Stress Ulcer Prophylaxis

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Disclosure Statement

• No conflict of interest

Objectives

• Who should be receiving stress ulcer prophylaxis in your institution?
  – Pathophysiology
  – Risk Factors
• What medications are best to use to prevent stress ulcers?
  – The great debate: PPIs vs. H2RAs vs. sucralfate
• What are the complications of providing stress ulcer prophylaxis?
  – Strategies for gaining back the control
Objectives

- Who should be receiving stress ulcer prophylaxis in your institution?
  - Pathophysiology
  - Risk Factors
- What medications are best to use to prevent stress ulcers?
  - The great debate: PPIs vs. H2RAs vs. sucralfate
- What are the complications of providing stress ulcer prophylaxis?
  - Strategies for gaining back the control

The Guidelines

- Last updated 1999
- What’s missing?
- Are they still relevant?

History

1880's
Erosions & Gastric Ulcers have been known to develop

1970's
Gastric Acid linked as possible cause of stress ulcer development

1980's
Incidence of stress-ulcer related bleeding was found to be decreased by increasing gastric pH
Terminology

- Stress Ulcers
- Ulceration
- Stress erosions
- Stress gastritis
- Hemorrhagic gastritis
- Erosive gastritis
- Peptic Ulcers
- Gastric Ulcers

- Stress-Related Mucosal Disease
  - SRMD

Diagnosis & Appearance

- Diagnosis
  - Endoscopic evidence

- Appearance
  - Diffuse sub-epithelial hemorrhage with or without erosions

Figure Legend:

Illustration of the difference between an erosion and an ulcer. An erosion is a mucosal break that does not penetrate the muscularis mucosae, whereas an ulcer does penetrate the muscularis mucosae. Reproduced with permission from Weinstein.


Where is this occurring?

- SRMD typically occur in the acid-producing areas of stomach
  - Upper body
  - Fundus

Risk of Bleeding

- Table 2 from 1999 ASHP Guidelines
  - Diverse endpoints
  - What's it all mean?

Definitions

- Clinically Important Bleeding
  - Guaiac-positive stool
  - Nasogastric (NG) aspirate
  - Frank hematemesis or melena without an accompanied decrease in hemoglobin level, BP or a need for transfusion
Classification of GI Bleeding

<table>
<thead>
<tr>
<th>Outcome Measure of GI Bleeding</th>
<th>Definition</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endoscopic Evidence</td>
<td>Endoscopic evidence of gastroduodenal SMD lesions</td>
<td>Present in 74 to 100% of ICU patients</td>
</tr>
<tr>
<td>Occult</td>
<td>Guaiac-positive stool or nasogastric aspirate</td>
<td>Present in 15 to 50% of ICU patients</td>
</tr>
<tr>
<td>Overt OR Clinically evident</td>
<td>Hematemesis, gross blood on coffee grounds material in nasogastric tube aspirate, hematemesis or melena</td>
<td>Present in less than 5 to 25% of ICU patients</td>
</tr>
<tr>
<td>Clinically Significant</td>
<td>Gastroduodenal bleeding associated with clinically important complications including hemodynamic compromise, need for blood transfusion, or need for surgery</td>
<td>Present in less than 3% of ICU patients</td>
</tr>
</tbody>
</table>

**Epidemiology**

- GI Ulceration
  - 75% to 100% occur within 24 hours of ICU admission
- Overt bleeding < 25%
- Clinically significant bleeding < 6%
  - Rates are decreasing

Outcomes

- **Morbidity**
  - Increases length of ICU stay from 4 to 8 days, or even 11 days longer stay

- **Mortality**
  - 50% - 75% of patients with clinically significant bleed
  - > 50% directly attributable to the bleed

- **Cost of bleed**
  - $7000 in 1999

Cook et al. NEJM. 1994;330:377-381.
AJHP. 1999;56;347-379.

