Opioid Induced Constipation

4/11/22

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What makes stool?

- Solid waste
  - Generally a moderate volume passing through small and large bowel is best
- Water Content
  - Essential to balance water content- not too much or too little
- Motility
  - Impaired by organic disease, mobility, and medication
    - Especially opioids

Opioid-Induced Constipation

- Occurs with all opioids
- 45-90% of patients
- The most common reason patients avoid and, or discontinue opioids
- Can increase hospital LOS
- Pharmacologic tolerance develops slowly, or not at all
- Dietary interventions alone usually not sufficient

Rome IV Diagnostic criteria

Table 1.

The Rome IV diagnostic criteria for opioid-induced constipation.

Diagnostic criteria
1. New, or escalating, symptoms of constipation when initiating, changing or increasing opioid therapy that must include two or more of the following: (a) Straining during more than one quarter of defaecations. (b) Lumpy or hard stools (BSFS 1–2) more than one-quarter of the time. (c) Sensation of incomplete evacuation more than one-quarter of the time. (d) Sensation of anorectal blockage/obstruction in more than one-quarter of defaecations. (e) Manual manoeuvres to facilitate more than one-quarter of defaecations. (f) Fewer than three spontaneous bowel movements per week. 2. Loose stools rarely present without the use of laxatives.

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BSFS: Bristol Stool Form Scale.

2 or more:
-Straining
-lumpy or hard
-sensation of incomplete evacuation more than ¼ of the time
-manual maneuvers
-less than 3 'Spontaneous' BM's

