

GASTROESOPHAGEAL REFLUX DISEASE

Raed Abughazaleh, PharmD, BCPS
PHAR 551: Pharmacotherapy I
Birzeit University

Background

- GERD: a condition that occurs when the refluxed stomach contents lead to troublesome symptoms and/or complications
- Esophageal GERD syndromes:
 - Symptom-based: heartburn, regurgitation, dysphagia, odynophagia, hypersalivation..
 - Tissue-injury based: esophagitis, Barrett esophagus, strictures, esophageal adenocarcinoma (AC)
- Occasional heartburn that is not painful or frequent enough to adversely affect the well being of pt is not considered GERD

Epidemiology

- Most common > 40 y/o
- Potentially significant impact on quality of life but no significant mortality risk
- Highest prevalence in Western countries
- No differences between M/F when excluding pregnancy
- Barrett esophagus is most prevalent in white adult males in Western countries
- Two- to sixfold increase in esophageal AC in past two decades

Pathophysiology

- Abnormal reflux of gastric contents
 - LES dysfunction
 - Abnormal esophageal anatomy
 - Reduced mucosal resistance to acid
 - Delayed gastric emptying
 - Reduced salivary buffering of acid
- Important factors in GERD development:
 - Composition of refluxate
 - Volume of refluxate
 - Exposure time to refluxate

Pathophysiology

A. LES Dysfunction:

1. Transient LES relaxations not related to swallowing
 - Accounts for 40% of reflux episodes in GERD
2. Transient increases in intra-abdominal pressure (IAP)
 - Straining, bending over, Valsalva maneuver
3. Atonic LES permitting free reflux (scleroderma..)
 - #2 and #3 more likely to occur if decreased LES pressure 2/2 smoking, fatty foods, gastric distention, medications..

Pathophysiology

- B. Direct mucosal aggravation
 - Foods such as spicy foods, orange juice, tomato juice, coffee
- C. Pregnancy
 - Hormonal, increased IAP,..
- D. Decreased esophageal clearance and saliva production
- E. Decreased mucosal resistance to acid
- F. Delayed gastric emptying and increased IAP
 - Smoking, high fat diet, obesity..
- G. Composition of refluxate

Clinical Presentation

- Clinical history is primary diagnosis tool
- Severity of symptoms does not always correlate with degree of tissue injury
- Typical symptoms: heartburn, hypersalivation, belching, regurgitation
- Atypical symptoms: asthma, chronic cough, hoarseness, pharyngitis, chest pain, dental erosions
- Alarm symptoms: dysphagia, odynophagia, unexplained weight loss..

Treatment

- Goals of treatment include alleviating symptoms, promoting healing of mucosa, and preventing complications
- *TAILORED* lifestyle modifications should be applied to all pts with esophageal symptoms
 - Weight loss, elevating head of bed if causes symptoms, eating smaller meals, avoid eating 3h before sleeping, smoking cessation, avoiding food and medicine that exacerbate GERD
 - Problem Meds: Anticholinergics, barbiturates, benzos, caffeine, DHP CCBs, ethanol, narcotics, nicotine, nitrates, estrogen, progesterone, bisphosphonates, aspirin, iron, NSAIDs..

Treatment

- Intermittent or mild symptoms
 - Lifestyle modifications *AND*
 - Patient-directed therapy: antacids, OTC H₂RAs (lower doses), OTC PPIs (QD) if available
 - Failure of patient-directed therapy after 2 wks indicates GERD and need for therapy escalation
- Symptomatic GERD
 - Lifestyle modifications *AND*
 - H₂RAs (normal dose) for mild GERD
 - PPIs (QD-BID) x 4-8 wks for mod-severe GERD

Treatment

- Treatment of erosive esophagitis or complications
 - PPI (BID preferred) x 4-16 weeks
 - Often requires chronic maintenance therapy on PPI
- Pts with GERD unresponsive to therapy course may require endoscopy (EGD)
- Refractory pts may be candidates for antireflux surgery

Treatment: Antacids

- Neutralize acid (buffer)
- Alginic acid coats mucosa with viscous solution and may reduce frequency of symptoms
- Provide immediate relief
- Used concurrently with other therapies
- Chronic use indicates need for therapy escalation
- Mg/Al hydroxide (Maalox) 30 mL after meals and HS as needed
- Calcium carbonate (Tums) 500 mg, 2-4 tabs PRN
- Antacid/alginic acid (Gaviscon) 2 tabs after meals and at bedtime

Treatment: Antacids

- Avoid Al-containing antacids in renal dysf.
- AEs: constipation, diarrhea, mineral imbalance, acid-base disturbance, bone demineralization with Al products
- Drug interactions
 - Fluoroquinolones: take 2h before or after antacids
 - Ferrous sulfate: take on empty stomach
 - TCN: take on empty stomach, or 4h after antacid
 - INH: levels decreased by antacids, separate

Treatment: H₂RA

- Cimetidine, famotidine, ranitidine..
- All agents equally efficacious
- Decrease acid secretion by inhibiting H₂R in gastric parietal cells
- Ranitidine
 - 75 mg QD- 150 mg BID
 - Dose adjustment for CrCl < 50 mL/min
- Long courses of treatment (up to 12 wks)
- Cimetidine has most drug-drug intxns
- Lower endoscopic healing rates (50%) than PPIs
- AEs: well-tolerated. HA, somnolence, fatigue

Treatment: PPIs

- Most superior acid suppressants
- Omeprazole, esomeprazole, pantoprazole, rabeprazole, lansoprazole, dexlansoprazole
- All equally efficacious
- Block gastric acid secretion by inhibiting H⁺/K⁺ pump in gastric parietal cells
- Available DR, EC granules, powder, IR, ODT, IV
- Take PPI early in AM 1h before meals except dexlansoprazole
- pH can be maintained > 4 even post-prandial

Treatment: PPIs

- Healing rates at 4 or 8 wks are similar (78%)
- Pantoprazole 40 mg QD-BID
- Omeprazole 20 mg QD-BID
- AEs: Well-tolerated. HA, vit B12 deficiency, possible relation to *C. Diff* infection, possible increased risk for other infections (e.g., PNA), possible fracture risk
- Drug-drug intxns: iron sulfate, clopidogrel..

Omeprazole	Esomeprazole	Lansoprazole	Dexlansoprazole	Rabeprazole	Pantoprazole
20 mg	20 mg	30 mg	30 mg	20 mg	40 mg

Treatment: Misc.

- Proton pump inhibitors
 - Cicapride, metoclopramide, bethanecol
 - Not recommended 2/2 lack of efficacy and due to safety profile
- Mucosal protectants
 - Sucralfate: nonabsorbable Alum salt
 - No role in treatment of GERD
- Maintenance therapy
 - May be needed for relapsing pts, pts with complications, or severe GERD
 - Lowest effective dose should be used
 - Typically PPIs will be used

Pediatric GERD

- Common with infants, typically with no clinical consequences
- Manifests in regurgitation (spitting up)
- Typically resolves spontaneously by 12-18 months of life, otherwise H₂RAs or PPIs are indicated
- Ranitidine, lansoprazole, esomeprazole, omeprazole are indicated for pediatric GERD