Journal of Pharmaceutical Research International

31(6): 1-7, 2019; Article no.JPRI.52271
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Implementation of Stress Ulcer Prophylaxis (SUP) in an Intensive Care Unit (ICU)

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Authors' contributions

This work was carried out in collaboration among all authors. Authors FS, HK and EH designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors FS and EH managed the analyses of the study. Author FS managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2019/v31i630326
Editor(s):
(1) Dr. Vasudevan Mani, College of Pharmacy, Qassim University, Buraidah, Kingdom of Saudi Arabia.
Reviewers:
(1) Manisha Aggarwal, Government Medical College, Patiala, India.
(2) N.S. Kannan, Sri Manakula Vinayagar Medical College and Hospital, India.
(3) Fabiana Lopes Joaquim, Brazil.
Complete Peer review History: http://www.sdiarticle4.com/review-history/52271

Original Research Article

Received 28 August 2019
Accepted 03 November 2019
Published 28 November 2019

ABSTRACT

Background: Critically ill patients are at high risk for developing stress ulcer bleeding, which may increase the length of hospitalization and mortality rate. Stress ulcer prophylaxis could be done either with PPIs or with H2 receptor blockers, which were prescribed in critically ill patients.
Aim: This cross-sectional study was accomplished in an intensive care unit to implement new stress ulcer prophylaxis.
Methods: This study was conducted in a tertiary hospital of Kermanshah province, west of Iran. Patients who were hospitalized for at least 72 hours and received SUP prophylaxis, were included in our study. Updated ASHP guideline was used for calculating SUP risk score. Patients received either PPIs or H2RA (intravenously or enteral). Efficacy and safety of early changes to enteral route were evaluated in one year and cost was calculated in three years' period.
Results: This study was conducted on 150 patients with a mean age of 58 ± 18 years old. More than half of patients (53.3%) were male. Stress ulcer prophylaxis was prescribed for all critically ill patients, regardless of the risk of GI bleeding while only 76.6% of patients had an appropriate

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indication for receiving SUP protocol. Six patients in the PPIs group (4 in intravenous and 2 in enteral) experienced gastrointestinal bleeding. Changing the route of administration from intravenous to intravenous over a three-year period resulted in a decrease in the mean use of pentoprazole vials from 12 to 4 per patient.
Conclusion: Early changing (within 72 hours) SUP from IV to enteral is safe and cost-saving approach.

Keywords: Anti-ulcer agents; critical illness; peptic ulcer; proton pump inhibitors.

1. INTRODUCTION

Since being first described in 1969, Stress Ulcer has been commonly known to be occurring in critically ill patients. Endoscopic evaluations have reported that as high as 74-100% of critically ill patients experience stress-related mucosal damage by passing 24 hours from admission [1]. At normal circumstances, oxygen supplies and bicarbonate neutralize excessive acids and subsequently prevent from mucosal injuries in the earlier mentioned patients [2]. Respiratory failure requiring mechanical ventilation, coagulopathy (e.g., INR> 1.5), hepatic and renal failure, circulatory shock, thermal injury, therapeutic doses of anticoagulants, and renal replacement therapy have been proposed risk factors for stress-related mucosal injuries [3,4]. Prophylactic treatments with Proton Pump Inhibitors [PPIs], type-2 histamine blockers [H2RA], and sucralfate have shown to reduce the incidence of stress-related injuries [2].

Several authorities have recommended some guidelines for stress ulcer prophylaxis [SUP] [5,6]. The guideline published by the American Society of Health System Pharmacist (ASHP) in 1999, before PPIs era, have suggested using either H2RA or sucralfate for SUP [6]. However, the newly published statements and guidelines have proposed either H2RA or PPIs for SUP in critically ill patients [7].

Stress ulcer prophylaxis regimens have been widely used for critically ill patients in pharmacoepidemiologic studies [8,9]. Most patients receive PPIs for SUP, which may increase the adverse effects and costs of prophylaxis [8].

Patients receiving omeprazole in bicarbonate solution have experienced an increase in their mean gastric PH values from 3.5±1.9 to 7.1±1.1, while being involved in no gastrointestinal bleeding [10].

The aim of the present single-center study was to investigate appropriateness of prescribed SUP and the implementation of early (i.e., within 72 hours) enteral omeprazole granule initiation, instead of intravenous dosage forms (e.g., pantoprazole or ranitidine) for SUP in critically ill patients in terms of the ASHP guidelines [6].

