# Drugs for treating Diarrhoea

**Dr. Badar Uddin Umar**
MBBS, MPhil

# Diarrhoea

- There is imbalance between secretion and reabsorption of fluid and electrolytes.
- Treatment is aimed at **restoration of fluid and electrolyte balance** first.
- Then treatment of the cause.

# Causes of Diarrhoea:

1. **Infection** with enteric organism
2. **Inflammatory bowel disease**
3. **Malabsorption** due to disease
4. **Disorder of gut motility**
5. **Secretory tumors** – rare

# Treatment

Fluid and electrolyte treatment:

Oral rehydration salt (ORS) The WHO/UNICEF recommended formulation is:

| | |
|---|---|
| Sodium chloride | 3.5 g/l |
| Potassium chloride | 1.5 g/l |
| Sodium citrate | 2.9 g/l |
| Anhydrous glucose | 20 g/l |

Total osmolarity 311mmol/l

# Treatment

Fluid and electrolyte treatment:

***'Reduced osmolarity Oral rehydration salt'*** (ORS) WHO/UNICEF recommended formulation is:

| | |
|---|---|
| Sodium chloride | 2.6 g/l |
| Potassium chloride | 1.5 g/l |
| Sodium citrate | 2.9 g/l |
| Anhydrous glucose | 13.5 g/l |

Total osmolarity 245 mmol/l

**This is also known as Neo Saline**

# Antidiarrhoeal drugs

Antimotility drugs:

- **Opioids:**
  - Codeine
  - Diphenoxylate
  - Loperamide
  - Opium tincture
  - Morphine

Drugs increasing viscosity of gut contents:

- Kaolin & Pectin
- Methylcellulose
- Chalk
- Activated Attapulgite

# Antidiarrhoeal drugs

Anticholinergics:

- Belladonna
- Atropine
- Propantheline
- Dicyclomine HCl
- Mebeverine

Miscellaneous:

- Peppermint oil
- Vegetable astringents

# Antimotility drugs

- **Opioids** have significant constipating effects
- They increase colonic phasic segmenting activity through **inhibition of presynaptic cholinergic nerves** in the submucosal and myenteric plexuses and lead to **increased colonic transit time** and fecal water absorption
- They also **decrease mass colonic movements and the gastrocolic reflex**

# Antimotility drugs cont….

- **Loperamide** is a nonprescription opioid agonist
- It does not cross the blood-brain barrier and has no analgesic properties or potential for addiction
- Tolerance to long-term use has not been reported
- It is typically administered in doses of 2 mg taken one to four times daily

# Antimotility drugs cont….

- **Diphenoxylate** is another opioid agonist
- Has no analgesic properties in standard doses
- Higher doses have CNS effects
- Prolonged use can lead to opioid dependence
- Commercial preparations commonly contain small amounts of atropine to discourage overdosage (2.5 mg diphenoxylate with 0.025 mg atropine)
- The anticholinergic properties of atropine may contribute to the antidiarrheal action

# KAOLIN & PECTIN

- **Kaolin** is a **naturally occurring** hydrated magnesium aluminum silicate (attapulgite)
- **Pectin** is an **indigestible carbohydrate** derived from apples
- Both appear to act as **absorbents of bacteria, toxins, and fluid,** thereby **decreasing stool liquidity** and number
- They may be useful in **acute diarrhea** but are seldom used on a chronic basis

# KAOLIN & PECTIN

- A common commercial preparation is **Kaopectate**
- The usual dose is 1.2-1.5 g after each loose bowel movement (maximum: 9 g/d)
- Kaolin-pectin formulations are **not absorbed** and have **no significant adverse effects** except constipation
- They *should not be taken within 2 hours of other medications* (which they may bind)

# C. Antimicrobial therapy

| *Cause* | *Drug of 1st choice* | *Alternative drug* |
|---|---|---|
| Cholera | For younger children: Erythromycin<br>For adults: Tetracycline | Co-trimoxazole |
| Shigellosis | Nalidixic acid<br>Co-trimoxazole | Pivmecillinam<br>Ampicillin |
| Acute intestinal amoebiasis | Metronidazole | Tinidazole |
| Acute giardiasis | Metronidazole | |

