

## Brief Communication

### Attachment to stress ulcer prophylaxis guideline in the neurology wards of two teaching and non-teaching hospitals: A retrospective survey in Iran

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#### ABSTRACT

**Objective:** In this study, we aimed to evaluate the attachment to stress ulcer prophylaxis (SUP) guideline in the neurology wards of two teaching and nonteaching hospitals.

**Methods:** A total of 243 patients were retrospectively reviewed in the neurology wards of two teaching and nonteaching hospitals. To assess the appropriate administration of SUP, an internal guideline was prepared using the American Society of Health-System Pharmacists (ASHP) protocol.

**Findings:** SUP prescriptions were noncompliant with ASHP guideline in about 93.1% and 84.6% of cases in the nonteaching and teaching hospitals, respectively.

**Conclusion:** SUP may be better practiced in teaching hospitals versus nonteaching ones.

**Keywords:** American Society of Health-System Pharmacists guideline; nonteaching hospital; stress ulcer prophylaxis; teaching hospital

## INTRODUCTION

Stress ulcer or stress-related mucosal disease is defined as "acute superficial inflammatory lesions of the gastric mucosa induced when an individual is subjected to abnormally elevated physiologic demands."<sup>[1]</sup> A backward glance shows that risk of bleeding from stress ulcers apparently declined from 20% to 30% in the 1970s to 1.5–14% in the 1990s.<sup>[2]</sup> In the late 1990s, the American Society of Health-System Pharmacists (ASHP) published guidelines on the use of stress ulcer prophylaxis (SUP) in medical, surgical, respiratory, and pediatric Intensive Care Unit (ICU) patients.<sup>[3]</sup>

In recent years, SUP practice has become more common in general medicine patients with little to no evidence to support it, though. To date, few studies have effectively examined the role

of SUP in non-ICU patients. In a retrospective case-control study at an American tertiary care center, it was demonstrated that hospital-acquired bleeding was uncommon in noncritically ill patients; therefore, routine prophylaxis was unnecessary in most hospitalized patients.<sup>[4]</sup> Likewise, another retrospective study showed that using SUP in the non-ICU setting brought about significantly high costs without any special benefit for the quality of care for patients.<sup>[5]</sup>

The present study was an effort to evaluate the appropriateness of SUP practice in the neurology wards of two teaching and nonteaching hospitals. It also aimed to assess the appropriateness of SUP practice in terms of drug choice, dose, route of administration, and duration of prophylaxis in both centers.

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## METHODS

The present work was a retrospective multicenter medication use evaluation (MUE) study from July 2009 to February 2010 in the neurology wards of two hospitals (one teaching and the other nonteaching) affiliated to Shiraz University of Medical Sciences (SUMS), Iran. The study was approved by the ethic committee of SUMS.

A total of 260 consecutive SUP prescriptions were retrospectively reviewed in these two centers. Patients who had received acid suppressing drugs (acid suppressing therapy [AST]) in the neurology ward of these hospitals were identified. They were excluded from the study if having either of the followings: (1) active gastrointestinal (GI) bleeding or active peptic ulcer(s) at the time of admission; (2) taken any AST as a home medication; and (3) taken AST for a specific indication (e.g., for treatment of gastroesophageal reflux disease, peptic ulcer disease, dyspepsia, recent acute, or suspected GI bleeding). Finally, 243 patients were included in the study.

A special data collection form was constructed containing the patients' demographic data such as age, gender, length of hospital stay, diagnosis, and disease state: Diagnosis and prescribed medications, past medical history/past medical treatment, lab tests including blood urea nitrogen, serum creatinine, coagulation tests, stress ulcer risk factors, and SUP regimen (agents used, dose, route, and duration) in addition to AST discharge medications. Once the patients were identified, the charts were reviewed to identify the indication for the SUP during whole hospitalization period. To assess the appropriate administration of SUP, an internal guideline was prepared based on ASHP protocol [Table 1]. Patients were considered eligible for SUP, if they had at least one absolute risk factor or two or more relative risk factors. The practice of SUP was classified as either appropriate or inappropriate regarding the indication for SUP, agents used, route, dose, and duration of the prophylaxis. In addition, SUP practice was compared across different hospital type (teaching vs. nonteaching). The appropriateness of doses was checked using ASHP guideline and DiPiro textbook.<sup>[3,6]</sup> SUP duration was defined proper as long as the indication for SUP was appropriate.

SPSS version 18.0 (SPSS, Inc., Chicago, IL, USA) was used for data analysis. Differences in proportions were tested by the Pearson Chi-square when assumptions were met; if not, the Fisher's exact test was used. For comparing the hospital duration stay across different hospital types, the non-parametric

test, Mann-Whitney, was used. All analyzes were carried out at the 0.05 significance level.

