

IBS CME Isfahan

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Session 7

Symptomatic therapy

Who is Who?

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Scenario 19: Case Presentation

- SN is a 32-year-old white woman who presents with symptoms of recurrent abdominal pain and loose stools. She states that she has experienced these symptoms since adolescence, with periods of improvement and worsening over the years. Over the past year, her symptoms have been occurring more frequently and with greater severity. She has loose stools approximately one half of the time and often will have 6-7 bowel movements per day. Diarrhea is annoying. It has small volume and frequent. It does not contain blood or pus, but sometimes it is mucoid. Although it does not wake up the patient at night, it leads to functional impairment during the day.
- Other than her gastrointestinal symptoms, she considers herself healthy. She has no chronic illnesses or prior surgeries. She has no family history of organic gastrointestinal diseases such as inflammatory bowel disease, malignancy, or celiac disease.
- Her weight and other vital signs are within normal limits.
- On physical examination, she is a well-developed, well-nourished woman in no acute distress. Her physical examination is notable for mild tenderness to palpation in the left lower quadrant, but there is no rebound tenderness, guarding, or other peritoneal signs. The remainder of the physical examination is unremarkable.

Question 19: Targeting Diarrhea

- 19-1 Bulking Agents
- 19-2 Opioids
- 19-3 Ondansetron
- 19-4 Bile pathway
- 19-5 Antibiotics

19-1 Bulking Agents

- Soluble fiber
 - Insoluble fiber (eg, bran) → bloating
 - Psyllium → constipation / diarrhea.
 - Increase bulk of stool
 - may alter the production of gaseous fermentation products
 - changes to the gut microbiome.
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- low starting dose
 - slowly titrated up based on response



19-2 Opioids

Opioid receptor modulators



- can modulate GI motility → directly affects visceral hypersensitivity and stool patterns.
- regulating GI motility, secretion, and visceral sensation
- **Loperamide:** peripheral μ -opioid receptor agonist → ↓ GI motility → ↑ the duration of enteral transit, → ↑ fluid absorption and ↓ stool frequency.
- **Asimadoline:** KOR agonist with high affinity and selectivity. → ↓ patients pain symptoms.
- **Eluxadoline:** peripherally acting MOR and KOR agonist and DOR antagonist
- decreased risk of constipation
- reduce abdominal discomfort

19-3 serotonin-3 receptor antagonists



- **Alosetron:** approved for the treatment of severe diarrhea-predominant IBS in female patients who have failed to respond to all other conventional treatment.
- decreasing colonic motility and secretion, and may improve abdominal pain.
- a global improvement in IBS symptoms and relief of abdominal pain and discomfort.
- It can be prescribed under restricted conditions, at a lower starting dose than previously approved, and by physicians enrolled in the alosetron prescribing program.
- **Ondansetron:**
- significantly improved stool consistency, frequency, and urgency but was not associated with a significant improvement in abdominal pain.

19-4 Bile pathway

- **Bile acid sequestrants** (eg, cholestyramine, colestipol, colesevelam)
- In patients with persistent diarrhea despite antidiarrheals
- However, their use is controversial
- GI side effects including bloating, flatulence, abdominal discomfort, and constipation.
- up to 50 percent of functional diarrhea and IBS-D have bile acid malabsorption. Bile acids → stimulating colonic secretion and motility.



19-4 Antibiotics

- **Rifaximin**



Scenario 20

- A 30-year-old woman presents with recurrent abdominal pain and hard stools. She states that she has experienced these symptoms since adolescence, with periods of improvement and worsening over the years. Over the past year, her symptoms have been occurring more frequently and with greater severity. For the past 6 months, she has been bothered by bloating and more severe constipation.
- The patient has hard stools approximately one third of the time and often has less than one bowel movements per 2-3 days. She denied any blood in the stool. She has had no nausea, vomiting, or change in weight. No relationship was found between her symptoms and her diet, including milk products, spicy foods, alcohol, and processed meats. She denies excessive hunger or anorexia symptoms.
- Other than her mentioned symptoms, the patient considers herself healthy. She has no chronic illnesses or prior surgeries. She has no family history of organic gastrointestinal diseases.