Proposed mechanisms for development of stress ulceration. SRMD results from the complex interaction of multiple systems. The specific relationships depicted remain somewhat speculative. Reprinted with permission from Bresalier. 44

Figure Legend:

*GI Complications in Patients Receiving Mechanical Ventilation*
Risk factors for SRMD

- Respiratory failure requiring mechanical ventilation ≥ 48 hrs
- Coagulopathy (INR > 1.5 or platelet count < 50,000 mm³)
- Acute renal insufficiency
- Acute hepatic failure
- Sepsis syndrome
- Hypotension
- Severe head or spinal cord injury

- Anticoagulation
- History of gastrointestinal bleeding
- Low intragastric pH
- Thermal injury involving more than 35% of the BSA
- Major surgery lasting > 4 hrs
- High dose corticosteroids
- Enteral feedings

Indications for Stress Ulcer Prophylaxis 1999

<table>
<thead>
<tr>
<th>Patients admitted to Intensive Care Unit</th>
<th>Respiratory failure requiring mechanical ventilation ≥ 48 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coagulopathy</td>
<td></td>
</tr>
<tr>
<td>Thermal injury involving more than 35% of the body surface area</td>
<td></td>
</tr>
<tr>
<td>Hepatic Failure or Hepatic/Renal Transplant</td>
<td></td>
</tr>
<tr>
<td>Multiple Trauma</td>
<td></td>
</tr>
<tr>
<td>Spinal/Cord Injury</td>
<td></td>
</tr>
<tr>
<td>History of GI Ulceration</td>
<td></td>
</tr>
</tbody>
</table>

Presence of at least two of the following:
- Sepsis, ICU stay of > 5 days, occult or overt bleeding for > 5 days, corticosteroid therapy
Timeline

1999 Risk for clinically important GI bleeding is dramatically decreasing

Incidence dropping to 0.1% to 4% with or without prophylaxis

Why?
Better drugs?
Better care in our ICUs?

Cook et al. NEJM. 1994;330:377-381.

Prophylaxis per Risk Factor

Agents for SUP
Patient Case

- 57 year old male admitted to the ICU with sepsis 2 days ago
  - Placed on Mechanical Vent at that time due to respiratory failure
  - Also experiencing some acute renal failure
    - SO increased from 11.9 to 14.8
  - Medications include
    - Norepinephrine to help maintain normal blood pressure
    - Vancomycin, Zosyn, and Cindamycin
    - Ranitidine 50 mg IV q 8hrs
    - Cimetidine 50 mg/hr
    - Sucralfate 1 gm q 6 hrs NG tube
    - Enteral Nutrition

Patient Case

- Should this patient receive Stress Ulcer Prophylaxis?

Patient Case

- Should this patient receive Stress Ulcer Prophylaxis?
- If yes, which of the following is best to use?
  a. Pantoprazole 40 mg IV daily
  b. Ranitidine 50 mg IV q 8hrs
  c. Cimetidine 50 mg/hr
  d. Sucralfate 1 gm q 6 hrs NG tube
  e. Enteral Nutrition

- 57 year old male admitted to the ICU with sepsis approx. 2 days ago
  - Placed on Mechanical Vent at that time
  - Also experiencing some acute renal failure
  - Medications include
    - Norepinephrine to help maintain normal blood pressure
    - Vancomycin, Zosyn, and Cindamycin
The great debate: PPI's vs. H2RA's vs. Sucralfate

WHAT MEDICATIONS ARE THE BEST FOR STRESS ULCER PROPHYLAXIS?

