



PASSION ACADEMIC TEAM



Sheet# 4

YU - MEDICINE

GASTROINTESTINAL SYSTEM

Lec. Title : Drugs for Constipation
(Purgatives or Laxatives) .

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Drugs for Constipation (Purgatives or Laxatives)

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Sheet 1

- OTCs (over the counter) are drugs that given with no need for doctor prescription.
- We need to know before studying of the treatment of constipation that the constipation is not a disease by itself, but it is a symptom for another disease so before giving drugs to the patient you should:
 - Ensure that this case is really constipation
(it could be change in the bowel habit: times going to bathroom or the consistency)
 - In order to diagnose We need to compare between the bowel habit for each person individually before and after the complaint.
 - Find the possible reasons for patient's constipation

Definition of Constipation: Too infrequent passage of stool that may be due to decreased motility in colon or due to difficulty in evacuation.

So constipation could be:

1-Decrease in frequency, or 2-hardening of stool and decrease of its water content, or 3-difficulty of evacuation in colon

Causes

- **Diet: Decrease in water intake and decrease in fiber contents of diet (dates, apples,...).**
- **Local Painful Conditions: Anal fissures, piles or varicose veins of rectum (hemorrhoids).**
- **Lack of muscular exercise (especially muscles of pelvic and lower abdominal wall).**
- **Drugs : Muscle relaxants, Anticholinergics, Calcium channel blockers**

Treatment of Constipation

General Measures (non-pharmacological):

1. adequate fluid intake.
2. high fiber contents in diet.
3. Regular exercise
4. Regulation of bowel habit.
5. Avoid drugs causing constipation.

We need to take care not to give laxatives directly to patients due to its side effects

Only Stimulant Purgatives are called cathartics

Drugs (laxatives, purgatives, cathartics, anti-constipating):

Drugs that hasten the transit of food through the intestine by several methods :

Classification of laxatives or purgatives

(they are one of the “Over The Counter” drugs)

1. Bulk Purgatives : Increase volume

of nonabsorbable solid residue or fibers to make a bulk in the intestine until it push a stress against the wall .

2. Osmotic Purgatives : Increase water

content in large intestine by absorbing fluids from the surrounding environment.

3. Stimulant Purgatives : Increase motility and secretion.

4. Fecal softeners (lubricants) : Alter the consistency of feces → easier to

pass by softening of the stools to decrease the surface tension between stools and the mucosa .

Sheet 2

- - it is better to choose a laxative drug that does not create an imbalance in electrolytes as Na, Ca, K, Mg .
- - another thing we need to care about patient's blood pressure state to avoid hypovolemic shocks .
- - it is preferred to use a fast acting laxative because some types need from 6 to 12 hours in order to act

I. Bulk Purgatives

Mechanism of Action

Non absorbed hydrophilic colloids → Increase the bulk of intestinal contents by water absorption → ↑ mechanical pressure on the walls of intestine → stimulation of stretch receptors → ↑ peristalsis.

Note: 1 gm of Carrot absorbs 20 gm of water.

Carrot is very important for bowel habit, Its healthy to eat carrot 20gm daily

Sheet 3

The difference between the bulk purgatives and the osmotic purgatives is that the bulk although it absorbs some water but its mechanism of action is form a bulk mass to stimulate stretch receptors in the wall of intestine so increase the peristaltic movement of smooth muscles, unlike the osmotic which absorb fluids to soft the stools.

- Bulk forming laxatives are the most suitable drugs for patients with irritable bowel syndrome and spasm
- We can detect GIT spasm by the stethoscope
- There is a difference between increasing tone and motility
 - Increasing tone is the same as increasing of spasm but without motility which is Colic
 - Increase of motility because of increase in tone could cause diarrhea

Members:

- 1. Dietary fibers : undigested polysaccharide
vegetables, fruits, grains, bran, pectin.**
- 2. Natural plant products & semi synthetic
hydrophilic colloids (very important)**
 - Psyllium seed, methyl cellulose**
 - Carboxymethyl cellulose (CMC).**
- 3. Synthetic non absorbed resins
Calcium polycarbophil.**

Avoid dairy product because it contain calcium which cause constipation

- except for yoghurt as it doesn't cause constipation because it contains some bacteria that stimulate GIT motility

Side Effects:

Very important: Focus on each onset of action for all laxatives

- 1. Delayed onset of action (several days 1-3).**
- 2. Intestinal obstruction (should be taken with enough water).**
- 3. Malabsorption syndrome, abdominal distention.**