Question 20: Targeting Constipation

- 20-1 Osmotic agents
- 20-2 Stimulants
- 20-3 Lubricants
- 20-4 Bile acid pathway

20-1 Osmotic agents

- PEG
- inexpensive
- widely available
- fewer side effects
- Improves constipation but not abdominal pain.
- start with 17 g → titrate up or down (to a maximum of 34 g daily)

- Side effects: bloating and abdominal discomfort
- In a randomized trial → no significant difference in the severity of bloating or abdominal pain in patients treated with PEG as compared with placebo.



20-2 Stimulants



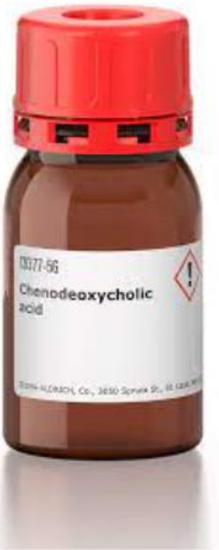
- bisacodyl, senna, and sodium picosulfate
- Mechanism: alteration of electrolyte transport//increase intestinal motor activity.
- can be used as short-term and rescue therapy.
- Chronic use ?
- Side effects: diarrhea, electrolyte abnormalities and abdominal pain
- No structural or functional impairment of the colon, nor does it increase the risk for colorectal cancer or other tumors.

20-3 Lubricants



- Lubricating agents; mineral oils (such as **Vaseline oil, Olive oil, Glycerin**)
- both orally and rectally;
- for acute or subacute management
- help fecal expulsion and create a soft fecal mass.
- lubricate the intestine and facilitate passage of stool by decreasing water absorption from the intestine.
- coat the colon and stool in a waterproof film allowing it to remain soft and easier to slip through the intestine while retaining its moisture, usually within 6-8 hours.
- May cause vitamin deficiencies / might interact with some medications
- Contraindication: Pregnancy/ difficulty in swallowing

20-4 Bile acid pathway



Emerging Constipation-predominant Irritable Bowel Syndrome Therapies Advantages/Disadvantages

Drug Class	Name	Advantages	Disadvantages
Bile acid modulators	CDCA	Double-blind placebo-controlled study showed acceleration in colonic transit and improved bowel function in 36 IBS-C patients. ⁵	Lower abdominal cramping/pain in over 40% of patients
	Elobixibat (A3309)	Three phase II trials in CC patients report improvement in the number of SBMs, stool consistency and decrease in straining. ⁶⁻⁸	No consistent amelioration of abdominal pain or bloating, except at the 15 mg dose

CDCA: Chenodeoxycholic acid

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Other

- Bulk-forming laxatives
- Lubiprostone
- Guanylate cyclase agonists — Linaclotide and plecanatide
- Sodium/hydrogen exchanger 3 (NHE3) inhibitor — Tenapanor,
- 5-HT₄ receptor agonists: Tegaserod
- Prucalopride
- Misoprostol



Scenario 21

- A 36-year-old woman presents with persistent abdominal pain and constipation. She states that she has experienced abdominal and bowel-related symptoms since she was in college. Her abdominal symptoms include intermittent cramps that typically occur in the left lower quadrant, nearly constant bloating that worsens during menstrual periods, and frequent episodes of constipation.
- When questioned about abdominal pain, the patient describes it as 5 (on a scale of 10) at its worst. Acute worsening occurs immediately before defecation, with significant improvement after defecation. She has had this pain at least once every week for the past 6 months.
- Upon inquiry, the patient admits that she limits many social events because of her abdominal pain. She reports that her symptoms, particularly the pain and bloating, are so debilitating that she skips work about 1 day per month.
- Physical examination and laboratory data were within normal limits.

