“Help! I Need Relief!” Constipation review

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Objectives

- Explain the physiological and behavioral causes of constipation in a specific patient
- Recommend appropriate pharmacological therapy based on a specific cause of constipation
- Recommend non-pharmacological therapy to treat or prevent constipation
- Work cooperatively with a team to make appropriate treatment recommendations for patients

Disclosures

- I have no conflicts of interest.

KW, 57 y/o male presents to the pharmacy and wants something "to help his bowels". He has hypertension, hypercholesterolemia, and chronic back pain. His medications include enalapril 20 mg daily, simvastatin 10 mg daily, and diclofenac 50mg bid for back pain. He had back surgery two weeks ago and is taking oxycodone 10/325mg every 4-6 hours for pain and zolpidem 10mg hs for sleep.

What are the best recommendations for your to make for KW?

A. Increase his exercise, drink more water and take docusate 100 mg: 2 capsules twice daily to soften his stool.
B. Stop the oxycodone and zolpidem, drink at least 16 oz. of water and increase his movement as tolerated.
C. Take PEG 3350 17 gms three times daily and docusate 240 mg now and again tomorrow morning plus walk as much as possible during the day.
D. Increase his movements as his pain allows, take one Senna 25 mg now plus two tablets tomorrow only if needed and increase his fluid intake.
E. Walk as much as pain will allow, drink 32-48 oz. of water per day, decrease oxycodone to twice daily and take Metamucil 2 heaping teaspoonsful tonight then up to 3 times daily as needed.
F. Drink 6-8 eight ounce glasses of water each day, increase activity as tolerated, take 2 bisacodyl 5mg tablets now then take 1-2 daily while on pain regimen.

A 60 y/o male asks you for something to help with constipation. He is 5'11' and weighs 215lbs. He just returned from a business trip to California. He usually has a bowel movement every day and at least every other day. He has not had a BM for 7 days and is uncomfortable. While on the trip, he did not eat his normal diet. He also admits to overeating on occasion, indulging in desserts often and consuming alcohol which he normally does not do. His normal exercise routine consists of a leisurely walk around the neighborhood on Sunday afternoons. When you ask about water intake, he replies that he does not really 'like' water. His normal diet includes:

Breakfast: Coffee, toast, poached egg

Lunch: Iced tea, sandwich (usually turkey or ham), chips and dessert

Dinner: Lean meat (chicken or turkey), a yellow or green vegetable and some kind of potatoes, iced tea, bread

Snack: Rice Krispies cereal about 9pm

What is the most appropriate ***FIRST*** recommendation for him?

A. Increase vegetables and fruits, PEG 3350 as directed on label, increase water
B. Increase exercise, glycerin suppository stat, increase fiber in diet
C. Increase water, docusate 240 mg daily, add fiber to diet
D. Reduce carbohydrates in his diet, bisacodyl 2 stat, then 1 daily x 3 days, change cereal to All Bran
E. No treatment necessary constipation most likely due to change in diet and habits while traveling

JA is a 56 y/o female who asks you to look at her medications to see if any of them could be causing her to have become constipated. Review the list below and make recommendations as necessary. Her normal habits include: She walks daily, rides horses twice weekly and tries to eat 'healthy' (Several fruits/veggies daily, lean meat). She drinks 3 cups of coffee daily and drinks 3 Route 44 Diet Cokes per day. She is a secretary and lately has been stressed due to an upcoming project.

Her medications include:

Stress formula vitamin plus iron daily x 5 years
Naproxyn 500mg bid x 1 year for arthritis
Lisinopril 10mg daily x 10 years for hypertension
Verapamil 120mg daily x 5 years for hypertension
Chlorthalidone 50mg daily x 2 weeks
Alprazolam 0.5mg bid and hs x 2 months
Calcium carbonate 500mg tid x 5 months

What are the most likely medications that are causing her constipation and what non-pharmacologic recommendations would you make for her?

A. Naproxyn, lisinopril and verapamil; Recommend: stress management and increased exercise
B. Chlorthalidone, alprazolam and calcium carbonate; Recommend: decrease coffee and tea and increase water intake
C. Iron in vitamin, chlorthalidone, and calcium carbonate; Recommend: increase exercise and intake of whole wheat grains
D. Verapamil, chlorthalidone, and calcium carbonate; Recommend: increase fiber in diet and increase water intake

"Muddiest points" information

- The information provided in the following slides will assist with our discussion.
- They may be used in your consideration of the application exercises.

