Drugs used in Peptic Ulcer

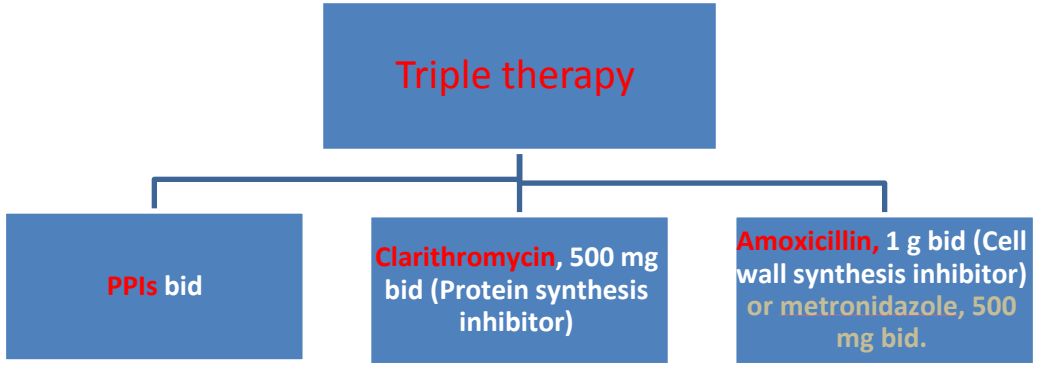
Drug	MOA	Pharmacokinetics	ADRs
1-Antiacids: These drugs are mainly inorganic salts (e.g.: NaHCO3; Ca CO3; most commonly used Al (OH)3; Mg (OH)2)	Antagonize acid; Also, Indirectly may decrease pepsin activity		constipation (from Al), diarrhea (from Mg), hypophosphatemia...others note: preparations that combine both Al and Mg hydroxides are used as their actions will cancel each other.
2- H2 –receptor antagonists: e.g: Cimetidine (prototype) most clinically use : Ranitidine (Zantac); Famotidine (most potent) ; Nizatidine **Used In :** • GERD (gastroesophageal reflux disease), (heartburn/ dyspepsia). • PUD(peptic ulcer disease): effective in nocturnal acid suppression & ulcer healing in moderate cases • Prevention of bleeding from stress-related gastritis. • Decrease the heartburn by NSAIDs. • Zollinger Ellison Syndrome (large doses).	They competitively & reversibly bind to H2-receptors on the parietal cells, thus decreasing the production of acid by these cells. * Highly selective on H2 receptors **Pharmacological Actions :** 1-Reduce basal & food-stimulated gastric acid secretion. 2-Reduce acid secretion stimulated by histamine, as well as by gastrin & cholinergic drugs. 3-Reduce pepsin activity. Block 90% of nocturnal acid secretion (which depend largely on histamine) ;Therefore, it is better to be given before night sleep	-Good & rapid oral absorption -Plasma half life (1-4 hr). -Duration (4-12 h) , given twice a day -First pass metabolism (50%, Except Nizatidine 100 % bioavailability). -Given before meals (all PU drugs are given on empty stomach) -Clearance by hepatic metabolism, glomerular filtration & renal tubular secretion. -Dose reduction is required in patients with moderate-severe renal (or severe hepatic) insufficiency. -50% clearance decline in elderly -Cross placenta & excreted in milk. * Ranitidine is more potent; 150 mg can give the therapeutic effect, compared to 400 mg for cimetidine.	-CNS effects: Headache,confusion, hallucination & agitation due to IV H2 antagonist (more with cimetidine in ICU especially (elderly –renal or hepatic dysfunction)) but not with Ranitidine. -Endocrine effects (For Only Cimetidine) : • -increases in serum prolactin (Galactorrhea in women). • -Inhibits binding of dihydro-testosterone to androgen receptors (gynecomasteia –impotence). -All cross placenta & breast milk, should not be given in pregnancy unless it is necessary. ranitidine can be given to pregnant woman. - Inhbition of Cty p450 by Cimetidine. (potential toxicity from other drugs administered concomitantly). -Leukopenea and thrombocytobenia and headache with ranitidine(rare). -GIT disturbances (Nausea & Vomiting) -Bradycardia & hypotension (rapid I.V)
3- Proton pump inhibitors.: e.g: : Omeprazole ; Lansoprazole ; Pentoprazole ; Raprazole **Used In :** • Gastric and duodenal ulcer • (H.pylori Eradication) • Zollinger–Ellison syndrome. (Ist) • GERD • NSAIDs associated ulcer • prevention of bleeding from stress-related gastritis. • PUD (4-8 weeks); faster & long- lasting ulcer relief.	• Irreversible inhibition of proton pump (H+/ K+ ATPase) that is responsible for final step in gastric acid secretion from the parietal cells. • 24 hr inhibition of basal & meal stimulated-acid secretion (90-98%).	-They are prodrugs. -All are taken orally. -Esomeprazole & pantoprazole are also available in IV formulation. Give to those who can't swallow because of bleeding. -All are given as enteric coated tablets/ capsules –To protect them from destruction by acidity in gastric lumen -They are rapidly absorbed from the intestine & converted to active form. -PPIs have plasma half life of 1.5 h -Long duration of action (> 12 h-24 h), because of the irreversible inactivation of the proton pump. -Once daily dose is sufficient -Bioavailability is reduced by food (50%). -Given 1 h before meal; on empty stomach. -Are metabolized in the liver by CytP450. So dose reduction is required in severe liver failure. They are more potent than H2 antagonists.	-Headache. -Diarrhea. -Nausea. -decreased gastric acid secretion lead to hypergastrinemia mucosal hyperplasia. prolonged acid suppression leads to: * subnormal B12 levels (because acid is required for its absorption). * risk of hip fracture if taking PPIs over a long period.(PPIs may reduce calcium absorption or inhibit osteoclast function). * colonization & infection of the stomach & intestine from ingested bacteria; increased risk of both community-acquired respiratory infections & nosocomial pneumonia. Note: Despite all the above PPIs are very save drugs.