2. MATERIALS AND METHODS

2.1 Study Protocol

This cross-sectional research was conducted during one-year period from May 2016 to May 2017 in a 16-bed general ICU in a tertiary hospital of Kermanshah province in west of Iran. No formal USP guideline was available in this hospital. Stress ulcer prophylaxis with intravenous pantoprazole (40 mg twice daily) was commonly utilized for nearly all patients who were admitted to emergency departments. The study protocol was prepared and updated according to the ASHP guidelines (Table 1), and was approved by the ethical committee of the mentioned university with an ID number of 96033. Early enteral nutrition was implemented for them as soon as possible. All critically ill patients were considered as SUP candidates in our study, if they had one very high risk or two high risk criteria and were hospitalized for more than one week (Table 1). Patients with the history of active bleeding (during present hospitalization in the previous month), and septic shock were excluded from the study. For the patients who were enrolled in the study, either enteral omeprazole or ranitidine was administered within 72 hours at a daily dose of 20 mg or 150 mg twice daily per physician discretion and compared with routine SUP regimes (intravenous pantoprazole or ranitidine). This investigation was done in an ICU, to evaluate the appropriateness of the currently implemented SUP protocol for 72 critically ill patients, who stayed at least 72 hours in the study ICU. The nurses were educated about the proper way of opening the capsules and intact administration of the granules. In the case of intolerance and bleeding, an intravenous route of administration was followed. All the patients' demographic data and disease severity scores

were recorded based on the Sequential Organ Failure Assessment (SOFA), Acute Physiology and Chronic Health Evaluation (APACHE-II), baseline biochemical parameters, rate of diarrhea-related clostridium difficile infections, bleeding events, and full blood cell count. They were followed up twice a week for their possible adverse effects during their ICU stays. To compare the economic impact of this protocol implementation, use of intravenous proton pump inhibitors were followed for 2 consecutive years.

Table 1. SUP check-list guidelines [6]

Very high risk
Mechanical ventilation >48 h
Coagulopathy (INR >1.5 or platelet count <50000 mm)
High risk
Sepsis
Renal failure (BUN/Cr)
Hepatic failure (AST, ALT, and ALP)
Hypotension (systolic blood pressure <100 mm Hg)
Trauma
Major surgery (lasting >4 h)
Burns (>35% BSA)
Anticoagulation
Spinal or head injury
MI
Neurologic surgery
Multiple organ failure
Ileus
High-dose corticosteroid (>250 mg)
Past history of gastric ulcer
Low intragastric PH level

2.2 Statistical Analysis

Descriptive statistics were used to report the data, because most of them were not amenable to inferential testing. The normally distributed and skewed data were presented as mean ± SD and a median (range), respectively. A student t-test or Mann-Whitney U-test was utilized at the appropriate time. The dichotomous data were compared using either Pearson's χ^2 or Fisher's exact test as appropriate. All the collected data were analyzed using SPSS-16 version.

3. RESULTS

During the study period, 150 from 400 admitted patients with a mean age of 58 ± 18 years old, fulfilled our study requirements. Eighty patients (53.3%) were male. Their baseline characteristics are shown in Table 2.

Stress ulcer prophylaxis were appropriately prescribed in only 115 patients (115/150, 76.6%), while 96 (83.5%), 17 (14.8%), and 2 (1.7%) patients received PPIs, H2RA, and sucralfate for SUP, respectively. Enteral SUP was initiated and continued in 66.08% of all patients (i.e., 67 and 9 in PPIs and H2RA, respectively). Enteral PPIs changed to an intravenous route in 11 out of 113 patients (9.73%) before 72 hours (Table 2). In addition, in those who were not SUP candidates, PPIs and H2RA in (26/35, 74.3%) and (9/35, 25.7%) of patients were prescribed, respectively. The mean SOFA score was significantly higher in the PPI, in comparison with H2RA group (p=0.046).

During the study period, three patients in enteral PPIs and three patients in intravenous PPIs experienced overt gastrointestinal bleeding. Clostridium-associated diarrhea occurred in 11 out of 150 patients, who received PPIs for SUP, however no significant differences were observed between these two different protocols (11/115 patients vs. 0/35 patients, p=0.21). Hypomagnesemia occurred in 21 out of 150 patients (14%), but its incidence was not significantly higher in the PPIs vs. H2RA receivers either [18/21 patients (85.7%) vs. 3/21 patients (14.3%), p=0.43].

During the study period, 55 episodes of ventilator-associated pneumonia were diagnosed by the ICU team. Most of them occurred in the PPI group [51/55 patients (92.7%) vs. 4/55 patients (7.3%), p=0.01]. Finally, after establishing the protocol, the use of intravenous pantoprazole vials significantly decreased from 11 to 7 and 4 per patients in Year 1 and 2 after the protocol establishment, respectively (p=0.02). This result was related to save approximately 1,400,000 Iranian rials for each patient without enhancing the risk of gastrointestinal bleeding.