Question 21: Targeting Pain

- 21-1 Neuromodulators
- 21-2 Serotonin Pathway
- 21-3 Antispasmodics

21-1 Neuromodulators

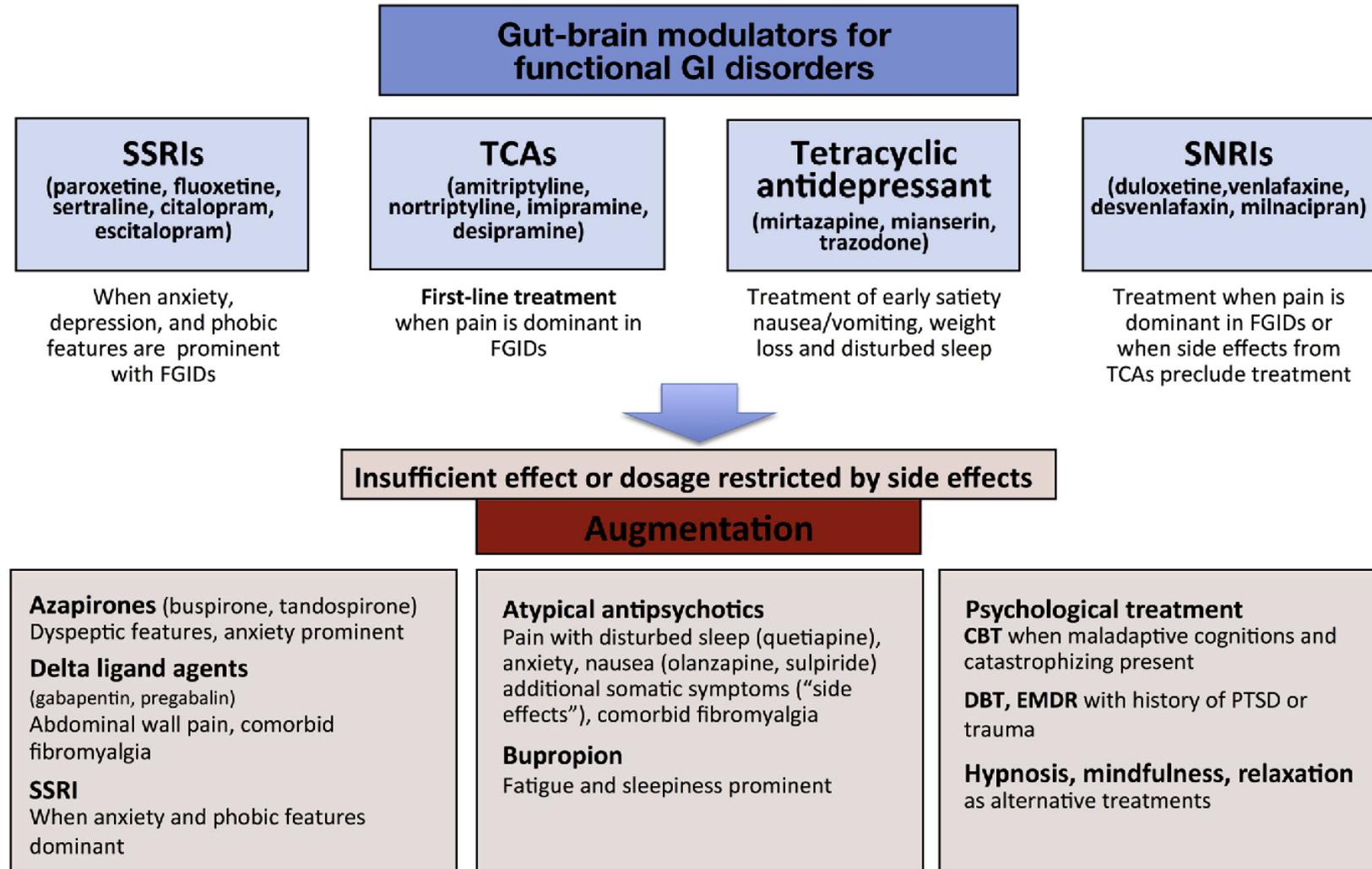


Figure 5. Summary of the clinical characteristics that can be considered when selecting gut-brain neuromodulating phar-

21-2 Antispasmodics

- as-needed basis and/or in anticipation of stressors
- short-term relief in symptoms of abdominal pain
- their long-term efficacy has not been established.
- 1. those that directly affect intestinal smooth muscle relaxation (eg, mebeverine and pinaverine),
- 2. those that act via their anticholinergic or antimuscarinic properties (eg, dicyclomine and hyoscyamine).
- The selective inhibition of GI smooth muscle by antispasmodics and peppermint oil → reduce stimulated colonic motor activity → may be beneficial in patients with postprandial abdominal pain, gas, bloating, and fecal urgency.



Other...

- **Probiotics**