# Some special diarrhoeal conditions:

- Travelers' diarrhoea
- Specific infective diarrhoea
- Drug induced diarrhoea
- Secretory diarrhoeas due to carcinoid tumor and vipomas treated with octreotide

- A VIPoma (also known as Verner Morrison syndrome
- A rare endocrine tumor, usually (about 90%) originating from non-β islet cell of the pancreas
- Produce vasoactive intestinal peptide (VIP)
- It may be associated with multiple endocrine neoplasia type

# Precautions

- Antidiarrhoeal agents may be used safely in patients with mild to moderate acute diarrhea
- However, they **should not be used** in patients with bloody diarrhea, high fever, or systemic toxicity because of the risk of worsening the underlying condition
- They should be discontinued in patients whose diarrhea is worsening despite therapy

# Other anti diarrhoeals

- **Bile salt-binding resins- cholestyramine and colestipol** decrease diarrhea caused by excess fecal bile acids
- The usual dose is 4-5 g one to three times daily before meals
- Adverse effects include-
  - bloating, flatulence, constipation, fecal impaction and exacerbation of fat malabsorption

# Octreotide

- **Somatostatin**, a 14 amino acid peptide, released in the gastrointestinal tract and pancreas from paracrine cells, D-cells, and enteric nerves as well as from the hypothalamus

# Effects of Somatostatin :

- It inhibits the secretion of numerous hormones and transmitters, including gastrin, cholecystokinin, glucagon, growth hormone, insulin, secretin, pancreatic polypeptide, vasoactive intestinal peptide, and 5-HT
- It reduces intestinal fluid secretion and pancreatic secretion
- It slows gastrointestinal motility and inhibits gallbladder contraction

# Effects of Somatostatin cont..

- It induces direct contraction of vascular smooth muscle, leading to a reduction of portal and splanchnic blood flow
- It inhibits secretion of some anterior pituitary hormones

# Octreotide

- Is a synthetic octapeptide with actions similar to somatostatin
- When administered intravenously, it has a serum half-life of 1.5 hours
- It also may be administered by **subcutaneous injection**, resulting in a **6 – 12 hour duration of action**
- A longer-acting formulation is available for **once-monthly depot intramuscular injection**

# Clinical Uses

- **Secretory diarrhea** caused by gastrointestinal neuroendocrine tumors (carcinoid, VIPoma)
- Diarrhea due to **vagotomy or dumping syndrome**
- Diarrhea caused by **short bowel syndrome or AIDS**
- **Pancreatic fistula**
- **Pituitary tumors**

# Nitazoxanide

- Rotavirus is a leading cause of morbidity and mortality in children younger than 5 years
- A 3-day course of nitazoxanide significantly reduced the duration of rotavirus disease in hospitalized paediatric patients

* The Lancet, Volume 368, Issue 9530, Pages 124 - 129, 8 July 2006

# Treatment of Constipation

# What is constipation?

# Laxatives/purgatives

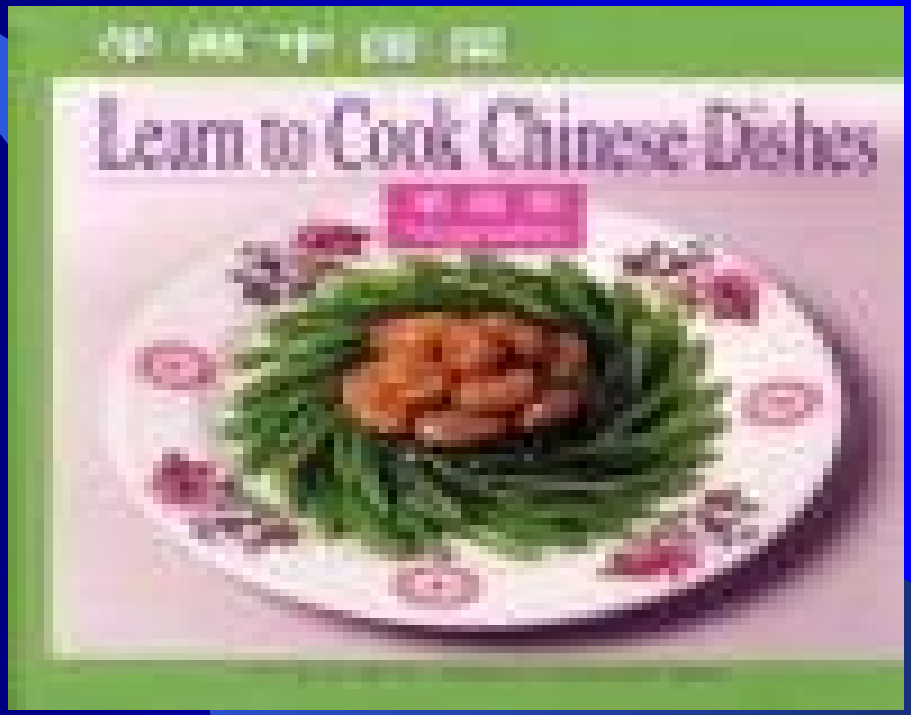
These are drugs that promote evacuation of bowels-

