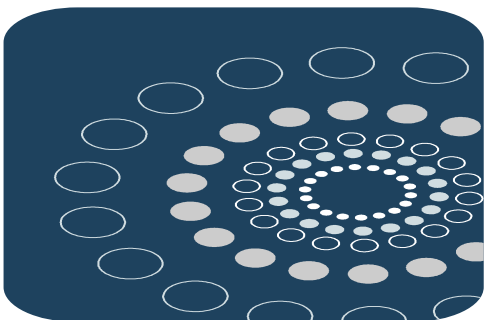
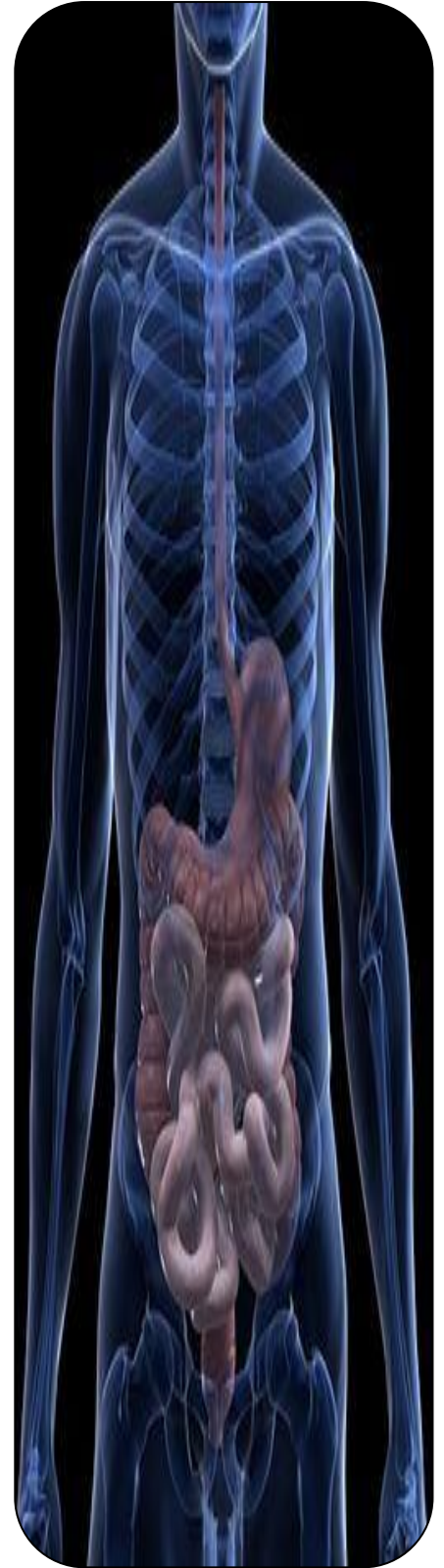


Pharmacology Team

**Drugs Treating
Constipation &
Irritable bowel
syndrome**



Done by :

- Nouf Hatim aboalsamh
- Abdulaziz Al-Subaie

Introduction

✓ What is constipation?

Infrequent defecation, often with straining and the passage of hard, uncomfortable stools.

✓ Accompanied by other symptoms:

Abdominal and Rectal pain, Flatulence, Loss of appetite, Lethargy and Depression

✓ Causes of constipations :

➤ Decreased motility in colon:

Decrease in water and fibre contents of diet. **(Most important)**

(Presence of water and fibres in the gastrointestinal tract induces motility / peristaltic movement)

➤ Difficulty in evacuation: (the patient is reluctant to pass stool)

1. Local painful conditions: Anal fissures, piles
2. Lack of muscular exercise

Anal fissure: is a break or tear in the skin of the anal canal

Piles = Haemorrhoids: are enlarged veins in the anus or lower rectum

➤ Drug-induced constipation :

- A. Anticholinergic agents (producing Atropine-like action)
- B. Anti-Acid Drugs (Aluminium or Calcium or Magnesium salts)
- C. Opioids (e.g.: Morphine)
- D. Antipsychotics (have Atropine-Like effect)
- E. Anti-Anaemia drugs (e.g.: Iron)

➤ Other conditions :

- A. Uremia
- B. Tumors obstructing
- C. IBS & IBD (sometimes come with constipations)

Treatment of Constipation :

1. Adequate fluid intake.
2. High fibre contents in diet. (Fibres enhance GIT motility e.g. : Corn , Almonds , Raspberries , spinach)
3. Regular exercise
4. Regulation of bowel habit.
5. Avoid drugs causing constipation.
6. Use drugs (**laxatives or purgatives**) to enhance GIT motility

