

DRUG RELATED PROBLEMS:

- “Reverse what you can reverse”
 - Assess whether any current medications may be causing the problem

PATHOPHYSIOLOGY:

- Weak lower esophageal sphincter → acid can backflow
- Inflammation in the esophagus
- Decreased gastric motility → allows food to collect in stomach → increases gastric acid production

MEDICATION CAUSES:

| Irritate esophagus | Increase acid reflux (Worsen GERD) |
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| <ul style="list-style-type: none"> • Oral bisphosphonates <ul style="list-style-type: none"> ◦ Alendronate ◦ Risedronate • Iron supplements • Quinidine • NSAIDs • Potassium supplement • Tetracycline | <ul style="list-style-type: none"> • Anticholinergics <ul style="list-style-type: none"> ◦ Oxybutynin • TCAs • CCBs • Nitrates • Progesterone • Quinidine • BZDs <ul style="list-style-type: none"> ◦ Diazepam ◦ Temazepam |

GERD TREATMENT APPROACH:

- Determined by symptom severity
- Typical GERD symptoms
 - Lifestyle measures
 - Empiric acid suppression therapy
- No response or complicated symptoms:
 - Diagnostic tests

TREATMENT APPROACHES:

- Decrease acidity of the refluxate
- Decrease gastric volume available to be refluxed
- Improve gastric emptying
- Increase lower esophageal sphincter (LES) pressure
- Enhance esophageal acid clearance

GOALS OF THERAPY:

- To alleviate or eliminate symptoms
- To decrease the frequency and/or duration of recurrence
- To promote healing of mucosal injury
- To prevent complications (stricture, perforation, cancer)
- To minimize adverse reactions of drug therapy

PATIENT EDUCATION:

- Effects of caffeine, EtOH and NSAIDs on GERD
- How/when to take medication
- Duration of therapy
- Alarm signs (worse than just GERD): when to go see a dr

LIFESTYLE MODIFICATIONS:

- Weight loss*
- Elevation of head of bed*
- Dietary modifications – generally unnecessary
 - Avoid trigger foods
- Avoid tightfitting garments
- Avoid tobacco and alcohol
- Abdominal breathing exercise

* = only modifications that have evidence

GERD THERAPY: PPI > H₂RA > prokinetic ~ placebo (in esophagitis healing)

PHARMACOTHERAPY ALTERNATIVES: antacids, H₂RA, PPI, promotility agents

H₂-RECEPTOR ANTAGONISTS:

EFFICACY:

- All H₂RA are equally effective
- After 8-12 weeks of therapy:
 - Sx improvement: 60-90% of pts
 - Endoscopy healing rates: 50-80%
- Sx improvement occurs faster than esophagus healing

DOSES:

- Cimetidine 400-800 mg BID → inhibits CYP 1A2, 2D6, 3A4
- Ranitidine 150 mg BID
- Famotidine 20 mg BID
- Nizatidine 150 mg BID

DURATION:

- 2-4 weeks initially
 - If no relief, double dose
- After symptoms are controlled, decrease dose by 50% every 2-4 weeks to identify lowest effective dose
- Total duration: 8 weeks

SAFETY:

- Generally well tolerated
- Rare to have serious AEs

| | |
|------------|--|
| CNS | Renal/hepatic disease, elderly: <ul style="list-style-type: none"> • Confusion • Depression • Agitation |
| | <ul style="list-style-type: none"> • Headache • Somnolence • Fatigue • Dizziness |
| GI | <ul style="list-style-type: none"> • Constipation • Diarrhea |
| HEME | <ul style="list-style-type: none"> • Leukopenia • Neutropenia • Thrombocytopenia |
| Cimetidine | Weak anti-androgenic effects: <ul style="list-style-type: none"> • Gynecomastia • Impotence |

PROTON PUMP INHIBITORS:

EFFICACY:

- All PPI are equally effective
- Sx relief in approx. 83% of pts
- Endoscopic healing rates 78% after 8 weeks of treatment