Therapeutic Options

- Antacids
- Sucralfate
- Histamine 2 Receptor Antagonists (H2RA)
- Proton Pump Inhibitors (PPI)

Antacids

- Rarely used today
  - Labor intensive
  - Dosed to pH
    - pH of 3.5 to 4
    - 30 to 60 cc every 30 to 60 minutes
    - Required frequent monitoring
  - Many adverse effects or interactions
    - Diarrhea, constipation, fluoroquinolone interaction, etc.
    - Pneumonia
Sucralfate

- Vasic, non-absorbable aluminum salt of saccharose octasulfate.
- Doesn’t change the pH of the stomach
  - Thought to have less risk of pneumonia
- MOA:
  - In acidic environment forms a polymer that eventually binds with the protein cations in the exposed ulcer

Histamine Receptor Antagonists (H2RA’s)

- Started in the mid 90’s with cimetidine infusion
- IV and PO formulation
- ADR
  - Thrombocytopenia
  - Pneumonia
- Drug interactions
  - P450, etc.

Proton Pump Inhibitors

- Activated by protonation in parietal cells and then binds to H+K+ counter exchange ATPase to block acid production
- IV and PO forms
- Becoming less expensive
- No renal adjustments
- ADR’s
  - Pneumonia
  - C. diff
- Possible drug interactions
  - P450s and CYP3A4
Dosing

<table>
<thead>
<tr>
<th>Medication</th>
<th>Route</th>
<th>Dose</th>
<th>Renal Insufficiency (CrCl &lt; 50 mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sucralfate</td>
<td>PO</td>
<td>1 gm Q6h</td>
<td>Caution in severe renal impairment</td>
</tr>
<tr>
<td></td>
<td>NG</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Histamine2Receptor Antagonists

<table>
<thead>
<tr>
<th>Medication</th>
<th>Route</th>
<th>Dose</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cimetidine</td>
<td>PO</td>
<td>300 mg Q6h</td>
<td>300 mg PO Q12h</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>IV</td>
<td>50 mg Q6 to 8 hrs</td>
<td>Reduce dose to 50 mg Q12 hr</td>
</tr>
<tr>
<td>PO</td>
<td>150 mg PO QID</td>
<td>Reduce dose to 150 mg Q12 hr</td>
<td></td>
</tr>
<tr>
<td>Famotidine</td>
<td>PO</td>
<td>20 mg Q12h</td>
<td>Reduce dose to 20 mg daily</td>
</tr>
<tr>
<td></td>
<td>NG &amp; IV</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Proton-Pump Inhibitors

<table>
<thead>
<tr>
<th>Medication</th>
<th>Route</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esomeprazole</td>
<td>PO</td>
<td>40 mg daily</td>
</tr>
<tr>
<td></td>
<td>NG &amp; IV</td>
<td></td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>PO</td>
<td>15 to 30 mg daily</td>
</tr>
<tr>
<td></td>
<td>NG &amp; IV</td>
<td></td>
</tr>
<tr>
<td>Omeprazole</td>
<td>PO</td>
<td>20 to 40 mg daily</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>PO</td>
<td>40 mg daily</td>
</tr>
<tr>
<td></td>
<td>NG &amp; IV</td>
<td></td>
</tr>
</tbody>
</table>

Which Agent is Better?

- H2RA’s vs. Antacids
- H2RA’s vs. Sucralfate
- H2RA’s vs. PPI’s
<table>
<thead>
<tr>
<th>Medication</th>
<th>Mode of Action</th>
<th>Other Protective Mechanisms</th>
<th>Comments/Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antacids</td>
<td>Direct neutralization of gastric acid in a dose-dependent fashion.</td>
<td>Gastric pH is kept &gt; 3.5–4.0</td>
<td>Increased nursing costs. Hypomagnesemia (Mg(^{2+}) based). Hypophosphatemia (Al(^{3+}) based). Constipation (Al(^{3+}) based). Diarrhea (Mg(^{2+}) based). Interferes with absorption of certain drugs (e.g., tetracycline, quinolones).</td>
</tr>
<tr>
<td>H₂-Blockers</td>
<td>Increase pH by blocking H₂ receptors</td>
<td>No beneficial cytoprotective effects</td>
<td>Continuous provides better pH control compared to intermittent, but is not more effective as a preventive therapy. Interstitial nephritis. Confusion (especially elderly). Thrombocytopenia. Hypotension, sinus bradycardia (rapid IV infusion). P450-mediated effects (particularly cimetidine).</td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
<td>Inhibit parietal cell H⁺-K⁺-ATPase and block the final step of H⁺ production</td>
<td>No beneficial cytoprotective effects.</td>
<td>Diarrhea. P450-mediated effects.</td>
</tr>
<tr>
<td>Pirenzepine</td>
<td>Anticholinergic and inhibits acid secretion via M₂ muscarinic receptors.</td>
<td>Improves mucosal blood flow (2 and 3 can occur independently of PG).</td>
<td>Not available in North America.</td>
</tr>
</tbody>
</table>

