

Drugs acting on GIT

Treatment of diarrhoea and constipation



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Anti-diarrhoeal drugs



Diarrhoea



- Refers to **frequent or liquid bowel** movements
- **Acute, chronic**
- May be mild **without complications**
- But in **infants & children** it is severe can cause **dehydration** quickly
- Diarrhoea results from an **imbalance** between **secretion & reabsorption of fluid & electrolytes**
- **Two major factors** in diarrhea are:
 - **Increased motility** of the GI tract
 - **Decreased absorption of fluid**

Causes of Diarrhoea



- **Infections** with enteric organisms:
 - Bacteria, viruses
 - Protozoa as amoebiasis & giardiasis
- **Food poisoning & traveler's diarrhoea**
- **Inflammatory bowel disease:**
 - Crohn's disease
 - Ulcerative colitis
- **Drugs:** antibiotics (Antibiotic-associated colitis)
- **Malabsorption**

- Examples of **serious diarrhoeal** diseases e.g. dysentery, cholera

Treatment of diarrhoea



- **Eliminating** the underlying **cause e.g. by specific antimicrobial agent**
- **Giving fluids and electrolyte replacement**
 - **Oral rehydration therapy**
- **Antidiarrhoeal drugs** provide symptomatic relief:
 - **Antispasmodics**
 - **Antimotility drugs**
 - **Adsorbants & Bulk forming agents**

Oral rehydration therapy (ORT)

- The **1st line** of treatment is **prevention** or treatment of **fluid** and **electrolyte depletion** particularly **in acute diarrhoea of children**
- Treat majority of **acute gastroenteritis (GE) of children (virus)**
- Important in **infants** and **elderly** patients
- **Is simple, effective, cheap & easy** to use

Oral rehydration preparations

- Replacement of fluid & electrolytes lost through diarrhoea can be achieved by giving **solutions** containing: Na, glucose, K, etc...
- For **acute diarrhoea**
- Intestinal absorption of **Na & water** is enhanced by **glucose**
- Suitable ORS should contain an **alkalinizing agent** to **counter acidosis**

Oral rehydration preparations

- Rehydration should be **rapid** over **3** to **4** hours
- Once rehydration is complete further dehydration is prevented by **encouraging** patients to **drink fluids**
- In infants **breast-feeding** should be **offered** between oral rehydration drinks
- **Severe** dehydration: **IV fluids & electrolytes**

Symptomatic Antidiarrhoeal Drugs

- These drugs **increase** intestinal content to control **acute diarrhoea**:
 - **Increase viscosity**
 - **Prolong transit time**
- Two types of **drugs** often used in combination:
 - **Opioids**
 - **Anti-muscarinics**

- These are used for **short-term** symptomatic **relief** of **acute** diarrhoea in **adults**
- **not** recommended:
 - For acute diarrhoea in **children** (under 2 years old), because of risk of respiratory depression
 - In **infective** diarrhoea
- **Caution** in ulcerative **colitis**
- These agents **delay** passage of intestinal **content** leading to:
 - increase water absorption
 - increase intestinal content viscosity.
- **Antidiarrhoeal action**

Codeine



- Codeine & other opioids produce constipation by **activation** of **opioid** receptors on **smooth** muscle of the gut **decreasing** forward **peristalsis** & increasing **segmentation**
- Codeine is useful for **non-infective** acute diarrhea in **adults**
- Contraindicated in:
 - **Infective** diarrhoea & **antibiotic-associated colitis** (AAC)
 - **Active inflammatory** bowel disease (as acute UC)

Codeine

- **Adverse effects:**
 - Nausea, sedation
 - **Respiratory depression**
 - **Dependence**

Diphenoxylate



- Its related to pethidine
- has actions on the bowel **similar to codeine**
- It is **used** as:
 - **Adjunct** to rehydration in **acute diarrhoea**
 - In **mild ulcerative colitis**
- It is usually mixed with small dose atropine (**lomotil**)
- Its $t_{1/2}$ is 3 hours
- **Overdose** may produce **respiratory depression** & manifestations of atropine poisoning.