Medications used in constipations :

Drugs that speed the passage of food through the gastrointestinal tract are called (**laxatives** or **purgatives**)

Classification of laxatives or purgatives:

1. **Bulk forming laxatives** (Fibre Laxatives):

Increase volume of non-absorbable solid residue. (Increasing the fiber content of the stool thus increasing the peristaltic movement)

2. **Osmotic laxatives:**

Increase water content in large intestine (by Osmosis)

3. **Stimulant or irritant laxatives:**

Act by direct stimulation of Enteric nerves system in colonic mucosa

4. **Stool softeners (lubricants):**

Alter the consistency (viscosity) of feces → easier to pass along the GIT

1. Bulk (fibre) Laxatives

Insoluble dietary fibers (Natural components):

- Indigestible parts of vegetables & fruits
- Bran powder “ النخالة ”

Hydrophilic colloids:

- ❖ Psyllium seed
- ❖ Methyl cellulose
- ❖ Carboxymethyl cellulose (CMC)

Hydrophilic: likely to withdraw water

Colloids: has high molecular weight

Mechanism of action :

Hydrophilic colloids are non-absorbed → Increase the bulk (volume) of intestinal contents by water retention → ↑ mechanical pressure on the walls of intestine → stimulation of stretch receptors located along the GIT → ↑ peristalsis → evacuation of soft stool.

Side Effects :

- Delayed onset of action (1-3 days).
- Intestinal obstruction (should be taken with enough water).
- Bloating, flatulence, distension
- Interfere with other drug absorption e.g. iron, cardiac glycosides. (because of the high molecular weight they adhere to other medication taken simultaneously at the same time and dragging them with the faeces)

Clinical use :

- Hemorrhoids
- Pregnancy
- Colostomy
- Anal fissures
- Chronic diarrhoea associated with diverticular disease (because there are substances stay long time in the diverticulum, body tries to get rid of it (diarrhea) but it cannot .. so we evacuate the diverticulum using this type of laxatives)

2. Osmotic Laxatives:

- ✓ Increase water content in the stool by enhancing the osmotic pressure thus producing Watery stool

1. Sugars : e.g. lactulose

Lactulose

- **Non absorbable** disaccharide (remain in the bowl and attract water by osmosis)
- Metabolized by bacteria in colon into “monosaccharide”: **fructose + galactose** → these sugars are further fermented into **lactic acid and acetic acid** that function as osmotic laxatives.

Lactic acid and acetic acid: stay in the colon and Drag more water which will result in softening / watering the stool

Uses:

- Prevention of chronic constipation
- **Hepatic encephalopathy (Hyperammonemia** =an excess of ammonia in the blood)

HOW?? Osmotic Laxatives are converted into active acids → Acidification of the intestine by increasing the H⁺ concentration in the gut thus changing the ammonia from its active form NH₃ “lipid soluble” to the non-absorbable “water absorbable “ form NH₄ → trapping NH₃ in the colon and reducing its diffusion into blood.

- Haemorrhoids (→the patient will not have to strain during defecation)

Side Effects

1. Delayed onset of action (2-3 days)

Regular use of lactulose can reduce the onset of action to (4-6) hours

2. Abdominal cramps and flatulence. → Because it's not absorbable
3. Electrolyte disturbances. **(Only In large doses)**

2. Salts (Saline laxatives)

A. Magnesium sulphate or hydroxide & B. Sodium or potassium phosphate.

- **Magnesium sulphate** (Epson's salt) / **Magnesium hydroxide** (milk of magnesia).
- **Sodium phosphate or potassium phosphate.**
- **Rapid effect** (within 1-3 h).
- Isotonic or hypotonic solution should be used.

Uses:

Treatment of **ONLY** acute constipation

Magnesium is the physiologic antagonist of calcium
sometime used IV in arrhythmia, eclampsia and cerebral palsy

Explanation: In general these drugs are not absorbed however, sometimes a little portion (10%) might be absorbed which can produce side effects in some certain situations like: Cardiac diseases, Renal failure...etc.

Side Effects

- Disturbance of fluid and electrolyte balance
- May have systemic effects.