4. DISCUSSION

The results of the present research demonstrated the SUP appropriateness in 76.6% of the patients according to the ASHP guidelines, while most of them (83.5%) received PPIs [6]. Similarly, a multicenter study performed by Barletta et al. revealed an appropriateness percentage of 78% in the ICU-admitted patients [8]. In contrast, in a recent study by masoompour et al. it was showed that the SUP was appropriately prescribed in only 28% of patients, and surprisingly more than 90% of patients were

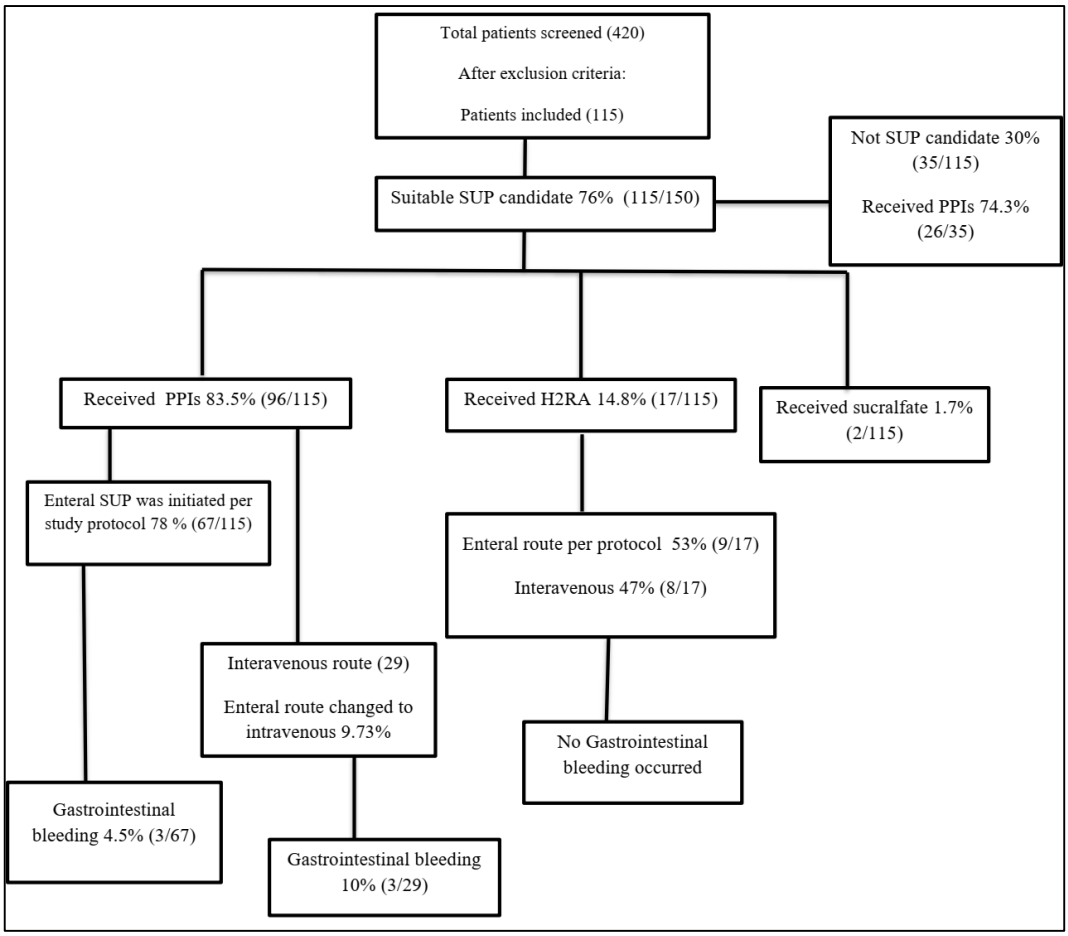

Fig. 1. Chart for included patients and experience outcome

Table 2. The patients' baseline characteristics

Parameter	PPI receiver	H2B receiver	P value
APACHEII. 1	17±5	12±4	0.137
APACHEII. 2	16±5	12±5	0.346
APACHEII. 3	16±5	12±4	0.335
SOFA. 1	8±2	5±1	0.046*
SOFA. 2	8±1	6±1	0.011*
SOFA. 3	7±2	5±1	0.411
Na1	140±6	137±4	0.031*
Na2	138±4	137±2	0.7
K1	3.9±.7	3. 9±.5	0.791
K2	3. 9±.5	3.7±.39	0.024*
WBC1	10±5	10±3	0.817
WBC2	11±5	10±3	0.770
Cr1	1.4±1.1	1. 1±0.6	0.738
Cr2	1. 4±1.3	1.1±0.5	0.767
INR	1. 2±.4	1. 1±.19	0.881
PLT1	205±98	210±68	0.258
PLT2	198±111	201±59	0.389
GFR	74±39	77±33	0.618

