

Management of Constipation

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Objective

- Define constipation, review its prevalence and pathophysiology, and identify commonly-affected populations.
- Discuss the assessment of patients for opioid-induced constipation
- Outline appropriate bowel care protocols to follow initiation of opioids
- Study the role of opioid antagonists in opioid-induced constipation
- Identify counseling tools, and pharmacist and patient resources for opioid-related constipation

Incidence

- Constipation: 2 % - 27 % in Western countries
- US: > 2.5 million visits, 92,000 hospitalizations
- Compared to adults: more prevalent in women, nonwhites, children, and the elderly
- “Severe constipation” requiring hospitalization or surgery: young women and the elderly.

Stewart WF et al. Epidemiology of constipation (EPOC) study in the United States: relation of clinical subtypes to sociodemographic features. *Am J Gastroenterol* 1999;94:3530-3540.

Pare P et al. An epidemiological survey of constipation in Canada: definitions, rates, demographics, and predictors of health care seeking. *Am J Gastroenterol* 2001;96:3130-3137.

Heaton KW et al. Defecation frequency and timing, and stool form in the general population: a prospective study. *Gut* 1992;33:818-824.

Definition

- Slow movement of feces through the large intestine
- Results in hard, dry stool that may be difficult to expel
- Patients describe:
 - Hard stools, infrequent stools, excessive straining, a sense of incomplete bowel evacuation, and excessive time spent on the toilet or in unsuccessful defecation
- Rome II describes:
 - Inability to evacuate stool completely and spontaneously three or more times per week
- Rome III (published April 2006):
 - Symptoms currently active 3 months
 - Use Bristol stool classification to define “constipation”

Drossman DA. The functional gastrointestinal disorders and the Rome III process. *Gastroenterol* 2006 130:1377-90.

Risk Factors for Constipation

- Diet and hydration
- Immobility
- Metabolic disease
 - Hypercalcemia, hypothyroidism, other chemical imbalances
- Concurrent disease
 - Parkinson's disease; Multiple sclerosis, CVA, Chronic Renal Failure
- Structural: tumors, strictures, diverticula
- Gender: female (hormonal and structural causes)

Drug-Induced Constipation

Therapeutic Category	Examples
Analgesics	Opioids (morphine), NSAIDs (ibuprofen)
Anticholinergics	TCA, antipsychotics (haloperidol), antiparkinsonian agents (benztropine), antihistamines (H1; diphenhydramine), antispasmodics (dicyclomine)
Cation-containing agents	Aluminum (antacids, sucralfate), calcium (antacids, supplements), bismuth, iron supplements, lithium
Chemotherapy	Vinca alkaloids (vincristine), alkylating agents (cyclophosphamide)
Antihypertensives	CCB (verapamil, nifedipine), diuretics (furosemide), centrally-acting (clonidine), antiarrhythmics (amiodarone), beta blockers (atenolol)
Bile acid sequestrants	Colestyramine, colestipol
5HT ₃ -receptor antagonists	Ondansetron
Laxatives	Chronic abuse

Branch RL, Butt TF. Drug-induced constipation. Adverse Drug Reaction Bulletin 2009;257.

Drug-Induced Constipation

Therapeutic Category	Examples
Excess fiber	Dietary or prescribed
Other antidepressants	Monoamine amine oxidase inhibitors
Other antiparkinsonian agents	Dopamine agonists
Other antispasmodics	Peppermint oil
Anticonvulsants	Carbamazepine
Miscellaneous	Barium sulphate, octreotide, polystyrene resins, oral contraceptives
	Vitamin C tablets, ¹³¹ I thyroid ablation, erythropoietin, baclofen
	Pamidronate, alendronic acid, PPI and H ₂ antagonists

Branch RL, Butt TF. Drug-induced constipation. Adverse Drug Reaction Bulletin 2009;257.

