Multimodal Management of Upper Gastrointestinal Bleeding Caused by Stress Gastropathy

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Abstract

Background: The 1999 ASHP (American Society of Health-System Pharmacists) recommendation regarding the prevention of stress-related mucosal disease and bleeding in critical care patients by using PPI and H2RA still holds. We tried to compare the results obtained by our group with the international data available and determine the benefits of this prophylactic therapy. Methods: The present paper presents a retrospective single center report of 36 patients with upper gastrointestinal (GI) bleeding caused by stress gastritis. Despite prophylaxis, the patients included in this study who were admitted in the ICU during a five year period (2003-2008) with various underlying conditions, had clinical and endoscopic diagnoses of bleeding from stress-related gastric mucosal disease. The initial treatment focused on patient stabilization first by medical intervention aimed at maintaining an elevated intragastric pH, in association with haemostatic drugs and blood transfusions; complementary endoscopic or surgical haemostatic therapy was employed for patients unresponsive to the initial management. Results: Despite prophylactic acid suppressive therapy, upper GI bleeding findings were consistently present in high risk patients, 69.4% presenting hematemesis and 55.6% presenting coffee-ground gastric content. Conclusions: Each institution needs to have guidelines in place to establish the patients that actually have sufficient risk factors to justify stress gastritis prophylaxis.

Keywords


Introduction

Although stress-related mucosal disease (SRMD) is very common in critically ill patients, significant upper gastrointestinal (GI) bleeding from stress-related mucosal disease is not [1]. Within the first 24 hours after ICU admission, approximately 75% to 100% of critically ill patients have some endoscopic evidence of gastroduodenal or upper GI lesions [2]. Clinical significant stress-related mucosal bleeding (gastroduodenal bleeding associated with clinically important complications, i.e. hemodynamic instability, need for blood transfusion or need for surgery) is a relatively infrequent event even when taking into consideration only ICU patients, with the incidence declining in the last 30 years [3] mainly due to the modern intensive care settings [4] and apparently independent of the use of prophylaxis. Implementation of a stress ulcer prophylaxis risk stratification scheme for ICU patients is necessary, since once this condition occurs, the mortality and morbidity associated are extremely high and the management options become very limited [5]. Prophylaxis of stress ulcers was shown to reduce the frequency of occurrence of major bleeding, but has not yet been shown to improve survival [6]. The cause of death is usually related to the underlying medical or surgical condition or to the multiple organ failure aggravated by the bleeding itself.

The present paper analyses the diagnosis, the treatment and the outcome in the management of patients with upper GI bleeding caused by SRMD in patients on mechanical ventilation for more than 48 hours.

Methods

This study is a retrospective single center case series report of 36 patients hospitalized in the St. Pantelimon University Emergency Hospital in Bucharest. All patients included in this study have received prophylaxis (acid suppressive therapy) for SRMD.

The following terms were used to define the study group: the critically ill patients at risk for developing SRMD are the patients admitted to the ICU and requiring
mechanical ventilation or having coagulopathy or an ICU stay longer than 1 week, with or without a history of active peptic ulcer disease in the previous year or corticosteroid therapy, regardless of the underlying condition (including sepsis, massive burn injury, polytrauma, severe trauma and multiorgan failure, head trauma associated with increased intracranial pressure). Upper GI bleeding was identified by clinical findings, laboratory data and endoscopic confirmation using multiple criteria: guaiac-positive stool and nasogastric aspirate, frank hematemesis or melena, defined as any episode of coffee-ground emesis requiring lavage, hematemesis or melena with or without a change in hemoglobin levels or hematocrit, accompanied or not by a decrease in hemoglobin level, a drop in blood pressure or need for blood transfusion. Severe (clinically important) gastrointestinal bleeding was identified by a spontaneous decrease in systolic blood pressure of 20 mm Hg or more, an increase in heart rate more than 20 beats per minute, or a decrease in hemoglobin level more than 2 g/dL and subsequent transfusion of blood after which hemoglobin levels do not increase by a value defined as the number of units transfused minus 2.

In order to assess the presence and the severity of upper GI bleeding in these patients, relevant clinical findings and laboratory data were gathered and documented. Once the clinical diagnosis of upper GI bleeding was established, the endoscopic examination was employed to confirm the presence of the gastrointestinal mucosal lesions and the etiology. The timeframe in which endoscopic examination was performed ranged from 15 minutes to 12 hours after the clinical diagnosis of upper GI bleeding. This represented approx. 12 hours to 5 days after admission to the ICU and it identified the hemorrhagic stigmata in patients with increased risk of continued or resuming bleeding. A subset of patients could not be managed medically or endoscopically and surgical intervention was warranted.

