UAB Hospital Trauma/Burn ICU Stress Ulcer Prophylaxis Guidelines

Background

Stress ulcers are superficial erosions involving the mucosal layer of the stomach or duodenum that develop after major stressors such as surgery or trauma, and may lead to clinically significant bleeding events.[1] The pathogenesis of stress ulcer development is multifactorial, due to a combination of acid hypersecretion, impaired mucosal protection, decreased mucosal blood flow, and increased concentrations of refluxed bile salts.[2,3]

In the absence of appropriate prophylaxis, it is estimated that 1.5 to 8.5% of ICU patients develop some degree of gastroduodenal hemorrhage.[4] The goal of prophylaxis is to prevent clinically relevant complications of stress ulcers such as hemorrhage severe enough to require transfusion, endoscopic therapy, or surgery.[5] In patients at highest risk for stress ulcers (8-10%) proton pump inhibitors (PPI) and histamine-2 receptor antagonists (H2RA) reduce clinically important bleeding by 3-5%.[6] Patient risk factors for development of clinically important bleeding should guide the need for stress ulcer prophylaxis.

The following guidelines are not intended for patients with known gastric or duodenal ulcer disease requiring acid suppression therapy. Patients with pre-existing indications for gastric acid suppression should continue home therapy when possible to avoid rebound acid hypersecretion.[6]

Clinical Practice Guidelines

I. Three risk factors for stress ulcer development have been found to independently predict an increased risk of clinically relevant bleeding - respiratory failure, chronic liver disease and coagulopathy. [6,7] Other factors have been identified as potential risk factors and warrant careful consideration.[7,8]

   a. Stress ulcer prophylaxis is indicated for patients with >4% risk of gastrointestinal bleeding due to any of the following factors:

      i. Respiratory failure requiring mechanical ventilation > 48 hours **without enteral nutrition**

      ii. Coagulopathy

         1. Platelet count < 50,000 mm^3
         2. INR > 1.5 or PT >20 seconds
         3. Concurrent dual antiplatelet therapy or combination anticoagulation

      iii. Chronic liver disease

         1. Portal hypertension
         2. Cirrhosis proven by biopsy, computed tomography scan, or ultrasound
         3. History of variceal bleeding
         4. History of hepatic encephalopathy

      iv. **<u>Two or more</u>** potential (moderate) risk factors

         1. Shock (defined by **at least 1** of the following):

a. Continuous infusion of vasopressors or inotropes
b. Systolic blood pressure < 90 mm Hg
c. Mean arterial pressure < 70 mm Hg
d. Plasma lactate level ≥ 4 mmol/L

2. Sepsis
3. Acute kidney injury or need for renal replacement therapy
4. Mechanical ventilation with enteral nutrition

b. Stress ulcer prophylaxis should be considered for patients with any of the following factors:
1. Spinal cord injury
2. Acute hepatic failure
3. Traumatic brain injury
4. Multi-trauma with ISS > 16
5. Thermal injury involving > 35% TBSA

c. Stress ulcer prophylaxis is not indicated in patients with the following as they have a <4% risk of clinically important bleeding:
1. <2 Moderate risk factors (see above)
2. Malignancy
3. Use of corticosteroids or immunosuppression

II. Choice of pharmacological agent

a. Proton pump inhibitors are recommended over H2 receptor antagonists for stress ulcer prophylaxis. While the two agents have similar efficacy, recent meta-analyses and controlled trials illustrate superior efficacy of PPIs when compared to H2RAs.[9] There is no clinically important difference between the two agents regarding mortality, hospital or ICU length of stay.[10]

b. Intravenous is preferred over enteral route of administration for patients with concern of malabsorption or non-functioning GI tract.

c. There is conflicting data regarding the efficacy of sucralfate for stress ulcer prophylaxis.[6] The results from the SUP-ICU trial suggest that sucralfate does not reduce the risk of clinically important bleeding when compared with placebo.[10] Therefore, sucralfate is currently not recommended for routine use.

Table 1

Drug name	Dosage Forms	Dose	Dose Adjustments	Adverse Effects
First Line				
Proton pump inhibitors				
Pantoprazole	Inj, Delayed Release Tab	40mg Daily	None	Abdominal pain, Diarrhea, Hypomagnesemia, increased risk of recurrent C. diff

Esomeprazole	Capsules	40mg Daily	Severe hepatic impairment(Child-Pugh C): Do not exceed 20 mg/day	Abdominal pain, Diarrhea, Hypomagnesemia, increased risk of recurrent C. diff
Second Line				
Histamine-2 Receptor Antagonists				
Famotidine	Inj, Tab	20mg BID	CrCl 30-60mL/min: 20mg Daily CrCl less than 30mL/min: 20mg Every other day	Constipation, Diarrhea, Headache, Thrombocytopenia

III. Duration of stress ulcer prophylaxis remains controversial. Some studies suggest an association between stress ulcer prophylaxis and hospital acquired pneumonia. Others suggest an association between stress ulcer prophylaxis and *C. difficile* infection. There is currently no data to suggest that any one agent may increase the risk of pneumonia or initial episode of *C. difficile* infection.[6]

a. Enteral feeding appears to have a protective effect against stress ulcer related bleeding and stress ulcer prophylaxis should be discontinued once tolerating goal tube feeds. [11] Stress ulcer prophylaxis likely provides no added benefit to patients receiving enteral nutrition.[12]

b. Continue prophylaxis until the patient is no longer critically ill or until the risk factor triggering prophylaxis is no longer present.[6]

IV. Prevention of recurrent stress ulcer related bleeding. [8]

a. Efficacy of medical therapy for prevention of recurrent stress induced bleeding has not been well studied.

b. Consideration should be given to increasing the dosage of the current prophylactic medication, adding a second agent, or switching to a different agent.

Summary and Recommendations

I. Stress ulcer prophylaxis is recommended for ICU patients with at least one independent risk factor and for ICU patients with two or more potential risk factors.

II. The use of proton pump inhibitors is currently recommended over H2 receptor antagonists. However, there are no differences in mortality or ICU length of stay between agents.[9]

III. Prophylaxis should be continued for patients in the ICU as long as risk factors persist or until tube feeds at full goal or diet is tolerated. As risk factors resolve, stress ulcer prophylaxis should be discontinued.[6]

IV. Stress ulcer related bleeding while on appropriate prophylaxis warrants consideration of increasing medication dosage, adding a second agent, or switching to a different agent.

References

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Additional resources:

13. Young PJ, et al. Effect of Stress Ulcer Prophylaxis With Proton Pump Inhibitors vs Histamine-2 Receptor Blockers on In-Hospital Mortality Among ICU Patients Receiving Invasive Mechanical Ventilation: The PEPTIC Randomized Clinical Trial. JAMA. 2020 Feb 18;323(7):616-626.

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