Opioid- Induced Constipation

- Opioids affect bowel function by:
 - Inhibiting propulsive peristalsis through the small bowel and colon
 - Colonic transit time is lengthened
 - Exacerbates fluid and electrolytes absorption, leading to dryer, harder stool
 - Occurs within 5-25 minutes of opioid use
 - Tolerance does NOT develop

Opioid- Induced Constipation

- Severity of symptoms probably influenced by a range of factors
 - Opioid-related
 - Oral probably > than transdermal
 - Codeine may be more likely than other opioids
 - Effects probably dose-related
 - Patient-related
 - Primary disease type and status
 - Comorbidities affecting bowel function
 - Age, nutrition, hydration status, and other factors

General Assessment

- Review the patient's medical history and presence of any disease affecting bowel functioning
- Assess hydration status: skin turgor, urinary output
- Medication history; including OTC
- Evaluate activity level and ability to use a toilet or bedside commode
- Physical/ abdominal exam

Alarm symptoms necessitating physician assessment

- Bloody stools
- Black/tarry stools
- Marked abdominal pain or discomfort
- Fever Nausea/vomiting
- History of family history of inflammatory bowel disease or colon cancer
- Symptoms persisting after two weeks of self-treatment

Bowel History

- What does the patient mean by “constipation”?
- Last time bowels moved
- Describe normal bowel habits
- Any blood or mucus noted with recent stools?
- Concurrent symptoms (bloating, abdominal pressure)
- Pain when moving bowels? Nausea?
- Efforts taken to relieve constipation

Constipation Assessment Scale

- Over the last 3 days; severe (2), some (1), no problems (0)
- Abdominal distention or bloating
- Change in amount of gas passed rectally
- Less frequent bowel movements
- Oozing liquid stool
- Rectal fullness or pressure
- Rectal pain with bowel movement
- Smaller stool size
- Urge but inability to pass stool

McMillan et al.

Analgesics - NSAIDs

Inhibit cyclooxygenase, blocking production of PGE both centrally and peripherally.

PGE Effects	Inhibition of PGE Effects
Decreases gastric acid secretion	Increased gastric acid secretion
Increases gastric mucus secretion	Decreased mucus secretion
Causes GI smooth muscle contraction	GI smooth muscle relaxation

NSAID discontinuation is more often due to constipation than dyspepsia.



Constipation

Non- Pharmacological Approach

- Prophylaxis!!!!
- Encourage fluid intake and increase dietary fiber (within reason)
 - High fiber diet may worsen discomfort and constipation, especially fiber without fluid
- Physical activity (within reason)

Pharmacological Approach

Laxative	Adverse effects	Mechanism of action
Stool softeners and emollients e.g. dioctyl sodium, docusate sodium	Few side effects, mainly bitter taste and nausea	Lubricates and softens stools
Stimulants and irritants e.g. senna and bisacodyl	Electrolyte imbalance, dermatitis, melanosis coli	Alters intestinal mucosal permeability; stimulates muscle activity and fluid secretions
Osmotic laxatives e.g. lactulose, magnesium salts, sorbitol	Electrolyte imbalance; excessive gas; hypermagnesaemia, hypocalcaemia and hyperphosphataemia in patients with renal dysfunction; dehydration	Osmotic effect of salts leads to greater fluid retention in bowel lumen and a net increase of fluid secretions in the small intestine
Bulk laxatives e.g. psyllium seed, bran	Increased gas; bloating; bowel obstruction if strictures present; choking if powder not taken with enough liquid	Increased fecal bulk and fluid retained in the bowel lumen
Non-absorbable solutions e.g. polyethylene glycol	Nausea; abdominal fullness; bloating	Volume lavage
Enema	Dehydration, hypocalcaemia and hyperphosphataemia in patients with renal dysfunction	Reflex evacuation

Agent	Onset of Action	Therapeutic starting dose	Comments/ Adverse Events
Stimulants Senna	6-12 hours	2- 4 tablets (17.2 mg – 34.4 mg) daily	Abdominal cramps, pain
Bisacodyl Tablets Suppository Microenema	6-12 hours 30 minutes 30 minutes	10 mg at bedtime 10 mg daily prn 10 mg daily prn	Diarrhea, hypokalemia Rectal administration can cause irritation
Osmotic Laxatives			
Lactulose	24-48 hours	15- 30 ml 1-2 times a day	Flatulence, abdominal cramps, nausea
Magnesium hydroxide	30 minutes- 3 hours	15- 30 ml 1-2 times daily	Hypomagnesemia, hypokalemia
Sodium phosphate oral solution	30 minutes – 3 hours	20- 30 ml daily	Hypocalcemia, hypokalemia, Hyponatremia
Glycerin Suppository	15 minutes- 1 hour	1 x 2.6 g suppository daily prn	Rectal irritation