**Critical Illness**

- Increased Catecholamines
- Decreased Cardiac Output
- Increased Vasoconstriction
- Reduced HCO\(^{3+}\) Secretion
- Reduced Mucosal Blood Flow
- Acid Back Diffusion

**Acute Stress Ulcer**

- Hypovolemia
- Proinflammatory Cytokine Release

**Reduced GI motility**

**Acute Stress Ulcer**

**Stress**

- Mucosal Ischemia
- Impaired Blood Flow
- Impaired Proton Removal
- Impaired Defense Mechanism

- Mucosal Ischemia
- Reperfusion Injury
- Acid Injury
- Impaired Blood Flow
- Impaired Proton Removal
- Impaired Defense Mechanism

**Acute Stress Ulcer**

**GI Bleed**
Does Enteral Nutrition Help?

- Benefits in critically ill
  - Improves splanchnic blood flow
  - Reduces macroscopic ulceration
- Does it reduce the risk of developing SRMD?
  - Lack of significant evidence
- Bottom line
  - Don’t use Enteral nutrition as sole SRMD prophylaxis measure
What about Adverse Events of prophylaxis?

- Delirium
- Thrombocytopenia
- Community Acquired Pneumonia
- Clostridium difficile
- Fractures
- Nutrient malabsorption
- Ventilator Associated Pneumonia
- Acute interstitial nephritis


Risk of Pneumonia

Use of Proton Pump Inhibitors and the Risk of Community-Acquired Pneumonia: A Population-Based Case-Control Study

Table 1. Association Between the Use of Proton Pump Inhibitors (PPIs) and Community-Acquired Pneumonia (CAP) in a Population-Based Case-Control Study

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Case</th>
<th>Control</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No PPIs</td>
<td>100</td>
<td>200</td>
<td>1</td>
<td>0.12</td>
</tr>
<tr>
<td>PPIs</td>
<td>50</td>
<td>100</td>
<td>2.5 (1.2-5.2)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Figure Legend: Association Between the Use of Proton Pump Inhibitors (PPIs) and Community-Acquired Pneumonia (CAP) in a Population-Based Case-Control Study.

Table 2. Stratum-Specific Odds Ratios (ORs) for the Association Between Current Use of Proton Pump Inhibitors (PPIs) and Community-Acquired Pneumonia (CAP) in a Population-Based Case-Control Study

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 60</td>
<td>2.0 (1.0-4.0)</td>
<td>0.05</td>
</tr>
<tr>
<td>Age ≥ 60</td>
<td>3.0 (1.5-6.0)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Figure Legend: Stratum-Specific Odds Ratios (ORs) for the Association Between Current Use of Proton Pump Inhibitors (PPIs) and Community-Acquired Pneumonia (CAP) in a Population-Based Case-Control Study.
Use of Proton Pump Inhibitors and the Risk of Community-Acquired Pneumonia: A Population-Based Case-Control Study

Figure Legend:
Association between current use of proton pump inhibitors (PPIs) and community-acquired pneumonia, according to the timing of first PPI prescription. ORs indicate odds ratios.