## RESULTS

The mean age of participants was  $56 \pm 18$  years (51% male). Among 243 patients included in this study, 205 patients had received SUP regimen (101 and 104 from the nonteaching and teaching medical centers, respectively). Although 7 patients had an indication for SUP, they had not received any AST. Of the 3 absolute risk factors, coagulopathy was the only absolute indication for SUP in the population under study. The list of patients' risk factors for stress ulcer is shown in Table 2.

In addition, it was found that about 84.6% of the total SUP prescriptions used in the teaching, and 93.1% of prescriptions in the nonteaching hospitals were noncompliant with the ASHP guideline. No statistically significant difference was observed among these two centers regarding the distribution of appropriate indication for SUP. On the other hand,

**Table 1: Internal guideline for stress ulcer prophylaxis prepared based on the American Society of Health-System Pharmacists protocol**

Absolute indications: Conditions in which prophylaxis must be given (mandatory)
Mechanical ventilation >48 h
Coagulopathy: Platelet <50,000/mm <sup>3</sup> ; INR >1.5; PTT >2 times normal value
History of GI bleeding or peptic ulcer disease within 1 year
Relative indications: Conditions in which prophylaxis could be given (optional): ≥2 conditions
Sepsis (core temperature >38.5°C or <35.0°C, WBC >15,000 or <3000/mm <sup>3</sup> , and positive blood culture)
Renal insufficiency (creatinine clearance rate <40 mL/min or serum creatinine concentration >2.8 mg/dL)
Hepatic impairment (bilirubin >8.8 mg/dL, serum AST >500 U/L, or albumin <4 g/L, or sign and symptom of hepatic coma)
Enteral feeding
Corticosteroids use (>250 mg/day hydrocortisone or equivalent)
Unfractionated or LMWH
Warfarin
NSAID use (>3 months)
An ICU stay of more than 1 week
Occult bleeding lasting 6 days or more
Spinal cord injury
Hepatic or renal transplantation
Head injury with GCS ≤ 10 or inability to obey simple commands
Thermal injury >35% BSA
Partial hepatectomy
Multiple trauma with ISS ≥ 16

WBC=White blood cell, AST=Aspartate aminotransferase, LMWH=Low-molecular-weight heparin, NSAID=Nonsteroidal anti-inflammatory drugs, ICU=Intensive Care Unit, GCS=Glasgow coma scale, BSA=Body surface area, ISS=Injury severity score, PTT=Partial thromboplastin time, INR=International normalized ratio, GI=Gastrointestinal

**Table 2: Patients' risk factors for stress ulcer in both teaching and non-teaching hospitals (n=243)**

Risk factor	Indication	N (%)
Coagulopathy	Absolute	11 (4.5)
Sepsis	Relative	10 (4.1)
Renal impairment	Relative	17 (7)
Hepatic impairment	Relative	6 (2.5)
Corticosteroid use (>250 mg hydrocortisone or equivalent)	Relative	19 (7.8)
Heparin or LMWH use	Relative	49 (20.2)
Warfarin use	Relative	7 (2.9)
Head injury with GCS ≤ 10 or inability to obey simple commands	Relative	1 (0.4)
Total patients with risk factors for SUP		120 (49.4)

LMWH=Low-molecular-weight heparin, GCS=Glasgow coma scale, SUP=Stress ulcer prophylaxis

**Table 3: Assessment of appropriateness of stress ulcer prophylaxis practice per hospital type**

SUP variable	Type of hospital (%)		P
	Non-teaching (n=101)	Teaching (n=104)	
Indication			0.055
Noncandidate	94 (93.1)	88 (84.6)	
Candidate	7 (6.9)	16 (15.4)	
Dose			<0.001
Appropriate	32 (31.7)	72 (69.2)	
Inappropriate	69 (68.3)	32 (30.8)	
Route			<0.001
Appropriate	31 (30.7)	91 (87.5)	
Inappropriate	70 (69.3)	13 (12.5)	
Dose and route			<0.001
Appropriate	10 (9.9)	71 (68.3)	
Inappropriate	91 (90.1)	33 (31.7)	
Acid-suppressant drugs			0.004
H <sub>2</sub> -RAs	37 (36.6)	62 (59.6)	
PPI	59 (58.4)	39 (37.5)	
Duplicate therapy	5 (5)	3 (2.9)	
Duration (days)	3.18 (±1.99)	4.99 (±1.83)	<0.001
Discharge on SUP			<0.001
Yes	31 (30.7)	67 (64.4)	
No	70 (69.3)	37 (35.6)	

SUP=Stress ulcer prophylaxis, H<sub>2</sub>-RAs=Histamine 2-receptor antagonists, PPI=Proton pump inhibitor

the other variables (dose, rout, regimen, agent used, duration of prophylaxis, and discharge on SUP) were significantly different between these two hospitals. The assessment of SUP practice in teaching and nonteaching hospitals was shown in Table 3.