Loperamide (**Imodium**)



- structurally similar to diphenoxylate
- Used as:
 - **Adjunct to rehydration** in acute diarrhoea in **adults & children over 4 years.**
 - In **mild chronic diarrhoea in adults.**
- Its contraindications are similar to the above drugs

Naloxone (opioid antagonist) antagonises actions of **codeine, diphenoxylate & loperamide** when there is overdose **intoxication**

Adsorbent & bulk forming agents

- Adsorbants such as **kaolin, pectin & chalk** are **no** more recommended for acute diarrhoea because of their **low** therapeutic **efficacy**.
- Bulk forming agents such as **ispaghula & methylcellulose** are useful in:
 - **Controlling faecal consistency & reducing its fluidity in ileostomy & colostomy**
 - **Controlling diarrhoea associated with diverticular disease.**

Specific drug therapy

- Helicobacter GE: **ciprofloxacin**
- Shigellosis: **ciprofloxacin**
- Typhoid fever: **ciprofloxacin, cefotaxime**
- AAC: **metronidazole, vancomycin**
- Amoebiasis: **metronidazole**
- Giardiasis: **metronidazole**
- **Octreotide** (a somatostatin analogue):
diarrhoea of **carcinoid**

Laxative agents





Constipation

- Is the passages of **hard stool less frequently** than the patient's own normal pattern.
- **Prevention** of constipation since childhood is important.
- Preventing constipation:
 - Regular **defecation**
 - Use of **balanced diet** containing adequate **fluid** intake and high **fibre** intake (vegetables, fruits and cereals)
- **Low fibre** diet has an important **aetiological** role in development of constipation, haemorrhoids and diverticulitis.

Therapeutic indications of laxative



- **Lower GIT procedures** as surgery, radiology and endoscopy
- **Anal lesions** like anal fissure and haemorrhoids
- **Mega colon** (Hirschprung disease) in children
- **Drug-induced** constipation (like opioid-induced)
- **Hepatic encephalopathy**
- **After antihelminthics** to encourage expulsion of worms to the outside

Routes of administration of laxatives

- Usually **orally**
- Occasionally **rectally** (suppositories or rectal enema)



Dangers of abuse of laxative



Regular or excessive or chronic use of laxative should be **avoided** because may produce the following risk:

- **Dependence and atonic** non-functioning colon
- **Water and electrolyte change** (hypokalaemia, hyponatraemia)
- **Steatorrhoea** (malabsorption of fat)
- **Hypocalcaemia and osteomalacia**

Contraindication of laxative



- **Undiagnosed abdominal pain**
- **Intestinal obstruction**
- **Inflammatory bowel disease**

Classification of laxatives

- **Bulk-forming laxative**
- **Osmotic laxative**
- **Faecal softeners**
- **Stimulant laxatives**



Bulk forming laxative

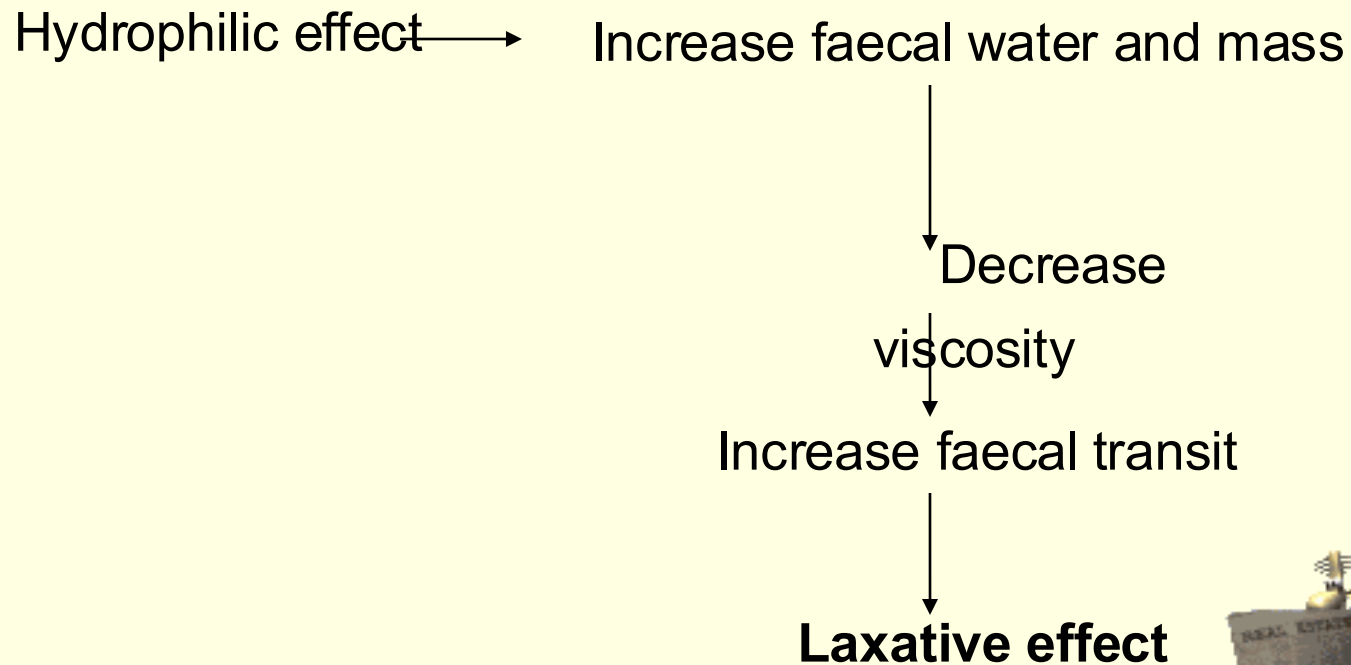
- Site of Action: **Small and large intestine**
- Onset of Action: **12 - 72 hours**
- Cause the stool to be **bulkier** and to **retain** more **water**, as well as forming an emollient gel, making it easier for peristaltic action to move it along.
- They should be **taken** with plenty of **water**.