Definition of Constipation

A syndrome characterized by bowel symptoms of hard, dry stool, a decrease in frequency, and/or difficult or incomplete bowel movements

Rome III classification: (Indicating need for Rx meds)

Symptoms for 6 months and ≥2 of the following occurring 25% of the time for the past 3 months:

- Straining
- Lumpy or hard stools
- Sensation of incomplete evacuation
- Sensation of obstruction/blockade
- Manual maneuvers

Alarm Symptoms

Contraindications to OTC therapy

- Hematochezia (bright red blood in stools)
- Anemia
- Weight loss of ≥ 10 lbs in the past 6 months
- New onset or worsening constipation (especially elderly)
- Family history of IBS or colon cancer
- Severe persistent or refractory constipation
- Fever
- Weakness
- Nausea/vomiting

Medical Causes of Constipation

- Anorexia Nervosa
- Colon Cancer
- Cystic Fibrosis
- Diabetes Mellitus
- Irritable Bowel Syndrome
- Metabolic Disorders
  - Hypercalcemia
  - Hypokalemia
  - Hypothyroidism
  - Hyperthyroidism
- Neurological Disorders
  - Multiple Sclerosis
  - Parkinson's Disease
  - Stroke
  - Dementia
- Pregnancy

- Drug-induced:
  - Antacids (aluminum or calcium)
  - Anticholinergics
    - Tricyclic antidepressants
    - Antihistamines
    - Antipsychotics
  - Antidiarrheals
  - Beta-Blockers
  - Calcium-Channel Blockers
  - Calcium Supplements
  - Diuretics
  - Oral Iron Supplements
  - Opioids
  - NSAIDs
  - 5-HT3 Receptor Antagonists

Treatment Options- Nonprescription/Lifestyle

- Non-pharmacological
  - Diet
  - Exercise
  - Toileting habits
- Pharmacological
  - Bulk-Forming Laxatives
  - Stool Softeners
  - Osmotic Laxatives
  - Saline Laxatives
  - Stimulants
  - Lubricants

Non-Pharmacological

- Provide Patient Education
  - What is “normal” (3 times a day to 3 times a week)
  - Assess for medications causing constipation
  - What has been tried
- Ensure adequate fluid (1.5 to 2 L per day)
- Exercise
- Fiber (20-35 grams per day)
  - Start low and go slow to avoid bloating and gas
  - Do not recommend if have more severe constipation
- Allow enough time for bowel movements
  - In the morning or 30 minutes before meals before meals
- Do not ignore the urge

Bulk-Forming Laxatives

- **Agents**:
  - Methylcellulose (*Citrucel*)
  - Polycarbophil (*FiberCon, Fiber-Lax)*
  - Psyllium (*Metamucil*)
- **MOA**: absorb water in the intestinal tract to increase the stool weight, increase colonic distension, and improve frequency
- **Adverse Effects**: gas and bloating, obstruction of esophagus and colon
- **Onset**: typically 12-72 hours
- **Contraindications/Precautions**:
  - Inability to drink adequate fluid
  - Difficulty swallowing
  - Fecal impaction or GI obstruction
- Dose other medications at least 1 hour before taking bulk-forming laxatives to avoid decreased absorption

Stool Softeners

- **Agents**:
  - Docusate calcium (*Surfak*)
  - Docusate sodium (*Colace, DOS, Enemeez*)
- **MOA**: decrease the surface tension of the stool to promote mixing with water
- **Adverse Effects**: diarrhea and cramping
- **Contraindications/Precautions**:
  - Do not use with mineral oil
    - can result in foreign body reaction in lymphoid tissue
- **Onset**: 12-72 hours

Osmotic Agents

- **Agents**:
  - Polyethylene Glycol (*Miralax, NuLYTELY*)
  - Glycerin
  - Lactulose (*Constulose, Generlac*)
  - Sorbitol
- **MOA**: pull fluid from tissues into the lumen of the colon and stimulate bowel movement
- **Adverse Effects**:
  - PEG 3350—urticaria, bloating, cramping, diarrhea, gas
  - Glycerin—rectal irritation
  - Sorbitol and Lactulose–Electrolyte imbalances, hyperglycemia, diarrhea, dry mouth, nausea and vomiting
- **Contraindications/Precautions**:
  - Sorbitol and Lactulose should be used with caution in DM, severe cardiopulmonary or renal impairment
- **Onset**: 12-96 hours

Saline Laxatives

- **Agents**:
  - Magnesium hydroxide
  - oral sodium phosphate liquid
  - magnesium citrate
- **MOA**: draw water into intestines and colon by osmosis to increase motility
- For occasional use only
- **Adverse Effects**:
  - Sodium phosphate—electrolyte abnormalities, hypotension, dizziness, headache, acute renal failure, bloating, abdominal pain, diarrhea, mucosal bleeding, nausea/vomiting, edema
  - Magnesium citrate/hydroxide—Mg accumulation in renal insufficiency, abdominal pain, gas, diarrhea, nausea/vomiting
- **Contraindications/Precautions**:
  - Sodium phosphate—CI in CHF, hyperparathyroidism, ascites, unstable angina
  - Magnesium citrate/hydroxide—Caution in renal insufficiency
- **Onset**:
  - Magnesium hydroxide: 30 min to 6 hours
  - Magnesium citrate, oral sodium phosphate: 30 min to 3 hours

