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ANTI-DIARRHOEAL AGENTS

- Diarrhoea: frequent passage of liquid or semisolid stools is called diarrhoea.
- Causes: enteric infection, food toxins, malnutrition, inflammation, drugs like reserpine, prostaglandins, metoclopramide, domperidone, cholinergic drugs, quinidine and purgatives.
- Dysentery: abdominal pain and passage of bloody stools and mucous due to infection or inflammation.

Management of diarrhea

1. Non-specific therapy:

- a) Oral and parenteral rehydration
- b) Anti-motility and anti-secretory agents:
 - i) Opioids: codeine, diphenoxylate, loperamide
 - ii) α -adrenergic receptor agonist: clonidine
 - iii) Octreotide.

2. Specific therapy: Antimicrobial agents

3. Antispasmodics: Atropine & oxyphenonium (antrenyl)

4. Adsorbants: Kaolin, pectin and chalk, bismuth subsalicylate

Non-specific therapy

Oral rehydration solution (ORS): 2.6 g NaCl, 1.5 g KCl, 2.9 g sodium citrate, 13.5 g glucose dissolved in 1 liter of water.

Super ORS: (boiled rice powder used instead of glucose)-also decreases frequency of diarrhoea along with rehydration.

Antimotility and antisecretory agents

- Codeine: opium alkaloid, reduces GI motility, also have antisecretory effects.
- Diphenoxylate: structurally related to pethidine, combined with small doses with atropine, side effects are constipation, paralytic ileus, banned in many countries.
- Loperamide: opiate analogue and important antidiarrhoeal than morphine.
- Interact with μ -receptor in the gut, reduces GI motility and increase anal sphincter tone.

DRUGS FOR CONSTIPATION

LAXATIVES

(Aperients, Purgatives, Cathartics)

These are drugs that promote evacuation of bowels. A distinction is sometimes made according to the intensity of action.

(a) Laxative or aperient: milder action, elimination of soft but formed stools.

(b) Purgative or cathartic: stronger action resulting in more fluid evacuation.

Many drugs in low doses act as laxative and in larger doses as purgative.

CLASSIFICATION

1. Bulk forming: Dietary fibre: Bran, Psyllium (Plantago) Ispaghula, Methylcellulose
2. Stool softener: Docusates (DOSS), Liquid paraffin
3. Stimulant purgatives (a) Diphenylmethanes, Phenolphthalein, Bisacodyl Sodium picosulfate
(b) Anthraquinones (Emodins) Senna, Cascara sagrada
(c) 5-HT₄ agonist Tegaserod (d) Fixed oil, Castor oil
4. Osmotic purgatives Magnesium salts: sulfate, hydroxide, Sodium salts: sulfate, phosphate
Sod. pot. Tartrate Lactulose

MECHANISM OF ACTION

All purgatives increase the water content of faeces by:

(a) A hydrophilic or osmotic action, retaining water and electrolytes in the intestinal lumen-increase volume of colonic content and make it easily propelled.

(b) Acting on intestinal mucosa, decrease net absorption of water and electrolyte; intestinal transit is enhanced indirectly by the fluid bulk.

(c) Increasing propulsive activity as primary action-allowing less time for absorption of salt and water as a secondary effect.

Laxatives modify the fluid dynamics of the mucosal cell and may cause fluid accumulation in gut lumen by one or more of following mechanism

- (a) Inhibiting Na⁺K⁺ATPase of villous cells impairing electrolyte and water absorption.
- (b) Stimulating adenylyl cyclase in crypt cells increasing water and electrolyte secretion.
- (c) Enhancing PG synthesis in mucosa which increases secretion.
- (d) Structural injury to the absorbing intestinal mucosal cells