Stress Ulcers (2008)

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Normal Gastric Mucosal Barrier Physiology

- Dynamic balance b/w gastroduodenal mucosal resistance and luminal contents
- Mucosal resistance includes:
  - Mucus
  - Mucosal and pancreatic bicarb. secretion
  - Epithelial integrity
  - Adequate mucosal blood flow

Prostaglandin Effects due to:

1. ↑ Bicarb. secretion
2. ↑ Mucus production
3. ↑ Mucosal cell integrity
4. ↓ Acid secretion
5. ↑ Mucosal perfusion

Definition of Stress Ulcers

Acute, superficial inflammatory lesions of the gastric mucosa induced when an individual is subjected to abnormally elevated physiological demands.

Stress vs. Nonstress Ulcers

Stress:

- Multiple
- Acid/pepsin secretory mucosa
- Lack of chronic inflammation
- Asymptomatic (most!)

Nonstress (PUD):

- Usually solitary
- Distal stomach/duodenum
- Chronic inflammation
- Symptomatic

Pathogenesis of Stress Ulcers

- Acid-not hypersecretion-exceptions: burns /head trauma
- Ischemia-Primary
- -Promotes:

1. Intramural acidosis
2. Free radicals
3. Increased cell permeability
4. Decreased bicarb.
5. Decreased acid-buffering capacity
6. Decreased mucus production

- *H.pylori* plays no role

Risk Factors

- ↑ risk with ↑ severity of illness?
- Multiple trauma, age > 65, corticosteroids, NSAIDs, major surgery, resp. failure, renal failure, hepatic failure, mult. organ failure, head injury, sepsis, burns > 30-35% BSA-↑ risk with ↑ # ?
- Coagulopathy, mech. ventilation, high dose corticosteroids only independent risk factors

Clinical Manifestations

- GI bleeding-minutes to hours
- 6-25 % endoscopic lesions→ clinically – sign. with 50-70% mortality
- Incidence has decreased due to: ventilation, nutrition, hemo monitoring, prophylaxis
- 25→ <1 - 2.8% clin.-relev. stress bleeding incidence

Criteria for Clinically-Relevant Overt Gastric-Stress Bleeding

- Drop at least 2 gm% Hgb concentration
- Need for transfusion of 2 units of packed RBCs
- Systolic BP < 90mm Hg (shock) for more than 3 hours
- Drop > 20mm Hg in systolic BP compared to prebleeding values

Management: Prophylaxis vs. Treatment

Prophylaxis:

- Antacids
- H-2 receptor antagonists
- Sucralfate
- Nutrition

PO Antacids

- Usually q 1 h dosing, dose based on gastric pH
- Side effects: GI, electrolytes, vol. leads to aspiration
- Drug-drug interactions
- Labor-intensive
- Interferes with endoscopic control
- Controversial whether pH monitoring needed: What should " cut-off" be?-no trials have evaluated different "cut-offs"- pH $\geq$ 4 "gold standard"

IV H2-Receptor Antagonists

- Continuous infusion superior to bolus injection (cimet. infusion FDA-approved)
- Paucity of data for ranitidine, famotidine
- May not be totally effective when used alone to incr. pH
- Side Effects: CV, CNS, hematologic
- Drug-drug interactions (see PUD lecture)
- Controversial whether pH monitoring needed (target pH$\geq$ 4)

PO Sucralfate

- Preservation of gastric acid barrier to bacteria
- Side effects: electrolytes, GI.
- Drug interactions: po anticoagulants, phenytoin, quinolones , thyroxine
- Interferes with endoscopic diagnosis/control

Enteral Nutrition

- Animal studies-nutritional supps>antacids or saline in preventing stress ulcers
- Supported by retrospective human studies:early enteral nutrition sing . superior to IV cimetidine 400 mg per 24h(+NG antacids or additional IV cimetidine prn to keep pH>= 4) in decreasing overt GI bleeding in severely burned patients
- Mechanism: -Buffering acid (minor)
  -Energy source to mucosa
  -? Modulate blood flow
  -? Release PGs
- TPN does not work !

Proton Pump Inhibitors

- Not a lot of data!
- PO/NG omeprazole 20-40mg/d effective in open and controlled (vs. H2RA) trials – 40 mg bid x 1 d $\rightarrow$ 40 mg qd is FDA-approved
- PO lansoprazole suspension via feeding tube
- IV pantoprazole? (equal to IV cimet. in 1 study)

Delivery

- NG tube-use IV H2 blockers, po antacids, po sucralfate
- ND, NJ tube-use IV H2 blockers only, or place NG tube to give PO agents
- Continuous gastric enteral feeding-? Need for prophylaxis at all or use sucralfate

Dosing Guidelines for Stress Ulcer Prophylaxis

Agent	Neonates	Infants	Children	Adults
Antacid	0.5-1.0 ml/kg/dose	2.5-5 ml/dose	5-15 ml/dose	30-60 ml/dose
Cimetidine	5-10 mg/kg/day	10-20 mg/kg/day	20-40 mg/kg/day	1200 mg/day
Ranitidine	1.5-2 mg/kg/day	2-3 mg/kg/day	2-6 mg/kg/day	150-300 mg/day
Famotidine	0.5 mg/kg/dose	1-2 mg/kg/day	1-2 mg/kg/day	40 mg/day
Omeprazole	ND	0.3-3.3 mg/kg/day	0.3-3.3 mg/kg/day	20-40 mg/day
Sucralfate	ND	ND	40-80 mg/kg/day (up to 2-4 g/day)	4g/day

Which Prophylaxis Works Best?

Meta-analysis of comparative trials:

Cook et al. JAMA 1996;275:308-314
(Table at end of handout)

Treatment

- Unsatisfactory
- Fluids improve perfusion
- Treat sepsis if present
- Vasopressin infusions-no benefit in RCTs
- Histamine H2 blocker-no benefit in RCTs
- Antacids – no benefit, aspiration risk due to volume
- PPIs -no data
- Sucralfate-no data
- Surgery: mortality rate 40-60% (combined V+P, gastric resection)