Lecture 4

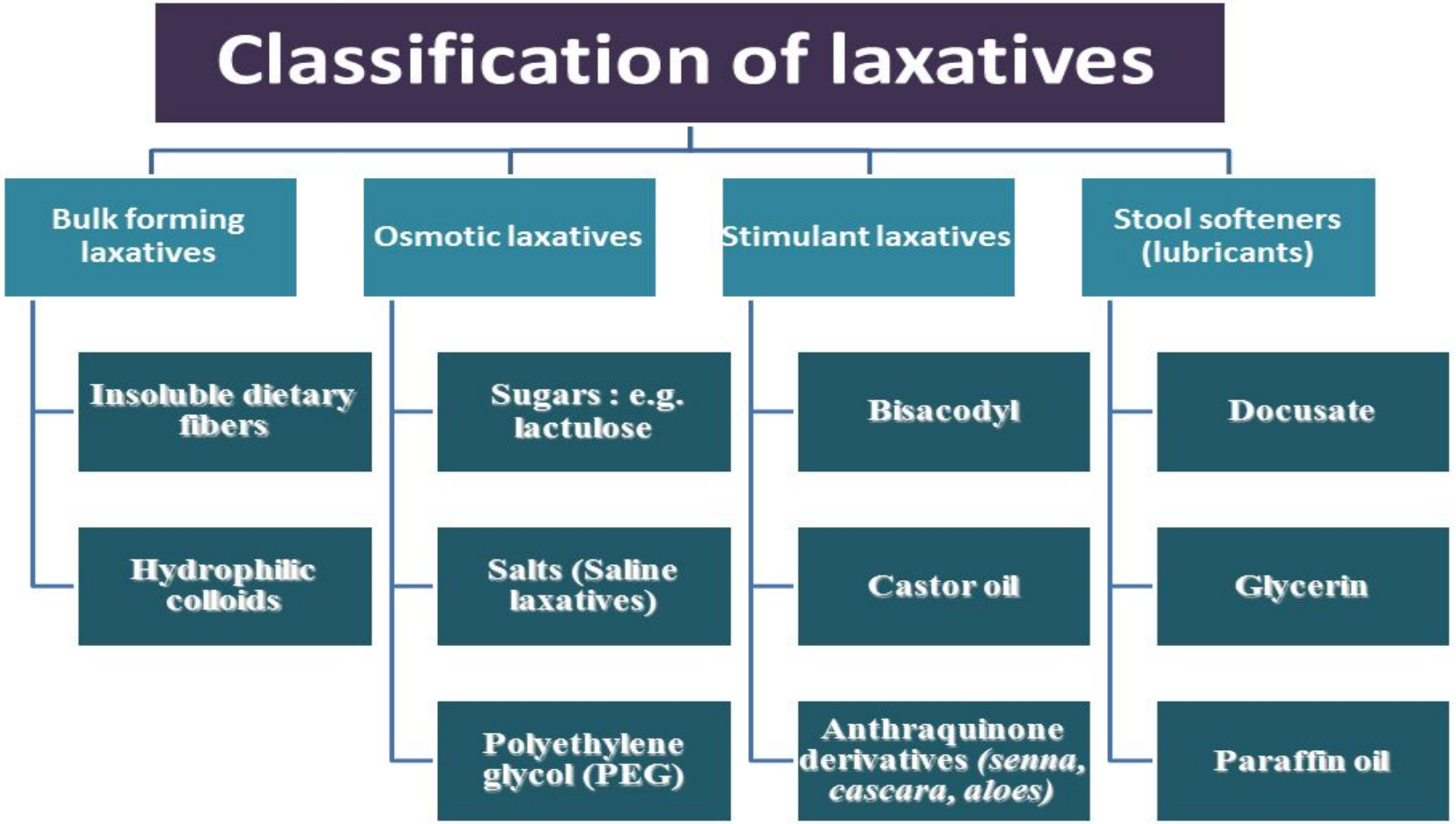
Drugs used in treating constipation and IBS

Objectives:

★ **NOT GIVEN**

- Additional Notes
- Important
- Explanation –Extra-

For any correction, suggestion or any useful information
do not hesitate to contact us: Pharmacology434@gmail.com



before starting, please check our GIT block correction

Introduction:

What is constipation?

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

What other symptoms may accompanied with constipation?

- ★ Abdominal and rectal pain
- ★ Flatulence
- ★ Loss of appetite
- ★ Lethargy
- ★ Depression

what are the causes of constipation?

1-Decreased motility in colon:

- ★ Decrease in water and fiber contents of diet.