Results

The study included 36 critical care patients, admitted to the critical care ward with a severe polytrauma diagnosis in 23 patients (21 motor vehicle accidents, 2 work related trauma), an underlying neoplasm with other than gastric location following surgical intervention in 7 patients or other causes (Table I).

All patients were mechanically ventilated for at least 48h and in one case for 18 days (Fig. 1). None had any underlying coagulopathy, such as a preexisting thrombocytopenia. Screening for hereditary coagulopathies was not performed.

In this group (Table II), only 2 (patients 5.55%) had a history of upper GI bleeding and 8 patients (22.22%) were receiving anti-acid medication at the time of bleeding. Patient history was significant for a previous episode of upper GI bleeding in 2 patients, previous history of peptic ulcer in 2 male patients and intermittent dyspeptic syndrome in 6 patients.

<table>
<thead>
<tr>
<th>Table I. Diagnosis of underlying conditions</th>
<th>Frequency (%)</th>
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<tbody>
<tr>
<td>Acute myocardial infarction</td>
<td>1 (2.8%)</td>
</tr>
<tr>
<td>Motor vehicle accident</td>
<td>21 (58.3%)</td>
</tr>
<tr>
<td>Work related trauma</td>
<td>2 (5.6%)</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>7 (19.4%)</td>
</tr>
<tr>
<td>Severe pneumonia</td>
<td>2 (5.6%)</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>2 (5.6%)</td>
</tr>
<tr>
<td>Entero-mesenteric infarction</td>
<td>1 (2.8%)</td>
</tr>
<tr>
<td>Total</td>
<td>36 (100.0%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table II. Previous GI patient history</th>
</tr>
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<tbody>
<tr>
<td>Cases (N=36)</td>
</tr>
<tr>
<td>male</td>
</tr>
<tr>
<td>--------------------------------------------</td>
</tr>
<tr>
<td>Previous GI bleeding</td>
</tr>
<tr>
<td>Acid suppressive therapy</td>
</tr>
<tr>
<td>Previous peptic ulcer disease (PUD) history</td>
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<tr>
<td>Surgical therapy attempted</td>
</tr>
<tr>
<td>Dyspeptic syndrome history</td>
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</tbody>
</table>

Twenty-one patients (58.33%) received histamine 2 receptor antagonists (H2RA) prophylaxis and 15 patients (41.66%) received proton pump inhibitors (PPIs). The average acid suppressive therapy duration was 2-3 days and in 4 patients - 7 days.

The initial upper GI bleeding diagnosis was clinical, followed by endoscopic confirmation. In 20 patients the nasogastric tube demonstrated coffee-ground-like gastric content; 6 patients presented with hematemesis and coffee-ground-like emesis. A subgroup of 7 patients presented with an association of hematemesis and melena/coffee ground emesis or melena and 7 patients presented with melena,
Upper GI bleeding caused by stress gastropathy

The endoscopic examination was performed as soon as the patient was hemodynamically stable, regardless of the presence of the endotracheal tube, with an average period of 6–8h after the start of the GI bleeding. The timeframe within which endoscopic examination was performed ranged from approx. 15 minutes to 12 hours after establishing the clinical diagnosis of upper GI bleeding, which represented a period of 12 hours to 5 days after admission to the ICU. In 4 cases immediate endoscopy was performed (Fig. 2).

Endoscopy revealed erosions or ulcers, often with stigmata of recent hemorrhage, such as adherent clots or petechiae. These lesions are usually more shallow, more diffuse and more numerous than those of peptic ulcers. In 3 cases (83%), the esophagogastrroduodenoscopy identified alongside the gastric lesions, associated duodenal lesions (erythema and erosions). The site of the gastric lesions was the upper 1/3 of the stomach in 14 patients (27.8%), the whole stomach in 17 patients (47.2%) and the antropyloric region in 10 patients (27.8%). The endoscopic examination revealed gastric ulcerations in 36 patients.

The techniques we used included thermocoagulation, epinephrine injection (0.5–1 ml dilution 1:10000), absolute alcohol and saline injections (saline used in order to achieve tamponade). Various other substances such as ethanol, polidocanol and sodium tetradecyl sulfate were employed in 4 cases, with good results in 3 cases: one patient required surgical intervention.