- Laxatives/ aperient:
  - Milder in action
  - Produces soft but formed stool
- Purgatives/ cathartics:
  - Stronger acting
  - Produces fluid stool

*Many laxatives in higher doses act as purgatives

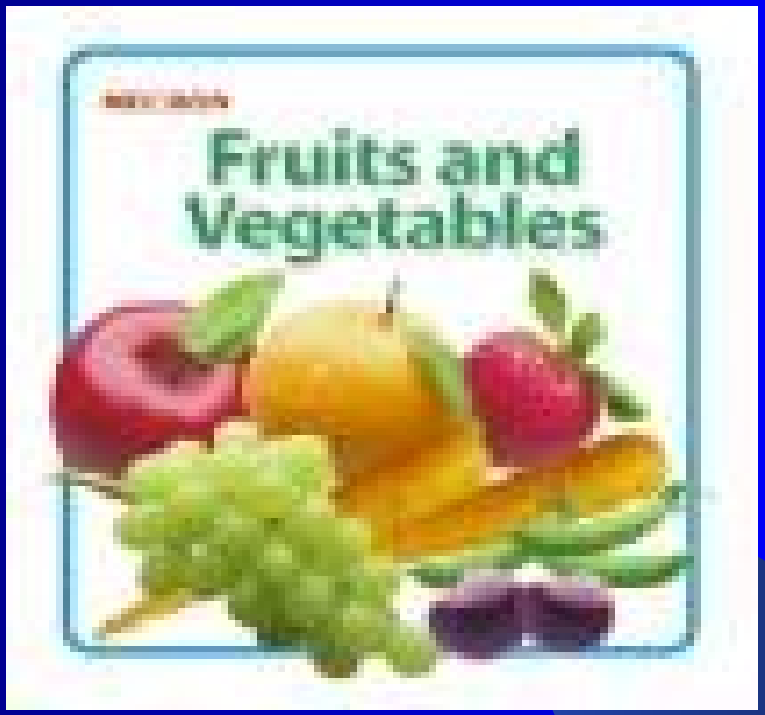
# Laxatives

Chronic use of laxatives may make you…
dependent



# Management of constipation

- Avoid highly refined diet
- Avoid aluminium containing antacids & Iron
- Take Plenty of vegetables, fruits and milk




**Don’t use laxatives**

# Eat a diet with high roughage

# Management of constipation

- Drink a cup of warm water/ tea/ coffee half an hour before breakfast
- Mild exercise for bed ridden patients, patients of old ages are required to improve tone of abdominal muscles
- Anxiety and worry to be avoided

# Drug classes used as laxatives/ Types of laxatives

- Bulk laxatives
- Faecal softeners
- Stimulant laxatives
- Osmotic laxatives

# Bulk Laxatives

- Isapghula husk
- Methyl cellulose
- Bran
- Psyllium (Plantago)
- Sterculin
- Indigestible vegetables

# Isapghula husk

How it should be taken?