2-Difficulty in evacuation:

- ★ Local painful conditions: anal fissures, piles
- ★ Lack of muscular exercise

3-Drug-induced:

- ★ Anticholinergic agents
- ★ Opioids
- ★ Iron
- ★ Antipsychotics

treatment of constipation

A-General Measures :

1. Adequate **fluid intake**.
2. **High fiber** contents in diet.
3. Regular exercise
4. Regulation of bowel habit.
5. Avoid **drugs** causing constipation.
6. Use drugs (laxatives or purgatives)

B-Medications used in constipations:

Drugs that hasten the transit of food through the gastrointestinal tract are called laxatives or purgatives.

Classification of laxatives:

I) Bulk forming laxatives:

Increase volume of non-absorbable solid residue.

II)Osmotic laxatives:

Increase water content in large intestine.

III) Stimulant or irritant laxatives:

Act by direct stimulation of nerve endings in colonic mucosa.

IV) Stool softeners (lubricants):

Alter the consistency of feces → easier to pass

Bulk (fiber) Laxatives

Include:	**Dietary fibers:** • **Indigestible parts of vegetables & fruits** • **Bran powder**	**Hydrophilic colloids** • **Psyllium seed** • **Methyl cellulose** • **Carboxymethyl cellulose (CMC)**
MOA	Dietary fibers and hydrophilic colloids are non absorbable substances → **increase** the bulk of intestinal contents by water retention → **-increase** mechanical pressure on the walls of intestine → stimulation of **stretch receptors** → increase -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.**	

Osmotic Laxatives

characteristics	● are **water soluble** compounds ● **Poorly absorbable** compounds (<u>salts or sugars</u>) ● They remain in the bowel, attract and retain water by **<u>osmosis</u>** thereby increasing the volume of feces → increase peristalsis → evacuation of stool.		
drugs	**1-Sugars :** **e.g. lactulose**	**2-Salts (Saline laxatives)** ● **Magnesium sulphate or hydroxide** ● **Sodium or potassium phosphate.**	**3-Polyethylene glycol (PEG)**

1-Lactulose

pharmacokinetic	● Semisynthetic disaccharide of **fructose** and **galactose**. ● **Non absorbable**. ● In colon, metabolized by bacteria into fructose and galactose. ● These sugars are fermented into **lactic acid** and **acetic acid** that function as <u>osmotic laxatives</u>.

Osmotic Laxatives

cont. 1-Lactulose

Uses

- prevention of chronic constipation
- Hepatic encephalopathy (Hyperammonemia)
- Hemorrhoids
- Liver cirrhosis HOW?!

★ **Lactulose increases the H^+ concentration (acidification of colon) in the gut (by lactic acid and acetic acid), This favors the formation of the non-absorbable NH_4^+ from NH_3, trapping NH_3 in the colon and reducing its back diffusion into blood.**

side effects

1- delayed onset of action (2-3 days)
2- abdominal cramps and flatulence
3- electrolyte disturbances

Dose

15 ml for constipation and 30 ml for liver cirrhosis

Osmotic Laxatives

2- Saline Laxatives

drugs	➔ **Magnesium sulphate** (Epson's salt). ➔ **Magnesium hydroxide** (milk of magnesia). ➔ **Sodium phosphate or potassium phosphate**
characteristic	• Are **poorly absorbable** salts • **Increase evacuation of watery stool.** • **have rapid effect (within 1-3 h).**(emergency) • **Isotonic or hypotonic solution should be used.**(if hypertonic then dehydration develop)
use	Treatment of **acute constipation**
side effect	• **Disturbance of fluid and electrolyte balance** • **May have systemic effects.**(because of the small amount that get absorbed)
contraindication	• **1)Sodium salts** in congestive heart failure **(CHF)** • **2)Magnesium salts** are contraindicated in: **Renal failure (it's site of execration),** **Heart block, CNS depression, Neuromuscular block(myasthenia gravis)**

Osmotic Laxatives

3-Balanced Polyethylene Glycol (PEG)

characteristic	Isotonic solution of **polyethylene glycol & electrolytes** (NaCl, KCl, Na bicarbonate). ★ Is a **colonic lavage solution**
uses	**Used for whole bowel irrigation prior to colonoscopy or surgery (4L over 2-4 hours)**
Advantages	• **Limited fluid or electrolyte imbalance** • **less flatulence and cramps**

Stimulant Laxatives

characteristic	are the **most powerful** group among laxatives and should be used with care.
MOA	act via direct stimulation of enteric nervous system→increase peristalsis & purgation.