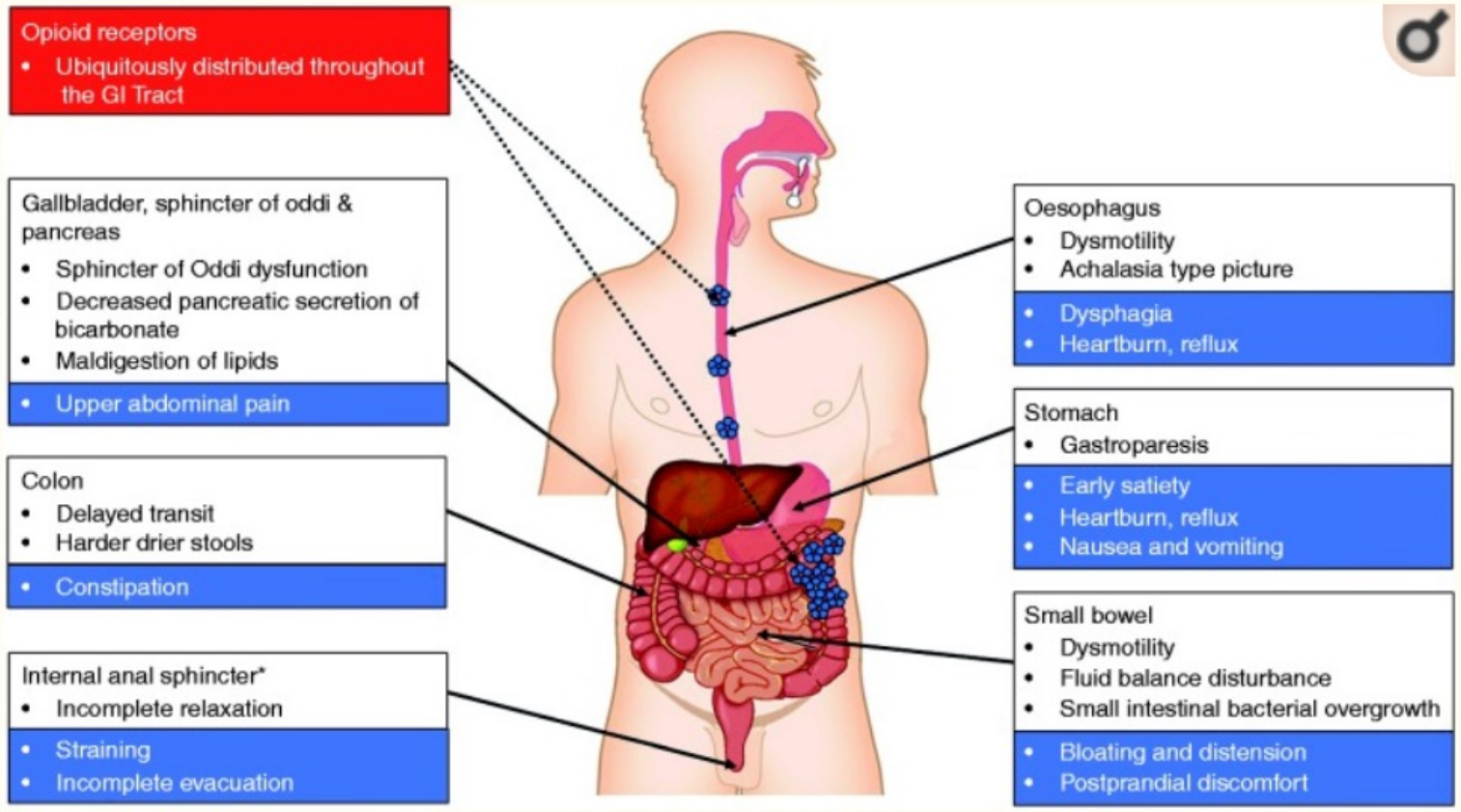

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Figure 1.

A schematic summary of the effects of opioids on the gastro-intestinal (GI) tract. Opioid receptors are distributed throughout the GI tract. *The function of other GI sphincters can also be influenced opioids such as the lower oesophageal sphincter and pylorus.

-Dysfunction of anorectal
-increased contraction of the internal anal sphincter

- Straining
- Haemorrhoids
- Sense of incomplete evacuation

Assessment

- Assess bowel function at every opportunity!!

- Establish patient's normal bowel schedule/pattern
- Take hx of recent changes pre/post opioid
- Physical exam
  - Rectal? Stoma?
  - Imaging?
- Check-in with caregivers
  - Functional challenges

THE BRISTOL STOOL FORM SCALE

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges (passed easily)
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces ENTIRELY LIQUID

Treatment

- Prevention

- Prevention

- Prevention

Prevention

- Co-prescribing
- Education
  - Constipation as potential side effect
  - Tips to reset pre-existing issues
  - Written hand out
- Rapid reevaluation after starting opioids

Treatments

- Fiber and Fluids
- Stool Softeners
- Stimulant Laxatives
- Osmotic Laxatives
- Lubricants & Large Volume Enema
- Prokinetic Agents
- Opioid Antagonists

Stimulant laxatives

- Mechanism: increasing enteric muscle contraction and GI motility

- Agents:
  - Prune juice -1/2 cup warm
  - Senna 8.6mg- 2 tab, up to 12 tab
  - Bisacodyl 10mg daily, up to 30mg
  - onset of action for oral senna and bisacodyl is around 6-12 hours
- Watch for cramping pain
  - Can address by dividing dose across the day

Combination treatment

- Combination stimulant / softeners are useful first-line medications
  - Senna + docusate sodium
- Tarumi et al. "Randomized, double-blind, placebo-controlled trial of oral docusate in the management of constipation in hospice patients." Journal of Pain & Symptom management. 44(1): 2-13, 2013 Jan
  - A total of 74 patients, hospice, PPS over 20%, No stoma, able to tolerate PO
  - No significant difference in: stool frequency, volume, or consistency, nor in difficulty or completeness of evacuation

Prokinetic Agent - Metaclopramide

- Potential agent for refractory constipation
- Stimulates enteral nervous system
- Not significantly effective for distal bowels

Stool softeners (detergent laxatives)

- Mechanism: break down fat in stool
  - Less fat → increase fluid penetration
  - Fat → fatty acids → osmotic effect