** significat difference*

discharged with SUP medications [Gastroenterol Nurs. 2017 Nov/Dec;40(6):491-495]. Mechanical ventilation for more than 48 hours, shock, and coagulopathy are the main risk factors for GI bleeding and initiation of SUP [4]. The minority of this study patients (14.7%) received H2RA for SUP, while about 30% of the patients in Barletta survey have received H2RA [8]. In the current research, SUP was universally prescribed for all the ICU-admitted patients, most of whom received PPIs.

Although our study had not been designed for comparing the enteral versus intravenous, no differences were found between the route of administration and incidence of gastrointestinal bleeding.

In our center, intravenous pantoprazole was commonly applied as an agent of choice for SUP initiation and maintenance, which might increase the treatment costs. In the present study, nasogastric or oral administration of omeprazole were initiated as soon as the patients could tolerate the enteral nutrition. GI bleeding rates were comparable in those patients who received enteral and parenteral PPIs. It should be noted that no differences were observed between the disease scores of SOFA or APACHE II, in those who received oral administration or intravenous route. The previous studies have compared the efficacies of nasogastric PPIs (omeprazole, rabeprazole, and lansoprazole) with that of H2RA [11–13]. Conrad, et al. evaluated the immediate-release formulation of omeprazole *vs*. intravenous infusion of cimetidine in their multicenter study on the ICU-hospitalized patients with APACH II score of 11 and higher for at least 48 hours. There was a significantly lower gastrointestinal bleeding rate in those patients who received immediate-release omeprazole [12]. In another study, Olsen and Devlin demonstrated that rabeprazole suppressed acid in critically ill patients, despite of its lower bioavailability [13]. The results obtained from different meta-analyses showed higher efficacy of PPIs in comparison with H2RA [14–16]. Therefore, one reason for high rate of PPIs prescription in our survey is PPIs efficacy in preventing from gastrointestinal bleeding.

In a recent meta-analysis, Alhazzani et al. reported the higher rate of pneumonia in the patients receiving PPIs for SUP [17]. Although our survey has not been designed to evaluate SUP adverse effects including pneumonia and Clostridium difficile infection, the patients who received PPIs had more clostridium-associated diarrhea and ventilator associated pneumonia episodes compared to those who received H2RA. Low-sample size of study and use of pantoprazole in high-risk patients might be responsible for higher pneumonia and diarrhea episodes in our study.

Furthermore, a very recent study compared the intravenous pantoprazole with placebo in critically ill patients at risk [18] representing clinically important events, such as bleeding, pneumonia, clostridium difficile infection, and myocardial infarction, which equally occurred in both groups [18]. It should be noted that 4.2% and 2.5% of the patients in the placebo and pantoprazole groups experienced clinically significant bleeding, respectively; however, the study was not powered to address secondary endpoints [19]. Therefore, not using SUP in critically ill patients at a high and very high risk of stress ulcer-related bleeding is not recommended.

In the present research, several medications (intravenous pantoprazole, enteral omeprazole, and enteral/intravenous ranitidine) were prescribed for SUP. Although a small sample size belonged to the patients was included in the study, no differences were observed between the enteral and intravenous regimens. Therefore, our protocol could be considered as a standard SUP, and initiated for the patients as soon as they could tolerate enteral nutrition. However, nasogastric tube obstruction was the main complication of such an approach [20].

As it was mentioned earlier, by passing three years from protocol implementation, a significant reduction in parenteral SUP were noted without significant increase in risk of GI bleeding. This is especially important for our hospital, because most of this hospital costs are afforded by government.

Our study had several limitations: first, our sample size was not adequate for properly detecting the differences between the different prophylaxis regimens (PPIs vs. H2RA); second, we were not able to measure intra-gastric PH levels.

5. CONCLUSION

Taken together, our research revealed that nasogastric administration omeprazole could serve as a safe, effective, and cheaper alternative for SUP.

CONSENT

As per international standard, patient's written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

The study protocol was prepared and updated according to the ASHP guidelines and was approved by the ethical committee of the mentioned university with an ID number of 96033.

ACKNOWLEDGEMENTS

This study forms part of a PharmD thesis (Elham Hosseini), and was supported financially by the Kermanshah University of Medical Sciences.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/52271