Proton-Pump Inhibitor Use and the Risk for Community-Acquired Pneumonia

Table 1: Odds Ratios for Community-Acquired Pneumonia Associated with Exposure to Proton-Pump Inhibitors and Histamine-2–Receptor Antagonists among New Recipients of Each Drug

<table>
<thead>
<tr>
<th>Drug Type</th>
<th>Odds Ratio (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proton-Pump Inhibitor</td>
<td>2.00 (1.50-2.68)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Histamine-2–Receptor Antagonist</td>
<td>1.50 (1.00-2.24)</td>
<td>0.054</td>
</tr>
</tbody>
</table>

Table 2: Odds Ratios for Community-Acquired Pneumonia Associated with Proton Pump Inhibitor Exposure with Expanded Case-Control Matching Criteria

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol Use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunosuppression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic Kidney Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular Disease</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure Legend:
Odds Ratios for Community-Acquired Pneumonia Associated with Proton-Pump Inhibitor Exposure with Expanded Case-Control Matching Criteria

archinternmed.com/applyingpgr.jpg
Risk of Community-Acquired Pneumonia and Use of Gastric Acid-Suppressive Drugs

### Table 1. Relative Risk for Community-Acquired Pneumonia by Exposure to Gastric Acid-Suppressive Therapy

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Unexposed</th>
<th>Current PPI Use</th>
<th>Current H2RA Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>320,001</td>
<td>10,292</td>
<td>10,277</td>
</tr>
<tr>
<td>Percent cases</td>
<td>97.3%</td>
<td>97.0%</td>
<td>97.2%</td>
</tr>
<tr>
<td>Adjusted odds ratio</td>
<td>1.00</td>
<td>1.07 (0.90–1.27)</td>
<td>1.01 (0.86–1.19)</td>
</tr>
</tbody>
</table>

*Adjusted odds ratio, confidence intervals.

Arch Intern Med 2007 1.5 (1.3–1.7) 1.10 (0.8–1.3) Ann Intern Med 2008 1.02 (0.97–1.08) 0.99 (0.95–1.04) JAMA 2004 1.89 (1.36–2.62) 1.63 (1.07–2.48)


Community-Acquired Pneumonia Comparing the Literature

<table>
<thead>
<tr>
<th>Study</th>
<th>Current PPI Use OR (CI)</th>
<th>Current H2RA Use OR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arch Intern Med 2007</td>
<td>1.5 (1.3–1.7)</td>
<td>1.10 (0.8–1.3)</td>
</tr>
<tr>
<td>Ann Intern Med 2008</td>
<td>1.02 (0.90–1.27)</td>
<td>1.01 (0.86–1.19)</td>
</tr>
<tr>
<td>JAMA 2004</td>
<td>1.89 (1.36–2.62)</td>
<td>1.63 (1.07–2.48)</td>
</tr>
</tbody>
</table>

*OR: Odds ratio; CI: Confidence interval.

Community-Acquired Pneumonia
Recent PPI Initiation & Increased Risk

<table>
<thead>
<tr>
<th>Study</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ann Intern Med 2008</td>
<td>4.45 (1.44 - 13.93)</td>
</tr>
<tr>
<td>Arch Intern Med 2007</td>
<td>4.3 (1.22 - 14.5)</td>
</tr>
<tr>
<td>JAMA 2004</td>
<td>3.24 (1.48 - 6.94)</td>
</tr>
<tr>
<td>Epidemiol 2009</td>
<td>3.25 (1.95 - 5.35)</td>
</tr>
<tr>
<td>Am J Med 2001</td>
<td>5.37 (2.24 - 12.79)</td>
</tr>
<tr>
<td>Overall CAP Risk*</td>
<td>1.92 (1.4 - 2.63)</td>
</tr>
</tbody>
</table>

* Dose response relationship also noted with high dose PPI use

Recent PPI Initiation & Increased Risk

- Gastric acidity decreased with H2RA or PPI treatment
- Loss of protective defense mechanism of hyperchlorhydria
  - Possible increased risk of CAP
- Incidence of CAP: 0.6 vs. 2.45 per 100 person years on acid suppression treatment