How Gastrooesophageal Reflux could be managed?

- Decrease gastric acidity (H2 blockers or PPIs).
- Increase tone of LOS (lower esophageal sphincter) and increase gastric emptying by Metoclopramide.
- Avoid drugs or foods that trigger GERD. (caffeine, alcohol, smoking).
- Avoid sleeping after meal and try to use two to three pillows.

Eradication Of H. Pylori

- Is a bacteria that causes chronic inflammation of the inner lining of the stomach.
- Duodenal ulcer -Gastric ulcer.
- Produces enzymes (tissue damage).
- Risk factor for gastric cancer.
- Eradication is important to prevent recurrence of ulcer.
- The best treatment regimen: Triple therapy (10-14 days).(PPIs bid ,Clarithromycin, Amoxicillin)



Summary:

- Most common cause (agent) in peptic ulcer H. Pylori infection. Others: smoking, caffeine, drugs…etc.
- Objective of treatment: (prevention of further ulcer recurring, Relieve pain; healing of ulcer).
- Best approach in treatment is the eradication of H. Pylori.
- Treatment available: antacids, H2-antagonist, and PPI.
- Antacids give symptomatic relief, Al and Mg hydroxides most commonly used.
- H2-antagonist: Ranitidine(more potent), cimetidine(enzyme inhibitor +anti-androgenic)
- All cross placenta.
- PPIs irreversibly inhibit proton pump (H/K ATPase).
- Do not use PPIs concomitantly with H2-antagonist.
- PPI are more potent than H2-antagonist.
- PPI side effects: diarrhea, nausea + hypergastrinemia + B12 deficiency + risk of hip fracture.
- PPIs are pro-drugs.
- One of the ways to manage Gastroesophageal reflux is to avoid sleeping after meal and try to use two to three pillows.
- Eradication of H. Pylori by triple therapy for (10-14) days. (chart above).
- Clinical uses of IPP include: Gastric and duodenal ulcer (H.pylori Eradication), Zolinger Elison syndrome. GERD, NSAIDs.
- Clinical uses of H2-antagonist: PUD (effective in nocturnal acid suppression), prevention of bleeding form stress-related gastritis.