Bisacodyl type: (Diphenylmethane)	Castor Oil type :(ricinoleic acid)	Anthraquinone glycosides (senna, cascara, aloes)
Is given **orally**, acts on **colon** Onset of action: **orally (6-12 h) per rectum (1 h)**	Given **orally**, 5-20 ml on empty stomach in the morning. acts in **small intestine** Vegetable oil degraded by **lipase** → **ricinoleic acid** + **glycerin** Ricinoleic acid is very irritating to mucosa. **Onset of action = 2-6 h.**	Act in **colon** Hydrolyzed by bacterial colon into **sugar+ emodin** (The absorbed emodin has direct stimulant action). **Emodin may pass into milk.** **Delayed onset of action (8-12 h).** Bowel movements in **12h (orally) or 2h (rectally)**. *Given at night

Side Effects	**1.Abdominal cramps may occur.** **2.Prolonged use → dependence & destruction of myenteric plexus leading to atonic colon.**
Contraindications	***Senna: is contraindicated in breast feeding.** ***Castor oil** **: in pregnancy→reflex contraction of uterus → abortion.**

Fecal Softeners

characteristic	- 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***		
Drugs	**Docusate** (Sodium dioctyl sulfosuccinate)	**Glycerin**	**Paraffin Oil**
Pharmacokinetics & Clinical Uses	- One type of **surfactants** - Act by decreasing surface tension of feces - Is given orally (12-72 hours, **Long**) , or enema** (5-20 min, **short**).	- **Lubricant** - Given rectally (suppository***)	- Is a mineral oil - Given orally - Acts as **lubricant** thus softening the feces and promoting defecation. - **Good for radiology preparation**
Side Effects	_	_	- **Not palatable** (bad taste) - **Impairs absorption of fat soluble vitamins.**

*(doing an effort during defecation) **(injected into the rectum) ***(تحميلة)

Irritable bowel syndrome (IBS)

Chronic bowel disorder characterized by :

- **Abdominal discomfort** (bloating, pain, distention, cramps) treated by Antispasmodics & Tricyclic antidepressants
- **Alteration in bowel habits** (diarrhea or constipation or both). .. treated by Laxatives & Antidiarrheal

Symptomatic treatment

Antispasmodics
e.g. **mebeverine**
(decrease GI Motility & decrease spasm)

Low doses of
tricyclic antidepressants
e.g. **amitriptyline**
act via:
- Anticholinergic action
(decrease GI motility)
- Reduce visceral afferent sensation

Laxatives in IBS-Constipation
e.g. **Tegaserod**

Antidiarrheals in IBS-Diarrhea
e.g. **Alosetron**

Alosetron (antidiarrheal)

M.O.A	★ **Selective 5HT3 antagonist** 5-HT3 receptors antagonism of the enteric nervous system of the gastrointestinal tract results into: - **inhibition of colon motility.** - **inhibition of unpleasant visceral afferent pain sensation** (nausea, pain, bloating).
Uses	- **IBS with severe diarrhea** (in women who have not had success with any other treatment.)
Side Effects	- **Constipation** - **Ischemic colitis may occur.**

Tegaserod

M.O.A	★ **5HT4 agonist** - Stimulation of 5HT4 of enteric nervous system of GIT > increases peristalsis.
Uses	- Short term treatment of **IBS-associated with constipation** (in women <55 years old with no history of heart problems.)
Side Effects	- **CVS side effects** - **May still be used in limited emergency situations.**

MCQS:

1. A patient was taking a laxative for long time. He suddenly developed atonic colon. What is the medication he was taking ?
A)Saline laxatives. B) Tegaserod.
C)Senna.
D)Paraffin oil

2. Which of the following is used in treatment of Hepatic encephalopathy ?

A) Lactulose
B) Magnesium salts
C) Sodium salts
D) Bisacodyl

3. Which of the following drugs is acting on small intestine ?

A) Bisacodyl
B) Castor oil
C) Lactulose
D) Paraffin oil

4. Which of the following is contraindicated in lactating women?

A) Castor oil
B) Senna
C) Docusate
D) Bulk purgatives

5. A patient was using a drug and suddenly he developed Neuromuscular Block. Which of the following he was taking ?
A) Magnesium salts
B) Sodium salts
C) Bisacodyl
D) Docusate

6. Which of the following is contraindicated in pregnant women ?
A) Castor oil
B) Senna
C) Docusate
D) Bulk purgatives

7. Which of the following is used in colonic lavage ?
A) Balanced Polyethylene Glycol (PEG)
B) Sodium salts
C) Lactulose
D) Anthraquinone glycosides

8. Which of the following Act by decreasing surface tension of feces ?
A) Bisacodyl B) Docusate
C) Lactulose D) Paraffin oil

9. A patient with IBS was treated by a drug and after a while he developed ischemic colitis . What was the drug he took ?
A) Tegaserod B) Anthraquinone glycosides C) Alosetron
D) Balanced Polyethylene Answers Glycol (PEG)

1-C
2-A
3-B
4-B
5-A
6-A
7-A
8-B
9-C

Good luck!

Done by Pharmacology team 434

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