Outline

- Definition
- Pathophysiology
- Mortality and morbidity
- Current Guidelines & Evidence
- Agent Selection & Administration
- Complications
- Role of pharmacist:

Stress ulcer defined

Stress ulcerations usually occur in the fundus and body of the stomach, but sometimes develop in the antrum, duodenum, or distal esophagus. They tend to be shallow and cause oozing of blood from superficial capillary beds. Deeper lesions may also occur, which can erode into the submucosa and cause massive hemorrhage or perforation. (1)

Pathophysiology

Etiology is complex

- Decreased mucous production:
  This barrier may be denuded by increased concentrations of refluxed bile salts or uremic toxins, which are common in critically ill patients. In addition, its synthesis may be decreased when there is poor gut perfusion caused by shock, sepsis, or trauma.

- Hyper secretion of acid: Hypersecretion of acid due to excessive gastrin stimulation of parietal cells has been detected in patients with head trauma. H. pylori infection may also contribute to stress ulceration (1)
Mortality and morbidity

Patients with Stress-related mucosal damage (SRMD) have much higher mortality rates than those without (57% vs. 24%) (3)

Current Guidelines & Evidence

Key guideline points (1)

The major four (start SUP if patient has one of these four factors):

1 - Coagulopathy
   - Platelet count of <50,000mm3
   - INR>1.5
   - PTT of >2 times the control

2 - Mechanical Ventilation Longer than 24 hours

3 - Recent GI ulcers/bleeding Within 12 months of admission

4 - Traumatic brain injury, traumatic spinal cord injury, or thermal injury (>35 percent of the body surface area)

The minor:

2 or more of the following:

1- sepsis
2- shock
3- ICU>1 week
4- Occult Bleeding within 6 days
5- High dose corticosteroids (250mg Hydrocortisone ,50mg Methylprednisone)
6- hepatic failure, renal failure,
7- organ transplantation
8- administration of nonsteroidal anti-inflammatory agent
9- ISS>15 .(Injury severity score).
**Note:**
The use of intragastric enteral nutrition may have additive cytoprotective effects when used in conjunction with H2RAs, but whether administration of intragastric enteral nutrition alone provides adequate protection is controversial. (4)

Among patients who are not considered high risk for gastrointestinal bleeding, we believe that stress ulcer prophylaxis should be administered on a case-by-case basis. Among the considerations are whether the patient is receiving enteral nutrition, how long the patient is expected to be without enteral nutrition, the severity of the patient’s illness, and the patient’s comorbidities. (1)

**The agents used: (1)**

<table>
<thead>
<tr>
<th>Family</th>
<th>Mechanism of action</th>
<th>Route of administration</th>
<th>Agent</th>
<th>Efficacy</th>
<th>Safety</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>H2 blockers</td>
<td>Histamine-2 receptor antagonists (H2 blockers) antagonize the H2 receptors on the parietal cell, resulting in diminished gastric acid secretion.</td>
<td>orally, via nasogastric tube, or intravenously</td>
<td>cimetidine, famotidine, ranitidine, nizatidine</td>
<td>-significantly lower rate of GI bleeding than antacids -decreased overt GI bleeding compared to sucralfate</td>
<td>ventilator-associated pneumonia was more frequent in the H2 blocker group, than sucralfate</td>
<td>intravenous H2 blockers are substantially less expensive than intravenous PPIs</td>
</tr>
<tr>
<td>Proton pump inhibitor</td>
<td>block acid secretion by irreversibly binding to and inhibiting the hydrogen-potassium ATPase pump that resides on the luminal surface of the parietal cell membrane.</td>
<td>orally, via nasogastric tube, or intravenously</td>
<td>omeprazole, lansoprazole, pantoprazole, esomeprazole</td>
<td>less GI bleeding than H2 blockers</td>
<td>higher incidence of nosocomial pneumonia among patients who received a PPI than those who received an H2 blocker</td>
<td>Oral PPI may be more cost-effective than intravenous H2 blockers. (This was a consequence of the lower cost of oral medication)</td>
</tr>
<tr>
<td>Drug</td>
<td>Description</td>
<td>Treatment Failures</td>
<td>Comparability</td>
<td>Rate of GI Bleeding</td>
<td></td>
<td></td>
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<tr>
<td>---------------</td>
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<tr>
<td>Sucralfate</td>
<td>Sulfated polysaccharide complexed with aluminum hydroxide. It exerts its effects by coating and protecting the gastric mucosa, without altering gastric acid secretion</td>
<td>ns and fewer treatment failures in the oral PPI group</td>
<td>No comparable study</td>
<td>Lower rate of clinically important GI bleeding than antacids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antacids</td>
<td>Neutralize gastric acid and protect the gastric mucosa</td>
<td>Higher incidence of nosocomial pneumonia than sucralfate</td>
<td>No comparable study</td>
<td>Higher GI bleeding than H2 blockers and PPI and sucralfate</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Carbonate bicarbonate Aluminum hydroxide:**
**Doses:** (1) (2) (3)

