

Drugs used in treating constipation and IBS

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- Main text
- Male slide
- Female slide
- Important
- Dr, notes
- Extra info

EDITING FILE

Objectives



Classify Laxatives.



Discuss the pharmacological properties of different classes of laxatives.



Outline drugs used to treat irritable bowel syndrome.

★ Dr: you should know the onset of action + the route of administration in this lecture since the drug of choice depends on them



Dr. Fouda Video

Constipation

Epidemiology

- ▶ Constipation affects all age groups
- ▶ Formula-fed baby are more likely to have constipation
- ▶ Over 700 drugs have constipation as a side effect.
- ▶ The elderly are most susceptible
- ▶ There is high incidence of females

Definition

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

May be accompanied by other symptoms:

- ▶ Loss of appetite
- ▶ Lethargy
- ▶ Depression
- ▶ Abdominal and rectal pain
- ▶ Flatulence "*accumulation of gas*"

Causes

Decreased motility in colon

Decrease in water and fiber contents of diet

Difficulty in evacuation

- Local painful conditions: anal fissures, piles "*hemorrhoids*"
- Lack of muscular exercise

Drug-Induced

- Anticholinergic agents
- Opioids
- Iron
- Antipsychotics

Treatment

General measures: "*Habits and lifestyle should be changed before prescribing drugs*"

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**): Drugs that hasten "*speed up*" the transit of food through the GIT.

Classification of Laxatives:

1- Bulk forming Laxatives	2- Osmotic Laxatives	3- Stool softeners (lubricants)	4- Stimulant or Irritant Laxatives
Increase the volume of non-absorbable solid residue	Increase water content in large intestine	Alter the consistency of feces → easier to pass	Act by direct stimulation of nerve endings in colonic mucosa

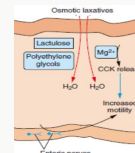
1. Bulk forming Laxatives

	Dietary fibers	Hydrophilic colloids
Types	<ul style="list-style-type: none"> ▸ Indigestible parts of vegetables & fruits ▸ Bran powder 	<ul style="list-style-type: none"> ▸ Psyllium seed (soluble fiber) ▸ Methyl cellulose ▸ Carboxymethyl cellulose (CMC)
M.O.A	Dietary fibers and hydrophilic colloids are non absorbable substances → increase the bulk of intestinal contents by water retention → → Distend the colon → → ↑ Mechanical pressure on the walls of intestine → → Stimulation of stretch receptors → → ↑ Peristalsis → Evacuation of soft stool .	
ADRs	<ul style="list-style-type: none"> ▸ Delayed onset of action (1-3 days) "<i>not used in acute</i>" ▸ Intestinal obstruction (should be taken with enough water). ▸ Bloating, flatulence, distension. ▸ Interfere with other drug absorption e.g. iron, cardiac glycosides. 	

2. Osmotic Laxatives

Overview

- Are water soluble, poorly absorbable compounds (**salts or sugars**).
- **M.O.A:** They remain in the bowel, **attract & retain water** by **osmosis** thereby increasing the volume of feces → ↑ Peristalsis → Evacuation of stool.



▸ **Include:**

A. Sugars: Lactulose

B. Salts (Saline laxatives):

- Magnesium sulphate or hydroxide

- Sodium or Potassium phosphate

C. Polyethylene glycol (PEG)

A. Sugars

Drug	Lactulose
P.K	<ul style="list-style-type: none"> ▸ Semi-synthetic disaccharide of fructose & galactose. ▸ Non absorbable. ▸ In the colon, metabolized by bacteria to fructose & galactose. ▸ These sugars are fermented into lactic acid & acetic acid that function as osmotic laxatives.
Uses	Prevention of chronic constipation
ADRs	<ul style="list-style-type: none"> ▸ Delayed onset action (2-3 Days) ▸ Abdominal cramps & flatulence. ▸ Electrolyte disturbance.

B. Salts (Saline laxatives)

Drugs	<ul style="list-style-type: none"> - Magnesium sulphate (Epson's salt) - Magnesium hydroxide (milk of magnesia) 	<ul style="list-style-type: none"> - Sodium phosphate - Potassium phosphate
P.K	<ul style="list-style-type: none"> ▸ Are poorly absorbable salts. ▸ Increase evacuation of watery stool. ▸ have rapid effect (within 1-3 h). "Used for acute constipation" ▸ Isotonic or hypotonic solution should be used. "<i>Hypertonic shouldn't be used because it causes vomiting & dehydration</i>" 	
Uses	<ul style="list-style-type: none"> ▸ Treatment of acute constipation. 	
ADRs	<ul style="list-style-type: none"> ▸ Disturbance of fluid and electrolyte balance. ▸ May have systemic effects. 	
#	Magnesium salts: <ol style="list-style-type: none"> 1. Renal failure (<u>Hypermagnesemia</u>). 2. Heart block. 3. CNS depression. 4. Neuromuscular block. 	Sodium salts: <ul style="list-style-type: none"> - congestive heart failure.