Surgery was attempted in 4 cases (11.11%) that did not respond to the medical or endoscopic therapy. The registered mortality was 7 cases (19.44%).

**Discussion**

Currently there are many terms used to identify the stress-related gastric damage in critically ill patients (stress ulcers/ulceration, stress erosions, stress gastritis, hemorrhagic gastritis, erosive gastritis and SRMD). The upper GI bleeding that can result from this condition can also be identified and graded according to multiple criteria (guaiac-positive stool and nasogastric aspirate, frank hematemesis or melena, accompanied or not by a decrease in hemoglobin level, drop in blood pressure, need for blood transfusion). Spontaneous decrease in systolic blood pressure of 20 mm Hg or more, an increase in heart rate > 20 bpm, a decrease in systolic blood pressure > 10 mmHg on sitting up, and a decrease in hemoglobin level more than 2 g/dL and subsequent transfusion of blood after which hemoglobin levels do not increase by a value defined as the number of units transfused minus 2, all identify clinically important GI bleeding and this definition has been used in previous studies [7].

According to a landmark multicenter prospective cohort study on 2,252 patients by Cook et al [7], approx. 2% to 6% of ICU patients had had overt bleeding (defined as any episode of coffee-ground emesis requiring lavage, hematemesis, or melena with or without a change in hemoglobin levels or hematocrit). Similar results were obtained in another study [8]. Once the upper GI bleeding occurs, the mortality rate in patients with endoscopic evidence of ulcer, bleeding, or both within 18 hours of admission to a medical ICU was 57%
compared with 24% in patients with either a normal mucosa, only nonhemorrhagic erosions or petechial changes [9]. The mortality for the critically ill patients with GI bleeding is 50% to 77%, and the cause of death is not that much the bleeding itself, but the underlying medical condition or the aggravated multiple organ failure.

According to the 1994 Cook study [7], prophylaxis against stress ulcers can be safely withheld from critically ill patients unless they have coagulopathy or require mechanical ventilation, since few critically ill patients have clinically important GI bleeding. The prophylaxis and the treatment for the GI bleeding determined by stress gastritis are guided by a well defined therapeutic protocol realized in 1999 by ASHP (The American Society of Health-System Pharmacists). This protocol defines the indications for medical, surgical, respiratory, and pediatric ICU patients and still holds [10]. Stress ulcer prophylaxis is recommended for adults admitted to the ICU who have coagulopathy, require mechanical ventilation for more than 48 hours, have a history of GI ulceration or bleeding within 1 year before admission or have at least two of the following risk factors: sepsis, ICU stay longer than 1 week, occult bleeding lasting 6 days or longer and use of more than 250 mg hydrocortisone or the equivalent [11]. The ASHP recommendations do not cover single system injuries such as head trauma, spinal cord injury or thermal injury [12].

Currently, in strong contrast to the initial 1994 and 1999 recommendation, the use of acid suppressive therapy as part of SRMD and associated upper GI bleeding prophylaxis has become increasingly more common in general patients, with little to no evidence to support it. As many as 71% of patients in general medicine wards are receiving some sort of acid-suppressive therapy without an appropriate indication, although this practice is currently not recommended or supported [10, 11], and despite the fact that any form of prophylaxis against stress ulcers is expensive [13, 14] and can have adverse effects [15].

Stress-related mucosal disease encompasses two types of mucosal lesions and the continuum that can be described between these two: (1) stress-related injury, which is diffuse, superficial mucosal damage, and (2) discrete stress ulcers, which are deep focal lesions that penetrate the mucosa to the submucosa. Both types are caused by mucosal ischemia [16] and both show a propensity for the acid-producing corpus and fundus [17].