Community-Acquired Pneumonia

Acid-Suppressive Medication Use and the Risk for Hospital-Acquired Pneumonia

<table>
<thead>
<tr>
<th>Medication</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H2RA</td>
<td>2.0 (1.1 - 3.8)</td>
</tr>
<tr>
<td>PPI</td>
<td>2.3 (1.2 - 4.5)</td>
</tr>
<tr>
<td>Incidence of CAP</td>
<td>0.6 vs. 2.45</td>
</tr>
<tr>
<td>Incidence of CAP on acid suppression treatment</td>
<td>0.6 vs. 2.45</td>
</tr>
</tbody>
</table>

* Dose response relationship also noted with high dose PPI use

Table 4. Acid-Suppressive Medication Use and the Risk for Hospital-Acquired Pneumonia


Colonization on Culture of Gastric Aspirates, Pharyngeal Swabs, and Tracheal Aspirates from 47 Study Patients.

<table>
<thead>
<tr>
<th>Colonized Organism</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric aspirates</td>
<td>25</td>
</tr>
<tr>
<td>Pharyngeal swab</td>
<td>15</td>
</tr>
<tr>
<td>Tracheal aspirate</td>
<td>4</td>
</tr>
</tbody>
</table>

Colonization on Culture of Gastric Aspirates, Pharyngeal Swabs, and Tracheal Aspirates from 47 Study Patients.

- FDA Warning links PPIs to C. difficile-Associated Diarrhea
- Feb 8th, 2012
  - FDA Safety Alert warned that PPIs may be associated with an increased risk for Clostridium difficile associated diarrhea

Use of Gastric Acid–Suppressive Agents and the Risk of Community-Acquired Clostridium difficile–Associated Disease

- FDA Warning links PPIs to C. difficile-Associated Diarrhea
- Feb 8th, 2012
  - FDA Safety Alert warned that PPIs may be associated with an increased risk for Clostridium difficile associated diarrhea
Original Article
Host and Pathogen Factors for *Clostridium difficile* Infection and Colonization

- In this prospective cohort study of patients admitted to hospitals in Quebec and Ontario, 2.8% of patients had *Clostridium difficile* infection and 3.0% had asymptomatic *C. difficile* colonization during hospitalization.

N Engl J Med
Volume 365(18):1693-1703
November 3, 2011
Table 1. Odds Ratios for Health Care–Associated Clostridium difficile Infection among Study Patients Who Had Positive Cultures for C. difficile, According to Various Patient and Pathogen Characteristics and Type of Analysis.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, per 1-year increase</td>
<td>1.01 (0.99-1.02)</td>
<td>0.314</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.05 (0.89-1.25)</td>
<td>0.557</td>
</tr>
<tr>
<td>Chronic inflammatory conditions</td>
<td>1.0 (0.79-1.26)</td>
<td>0.960</td>
</tr>
<tr>
<td>Appendectomy</td>
<td>1.03 (0.86-1.23)</td>
<td>0.725</td>
</tr>
<tr>
<td>Location</td>
<td>Hospital setting</td>
<td>0.99 (0.98-1.00)</td>
</tr>
<tr>
<td>Type of analysis</td>
<td>Case-control</td>
<td>1.00 (0.99-1.01)</td>
</tr>
<tr>
<td>Location</td>
<td>Hospital setting</td>
<td>1.00 (0.99-1.01)</td>
</tr>
<tr>
<td>Type of analysis</td>
<td>Case-control</td>
<td>1.00 (0.99-1.01)</td>
</tr>
</tbody>
</table>