C. Balanced Polyethylene Glycol (PEG)

P.K	<ul style="list-style-type: none"> ▸ Isotonic solution of polyethylene glycol (PEG) & electrolytes (NaCl, KCl, Na bicarbonate) ▸ A colonic lavage solution "<i>to empty the colon before procedures</i>"
Uses	Used for whole bowel irrigation prior to colonoscopy or surgery (4L over 2-4 hours) before surgery.
ADRs	<ul style="list-style-type: none"> ▸ Safe for all patients & Limited fluid or electrolyte imbalance. ▸ Less flatulence and cramps.

3. Stool softeners (Lubricant)/Surfactants

Drugs	Docusate	Glycerin	Paraffin Oil
M.O.A	<ul style="list-style-type: none"> ▸ Are non absorbed drugs. ▸ Act by either decreasing surface tension (allowing water to interact with the stool) or by softening the feces thus promoting defecation. 		
P.K	<ul style="list-style-type: none"> ▸ Sodium dioctyl sulfosuccinate. ▸ One type of surfactants. ▸ Act by decreasing surface tension of feces. ▸ Given orally (12-72 hours) or enema "<i>injected into rectum</i>"(5-20 min) in hospitalized patients. 	<ul style="list-style-type: none"> ▸ Lubricant. ▸ Given rectally (suppository). 	<ul style="list-style-type: none"> ▸ A mineral oil, given orally. ▸ Acts as lubricant thus softening the feces and promoting defecation. ▸ Good for radiology preparation. ▸ Unpalatable. "<i>bad taste</i>" ▸ impairs absorption of fat soluble vitamins.
Uses	<ul style="list-style-type: none"> ▸ Treat constipation in patients with hard stool or specific conditions and for people who should avoid straining. "<i>patients that can't push hard post surgeries</i>" 		

4. Stimulant Laxatives

Types	Anthraquinone derivatives	Diphenyl-methane	Ricinoleic Acid
Drugs	Senna / Cascara / Aloe vera	Bisacodyl	Castor Oil
M.O.A	<ul style="list-style-type: none"> ▶ The most powerful group among laxatives and should be used with care. ▶ Act via direct stimulation of enteric nervous system → increased peristalsis & purgation and increased fluid and electrolyte secretion. 		
P.K <i>It's important to know the site and onset of action + route of administration.</i>	<ul style="list-style-type: none"> ▶ Act in colon ▶ Hydrolyzed by bacterial colon into sugar + emodin (The absorbed emodin has direct stimulant action) ▶ Emodin may pass into milk "lactating women" ▶ Delayed onset of action (8-12 h) ▶ Bowel movements in 12 h (orally) or 2 h (rectally as suppository) ▶ Given at night 	<ul style="list-style-type: none"> ▶ Given orally, Acts on colon. ▶ Onset of action: orally (6-12 h) / or per rectum (1h) 	<ul style="list-style-type: none"> ▶ Obtained from the seeds of <i>Ricinus communis</i> ▶ 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 ▶ Could be employed after oral ingestion of a toxin.
ADRs	<ul style="list-style-type: none"> ▶ Abdominal cramps may occur ▶ Prolonged use → dependence & destruction of the myenteric plexus leading to atonic colon 		
#	Senna: breastfeeding	-	Pregnancy → reflex contraction of the uterus → abortion

5. Other Anti-Constipation Drugs

Prucalopride	A selective, high affinity serotonin (5-HT ₄) receptor agonist with enterokinetic activities
Lubiprostone	Used for chronic constipation & IBS-C, It stimulates type 2 chloride in the small intestine
Linacotide	Stimulate chloride secretion, Approved for chronic constipation & IBS-C
Methylnaltrexone	(μ-receptor antagonist) is used in opioid induced constipation in advanced illness.