Stimulants

- **Agents**:
  - Sennosides (*Senokot, etc.*)
  - Bisacodyl (*Dulcolax, etc.*)
- **MOA**: Stimulation of the Enteric Nervous System (ENS) and inhibition of water reabsorption
- **Adverse Effects**: abdominal pain/discomfort, electrolyte disorders, allergic reactions, melanosis coli (with prolonged use of sennosides)
- **Contraindications/Precautions**:
  - Intestinal obstruction
  - Acute intestinal inflammation
  - Ulcerative coliti
  - Abdominal pain of unknown origin
  - Pregnancy—avoid long-term use
- **Onset**:
  - Oral: 6-10 hours, possibly up to 24 hours
  - Rectal: 15-60 minutes

Lubricants

- **Agent**: Mineral Oil
- **MOA**: coats the stool and intestinal lumen with a waterproof substance to help the stool retain fluid
- **Adverse effects**: abdominal cramps, diarrhea, nausea, vomiting, lipid pneumonitis with aspiration, and large doses may cause anal itching, irritation, hemorrhoids, perianal discomfort, soiling of clothes
- **Contraindications/Precautions**:
  - Aspiration risk in bedridden patients or those with difficulty swallowing (Parkinson's, stroke, Alzheimers)
- **Onset**:
  - Oral: 6-8 hours
  - Rectal: 2-15 minutes

Pregnancy

- **First-line**:
  - Dietary fiber
  - Increased fluid intake
  - Exercise
  - If need laxatives, bulking agents thought to be safer since not absorbed systemically
- **Second-line**: lactulose, glycerin, sorbitol
- Senna is safe for use in pregnancy at normal doses for short-term but ***caution*** if used near term or pregnancy is unstable

Elderly

- **Main Etiologies of Constipation**:
  - Lack of mobility
  - Polypharmacy
- **Non-pharmacological Therapy**:
  - Review medications and if possible, discontinue or decrease medications that cause constipation
  - Counsel on lifestyle modifications
- **Pharmacological Therapy considerations**:
  - For immobility, stimulants are better than bulking agents
  - Osmotic agents are good for chronic constipation
  - Avoid saline laxatives due to risk of electrolyte abnormalities
  - Avoid bulking if immobile or have difficulty swallowing
  - Ensure **NO** impactions before recommending fiber or bulking agents

Children ≥1 years of age

- Generally constipation etiology is from diet and bad toileting habits and not underlying disease
- **First line**: high fiber diet and increased fluids
- Avoid excessive milk consumption
- **Pharmacological Therapy**:
  - PEG 3350, Lactulose or Sorbitol
  - Magnesium Hydroxide
  - Mineral Oil
  - Stimulants as rescue therapy only to avoid impaction

Opioid-Induced Constipation

- **Etiology**:
  - decreased motility due to decreased Ach
  - increased water and electrolyte reabsorption
  - decreased intestinal secretions
  - impaired defecation response
- **First-line**: **Stimulants** +/- stool softener
- Lactulose or sorbitol can be used as alternates
- **DO NOT RECOMMEND** increased fiber or bulking agents
- Try drug with less potential cause constipation such as fentanyl over morphine and parenteral over oral
- Opioid-antagonists (methylnaltrexone, naltrexone) may be necessary in advanced illness with resistance to laxative therapy

Prescription options for treatment

If nonprescription and nonpharmacologic measures fail

Lubriprostone

- **MOA**: acts locally in intestine as a chloride channel activator, increasing intestinal fluid secretion and intestinal motility
- **Uses**: Chronic idiopathic constipation and for IBS with constipation in ***women***
- **Adverse Effects**: Nausea (dose dependent; give with food or decrease to once daily), diarrhea, other GI, dyspnea, headache, allergic reactions (rare)
- **Contraindications/Precautions**:
  - Mechanical bowel obstruction
  - Caution in hepatic impairment

Linaclotide

- **MOA**: guanylate cyclase-C agonist that increases intestinal fluid and decreases transit time
- **Uses**: Chronic idiopathic constipation, IBS with constipation in adults
- **Adverse Effects**: Diarrhea (may be severe; if so discontinue), abdominal pain, headache, upper respiratory infection
- **Contraindications/Precautions**:
  - CI in pediatric patients ≤6 years old. Avoid use in 6-17 years.
  - CI in known or suspected mechanical GI obstruction

Methylnaltrexone

- **MOA**: peripheral opioid receptor antagonist that does not cross the CNS
- **Use**: second line treatment of opioid-induced constipation
  - after laxatives have been tried
- Weight based dosing administered Sub-Q
- **Adverse effects**: abdominal pain, flatulence, nausea
- **Contraindications/Precautions**:
  - Dose adjust in renal impairment
  - CI in known or suspected mechanical bowel obstruction
  - Possible risk of intestinal perforation in patients with compromised GI integrity
  - Use beyond 4 months has not been studied