DOSAGES:

- Omeprazole
 - Mild-mod: 20 mg daily
 - Mod-sev: 20 mg BID or 40 mg daily
- Esomeprazole 20 mg daily
- Lansoprazole 15-30 mg daily
- Dexlansoprazole 30-60 mg daily
- Pantoprazole sodium 20-40 mg daily
- Pantoprazole magnesium 40 mg daily
- Rabeprazole 20 mg daily

SAFETY:

- Generally well tolerated

| | |
|------|--|
| CNS | <ul style="list-style-type: none"> • Headache • Somnolence • Fatigue • Dizziness |
| GI | <ul style="list-style-type: none"> • Nausea • Constipation • Diarrhea |
| HEME | <ul style="list-style-type: none"> • Leukopenia • Neutropenia • Thrombocytopenia |

- Controversies with long-term use
- ?? Increased risk of:
 - Pneumonia
 - C difficile infection
 - CV events
 - Fractures
 - Hypomagnesemia
 - Acute interstitial nephritis

DRUG INTERACTIONS:

- All PPI metabolized via CYP isoenzymes
 - Omeprazole: inhibits CYP2C19 = ↑ diazepam, warfarin, and phenytoin
- Most interactions not clinically relevant
- Elevation of gastric pH may affect absorption of oral medications
 - ↑ absorption: ampicillin, pancreatic enzymes
 - ↓ absorption: digoxin, itraconazole, ketoconazole, iron

PROMOTILITY AGENTS: efficacy & safety issues

- Metoclopramide, domperidone, bethanechol (cisapride no longer on market)
- Role: if has known or suspected motility disorder
 - Combination with PPI if failed high dose PPI therapy (decrease sx severity)
 - Adding to PPI therapy: no change in relief of sx or endoscopic changes

| THERAPEUTICS: | |
|-----------------------------|---|
| Intermittent Mild Heartburn | <ul style="list-style-type: none"> • < 2 episodes per week • Non-drug therapy (lifestyle modifications) • Antacids (if < 1 episode per week): on demand • Low dose (OTC) H₂RA |
| Mild-moderate GERD | Lifestyle modifications PLUS H ₂ RA x 2 -4 weeks (tachyphylaxis with prolonged use) or PPI x 2 -4 weeks |
| Mod-severe GERD | <ul style="list-style-type: none"> • Lifestyle modifications • PPI x 6-12 weeks <ul style="list-style-type: none"> ○ Initial trial 2-4 weeks ○ Re-assess → if no response then double the dose (twice daily) x 4 more weeks |
| Persistent GERD | <ul style="list-style-type: none"> • Step down (PPI → H₂RA) • Step up (antacids → H₂RA → PPI) <ul style="list-style-type: none"> ○ Historically step up approach used ○ PPI decreased severity of symptoms and greater symptom free days vs. H₂RA (step up and step down) • Neither step up nor step down has been shown to be more effective or more cost effective |
| Maintenance Therapy | <ul style="list-style-type: none"> • D/C after 12 weeks <ul style="list-style-type: none"> ○ Approx. 80% of pts experience relapse within a year after D/C therapy |
| Recurrence/Relapse | <ul style="list-style-type: none"> • On-demand (intermittent) therapy with PPIs may be effective • Long-term therapy often necessary <ul style="list-style-type: none"> ○ Restart PPI at previous effective dose ○ Determine lowest effective dose <ul style="list-style-type: none"> ▪ After 2 weeks, decrease dose by 50% q2 weeks to determine minimum effective dose |
| Ineffective drug therapy | <ul style="list-style-type: none"> • After 8 weeks of drug therapy (on BID dosing of PPI for at least 4 weeks), if still symptomatic, REFER <ul style="list-style-type: none"> ○ Endoscopy ○ May try PPI + promotility agent ○ Consider H. pylori treatment ○ Explore antireflux surgery |