Indigestible vegetables: act within 1-3 hrs

# Isapghula husk

- Contain natural colloidal mucilage
- Absorbs water in the gut
- Forms a gelatinous mass

# Stimulant Laxatives (Contact Laxatives)

- Bisacodyl (Dulculax):
  - Powerful purgatives
  - Orally given, act within 6-10 hrs.
  - Suppository act within 15-30 min.
- Senna (Laxena):
  - Acts within 8-12 hours
- Castor oil (Fixed oil)

# Mechanism of action of stimulant purgatives

- Stimulate motor activity by irritating the mucosa
- Causes accumulation of water and electrolytes in the gut lumen by
  - altering  absorption
  - inhibit $Na^{+}K^{+}$ATPase at the basolateral membrane of villous cells
  - cAMP activation leads to increased secretion
  - PG synthesis also increases secretion

# Adverse effects of stimulant purgatives

- Excessive purgation
- Fluid and electrolyte imbalance
- Hypokalemia
- Colonic atony in long term use
- Contra-indicated in-
  - pregnancy as it can cause abortion
  - subacute or chronic intestinal obstruction

# Osmotic Laxatives

- Lactulose( Disaccharide):
  - Very good in hepatic encephalopathy
  - Fermented to Lactic & Acetic acid and prevents ammonia producing organisms
- Magnesium sulfate:
  - Useful when  powerful effect is required

# Osmotic Laxatives

- Remain unabsorbed in GIT
- Retain water osmotically
- Distend in the gut
- Increase peristalsis
- Mg ions release cholecystokinin adding to their purgative action

Mg salts are contraindicated in renal failure, sodium salts are contraindicated in CHF

# Lactulose

- Semisynthetic disaccharide of fructose and lactose
- Not digested, not absorbed in small intestine
- Retains water
- In the colon broken down by bacteria in to osmotically active products

# Adverse effects of lactulose

- Flatulence
- Cramps and
- Nausea due to very sweet taste

# Faecal Softeners

- Milk of magnesia
- Liquid paraffin:
  - For short term use only
  - Has lot of complications
- Mineral oil

# Common indications for laxatives

1. Functional constipation
   - Spastic constipation
   - Atonic constipation
1. Bed-ridden patients

   Myocardial infarction, stroke, fracture and post-operative pts.
1. To avoid straining at stool
2. Preparation of bowel for surgery, colonoscopy & radiography
3. After certain anthelmintics
4. Food/ drug poisoning

# Contraindications of laxatives

- Undiagnosed abdominal pain, colic or vomiting
- Secondary constipation due to
  - Stricture, obstruction etc.
  - Hypothyroidism
  - Hypercalcemia
  - Malignancies
  - Some drugs like-opiates, sedatives, anticholinergics, antidepressants, antihistamines, iron, clonidine, verapamil, laxative abuse itself

# SLOs

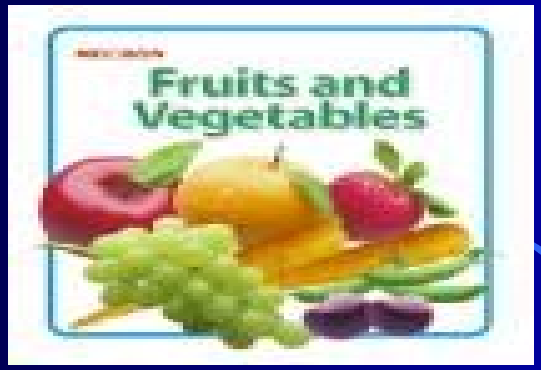
At the end of the lecture students should be able to-

43.1 list the drugs used in the treatment of constipation

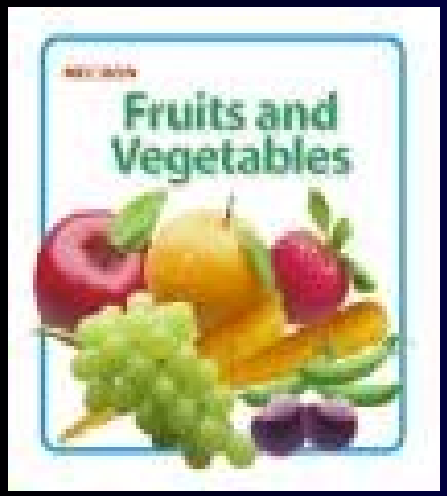
43.2 list the drugs used for the treatment of diarrhoea

43.3 Describe the mechanism of action of drugs acting in constipation and list other uses of these drugs

43.4 Describe mechanism of action and side effects of antidiarrhoeals




# Questions?




# Thanks