Drugs Used for Peptic Ulcer

Pharma Team

SUMMARY IN CHARTS & TABELS

DRUG TREATMENT OF PEPTIC ULCER

- Gastric hyposecretory drugs (reduce gastric acidity)
  - H2 receptor blockers
    - Cimetidine (prototype)

      Most clinically used are:
    - Ranitidine
    - Famotidine (most potent)
    - Nizatidine

    See the figure of comparison Page 6
  - Antimuscarinic drugs
  - proton pump inhibitors
    - Omeprazole (prototype)
    - Lansoprazole
    - Pantoprazole
    - Esomeprazole
    - Rabeprazole
- Neutralizing agents (antacids).
- Mucosal cytoprotective agents
  - Sucralfate
  - Prostaglandin analogues
  - Colloidal bismuth
- Eradication of H. pylori infections
  - Is a bacteria that causes chronic inflammation of the inner lining of the stomach.
  - Duodenal ulcer -Gastric ulcer
  - Produce enzymes (tissue damage)
  - Risk factor for gastric cancer.
  - Eradication is important to prevent recurrence of ulcer.
  - The best treatment regimen: Triple therapy (for 14 days)
    - ✓ PPIs bid (twice daily)
    - ✓ Clarithromycin, 500 mg bid
    - ✓ Either Amoxicillin, 1 g bid/ or metronidazole, 500 mg

Combination of all drugs bellow

	H2 receptor blockers (selective on H2 receptors)	Proton Pump Inhibitors (PPIs)
MOA	• They competitively & reversibly bind to H2-receptors on the parietal cells, thus - decreasing the production of acid by these cells. See the figure below	• Irreversible inhibition of proton pump (H^+/ K^+ ATPase) that is responsible for final step in gastric acid secretion from the parietal cells. See the figure below
PK	- Good & rapid oral absorption - Plasma half life >> (1-4 hr). - Duration >> (4-12 h). - Given before meals. - First pass (50% bioavailability Except Nizatidine 100%) - Clearance by hepatic metabolism, glomerular filtration & renal tubular secretion SO Dose reduction is required in patients with moderate-severe renal (or severe hepatic) insufficiency. - 50% clearance decline in elderly - Cross placenta & excreted in milk.	- They are rapidly absorbed from the intestine & converted to active form - plasma half life >> 1.5 h - Duration >> Long (> 12 h-24 h) Beca. of irreversible inactivation of PP - Given 1 h before meal; on empty stomach. - Bioavailability is reduced by food (50%). - Are metabolized in the liver by CytP450 SO Dose reduction is required in severe liver failure. - All are taken orally except Esomeprazole & pantoprazole are also available in IV formulation. - All are given as enteric coated tablets/ capsules To protect them from destruction by acidity in gastric lumen - Once daily dose is sufficient - ***They are more potent than H2 antagonists.***
action	1. Reduce basal & food-stimulated gastric secretion. 2. Reduce acid secretion stimulated by histamine, as well as by gastrin & cholinergic drugs. 3. Reduce pepsin activity. 4. Block90%of nocturnal acid secretion(which depend largely on H) & 60-70% of total 24 hr acid secretion	1. 24 hr inhibition of basal & meal stimulated-acid secretion (90-98%) 2. Inhibit the final step of Gastric Acids secretion
Uses	- GERD (heartburn/ dyspepsia). - PUD: effective in nocturnal acid suppression & ulcer healing in moderate cases - Zollinger Ellison Syndrome (large doses). - Prevention of bleeding from stress-related gastritis.	- Zollinger Ellison syndrome (1st choice). - PUD (4-8 weeks); faster & long- lasting ulcer relief. - GERD. - prevention of bleeding from stress-related gastritis. - H. pylori-associated ulcer & NSAID-associated ulcer.

	H2 receptor blockers	Proton Pump Inhibitors (PPIs)
ADRs	- **GIT disturbances (Nausea & Vomiting)** - **2.CNS effects** - **3. Bradycardia & hypotension (rapid I.V)** - **4. 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.**	- **GIT disturbances** - **Prolonged acid suppression leads to:** - **subnormal B12 levels** - **risk of hip fracture if taking PPIs over a long period** - **colonization & infection of the stomach & intestine from ingested bacteria; increased risk of both community-acquired respiratory infections & nosocomial pneumonia.**
Drug intera-ctions	- **-Cytochrome P450 inhibition (mostly with cimetidine , then ranitidine)** - **It decreases metabolism & prolong $t_{1/2}$ of:** - **warfarin, phenytoin, theophylline.** - **-H2 antagonists compete with creatinine & certain drug (procainamide; antiarrhythmic) for renal tubular secretion.**	———————

H2 Blockers	PPIs
block one of the 1st stimuli for acid production	block the final step in the pathway of acid secretion (greater suppression)
usually only work up to 12 hours.	work for a longer period of time; (up to 24 hr) & the effects may last up to 3 days.

	CIMETIDINE	RANITIDINE	FAMOTIDINE	NIZATIDINE
Efficacy	+++	++ +	+++	+++
Potency	+	++	+++	++
Dose	400 mg bid	150 mg bid	20mg bid	150 mg bid
Route	orally, IV	orally, IV	orally, IV	orally
T 1/2	short (2 h)	longer (3h)	longer (3h)	shortest (1
Duration	5-6 h	10 h	12 h	11 h
CYT P 450	++	-	-	-
Antiandrogenic	++	-	-	-
Drug interactions	many	No	No	No