<table>
<thead>
<tr>
<th>family</th>
<th>Agent</th>
<th>doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>H2 blockers</td>
<td>cimetidine, famotidine, ranitidine,</td>
<td>300 mg orally or IV Q 6-8 H</td>
</tr>
<tr>
<td></td>
<td>nizatidine</td>
<td>20 mg twice daily orally OR IV</td>
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<tr>
<td></td>
<td></td>
<td>150 mg twice daily(oral)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50 mg every 6-8 hours(IV)</td>
</tr>
<tr>
<td>Proton pump inhibitor</td>
<td>omeprazole, lansoprazole, pantoprazole, esomeprazole</td>
<td>40 mg orally</td>
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<tr>
<td></td>
<td></td>
<td>30mg PO Q24 Hours</td>
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<tr>
<td></td>
<td></td>
<td>40 mg (Q12-24h)IV or orally</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20-40 mg</td>
</tr>
<tr>
<td>Sucralfate</td>
<td>-</td>
<td>1 gram four times per day orally</td>
</tr>
<tr>
<td>Antacids</td>
<td>Aluminum hydroxide magnesium hydroxide Calcium carbonate</td>
<td>300 mg tab</td>
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<tr>
<td></td>
<td></td>
<td>150 mg tab</td>
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<tr>
<td></td>
<td></td>
<td>1-2 tablets</td>
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</table>

**About drugs:** (4) (5)

- Histamine2 Receptor Antagonists are equally efficacious, so the choice of which H2RA to use varies according to adverse effects, ease of administration, formulary availability, and institution-specific cost. The clinically relevant adverse effects attributed to H2RAs in the critically ill patients include thrombocytopenia (especially pediatric), confusion (especially elderly), interstitial nephritis, rapid infusion-related hypotension and sinus bradycardia, and possibly pneumonia.

- Despite pharmacokinetic differences, PPIs are equally efficacious for maintaining gastric pH > 4. However, only lansoprazole and omeprazole have been studied for stress ulcer prophylaxis. While tolerance does not occur with PPIs (occurred in H2-blocker), the development of rebound acid hypersecretion is common after discontinuation of PPI therapy. Other clinically relevant adverse effects associated with PPIs include diarrhea, interstitial nephritis, possibly pneumonia associated with gastric microbial growth, neurologic effects of high-dose intravenous omeprazole administration (hearing and vision disturbances, seizures), and hypophosphatemia and metabolic alkalosis associated with enteral administration of the bicarbonate method.
The most common adverse events of Sucralfate are constipation, occlusion of the feeding tube, gastrointestinal bezoar formation, electrolyte disturbances (hypokalemia and hypophosphatemia), aluminum toxicity (especially in the presence of renal dysfunction), and drug binding warfarin, phenytoin, digoxin, fluoroquinolones, theophylline, quinidine, L-thyroxin) or feeding interactions. Sucralfate has not been shown to increase the risk of aspiration pneumonia but has been associated with acid aspiration to cause aspiration pneumonitis.

**Duration:**

Discontinue prophylaxis when the patient is no longer at high risk for stress ulceration (1).

**Role of pharmacist:**

*Document* the indication for ongoing therapy
- The major
- The minor

*Discontinue* therapy if not indicated, so Reduce the risk to patients, Reduce costs.

*Discuss* the indications with the patient/provider.

**Summary:**

- Give Stress Ulcer Prophylaxis therapy when indicated (major and minor)

- Stress Ulcer have a high mortality (nearly \( \frac{1}{2} \))

- Discontinue Stress Ulcer Prophylaxis when no longer indicated

- Stress Ulcer Prophylaxis has risks (HAP, C diff, Osteoporosis).

- The pharmacist role: Document, Discontinue, Discuss
References:
(1) Gerald L Weinhouse, MD. Stress ulcer prophylaxis in the intensive care unit. (UPTODATE.COM)
(2) drugs.com