- Agents: Sodium docusate, Calcium docusate, Phospho-soda enema

Osmotic laxatives

- Mechanism: Increased osmotic load draws liquid into lumen
- Onset of action 12-48 hours
- Agents
  - Lactulose or sorbitol
    - lactulose is 15 ml, and 30 ml for 70% sorbitol solution, up to lactulose is 60 ml, and for sorbitol is 150 ml
  - Milk of magnesia (other Mg salts)
    - Avoid in renal disease
  - Magnesium citrate
  - Polyethylene glycol- 17 g, up to 68g
    - "Tasteless" and inert
    - Requires 125ml liquid per 17gm
- Caution with non-absorbed sugars as they can ferment in the gut and add to bloating, pain

Lubricants / Enemas

- Mechanic: softens stool and volume distension stimulates peristalsis
- Onset 10-15 min, can repeat every 2 hours in a well pt
- Agents
  - Glycerin suppositories
  - Phosphate enema
  - Mineral Oil enema
  - Milk and Molasses et al
  - Tap water, 500 – 1,000 ml

Fiber and Fluids???

- Mechanism: increase in stool volume. Stretch receptors within the colon stimulate peristalsis
- Agents: Psyllium, polycarbophil
- HOWEVER
  - Dehydration and delayed bowel transit make use of fiber supplements counterproductive
  - **Avoid bulk-forming agents in debilitated patients**

Exercise

- ??
- No clear recommendations on exact amount
- Unique from patient to patient
- Numerous limitations

Lubiprostone (Amitiza; PO)

- FDA Indications: IBS, chronic idiopathic constipation, opioid-induced constipation
- Mechanism of Action
  - Activates chloride channels
    - Increases intestinal fluid secretion
    - Increases intestinal motility
    - Reduces intestinal permeability
- 40% have BM in 24h, 60% within 48h; 27% with >3 BM/week

Opioid Antagonists

- Naloxone/Naltrexone (PO)
  - 80% have BM within 1-4 hours
    - 2/3 reported some loss of analgesia; 1/3 reported withdrawal symptoms
    - Dose: 0.8-12mg

