

Drugs used in constipation and IBS

Drug	MOA	Uses	Pharmacokinetics	ADRs
1-Bulk purgatives 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	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.	-Hemorrhoids; Pregnancy; Colostomy; ileostomy; anal fissure; IBS, UC, -Chronic diarrheas with diverticular disease. (a disease characterized by outpocketings of the colonic mucosa and submucosa through weaknesses of muscle layers in the colon wall.)		-Delayed onset of action (several days 1-3). -Intestinal obstruction -Malabsorption syndrome, abdominal distention. -Interfere with other drug absorption e.g. iron, calcium, and cardiac glycoside (digoxin). So we should separate the drug in time
2- Osmotic Purgatives Water Soluble but non absorbable compounds ,Increase water content in large intestine				
A) Organic (Sugars): lactulose (semisynthetic disaccharide of fructose and galactose).	-Metabolized by colonic bacteria into fructose and galactose. -These sugars are fermented into lactic acid and acetic acid that function as osmotic laxatives.	<ul style="list-style-type: none"> Prevention of chronic constipation Treatment of hepatic encephalopathy 	<ul style="list-style-type: none"> Delayed onset of action (2-3 days) 	<ul style="list-style-type: none"> Abdominal cramps and flatulence. Electrolyte disturbance. (Because of the water drainage)
B) Non-organic (Saline purgatives): Magnesium salts, sodium or potassium salts Contraindicated : -Elderly patients -Renal insufficiency. -Sodium salts: in CHF -Magnesium salts : renal failure, heart block, CNS depression, neuromuscular block	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.	<ul style="list-style-type: none"> Treatment of acute constipation because it has rapid action Prevention of chronic constipation 	<ul style="list-style-type: none"> Rapid effect (within 1-3h). Isotonic or hypotonic solution should be used 	<ol style="list-style-type: none"> Intravascular volume depletion. Electrolyte fluctuations: severe in children May have systemic effect

Balanced polyethylene glycol (PEG*)

- Balanced **isotonic solution** of **osmotically** active sugar, NaCl, KCl, Na bicarbonate
- 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)
- small doses used for treatment or prevention of chronic constipation

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3 - Stimulant Purgatives (cathartics) act via direct stimulation of enteric nervous system → peristalsis & purgation and it's ADRs are: 1-Abdominal cramps may occur 2-Prolonged use → dependence & destruction of myenteric plexus and atonic colon.				
a. Bisacodyl.	-Acts on large intestine (weak).		-Onset time 6-10 h, taken at night.	
b. 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. -Emodin may pass into milk	-Causes brown pigmentation of the colon (melanosis coli). Senna is contraindicated in : Lactation
c. Castor oil. -Fixed oil degraded by lipase in upper small intestine → ricinoleic acid + glycerin Acts on small intestine (strong). -5-20 ml on empty stomach in the morning. -Ricinoleic acid irritates mucosa. -D.T. = 4 h.				Contraindicated in : Pregnancy → abortion
4 - Fecal Softeners (Lubricants) <ul style="list-style-type: none">Are non absorbed drugs that soften the feces ,thus promoting defecation.May be given orally or rectally(faster).				
A)Surfactants e.g. Docusate (sodium dioctyl sulfosuccinate).	decrease surface tension of feces	Is commonly prescribed in hospitalized patients to minimize straining.	<ul style="list-style-type: none">is given orally or enema.	
B)Glycerin (Suppository)		(Usually given twice after surgery to avoid any damage to the Surgery) and it's preferable with children		
C)Mineral oil (Liquid Paraffin)		(Good for radiology preparation) given in enema in that case.	<ul style="list-style-type: none">Not palatable (bad taste)Impairs absorption of fat soluble vitamins.Increase activity of oral anticoagulant.	

Treatment of IBS

- Antispasmodics e.g. mebeverine (**atropine like action**)
- Low doses of tricyclic antidepressants (amitriptyline) : * Anticholinergic action * reduce visceral afferent sensation
- Alosetron (diarrhea)
- Tegaserod (constipation)

	Alosetron	Tegaserod
MOA	5-HT₃ receptor antagonists	5-HT₄ partial agonist
USES	Woman with IBS and severe diarrhea	Woman with IBS and constipation
Side effects	Constipation; Ischemic Colitis	Diarrhea; Headache