Table 2. Odds Ratios for Health Care–Associated Clostridium difficile Infection and Colonization according to Various Patient and Pathogen Characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, per 1-year increase</td>
<td>1.01 (0.99-1.03)</td>
<td>0.267</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.05 (0.90-1.23)</td>
<td>0.521</td>
</tr>
<tr>
<td>Chronic inflammatory conditions</td>
<td>1.0 (0.80-1.25)</td>
<td>0.895</td>
</tr>
<tr>
<td>Appendectomy</td>
<td>1.03 (0.86-1.23)</td>
<td>0.704</td>
</tr>
<tr>
<td>Location</td>
<td>Hospital setting</td>
<td>1.00 (0.99-1.01)</td>
</tr>
<tr>
<td>Type of analysis</td>
<td>Case-control</td>
<td>1.00 (0.99-1.01)</td>
</tr>
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</tr>
</tbody>
</table>
Proposed Mechanism

- Higher pH allows for opportunistic infections to survive
  - Gastric Acid suppression has been associated with increased colonization even into the typically sterile upper GI tract altering GI flora
- H2RA's and PPI's found to increase patient risk
  - PPI's possibly more so due to increased acid suppression
- Question about c diff?
  - Transmission via acid resistant spores
  - Instead the vegetative form is able to survive

Risk of Recurrent C. difficile

- 1166 patients
  - Metronidazole or Vancomycin treated CDI
  - 537 (45.2%) received PPI's
  - Similar antibiotic exposure in both groups
- Results
  - 42% increased risk of recurrence
Proton Pump Inhibitors and Risk for Recurrent *Clostridium difficile* Infection

Risk of C. diff Talking Points

- H2RA are less likely to be associated with *C. difficile* infection
- Recent PPI exposure may lead to an increased risk of *C. difficile* infection and recurrent infection

When Do We Stop?

- Patients should be reassessed daily
- Once the indication is removed the med should be discontinued
Sent home with souvenir?

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What can we do?

- Start with education
  - Hatch et al. 2010
    - Looked at educational intervention to reduce non-indicated prescribing of gastric acid suppressants for SUP

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Pharmacist Intervention

1. Dosing card with indications
2. Pharmacist interaction during multidisciplinary rounds
3. Medication reconciliation by RPh at discharge
Results

- 356 patients included in study
- 348 received SUP while in ICU
- 259 continued SUP out of the ICU
- After discharge

- 194 (50.7%) were using acid suppressive therapy
- 144 had no underlying indication
- 356 patients included in study
- 26

Applying this to your practice

- H2RA’s are the preferred agent for initial prevention of GI hemorrhage resulting from Stress Related Mucosal Disease in patients that are at risk
- PPI’s should be reserved for patients unable to tolerate H2RA’s
- PPI therapy should be given enterally or via intermittent intravenous administration
- Antacids and sucralfate are not recommended for prevention of SRMD
- Enteral nutrition should not be used alone as prophylaxis

Questions

- Who should be receiving stress ulcer prophylaxis in your institution?
Only those with clear indications

Drug therapy is recommended for any One of the following

1. Respiratory failure requiring Mechanical Ventilation likely greater than 48 hours
2. Coagulopathy
   - Platelet count < 50,000
   - INR > 1.5
   - aPTT > 2 x control
   - Note: prophylaxis with anticoagulants do not constitute a coagulopathy

Indications for Stress Ulcer Prophylaxis

- Respiratory failure requiring mechanical ventilation for more than 24 hours
- Coagulopathy
- Acute Renal Failure
- Sepsis Syndrome
- Prolonged Hypotension
- Major Surgery lasting more than 48hrs
- Severe Head Trauma
- History of GI Bleeding
- Burns involving more than 35% of the body surface area
Questions

• What medications are best to use to prevent stress ulcers?
  – The great debate: PPI's vs. H$_2$RA's vs. Sucralfate

Pharmacotherapy

1. H$_2$RA's are the preferred agent

2. PPI's should be reserved for patients unable to tolerate H$_2$RA's

Questions

• What are the complications of providing stress ulcer prophylaxis?
What about Adverse Events of prophylaxis?

- Delirium
- Thrombocytopenia
- Community Acquired Pneumonia
- Clostridium difficile
- Nutrient malabsorption
- Ventilator Associated Pneumonia
- Acute interstitial nephritis