Contraindications

A. **Sodium salts:**

in cardiac patients → results in Tachycardia

B. **Magnesium salts** are contraindicated in:

1. Renal failure **2. Old age** **3. Heart block**,

4. CNS depression **5. neuromuscular block**

Magnesium is excreted by the kidney, so In case of old age or renal failure (kidneys are unable to completely clear the body from the Magnesium). This will result in the accumulation of Magnesium (**Hypermagnesaemia**) causing Toxicity as well as producing systemic side effects such as (Bradycardia, CNS depression, Muscle relaxation)

In **heart block** we want Calcium to activate the heart, **we don't want magnesium** (contraindication) since it's an antagonist to Calcium, vice versa for arrhythmia (indication)

3. **Balanced Polyethylene glycol (PEG)** (Very Effective)

- **Isotonic solution of polyethylene glycol & electrolytes** (NaCl, KCl, Na bicarbonate).
- **Colonic lavage solution** (complete clearance)
- **Used for whole bowel irrigation prior to colonoscopy or surgery** (4L over 2-4 hours).

Advantages

- ✓ **Limited fluid or electrolyte imbalance (iso-osmotic).**
- ✓ less flatulence and cramps

3. Stimulant Laxatives (Irritant Laxatives)

- ✓ The **most powerful** among laxatives and should be used with care.

Mechanism of Action:

Act **via direct stimulation of enteric nervous system** → increased peristalsis.

Bisacodyl

- ✓ **Acts on colon**
- ✓ Onset of action = orally (6-12 h)/ per rectum “suppository” (1 h) (depending on the route of administration)

Castor Oil (زيت خروع)

- ✓ **Acts in small intestine**
- ✓ Vegetable oil degraded by lipase → **ricinoleic acid** + glycerin
- ✓ **Ricinoleic acid is very irritating to mucosa thus increasing the peristaltic movement.**
- ✓ **Rapid** Onset of action = 2-6 h.

Anthraquinone glycosides

e.g. **senna, cascara, aloe**

- ✓ **Act in colon**
- ✓ Hydrolyzed by bacterial colon into **sugar + emodin** (**The absorbed emodin has direct stimulant action on the Enteric Nervous system**).
- ✓ Emodin is excreted into milk.
- ✓ Delayed onset of action (8-12 h).

Side Effects :

1. Abdominal cramps.
2. **Prolonged use** → atonic colon due to **dependence & destruction of myenteric plexus**

Atonic colon: Lack of normal muscle tone or strength

Contraindications:

- **Senna** is contraindicated in lactation (**because it is excreted in the milk**) → Diarrhoea to the **Baby**
- **Castor oil** is contraindicated in **pregnancy** → **reflex contraction of uterus** → **abortion**.

4. Fecal Softeners (Lubricants)/surfactants

Surfactants: Reduce surface tension = allow penetration of water into the stool

- **Are non-absorbed drugs**
- Act by either decreasing surface tension or by softening the feces thus promoting defecation.
- Treat constipation in patients with hard stool or specific conditions and for people who should avoid straining.

Docusate

sodium dioctyl sulfosuccinate)

- One type of Surfactants
- Act by decreasing surface tension of feces
- Is given orally (1-3 days) or enema (5-20 min "Rapid ").

Enema: introducing liquids into the rectum and colon via the anus

Paraffin oil

- Mineral oil, lubricant
- Not palatable (Unpleasant taste)
- Impairs the absorption of fat soluble vitamins (A, D, E, and K).

Glycerin

- Lubricant
- Given ONLY rectally (suppository)
 - ✓ Very favourable because it doesn't cause any side effects

Irritable bowel syndrome (IBS)

Definition: Chronic bowel disorder characterized by abdominal discomfort (bloating, pain, distention, cramps) associated with alteration in bowel habits (diarrhea or constipation or both).

- ✓ Causes of IBS are Idiopathic, so there is no absolute cure thus treatment is only symptomatic

Symptomatic treatment of IBS :

- ✓ Antispasmodics e.g. mebeverine → smooth muscle relaxant
- ✓ Low doses of tricyclic antidepressants (amitriptyline)
 - Anticholinergic action
 - reduce visceral afferent sensation
- ✓ Laxatives in IBS-Constipation
- ✓ antidiarrheal in IBS-Diarrhea
- ✓ **Alosetron** (IBS with Diarrhea)
 - Selective 5HT₃ antagonist
 - block 5-HT₃ receptors of the enteric nervous system of the gastrointestinal tract
 - Inhibition of colon motility + Inhibition of unpleasant visceral afferent pain sensation (nausea, pain, bloating).