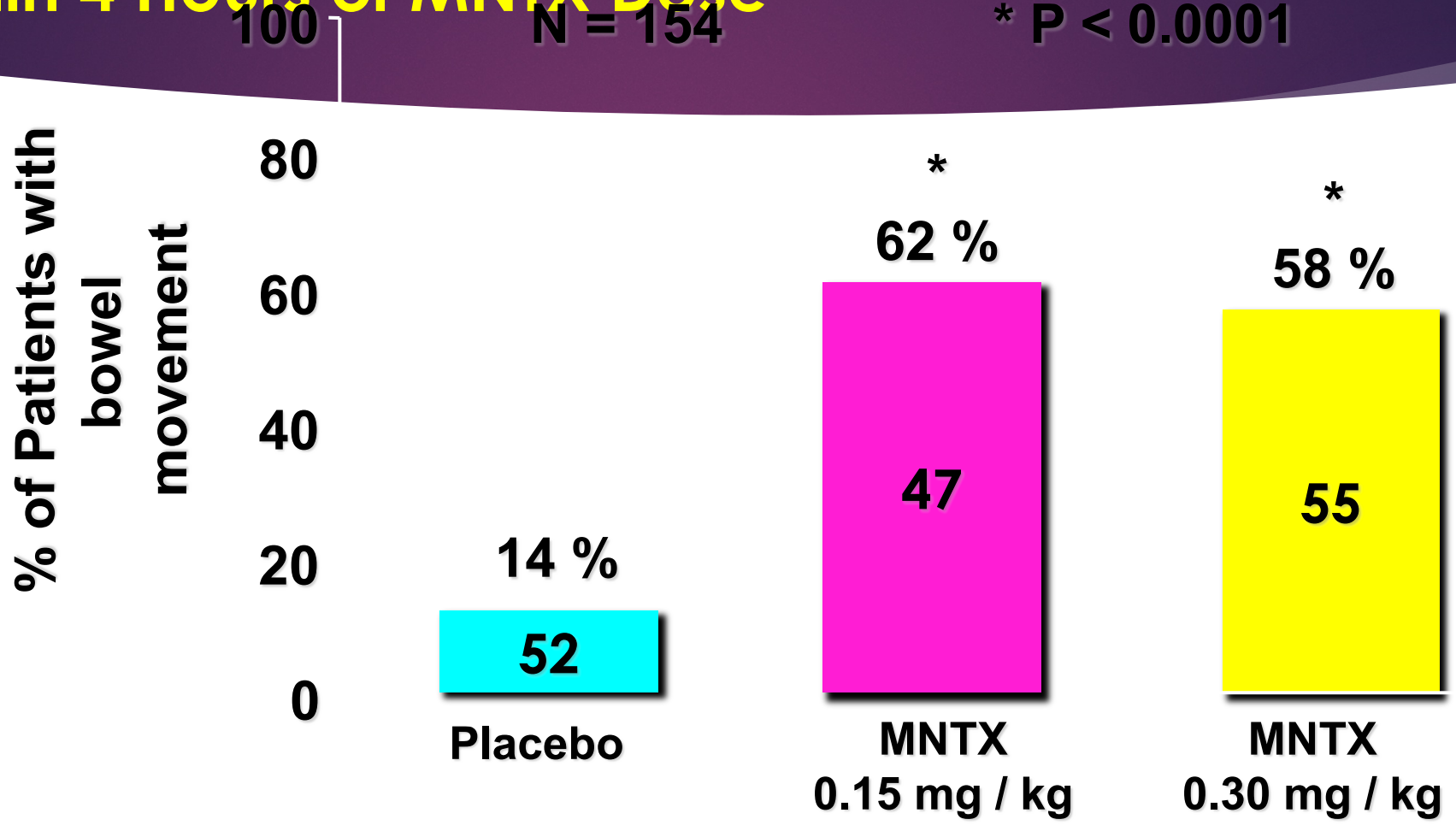
Opioids Antagonists

- Methylnaltrexone (SC; weight-based)
  - peripherally-acting μ-opioid receptor antagonist
  - subcutaneous injection, $55 per dose, Dose Q 48
  - Less able to cross the blood brain barrier, reducing the risk of altering analgesia or inducing central opioid withdrawal. An industry-funded randomized controlled trial of chronic opioid users showed that weight based methylnatrexone dosing led to laxation in nearly
  - half of subjects had BM within 4 hours
  - (NNT) is 3 for OIC patients that have failed to respond to standard laxative therapy
  - **Contraindicated** when bowel obstruction is suspected or for patients with compromised bowel integrity
  - Side effects are nausea, diarrhea, and cramping

Opioids Antagonists

- Naloxegol (Movantik; PO) – FDA indication: Opioid-induced constipation in non-cancer patients
  - Increase from 1 to >3 BM/week
    - alvimopam- only approved for post-operative ileus
- Significant improvement in a subset of patients who had failed traditional laxative therapy as well
- 12.5 mg and 25 mg have been studied, 25 mg dose has a higher success rate but is associated with more abdominal pain
- Side effects: nausea, vomiting, abdominal pain, and diarrhea
- Its current price is approximately $300 for 30 pills.

% Patients with Bowel Movement Within 4 Hours of MNTX Dose



The Bottom Line

- Educate!
  - signs and symptoms of OIC , ask early and often
- Start a stimulant with every opioid
  - Senna 2 tabs twice daily (unless unique concern)
- The goal for the bowel regimen should be an unforced bowel movement at least every other day.
- No BM in 48 hours?
  - increase stimulant laxative dose and/or adding an osmotic laxative is appropriate
- Failure of oral laxative therapy?
  - rectal based interventions and/or one of the newer treatment modalities

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