Irritable Bowel Syndrome (IBS)

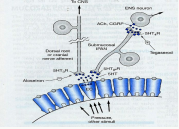
Definition

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

Symptomatic Treatment of IBS:

- **Antispasmodics** e.g. mebeverine.
- **Antidiarrheals** in IBS with Diarrhea (diphenoxylate, loperamide).
- **Alosetron (IBS-D).**
- **Tegaserod (IBS-C).**
- Low doses of **TCA** (amitriptyline) act via: Anticholinergic action, reduce visceral afferent sensation.
- **Laxatives** in IBS with Constipation.

Alosetron

M.O.A	<ul style="list-style-type: none"> • Selective 5-HT₃ antagonist. • 5-HT₃ receptors in the GIT activate visceral afferent pain sensation. • 5-HT₃ receptors antagonism of the enteric nervous system of the GIT results into: <ul style="list-style-type: none"> - inhibition of colon motility - inhibition of unpleasant visceral afferent pain sensation (nausea, pain, bloating). 	
Uses	Used in IBS with severe diarrhea in women who have not had success with any other treatment. <i>"Not a first choice"</i>	
ADRs	Constipation and ischemic colitis may occur. (People taking must sign a Consent form before starting to take the medicine)	

Tegaserod

M.O.A	<ul style="list-style-type: none"> • 5-HT₄ agonist • Stimulation of 5-HT₄ 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, may still be used in limited emergency situations.
ADRs	CVS side effects

Summary

- **Bulking agents** (Oral, 48-72 hours)→ chronic constipation
- **Stool softeners** (Oral, 24-72 hours Rectal, 5-20 minutes)→ Prevention of straining after rectal surgery and in acute perianal disease
- **Osmotic laxatives "lactulose"** (Oral, 24-72 hours)→ Chronic constipation, **Hepatic encephalopathy**, Opioid constipation.
- **Saline laxatives** (Oral, 0.5-3 hours; Rectal, 30 minutes)→ short -term treatment of moderate to severe constipation; acute constipation; bowel preparation for colonoscopy

1. A 27-year-old woman who is 34 weeks' pregnant is on bed rest and is experiencing mild constipation. Which drug is most appropriate for her?

- | | | | |
|---------------|--------------|----------------|---------|
| A. Castor oil | B. Lactulose | C. Mineral oil | D. None |
|---------------|--------------|----------------|---------|

2. What is the mechanism of action for Alosetron

- | | | | |
|------------------------------|---------------------------------|---------------------------------|------------------------------|
| A. 5-HT ₄ agonist | B. 5-HT ₄ antagonist | C. 5-HT ₃ antagonist | D. 5-HT ₃ agonist |
|------------------------------|---------------------------------|---------------------------------|------------------------------|

3. a patient complained of severe constipation, upon taking history it was found that he is undergoing chemotherapy and radiotherapy for the treatment of Glioblastoma. Which drug should you prescribe?

- | | | | |
|-----------------------|---------------------|-------------|---------------------|
| A. Magnesium sulphate | B. sodium phosphate | C. Docutase | D. Methylnaltrexone |
|-----------------------|---------------------|-------------|---------------------|

4. an elderly patient presented with abdominal pain, blood with stool and weight loss. after consultation the doctor ordered a colonoscopy, which of the following drugs should be administered prior to the colonoscopy?

- | | | | |
|---------------------|--------|-----------------|---------------------|
| A. sodium phosphate | B. PEG | C. lubiprostone | D. Methyl cellulose |
|---------------------|--------|-----------------|---------------------|

5. which of the following is preferable in radiological preparations?

- | | | | |
|---------------|-----------------|-------------------|---------|
| A. Castor oil | B. paraffin oil | C. psyllium seeds | D. None |
|---------------|-----------------|-------------------|---------|

6. which of the following could lead to atonic colon upon prolonged usage?

- | | | | |
|------------------------|---------------------------|----------------------|---------|
| A. stimulant laxatives | B. bulk forming laxatives | C. osmotic laxatives | D. none |
|------------------------|---------------------------|----------------------|---------|

7. which of the following is used for hepatic encephalopathy?

- | | | | |
|-------------|--------|--------------|-----------------|
| A. Docutase | B. PEG | C. lactulose | D. lubiprostone |
|-------------|--------|--------------|-----------------|

01

a patient is complaining from severe constipation what can the doctor prescribe for him?

saline laxatives

02

give examples for the class mentioned in Q1

Magnesium sulphate, magnesium hydroxide, sodium phosphate, potassium phosphate

03

mention the side effects associated with the drugs mentioned in Q2

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

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