Uses of Alosetron : Used in severe IBS with diarrhea in women

Adverse effects : Constipation and ischemic colitis may occur.

✓ **Tegaserod** (IBS with constipation)

- 5HT₄ agonist
- Stimulation of 5HT₄ of enteric nervous system of GIT → increases peristalsis
- Used In Short term treatment of IBS-associated with constipation in women
- Restricted to special patients that require hospitalization.

Serotonin acting Drugs (Alosetron / Tegaserod) → These Drugs Are only reserved for only SEVERE situations when the patient is not responding to all the other medication

WHY?? Because of the dangerous side effects induced by these drug

SUMMARY

- 1- **Bulk Purgatives** like grains, bran, and Psyllium seed : **Increase volume of non-absorbable solid residue** we should take them with water.
 - a. They are used in Hemorrhoids; Pregnancy, Chronic diarrheas with diverticular disease.
 - b. They have **delayed onset of action**,
 - c. may cause **Intestinal obstruction** (should be taken with enough water).
- 2- **Osmotic Purgatives**: are Water Soluble but non absorbable compounds that **Increase water content in large intestine**.
 - a. **lactulose is used in liver cirrhosis**
 - b. **Magnesium salts** are poorly absorbed salt that function as an osmotic purgatives. They are used in **acute cases** of constipation, **contraindicated in renal failure**, and its main side effects are: Intravascular volume depletion, electrolyte fluctuations: severe in children
 - c. **Balanced polyethylene glycol** (PEG) “ **movicol** “ : is a balanced isotonic solution of osmotically active sugar, NaCl, KCl, Na bicarbonate, which is used for complete cleansing prior to gastrointestinal **endoscopic procedures** (High doses), **treatment or prevention of chronic diarrhea**
- 3- **Stimulant Purgatives**: act via **direct stimulation of enteric nervous system** > peristalsis
 - a. Bisacodyl has a weak effect on the large intestine.
 - b. Anthraquinone derivatives are hydrolyzed by bacteria into emodin (stimulate myenteric plexus) + sugar. It causes brown pigmentation of the colon
 - c. Castor Oil is a Fixed oil degraded by lipase in upper small intestine > ricinoleic acid + glycerin. **Ricinoleic acid irritates the mucosa** .(acts on strongly on the small intestine)
 - d. **Senna** is contraindicated in **lactation**. **Castor** oil in pregnancy > reflex contraction of uterus > **abortion**.
- 4- **Fecal softeners** (lubricants): Are non absorbed drugs that soften the feces, thus promoting defecation
 - a. Surfactants: like **Docusate** (sodium dioctyl sulfosuccinate): decrease surface tension of feces, and is commonly prescribed in hospitalized patients to minimize straining.
 - b. **Glycerin** (Suppository). (Usually given twice after surgery to avoid any damage to the Surgery)
 - c. Mineral oil (Liquid **Paraffin**) (**good for radiology preparation**) given in enema in that case. Side effects of liquid paraffin: Not palatable (bad taste), **impairs absorption of fat soluble vitamins(A,D,E,K)**, and Increase activity of oral anticoagulant.

Irritable bowel syndrome (IBS) treatment :

- 1- Antispasmodics e.g. **mebeverine** (atropine like action)
- 2- Low doses of tricyclic antidepressants (**amitriptyline**) : has an Anticholinergic action and reduces visceral afferent sensation
- 3- **Alosetron** , serotonin **antagonist** (used in IBS-diarrhea)
- 4- **Tegaserod**, serotonin **agonist** (used in ISB-constipation)

Q1- patient has bleeding per rectum is going to do colonoscopy, which one of the following drugs is best to clean prior to the procedure ?

- 1- Bisacodyl
- 2- Docusate
- 3- Lactulose
- 4- Balanced polyethylene glycol

Q2 – which one of the following drugs is used in IBS-associated constipation in women ?

- 1- Alosetron
- 2- Ondansetrone
- 3- Zucopride
- 4- Tegaserod

Q3- which of the following laxatives is used in liver cirrhosis ?

- 1- Bisacodyl
- 2- Castrol oil
- 3- Sorbitol
- 4- Lactulose

Q4- which of the following laxatives is best used in pregnancy ?

- 1- PEG
- 2- Glycerine
- 3- Magnesium
- 4- Fibers

Q5- which of the following laxatives is used only in acute constipations ?

- 1- PEG
- 2- Glycerin
- 3- Fibers
- 4- Magnesium sulphate

Answers : 4 for all

GOOD LUCK :D