Original Research Article

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

Abstract

Critically ill patients are at high risk for developing stress ulcer bleeding that may increase the length of hospitalization and mortality rates. Stress ulcer prophylaxis may be done with either PPIs or H2 receptor blockers in critically ill patients was prescribed. This cross-sectional study was conducted in a intensive care unit. Patients who hospitalized for at least 72 hours and received SUP prophylaxis were included in our study. Updated ASHP guideline was used for SUP risk score calculation. Patients received either PPIs or H2RA (intravenously or enteral). Efficacy and safety of early changes to enteral rout was evaluate in one year and cost calculated in three years' period. This study was conducted in 150 patients with a mean age of patients were 58 ± 18 years. More than half of patients (53.3%) patients 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 indication to receive SUP protocol. Six patients in the PPIs group (4 in intravenous and 2 in enteral) experienced gastrointestinal bleeding. Changing administration rout from intravenous to enteral was done in During three-year period mean pantoprazole vial use reduced from 12/patients to 4/patients. Early changing (within 72 hours) SUP from IV to enteral is safe and cost-saving approach.

Key words: Stress ulcer prophylaxis, Protocol implementation, Critically ill patients

Introduction

Since being first described in 1969, Stress Ulcer Prophylaxis (SUP) has been commonly known to occur in critically ill patients. In addition, endoscopic evaluations have reported that as high as 74-100% of critically ill patients experience stress-related mucosal damage within 24 hours after admission (1). In normal situations, oxygen supplies and bicarbonate-neutralized excessive acids can prevent mucosal injuries in the mentioned patients (2). Such risk factors as respiratory failure requiring mechanical ventilation, coagulopathy, hepatic and renal failure, circulatory shock, thermal injury, anticoagulants, and renal replacement therapy have been proposed 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 SUP (5,6). The guidelines published by the American Society of Health System Pharmacist (ASHP) in 1999 have suggested 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).

SUP has been widely used in critically ill patients in pharmacoepidemiologic studies (8,9). Most patients receive PPIs for SUP, which may increase 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 (11).

The aim of the present single-center study was to investigate the implementation of enteral omeprazole granule administration instead of intravenous pantoprzole/ ranitidine for SUP in critically ill patients according to the ASHP guidelines (6).

Material and Method

This research was conducted in a 16-bed general ICU in a tertiary hospital with no local guidelines for SUP. SUP with intravenous pantoprazole at a dose of 40 mg is commonly utilized for nearly all the patients admitted to emergency departments. 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. After assessing their tolerations of enteral medication, administration of enteral omeprazole granules was initiated at a daily dose of 20 mg. The nurses were educated about the proper way of opening the capsules and administering the granule intakes. In the case of intolerance and bleeding, an intravenous route of administration was followed. All the patients' demographic data and disease severity scores 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 were recorded. The intravenous prophylactic regimens were changed to enteral omeprazole regimens for the patients as soon as they began to tolerate enteral

nutrition. Omeprazole was administered at a daily dose of 20 mg. The patients with active bleeding, a history of gastrointestinal bleeding in the previous month, and septic shock were excluded from the study. They were followed up twice a week for their possible adverse effects during their ICU stays. Early enteral nutrition was implemented for them as soon as possible. In the 2^{nd} and 3^{rd} years, only the data regarding pantoprazole uses were recorded.

Study protocol

This study was conducted in a 16-bed ICU in Kermanshah University of Medical Sciences. The study protocol was prepared and updated according to the ASHP guidelines (Table 1) and approved by the ethical committee of the mentioned university with an ID number of 96033. The patients would be considered as SUP candidates if they met a very high risk or two high risk criteria. For these patients, omeprazole was administered at a dose of 20 mg compared with routine SUP regimes.

Descriptive statistics were used to report the data since 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 when appropriate. The dichotomous data were compared using either Pearson's $\chi 2$ or Fisher's exact test as appropriate. All the collected data were analyzed using SPSS-16 version.