The stress-related erosive syndrome can be caused by multiple factors, ranging from sepsis, massive burn injury, polytrauma, head trauma associated with increased intracranial pressure, and multiorgan failure [7]. The pathophysiology is multifactorial and includes major factors such as reduced blood flow, mucosal ischemia, hypoperfusion, and reperfusion injury [11]. Still, despite the postulated pathogenetic role of ischemia in stress gastritis, selective vasopressin infusion in the left gastric artery achieves hemostasis in 80% of cases [18]. In patients on mechanical ventilation, positive pressure-induced splanchnic hypoperfusion appears to play a central role in the etiology of SRMD, associating also other two dreaded complications - GI hypomotility and diarrhea [19]. The inflammatory response in severely ill patients can severely affect the patient’s gastric mucosa perfusion, even without influencing peripheral oxygen saturation levels [20]. Luminal acid secretion can be increased by psychological factors and leads to multiple erosive lesions, independent of previous H. pylori infection status or NSAIDs exposure, enhancing the aggressive factors that predispose to peptic ulcer or exacerbating preexisting ulcer disease. The identified risk factors for clinically important GI bleeding include major burns, head injury, previous peptic ulcer disease in the last 6 weeks, organ transplants, upper GI bleeding in the previous 42 days [7], respiratory failure requiring mechanical ventilation for longer than 48h, the presence of a coagulopathy [7], and as probable risk factors older age, repair of abdominal aortic aneurysms, severe burns, multiple organ failure, neurological trauma, sepsis or septic shock, and high-dose corticosteroid therapy (intravenous or oral ≥40 mg/day) [2].

Currently, the indications for prophylactic treatment are to some degree arbitrary. Since hypotension is a known risk for decreased mucosal perfusion, maintenance of the hemodynamic stability is very important. It is extremely important to prevent gastric injury by prompt and appropriate therapy of the underlying systemic disease, including reversal of hypoxemia and hypotension and by avoidance of gastrotoxic medications such as aspirin or other NSAIDs [21]. In 2002, 86% of critically ill patients admitted to the ICU received some sort of stress ulcer prophylaxis [22]. The agents used are H2RA, sucralfate and PPIs [2], with a tendency towards using PPI more frequently. Proton pump inhibitors provide more consistent pH control than H2RA. There is no consensus on the drug of choice for stress ulcer prophylaxis with several meta-analyses providing conflicting results on the superiority of any medication [19]. Now, H2RA are the most widely used class of agents for SMRD prophylaxis, although PPIs are gaining in acceptance and are proved to be as effective as H2RA [5]. H2RA are more effective than sucralfate [23].

It has not been established whether enteral feeding is protective or just a marker for a patient that has a less severe condition, although it is established that it optimizes splanchnic distribution and lessens macroscopic ulceration [5]. Proper randomization is difficult to perform in the studies that address enteral feeding and can theoretically invalidate the consistent result in various studies that early enteral feeding is associated with a less likely tendency to bleed than in patients who are not tolerating enteral feeding. A remarkable result is presented in a study by Raff et al [24], who concluded that enteral feeding initiated within 12 h of trauma (if tolerated by the patient and this in itself is a marker of the patient’s condition) was as effective in reducing the risk of clinical significant upper GI bleeding as H2RA therapy and/or anti-acids [25].

The incidence of stress related mucosal bleeding is decreasing [5]. This is attributed to both improvements in
critical care and to the prophylactic administration of acid suppressive therapy [26, 27]. Recent trials [27-29] emphasize that prophylactic therapy seems not to alter the already low incidence of stress-related clinically important bleeding even in high risk patients or to justify the cost of the treatment; this raises the questions whether there will be a time when routine prophylaxis for SRMD will no longer be necessary [5] and whether there is a need for a review of the 1999 ASHP recommendation.

In our institution, the underlying management principle for upper GI bleeding caused by stress-gastritis in the critically ill patients is prophylaxis, by critically ill patients identifying the patients admitted to the ICU and requiring mechanical ventilation or having coagulopathy or ICU stay longer than 1 week. A history of active peptic ulcer disease in the previous year or corticosteroid therapy are also considered indications for prophylaxis. Gastric contents pH monitoring provides an objective variable to determine the current status of the patient and the efficiency of the therapy, but it is not routinely performed. The target pH value should be greater than 4.0. Anything less should prompt the clinician to double the dose of the agent used if the patient was previously on prophylaxis.

The prophylaxis of upper GI bleeding caused by stress gastropathy should be applied by first identifying the major risk patients and then by taking into account economic factors, since these determine the futility of large scale implementations. For each patient, the therapeutic decision should be individualized according to the severity of the presenting hemorrhage and the coexisting morbidities. We observed that this approach still does not manage all cases of this rare condition, raising the question whether there is an economic justification to the current prophylactic symptomatic approach.

Conclusion

We recommend that each institution has guidelines in place to determine what patients actually have sufficient risk factors to require stress gastropathy prophylaxis. The type of therapy applied must be tailored to the patient’s presentation, taking into consideration the gravity of the bleeding, the associated morbidities and the general status of the patients.

Conflicts of interest
No conflict to declare.

References
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