## DISCUSSION

There seems to be a rapidly growing increase in SUP prescriptions for medical patients in hospitals, which may lead to the rising costs and health problems

associated with this over usage. This study was the first in the country to asses and compares the pattern of SUP prescribing in the neurology wards of two teaching and nonteaching hospitals. Our results showed that 84.6% of patients in the teaching and 93.1% in the nonteaching hospitals received unjustified SUP in accordance with the ASHP guideline for SUP. However, no statistically significant difference was observed among these two centers.

Several surveys have investigated the SUP prescribing behavior in both teaching and nonteaching hospitals worldwide. In a retrospective study conducted on 320 patients admitted to general wards of a governmental hospital, it was revealed that the majority of patients (92%) were not eligible for using SUP. The result was similar to our results in the investigated nonteaching hospital.<sup>[7]</sup> Another study investigating the pattern of SUP prescription in the infectious ward of a teaching hospital in our country, Iran, showed that 91.5% of patients who received AST did not have an indication for SUP. This result was somewhat similar to our result in the teaching hospital.<sup>[8]</sup>

To date, few studies have compared SUP practice in teaching and nonteaching hospitals. In a large multicenter prospective MUE, 16 hospitals (six teaching and ten nonteaching hospitals) from all parts of Lebanon were included in the study. According to its result, 62.2% of patients in the teaching and 70.3% of patients in the nonteaching hospitals were not eligible for SUP. Inappropriate usage of SUP was significantly less practiced in teaching hospitals versus nonteaching ones.<sup>[9]</sup> In another study performed in 2 academic and 2 nonacademic hospitals, about 100 proton pump inhibitor (PPI) prescriptions were reviewed retrospectively in each center. It revealed that PPI prescriptions initiated by academic hospitals were significantly more likely to be compliant with the guidelines compared to those initiated by nonacademic hospitals (50% vs. 29%, *P* < 0.05).<sup>[10]</sup>

Concerning the choice of the AST, PPIs and histamine 2-receptor antagonists (H<sub>2</sub>-RAs) were drug classes prescribed in our study with a higher frequency use of PPIs in the nonteaching (58.4%) and H<sub>2</sub>-RAs in the teaching centers (59.6%). Differences in choosing AST class in teaching and nonteaching hospitals, in our study, may show different prescribing behaviors in these centers where intravenous (IV) PPIs had been used as a routine practice for SUP in the nonteaching hospital due to the misconception that parenteral medications are more effective than the oral ones. However, studies have failed to show any efficacy or safety advantages of one formulation over the other.<sup>[11]</sup>

Overall, according to this investigation, 68.3% of the patients had received incorrect doses of SUP in the nonteaching and 30.8% in the teaching hospitals. More inappropriate AST dose in the nonteaching hospital in our study might have happened as a result of over usage of parenteral PPIs.

According to the ASHP guideline, prophylaxis should be discontinued upon discharge from the hospital or after the resolution of risk factors.<sup>[3]</sup> No evidence-based data support the continuation of AST at discharge. In addition, long-term administration of ASTs was associated with an unnecessary increase in the costs and an increased risk of pneumonia, hip fracture, and *Clostridium difficile* colitis.<sup>[12]</sup> In our study, a large number of patients (64.4%) in the teaching hospital were discharged on AST, whereas just about 30.7% of patients in the nonteaching hospital stayed on AST following discharge. This difference may have happened as a result of using various AST administration routes in these two hospitals, more IV therapy in the nonteaching hospitals and, therefore, less AST prescription at discharge.

The current study had several limitations. First, it was of a retrospective nature, which may lead to some data missing due to the patients' incomplete charts. Second, we were not able to follow patients for side effects happening as a result of the inappropriate continuation of AST at discharge and also its unwanted costs. Third, this study was carried out in only one medical ward of two teaching and nonteaching hospitals; therefore, it lacks generalizability.

Results of this study were in accordance with those of several previous studies. It has been revealed that SUP was significantly better practiced in teaching hospitals versus nonteaching ones.<sup>[9-10]</sup> Such results are not surprising because teaching hospitals are more likely to implement standard guidelines. In addition, writing and practicing guidelines by pharmacists for appropriate uses of SUP in noncritical care settings can be mentioned as a useful strategy to reduce AST misuse and its related expenses in both teaching and nonteaching hospitals.

## AUTHORS' CONTRIBUTION

Farzaneh Foroughinia contributed in the idea of research, study design, data gathering, data analysis, and manuscript preparation.

Mohammad Madhooshi contributed in study design, data gathering, data analysis, and preparing first draft of the manuscript.

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## Conflicts of interest

There are no conflicts of interest.

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