Results

During the study period, 150 patients with a mean age of 58±18 years fulfilled our study requirements. 80 out of 150 patients (53.3%) were male. Their baseline characteristics are shown in Table 2.

Only 115 out of 150 patients (76.6%) were SUP candidates, while 96 (83.5%), 17 (14.8%), and 2 (1.7%) patients received PPIs, H2RA, and sucralfate for SUP, respectively. 26 (74.3%) and 9 (25.7%) out of 35 patients, who were not SUP candidates, received pantoprazole and ranitidine, respectively. Most PPI receivers (70.8%) were treated based on enteral SUP protocol either at initiation or after 72 hours. Enteral PPIs changed to an intravenous route in 11 out of 113 patients (9.73%) (Table 3).

During the study period, 6 patients experienced overt gastrointestinal bleeding and needed to be treated with either intravenous pantoprazole (4 patients) or enteral omeprazole (2 patients). The mean SOFA score was significantly higher in the PPI compared with H2RA group (p=0.046). Clostridium-associated diarrhea occurred in 11 out of 150 patients, who received PPIs for SUP, but no significant differences were seen between the 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 PPI 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 the protocol was established, the use of intravenous pantoprazole vials significant 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 corresponding to saving approximately

1,400,000 Iranian rials for each patient without increasing risk of gastrointestinal bleeding.

Discussion

The results of the present research showed 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% among the ICU-admitted patients (8). 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 our patients (14.7%) received H2RA for SUP, while about 30% of the patients in Barletta survey had received H2RA (8).

In the current research, SUP was universally prescribed for all the ICU-admitted patients, most of whom received PPIs.

In our survey, no differences were found between the route of administration and incidence of gastrointestinal bleeding.

In our center, intravenous pantoprazole was commonly applied as an alternative agent 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 showed toleration. GI bleeding rates were comparable in the patients, who received enteral and intravenous PPIs. No differences between the disease scores of SOFA or APACHE II were observed 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 (12–14). 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 sore of 11 and higher for at least 48 hours. There was a significantly lower gastrointestinal bleeding rate in the patients, who received immediate-release omeprazole (13). In another study, Olsen and Devlin showed that rabeprazole suppressed acid in critically ill patients despite its lower bioavailability (14).

In our survey, the patients, who received PPIs, had more clostridium-associated diarrhea. The results obtained from different meta-analyses showed the higher efficacy of PPIs compared with H2RA, yet with different rates of adverse effects (15–17). In a recent meta-analysis, Alhazzani et al. reported the higher rate of pneumonia in the patients, who received PPIs for SUP (18). The uses of a low-sample size and pantoprazole in high-risk patients might be responsible for higher pneumonia episodes in our study.

Furthermore, a very recent study compared intravenous pantoprazole vs. placebo in critically ill patients at risk (19) representing clinically important events, such as bleeding, pneumonia, clostridium difficile infection, and myocardial infarction, which equally occurred in both groups (19). 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 (20). Therefore, we cannot recommend not using SUP in critically ill patients at a high and very high risk of stress ulcer-related bleeding.

In the present research, several medications (intravenous pantoprazole, enteral omeprazole, and enteral/intravenous ranitidine) were prescribed for SUP. Although a small sample size of the patients was included in the study, no differences were seen 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 (21).

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

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

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267 ***Table 1: SUP check-list guidelines***

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

285 ***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

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290 ***Table 3: The route of administration at the time of admission and its changes***

291 ***during ICU stay***

SUP route of administration in the candidate groups	PPI receivers	H_2RB receivers
Intravenous (IV) administration	22/113 (19.5%)	6/17 (35.3%)
Enteral administration	37/113 (32.7%)	6/17 (35.3%)
Change of IV to enteral administration	43/113 (38.1%)	9/35 (25.7%)
Change of enteral to IV administration	10/113 (8.8%)	3/35 (8.6%)
Change of IV to continuous infusion	1/113 (0.9%)	

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