Bran



- Is **hydrophilic indigestible** vegetable **fibres** obtained from cereals
- Is the **residue** obtained when **flour** is made from **cereals** and consists of the cell wall of cereals
- Wheat bran is **taken** with **food or fruit juice**
- Is the **most effective** bulk-forming preparation
- Bran contain **~40% fibres** which are not digestible by human enzyme

Mechanism of action of bran



Therapeutic uses of bran

- **Prevention of constipation** in people with small hard stools resulting from low-fibre diet
- **Irritable bowel syndrome (IBS) and diverticulosis**
- **Colostomy and ileostomy**
- **Anal lesion** as anal fissure and haemorrhoids

Adverse effects of bran

- **Flatulence**
- **Intestinal obstruction**, may avoid with adequate fluid intake
- **Interference with absorption** may occur like of glucose, calcium and drugs.

Methylcellulose



- **Useful** for patients who **cannot tolerate bran**
- It takes water to swell to a colloid about 25 times its original volume resulting in laxative effect

Osmotic laxatives

- These cause the intestines **to hold more water** within, **softening** the stool.
- There are **two** principal types, **saline and hyperosmotic**

Osmotic
laxative



Saline Osmotic:

Magnesium sulphate (Epsom salt)

- Site of Action: **Small and large intestine**
- Onset of Action: **0.5 - 6 hours**
- Is an inorganic **powerful osmotic purgative**
- It **acts within 3 hrs** by its osmotic effects
- It should be **used on empty stomach** and **with fluids**
- **Useful** when **rapid clearing** and **evacuation** of the colon is required as **before**:
 - **Endoscopy**
 - **Surgery**
 - **radiology**

Mg₂SO₄ side effects

- May cause **nausea** and intestinal **colic**
- May alter a patient's **fluid and electrolyte balance**.
- Should be **avoided** in **renal impairment** because of its potent effect and toxicity resulting from absorption of Mg

Hyperosmotic: Lactulose



- Is a synthetic **disaccharide**, which is **not affected** by intestinal **disaccharidase** and so **not absorbed** from GIT
- Site of Action: **Colon**
- Onset of Action: **0.5 - 3 hours**
- works by the osmotic effect, which **retains water** in the **colon**, **lowering the pH** and **increasing colonic peristalsis**
- It **discourages** the proliferation of ammonia-producing microorganisms.
- Is **useful** in **hepatic encephalopathy** (portal systemic) to prevent onset of hepatic coma
- May produce **flatulence and colic**

Hyperosmotic: Glycerin



- Used as **suppositories**
- Has a mild **stimulant** action on the **rectum** by the **irritant action**

Stimulant laxatives

- These **increase** intestinal **motility** and often **cause** abdominal **colic**
- **Prolonged used** may cause **atonic non-functioning colon** and **hypokalaemia**
- Action site: **colon**

Bisacodyl (Dulcolax)



- Produce direct **stimulation** of sensory **nerve** ending in the **colon** from the lumen
- May used orally (action in 6-10hr) or rectally (1hr)
- Useful in:
 - **Constipation**
 - **Before surgery**
 - **Endoscopy**
 - **Radiology of the lower GIT**

Senna



- Is **absorbed** in the **small intestine** and **excreted** into the **colon** where it stimulates **bowel motility**
- Is **widely used**:
 - **Constipation**
 - **Before surgery**
 - **Before endoscopy**