related mucosal damage prophylaxis practice. *Clinicoecon Outcomes Res*. 2019;11: 111-6.
- Tasaka CL, Burg C, Van Osdol SJ, Bekeart L, Anglemeyer A, Tsourounis C, An Interprofessional Approach to Reducing the Overutilization of Stress Ulcer Prophylaxis in Adult Medical and Surgical Intensive Care Units. *Annals of Pharmacotherapy*,2014; 1–8
- Thomas L, Culley EJ, Gladowski P, Goff V, Fong J, Marche SM. Longitudinal analysis of the costs associated with inpatient initiation and subsequent outpatient continuation of proton pump inhibitor therapy for stress ulcer prophylaxis in a large managed care organization. *J Manag Care Pharm*. 2010;16(2):122-9.
- Pham CQ, Regal RE, Bostwick TR, Knauf KS. Acid suppressive therapy use on an inpatient internal medicine service. *Ann Pharmacother*. 2006;40(7-8):1261-6.
- Farley KJ, Barned KL, Crozier TM. Inappropriate continuation of stress ulcer prophylaxis beyond the intensive care setting. *Crit Care Resusc*. 2013;15(2):147-51.
- Hatch JB, Schulz L, Fish JT. Stress ulcer prophylaxis: reducing non-indicated prescribing after hospital discharge. *Ann Pharmacother*. 2010;44(10):1565-71.
- Santos YA, Younes-Ibrahim MS, Crozatti LL, Raglione D, Cardozo Junior LC, Besen BA, et al. Adherence to a stress ulcer prophylaxis protocol by critically ill patients: a prospective cohort study. *Rev Bras Ter Intensiva*. 2020;32(1):37-42
- Vazin A, Mousavinasab R, Sabetian G. Evaluation of Stress Ulcer Prophylaxis Guideline in the Intensive Care Units of a Teaching Hospital: A Cross Sectional Study. *J Pharm Care* 2020; 8(2): 65-9.
- Foroughinia F, Madhooshi M. Attachment to stress ulcer prophylaxis guideline in the neurology wards of two teaching and non-teaching hospitals: A retrospective survey in Iran. *J Res Pharm Pract* 2016; 5(2): 138-41.
- Hammond DA, Killingsworth CA, Painter JT, Pennick RE, Chatterjee K, Boye B, Meena N. Impact of targeted educational interventions on appropriateness of stress ulcer prophylaxis in critically ill adults. *Pharmacy Practice* 2017;15(3):948. [https:// doi.org/ 10.18549/ PharmPract.2017.03.948](https://doi.org/10.18549/PharmPract.2017.03.948).
- Barletta JF, Erstad BL, Fortune JB, Stress ulcer prophylaxis in trauma patients. *Critical Care*. 2002 ;6 (6):526-30.
- Shahbazi F, Karimpur H, Hosseini E, Implementation of Stress Ulcer Prophylaxis (SUP) in an Intensive Care Unit (ICU). *Journal of Pharmaceutical Research International* 31(6): 1-7, 2019; Article no. JPRI.52271
- Chen P, Reddy N, Loesch E, Agrawal S, Appropriateness of Stress Ulcer Prophylaxis in Hospitalized Patients. *J Gastric Disord Ther*,2016; 2(3): doi <http://dx.doi.org/10.16966/2381-8689.122>.
- Barkun AN, Bardou M, Pham CQD, Martel M. Proton pump inhibitors vs. histamine 2 receptor antagonists for stress related mucosal bleeding prophylaxis in critically ill patients: a meta-analysis. *Am J Gastroenterol*. 2012;107: 507-20.
- Lin P, Chang CH, Hsu PI, Tseng PL, Huang YB. The efficacy and safety of proton pump inhibitors vs. histamine-2 receptor antagonists for stress ulcer bleeding prophylaxis among critical care patients: a meta-analysis. *Crit Care Med*. 2010;38: 1197-205.
- Alhazzani W, Alenezi F, Jaeschke RZ, Moayyedi P, Cook DJ. Proton pump inhibitors versus histamine 2 receptor antagonists for stress ulcer prophylaxis in critically ill patients: a systematic review and meta-analysis. *Crit Care Med*. 2013;41: 693-705.
- Katzung, Betram G., and Bertram G Katzung. *Basic & Clinical Pharmacology / by Betram G. Katzung*. 14th edition. New York: McGraw-Hill, 2018. Print.
- J. Larry Jameson, Anthony Fauci, Dennis Kasper, Stephen Hauser, Dan Longo, Joseph Loscalzo, *Harrison's Principles of Internal Medicine, Twentieth Edition (Vol.1 & Vol.2)* 20th Edition