Agent	Onset of Action	Therapeutic starting dose	Comments/ Adverse Events
PEG 3350	2- 3 days	17 g daily dissolved in 250 ml water	Nausea, bloating, retching, abdominal cramps
<u>Bulk forming</u>			
Psyllium	12- 72 hours	7 g 1- 3 times a day	Abdominal distention
<u>Rectal Agents</u>			
Phosphate enema	2 – 15 minutes	118 ml single dose as needed	Abdominal distention, vomiting, hypocalcemia
Mineral oil enema	4- 8 minutes	100- 250 mL single dose as needed	Incontinence
Stool Softner			
Docusate Sodium	12- 72 hours	100 mg twice daily	Nausea, abdominal cramps

Management of Opioid Induced Constipation

- Relistor ® (Methylnaltrexone)
 - New kid on the block for treatment and prevention of opioid induced constipation
 - Peripherally-acting mu-opioid receptor antagonist for use in patients with advanced illness receiving palliative care
 - Does not reverse analgesia
 - Contraindicated if patient has mechanical bowel obstruction.
- Typically dosed 8-12 mg (wt based) SQ every other day (up to Q 24 hours)
- Cost 12 mg vial \$50

Adverse Effects

Common Adverse Effects	Relistor ®	Placebo
Abdominal Pain	29%	10%
Flatulence	13%	6%
Nausea	12%	5%
Dizziness	7%	2%
Diarrhea	6%	2%

Opioid- Induced Constipation

- History of colicky abdominal pain, IBS, hepatic primary or mets, confusion or encephalopathy with constipation?
 - Yes, but nauseated- Sorbitol
 - Yes, no nausea present – Lactulose
- If no history of above, institute standard bowel protocol
 - stool softner and laxative (Senokot S 2 tabs bedtime, titrate up to 8 tabs daily)

Lubiprostone (Amitza®)

- Selectively activates type 2 chloride channels (ClC-2) in apical membrane of the gastrointestinal tract
- Increased fluid secretion into lumen
- No significant systemic absorption
- No data on efficacy and safety in nursing home setting, or patients with significant co-morbidities

Constipation Remedy

- Roll/ squeeze vaseline into “pea-sized” balls.
- Roll in confectioners sugar (for taste).
- Freeze balls.
- Have patient swallow 2-3 balls; will lubricate bowel and ease defecation.



Surgery

For refractory constipation

- Total colonic resection and ileorectostomy
 - Patient does not have defecatory disorder
 - After medical therapies have failed
- Colonic resection is generally reserved for patients with slow-transit constipation
- A review of 32 studies showed that between 39 percent and 100 percent of patients were satisfied after colectomy
- Very little data in older patients (>95% of studies patients are young (25-45 years) and female

Surgery

- Complications of surgery: obstruction of the small bowel, diarrhea, and incontinence
- Diarrhea and incontinence improved after the first year
- Patients with upper-gut dysmotility (gastroparesis or pseudo-obstruction) or psychological disturbances have poorer outcomes
- Laparoscopic subtotal colectomy is as effective as laparotomy
- Rectal surgery: only in patients with functionally significant rectocele whose constipation is relieved with application of digital vaginal pressure to facilitate defecation.

Patient and Family Education

- Discuss the importance of reporting bowel functioning, including frequency, amount and consistency of stools and any discomfort associated with defecation to the health care team.
- Maintain good fluid intake, increase bulk in diet
- Encourage warm liquids with meals
- Use and dosing of laxatives
- Report cramping, bloating, stool leakage, or diarrhea associated with laxative use
- Avoid bulk-forming laxatives with opioid-induced constipation

