

~~LITHIUM~~

PEPTIC ULCER

Antacids

weak bases $\rightarrow$ neutralise acid.
inhibit formation of pepsin

pepsinogen $\xrightarrow{\text{acidic pH}}$ pepsin

$\rightarrow$ faster pain relief, relief of dyspepsia

DOA $\rightarrow$ 30 min (empty stomach)
2 hours after a meal

ADR

$\text{Al}^{3+} \rightarrow$ constipation, hypophosphatemia, osteomalacia

$\text{Mg}^{2+} \rightarrow$ osmotic diarrhoea

- $\rightarrow$ renal failure - Aluminium toxicity, encephalopathy

systemic antacids - alkalis
acid rebound - increased acid production

Potency: - No. of mEq of 1N HCl brought to a pH of 3.5 in 15 min by unit dose of antacid preparation

* Rationale for combining $\text{Al}(\text{OH})_3$ & $\text{Mg}(\text{OH})_2$ in antacids

- fast and sustained neutralizing capacity

$\text{Mg} \rightarrow$ rapid, Al - slow

- Bowel movements are least affected
 Mg - laxative, Al constipation

- Gastric emptying not least affected.
- Dose of individual drug can be reduced.

NaHCO_3

Use $\rightarrow$ alkalinisation of urine.
t/2 of audience

ADR $\rightarrow$ alkalosis, Na overload, and rebound CO_2 retention in stomach causing distension

MAGALDRATE $\rightarrow$ hydrous magnesium aluminate.
rapidly reacts with water, release $\text{Al}(\text{OH})_3$.

H_2 Receptor antagonists

- Reversible competitive inhibitors of H_2 receptors
- Highly selective.
- Suppress Basal, neurogenic, gastric phase.
- Secretin & IF reduced.
- block secretory response to histamine, gastrin, Ach, alcohol, food.

PK: well absorbed.

FPM BA 60-80%.

cross placenta, secreted in milk.

2/3rd unmetabolised.

excreted in urine.

dose redⁿ in severe renal and hepatic disease.

Use $\rightarrow$ duodenal, gastric, stress ulcers, gastritis, ZES
GERD, asp. pneumonia prophylaxis.

APR : GI upset, headache, fatigue,
myalgia, dizziness & hypotension on rapid IV
infusion due to histamine release
↑ concentration of aminoketones

- Cimetidine & Gynecomastia / Impotence
- displaces DHT from receptors
 - inhibits metabolism of estrogens
 - increases prolactin release

DI : cimetidine inhibits CYP 450.
↑ conc. of warfarin, theophyllin, phenytoin,
ethanol

FAMOTIDINE : All H_2 antagonists except famotidine
inhibit FPM of ethanol and increase its BA.
D.O.C to take before alcohol consumption to
avoid gastric irritation.

Proton Pump Inhibitors substituted benzimidazoles

MOA :

- produces - activation in acid environment
- accumulate in canaliculi of parietal cell
- sulfenic acid, sulfenamide metabolite - Active.
- Binds covalently to extracellular domain of $H^+K^+ATPase$.
- irreversible inhibitor of $H^+K^+ATPase$ (recombination takes 15-20 hours)

Actions : Totally abolish acid secretion
only acid secretion is affected, (pepsin, H^+ not affected)
Decrease all phases
Both basal & stimulated secretion - Ach, Food

Pharmacokinetics

enteric coated capsules

BA varies - digestion by acid

BA decreases with food

Metabolism - CYP 2C9, CYP 3A4

Metabolites - urine

(lit and excreting drugs) $t_{1/2} = 1 - 3.5$ hrs.

ADRS

- GI upset
- Rash
- Vit B12 and Ca deficiency
- Leukopenia
- Hepatic dysfunction
- Suprarenal and carcinoid tumours in man

DI

Inhibit CYP 2C9
+ metabolism of warfarin, phenytoin, diazepam

Pantoprazole & rabeprazole have no significant DI.

MISOPROSTOL

PGE1 analogue

inhibits acid production + mucosal protection

stimulates mucus & bicarbonate secretion

↑ mucosal blood flow

Use → prevention of NSAID induced ulcer + $t_{1/2}$ short $t_{1/2} \rightarrow 30$ min

Needs 4 times a day

ADR $\rightarrow$ D, Abdominal pain, uterine bleeding.

SUCRALFATE

- $\rightarrow$ Aluminium salt of sulfated mucose.
- $\rightarrow$ Acidic pH - polymerises to viscous gel that adheres to ulcer crater (binds to proteins) physical barrier.
- $\rightarrow$ Augments gastric mucosal PG synthesis.
- $\rightarrow$ prevents acid, bile coming in contact with ulcer base.
- Taken on empty stomach, 1 hour before 3 major meals.

ADRs constipation, hypophosphatemia, dry mouth.
Not absorbed, hence no systemic ADR.

Uses : promote healing of ulcers.
prophylaxis of stress ulcers.

typical - ulcers, bedsores, diabetic ulcers.

COLLOIDAL BISMUTH COMPOUNDS:

- $\rightarrow$ coats ulcer, produce layer.
- $\rightarrow$ Stimulates PG, mucus, NO_2 secretion.
- $\rightarrow$ Direct antimicrobial activity against *H. pylori*.

ADR $\rightarrow$ blackening of stools / tongue.
Bismuth toxicity - encephalopathy.
CI in renal failure patients.

- Pregnancy - Antacids / Sucralfate.
- heartburns - Antacids (fast).

H. Pylori Gastritis

Triple therapy.

- Metronidazole - 400 mg TDS.
- omeprazole - 40 mg OD.
- amoxicillin - 500 mg TDS.

2 weeks followed by PPI - 4-6 weeks.

Quadruple therapy. (COMT)

- colloidal bismuth subcitrate - 120 mg QID.
- Omeprazole - 20 mg BD.
- Metronidazole 400 mg TDS.
- Tetracycline - 500 mg QID.

GERD.

PPI, H₂ blockers, Antacids, Sodium alginate, prokinetics

- Sodium alginate - from algae, gel covering floats on gastric contents as a thick fatty layer prevent contact of acid with esophagus.

- prokinetics.

- ① Metoclopramide.
- 5HT₄ antagonist
- D2 blocker.
- 5HT₃ antagonist

- Domperidone
- D₂ blocker.

↑ tone of LES, facilitate gastric emptying