Ho Medical ANAESTHESIA

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Gastrointestinal Pharmacology

Pharm-05A6/02A14/98A12/96B15 Briefly outline pharmacological methods of reducing gastric acidity (and volume). Indicate the mechanisms of action,advantages and disadvantages of each.

1. The parietal cells of the stomach produce hydrochloric acid which accounts for the acidic environment of the stomach.
2. Mechanism of gastric acid production: produced by parietal cells
    a. Steps:
        i. $CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-$
        ii. HCO_3^-/Cl^- exchange at basolateral membrane
        iii. H^+/K^+-ATPase pump exchange at apical membrane
        iv. K^+ gradient maintained by Na^+/K^+-ATPase pump
    b. Control:
        i. ↑ pump activity:
            1. H_2 – G_sPCR → ↑cAMP
            2. $M_{1/3}$ - G_qPCR → ↑Ca^{2+}
            3. Gastrin - ↑Ca^{2+}
        ii. ↓ pump activity:
            1. Prostaglandin E_2 receptor – G_iPCR → ↓cAMP

Drug	Mechanism	Assessment
Acid reduction		
Proton Pump Inhibitors: Omeprazole	Pro-drug (protonated in stomach) Non-competitive irreversible block H/K ATPase	Adv: most effective ↓acid drug as it blocks the final common pathway Dis: minimal toxicity includes GI upset, headache, mild inhibition CYP 450
H_2 antagonists: Cimetidine	Competitive reversible blockade H_2 receptors → ↓cAMP H_2 receptors also on cardiac, mast cells.	Adv: effective ↓ acid Dis: not as effective as PPIs, ↓ hepatic BF, CYP450 inhibition, anti-androgenic (cimetidine), fast IV infusion can cause ↓BP/HR.
Anti-muscurinics: Pirenzepine	Competitive reversible blockade $M_{1/3}$ receptors → ↓IP_3 and DAG → ↓Ca^{2+}	Adv: effective ↓acid, anti-emetic properties Dis: less effective than H_2 blockers, anti-muscurinic side-effects – tachycardia, dry eyes/mouth, confusion.
Prostaglandins: Misoprostol	PGE_1 analogue → ↓cAMP → ↓H/K ATPase pump, ↑ mucosal secretions	Adv: additional ↑mucous protection, metabolism not dependent on hepatic/renal function Dis: ↑uterine tone → miscarriage, diarrhoea, GI upset, ↓BP large doses, multiple daily dosing
Antacids: Al salts Mg trisilicate Na citrate	Bases which neutralise luminal acid by buffering H^+ forming → $MgCl_2$, $NaHCO_3$	Adv: promotes ulcer healing, minimal systemic absorption, fast speed onset Dis: short duration, Mg causes diarrhoea, Al causes constipation, less effective
Volume reduction		
Metaclopramide (Benzamide)	D_2 blocker, $5HT_4$ agonist, Muscurinic agonist → ↑LOS tone, relaxation pylorus	Adv: effective anti-emetic Dis: high dose EPSE, NMS, no effect on acid secretion, high dose IV bolus can cause ↓BP
Domperidone (Butyrophenone)	Peripheral D2 blocker	Adv: does not cross BBB, no EPSE Dis: arrhythmia high dose
Erythromycin	Uncertain	Adv: effective macrolides antibiotic
Ipecacuanha	Direct gastric irritant	Dis: causes vomiting

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