Stress Ulcer Prophylaxis in the ICU:
If you can’t feed them, proton pump inhibit them

Karen Lo
University of Colorado, PGY4
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Stress Related Mucosal Injury
Overview

- History
- Physiology
- Who is at risk?
- The medications:
  - Why PPIs are better
Stress Related Mucosal Injury History

- 1800s: Curling described ulcers in burn patient
- 1969: Skillman reported stress ulcers in ICU patients
- 1970s: Lucas coined the term stress related mucosal damage
- 1980s incidence of stress ulcers decreasing by increasing gastric pH

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- Endoscopic studies have shown nearly all critically ill patients develop upper GI erosions
  - 90% ICU patients have gastric erosions by ICU day 3

Stress Related Mucosal injury
Pathophysiology

Critical Illness

- Increased catecholamines
- Increased vasoconstriction
- Hypovolemia
- Proinflammatory cytokine release
- Cardiac output

Splanchnic hypoperfusion

- Reduced HCO$_3^-$ secretion
- Reduced mucosal blood flow
- Decreased GI motility
- Acid back diffusion

Acute stress ulcer

Source: Curr Med Res Opin © 2005 Librapharm Limited
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Who is at risk?

Level 1

- Mechanical ventilation over 48 hours
- Coagulopathy
  - INR >1.5 or plt<50
- Traumatic brain injury
- Major burn

Level 2

ICU pt with:
- Multi-trauma
- Sepsis
- Acute Renal failure

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Prophylaxis:

What drug do I use?

- Antacid
- Carafate
- H2 blockers
- PPI
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the other meds:

Antacids

- Neutralizes the acid of the stomach
- Oral
- Re-dose every 1-2 hours
- Aspiration pneumonia
- Toxicity:
  - Hypermagnesium
  - Hyperphosphotemia
  - Hypercalemia
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the other meds: Sucralfate

- Oral
- Coats and adheres to gastric mucosa
- Does not change gastric pH
- Decreases absorption of some medications
- Aluminum toxicity
Stress Related Mucosal Injury
the other meds:
Sucralfate

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Stress Related Mucosal Injury
the other meds:
Histamine Receptor Antagonist

- Oral and IV
- Ranitidine superior to sucralfate in preventing UGI bleed in ICU Pt *
- Reversibly binds to H₂ receptor of parietal cells

*Cook, Risk factors for clinically important UGI bleeding in pts requiring mechanical Ventilation. Critical Care Med 1999 Dec 27(12):28 12-7
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the other meds:
Histamine Receptor Antagonist

- Does not acid stop stimulation from Acetycholine and Gastrin receptors
Stress Related Mucosal Injury
the other meds:

Histamine Receptor Antagonist

- Less gastric acid control
- Multiple daily dosing
- Unwanted side effects: 7% adverse reactions
  - Altered mental status, neutropenia, thrombocytopenia
- Increased incidence of hospital acquired pneumonia
- Drug Resistance: Tachyphylaxis
Stress Related Mucosal Injury

PPI

- Irreversibly binds to Proton pump
  - Inhibiting the final step in acid production
  - Rapid onset of action
  - Longer duration of action

![Diagram showing the proton pump and its receptors](Figure 1a)

Figure reproduced with permission from Lars Olbe, Enar Carlsson, and Per Lindberg. A Proton-Pump Inhibitor Expedition: The Case of Omeprazole and Esomeprazole. Nature Reviews Drug Discovery (www.nature.com) 2003;2:132-139
Stress Related Mucosal Injury

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Figure 1a

The proton pump

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PPI

- Safe
- Do not increase the risk of hospital acquired pneumonia

Stress Related Mucosal Injury
Oral PPI versus IV H2B

- Direct comparison omeprazole versus ranitidine in 77 trauma patients
- Prospective RCT
- Single institution

**TABLE 3. CLINICAL OUTCOMES***

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<th>Omeprazole</th>
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<td>5 (14%)</td>
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* Clinically significant bleeding, secondary to stress ulcers, occurred at a statistically significant more frequent rate in those patients receiving ranitidine as compared to omeprazole. Nosocomial pneumonia also occurred more frequently in patients given ranitidine; however, the difference was not statistically significant.

Stress Related Mucosal Injury
PPI versus H2B

- **PPI** less incidence of stress ulcer bleed: 6%
- **H2B** increased incidence of stress ulcer bleeding: 31%

LEVY, Comparison of Omeprazole and Ranitidine for Stress Ulcer Prophylaxis, Digestive Diseases Science. 1997; 42; 6

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Stress Related Mucosal Injury

PPI versus H2B

- H2B do increased the risk of hospital acquired Pneumonia
- PPIs do not increase the risk of hospital acquired Pneumonia

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Stress Related Mucosal Injury
Oral PPI versus IV H2B

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Any overt bleeding included both end point and non-end point bleeding. Inadequate pH control was defined as two consecutive gastric pH determinations of ≤4 at least 1 hr apart on any given day of treatment; tabulated patients experienced inadequate pH control at least once during the trial. The difference in rates was calculated as omeprazole-cimetidine.

<sup>a</sup> Noninferiority analysis, one-sided 97.5% confidence interval; <sup>b</sup> two-sided 95% confidence interval, p = .005; <sup>c</sup> two-sided 95% confidence interval, p < .001.

Conrad. Randomized, double blind comparison of immediate-release omeprazole oral suspension vs IV cimetidine for prevention of UGI bleed in Critically ill patients, Critical care med 2005;33 760-765
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PPI versus H2B cost

Observational study of ICU patients

- 32 pts on Cimetidine
- 25 pts on Cimetidine who were changed to lansoprazole
- 31 pts on Lansoprazole

Stress Related Mucosal Injury
PPI versus H2B cost

- Of 32 patients on Cimetidine
  - 5 failed
- All 31 patients on Lansoprazole had successful treatment

Stress Related Mucosal Injury
PPI versus H2B

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<td>Cimetidine</td>
<td>Omeprazole</td>
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<tr>
<td>Potency to reduce gastric acid secretion</td>
<td>++</td>
<td>++++</td>
</tr>
<tr>
<td>Common side effects</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Drug interactions</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Tachyplaxis</td>
<td>+</td>
<td>None</td>
</tr>
<tr>
<td>Cost-effectiveness</td>
<td>++++</td>
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Ali, Stress -Induced Ulcer Bleeding in critically Ill patients, Gastroenterology 2009 245-265
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- McCarthy, Management of bleeding peptic ulcers: Current status of intravenous proton pump inhibitors, Best Practice and Research Clinical Gastroenterology 2004; 18: 7-12
- Mohebbi, L et al. Stress Ulcer Prophylaxis in the ICU, Pharmacology Notes 2009; 22(4):373-376