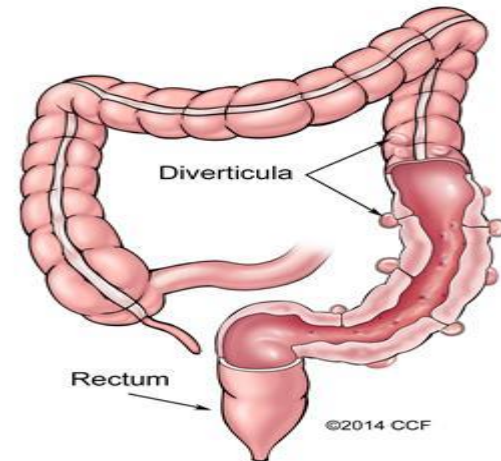
Because it disrupts the process of normal intestinal absorption (eg: some kinds of drugs, iron supplements, normal nutritional substances)
- 4. Interfere with other drug absorption e.g. iron, calcium, and cardiac glycosides.**

Clinical Uses

a surgical operation in which a piece of the colon is diverted to an artificial opening in the abdominal wall so as to bypass a damaged part of the colon.

Hemorrhoids; Pregnancy; Colostomy; ileostomy; anal fissure; IBS, UC, Chronic diarrhea ass with diverticular disease.

Because in late pregnancy months, the uterus may form some kind of pressure on the GI tract



II - Osmotic Purgatives

- **Water Soluble but non absorbable compounds**
- **Increase water content in large intestine.**

Members:

Very important drug and one of the most common prescribed drugs in medicine

1. **Organic (Sugars) : lactulose (semisynthetic disaccharide of fructose and galactose).**
2. **Non-organic (Saline purgatives) : Magnesium salts, sodium or potassium salts.**

1. Organic Osmotic (Lactulose)

- **Metabolized by colonic bacteria into fructose and galactose.**
- **These sugars are fermented into lactic acid and acetic acid that function as osmotic laxatives.**

Side Effects

1. **Delayed onset of action (2-3 days)**
2. **Abdominal cramps and flatulence.**
3. **Electrolyte disturbance.**



Because of fermentation and gas production in the GIT

Sheet 4

- We know from the previous slide that this sugar is fermented finally into lactic acid and acetic acid and these acids raise the pH of the medium making it hard for the normal flora to compensate this acidic media and then die and some types of this flora is responsible for the synthesis of vitamin K which is important to the body making that a big disadvantage for this drug).
- -In another point of view, this laxative could help some anti-coagulants drugs that rely in its mechanism on preventing the synthesis of vitamin K dependent coagulation factors
- -In patients with hepatic dysfunction or liver cirrhosis, the ability to convert ammonia (produced by normal flora) to urea is decreased and ammonia is toxic for CN system (cause hepatic encephalopathy) so lactulose is a good choice for them

Why Lactulose is commonly used in liver cirrhosis?

Mechanism:

- Lactulose \longrightarrow Lactic acid + Acetic Acid \longrightarrow

acidification of the colon \longrightarrow

↓ ammonia absorption

- **Dose: 15 ml for constipation and 30 ml for liver cirrhosis** (the dose is from one fourth to half of the whole bottle)

2. Saline Purgatives (e.g: Magnesium)

Mechanism of Action

Are poorly absorbed salts. They remain in the bowel and retain water by osmosis thereby increasing the volume of feces → ↑ distension → ↑ peristalsis → evacuation of watery stool.

- **Rapid effect (within 1-3h).** The fastest laxative groups ever
- **Magnesium sulphate (Epson's salt).**
- **Magnesium oxide (milk of magnesia).**
- **Sodium phosphate.**

Uses

Because of its fast onset of action

1. Treatment of acute constipation

2. Prevention of chronic constipation

Side Effects

Could cause Hypotension or Hypovolemic shock

1. Intravascular volume depletion.

2. Electrolyte fluctuations: severe in children

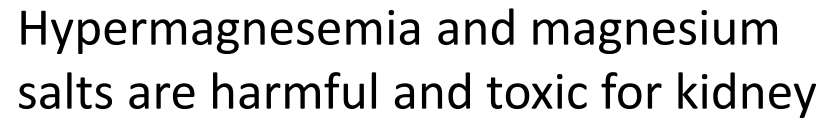
-Please be aware that sodium salts could cause water retention and thus increasing blood volume and blood pressure, so it's contraindicated for people with hypertension

-In general, we mustn't give any individual mineral salt for people with unstable blood pressure, instead we can give them (Balanced polyethylene glycol (PEG))

Contraindications

1. Elderly patients
2. Renal insufficiency.
3. Sodium salts in CHF (congestive heart failure) or in hypertension.
4. Magnesium salts renal failure, heart block, CNS depression, neuromuscular block .

Hypermagnesemia and magnesium salts are harmful and toxic for kidney



Because Mg cause relaxation of the muscles so whet it is given with muscle Relaxant it could make a neuromuscular block
Note: Mg is opposite to Ca in function

Very important drug
Study it well because Dr. focused a lot on it

Balanced polyethylene glycol (PEG)

- **Balanced isotonic solution of osmotically active sugar that contain: polyethyleneglycole and , NaCl, KCl, Na bicarbonate**

Note: isotonic solutions have no fluid absorption or shift effect

→ **✿ Very important feature ✿**

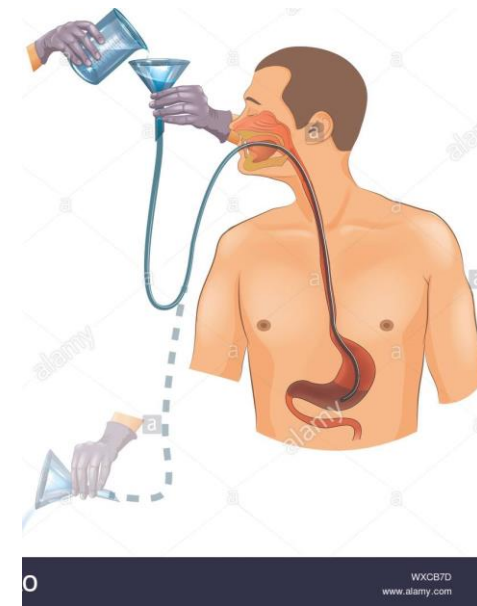
-No intravascular fluids or electrolyte shifts

-No flatus or cramps

-Lavage solution →

-Used for complete cleansing prior to gastrointestinal endoscopic procedures (4L over 2-4 hours).

-Also, small doses used for treatment or prevention of chronic constipation.



III - Stimulant Purgatives (cathartics)

Mechanism of Action :

**act via direct stimulation of enteric nervous system
→ peristalsis & purgation of wall's smooth muscle.**

Members

1. **Bisacodyl.**
2. **Anthraquinone derivatives** (natural compounds found at the Attar ant not commonly prescribed).
3. **Castor oil.**

Are the most important, memorize all the upcoming information about them and the differences between them
Also they are acting on intestine from inside the lumen unlike Anthraquinone derivatives which act from the blood after being absorbed

Bisacodyl

You need to know the Differences very well

- Acts on large intestine (weak).
- Onset time 6-10 h, taken at night.

Castor Oil

- Fixed oil degraded by lipase in upper small intestine → ricinoleic acid + glycerin
- Ricinoleic acid irritates mucosa.
- Acts on small intestine (strong).
- 5-20 ml on empty stomach in the morning.
- O.T. = 4 h. → The fastest drug after purgatives

Anthraquinone derivatives

(Senna, Cascara, Aloes)

- **In colon, glycosides are hydrolyzed by bacteria into emodin + sugar**
- **The absorbed emodin has direct stimulant action on myenteric plexus → ↑ smooth muscle contraction → defecation.**
- **Bowel movements in 12 h (orally) or 2 h (rectally).**
- **Given at night.**
- **Brown pigmentation of the colon (melanosis coli).**

The effective material

Disadvantage or side effect

Side Effects of Stimulant Laxative

- 1. Abdominal cramps may occur.**
- 2. Prolonged use → dependence & destruction of myenteric plexus and atonic colon. Leading to chronic constipation**

Contraindications

- 1. Senna in lactation**
- 2. Castor oil in pregnancy → reflex contraction of uterus → abortion.**

Sheet 5

- - stimulant laxatives obligate the smooth muscle of the intestinal wall to peristalsis so In cases of high and prolonged use it could lead to dependence of muscles and destruction of myenteric plexus and consequently to paralysis and then atonic colon and accordingly to chronic constipation
- Also, these drugs are contra indicated for patients with cramps or those we expect that they have spasm

IV - Fecal Softeners (Lubricants)

- **Are non absorbed drugs that soften the feces thus promoting defecation.**
- **May be given orally or rectally.**

Members :

1. Surfactants

- **decrease surface tension of feces**
- **e.g. Docusate (sodium dioctyl sulfosuccinate).**
- **is given orally or enema.**
- **Is commonly prescribed in hospitalized patients to minimize straining and surface tension between stools and intestine mucous membrane.**

2. Glycerin (Suppository). (Commonly used after Surgery)

3. Mineral oil (Liquid Paraffin) (good for radiology preparation)

Side effects of liquid paraffin

1. Not palatable

2. impairs absorption of fat soluble vitamins.

3. Increase activity of oral anticoagulant.

-Fat soluble vitamins are (A, K, E, D) and both glycerin and liquid paraffin are lipophilic so they maybe bind fat with it soluble vitamins and be evacuated outside the body

-It could be helpful in people having warfarin (stopping synthesis of vitamin k dependent coagulation factor)

-Can be given in chronic constipation but with vitamin supplements

