

Movement Beyond Laxatives: Evolving Pharmacologic Options for IBS-C and CIC

Ashish Advani, PharmD

Home Study Webcast Handout

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ACTIVITY DESCRIPTION

IBS-C and CIC are highly prevalent conditions that negatively impact Quality of Life and pose a significant economic burden on the healthcare system. Because so many patients self-treat the conditions, estimates of the number of Americans that suffer from IBS-C and CIC vary widely ranging from 2% to 27% of the population. Despite the \$400 million dollars that are spent on laxatives each year, constipation still accounts for 2.5 million physician visits annually in the U.S. revealing a desperate need for improved patient counseling and knowledge of pharmacologic options beyond laxatives in pharmacies around the nation where millions of patients seek pharmacist recommendations. When traditional treatments, such as dietary manipulation and standard laxatives do not adequately treat or fail to treat IBS-C and CIC, pharmacists must be prepared to educate patients regarding the pharmacologic options available to relieve these frustrating and costly conditions.

TARGET AUDIENCE

The target audience for this activity is **pharmacists, pharmacy technicians, and nurses** in hospital, community, and retail pharmacy settings.

LEARNING OBJECTIVES

After completing this activity, the **pharmacist** will be able to:

- Outline etiology and epidemiology of IBS-C and CIC in the U.S.
- Describe the FDA approved pharmacologic treatment options for IBS-C and CIC, beyond laxatives, to include novel targets, efficacy data, primary contraindications, and adverse effects.
- Identify strategies for pharmacists to assist in identifying inadequately treated patients and providing patient counseling regarding prescription treatment options that will facilitate communication with the physician.

After completing this activity, the **pharmacy technician** will be able to:

- Identify common causes of IBS-C and CIC in the U.S.
- Identify FDA approved pharmacologic treatment options for IBS-C and CIC
- Recognize effective patient communication skills with the physician.

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Ashish Advani, PharmD

Clinical Associate Professor, Mercer University, Founder, InPharmD

ABOUT THE AUTHOR

Dr. Ashish Advani received his PharmD degree from the University of Georgia in 2007, after completing his undergraduate coursework at the University of Georgia and Oxford University in England.

After graduating, he completed a Drug Information residency at Mercer University and Solvay Pharmaceuticals, Inc., centered around skills of literature searching, literature evaluation, and medical communication, all in support of the practice of evidence-based medicine (under Dr. Marsh!).

Since, Dr. Advani has worked as a Clinical Associate Professor and Director of the Drug Information Center at Mercer University College of Pharmacy. He has published 11 articles in peer reviewed journals, brought in \$1 M in research/grant funding (100% as principle investigator), served as Guest Editor of the Journal of Pharmacy Practice, blogs at Forbes, Huffington Post, and Kevin MD, served as a Drug Information specialist at Atlanta Medical Center, and held several committee and board appointments, including the Georgia State Drug Utilization Review Board and Georgia Pharmacy Association Board.

In partnership with the University, Dr. Advani is currently working on a technology called InpharmD, which aims to revolutionize the practice of evidence-based medicine.

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Movement Beyond Laxatives: Evolving Pharmacologic Options for Irritable Bowel Syndrome- Constipation Predominant (IBS-C) and Chronic idiopathic Constipation (CIC)

Faculty: Ashish Advani, PharmD



Objectives



Participants should be able to:

- Outline etiology and epidemiology of irritable bowel syndrome – constipation predominant (IBS-C) and chronic idiopathic constipation (CIC) in the U.S.
- Describe the Food and Drug Administration (FDA)-approved pharmacologic treatment options for IBS-C and CIC, beyond laxatives, to include novel targets, efficacy data, primary contraindications, and adverse effects.
- Identify strategies for pharmacists to assist in identifying inadequately treated patients and providing patient counseling regarding prescription treatment options that will facilitate communication with the physician



Background- Constipation



- Symptoms include bloating, difficulty evacuating, and abdominal pain
- Descriptors of constipation will vary from patient to patient:
 - Decreased bowel movement frequency
 - Changes in stool size or consistency
 - Straining
 - Sensation of incomplete evacuation
 - Inability to defecate at will
- CIC ≠ IBS



Background- IBS



- Functional bowel disorder
 - Occurs in approximately 20% of the population of industrialized countries
 - Responsible for approximately 12% of U.S. primary care visits
- Incidence increases during adolescence and peaks in 30's and 40's
- Female: male ratio = 2: 1
- Nearly 50% of patients have psychiatric abnormalities



Signs and Symptoms



- Abdominal bloating ± distention, fullness, gas
- Abdominal pain
 - Comes and goes
 - Is reduced or goes away after a bowel movement
 - Occurs after meals
- Chronic and frequent constipation= IBS-C
- Chronic and frequent diarrhea= IBS-D (FYI)
- Emotional distress
- Loss of appetite



Pathophysiology/ Etiology



- Characterized by abdominal pain/ discomfort associated with altered bowel function
 - Structural/ biochemical abnormalities absent
 - Thought to be due to altered somatovisceral and motor function of the intestine
 - Two types of serotonin found in the gut:
 - Type 3 (5-HT3) and Type 4 (5-HT4)
- Genetic factors could modulate processing of gastrointestinal signals centrally and inflammatory and immune responses locally
 - Psychosocial nature and response to environmental factors influence expression



Diagnosis



- Criteria to identify a combination of symptoms to diagnose the condition: Manning, Rome I-III
- Rule out lactose maldigestion
- Colonic imaging in patients with no “alarm features” unlikely to reveal structural disease
 - Alarm features= Rectal bleeding, weight loss, iron deficiency anemia, nocturnal symptoms, and a family history of selected organic diseases including colorectal cancer



Diagnosis

Manning Criteria



Chronic or recurrent abdominal pain for at least 6 months and *two or more of the following*:

- Pain relief with defecation
- More frequent stools
- Looser stools
- Feeling of incomplete evacuation after defecation
- Mucus in stools
- Abdominal distension



Diagnosis

Rome III Criteria



Recurrent abdominal pain or discomfort at least 3 days/month in the last 3 months associated with *two or more of the following*:

- Improvement with defecation
- Onset associated with a change in frequency of stool
- Onset associated with a change in form (appearance) of stool



Exacerbating Factors



- Stress
- Small intestinal bacterial overgrowth (SIBO)
- Diet
 - Food allergies may trigger symptoms
 - Quantity of portions and fat content can alter the gastrocolic reflex
 - ↑ quantity, ↑ fat meals stimulate bowel movement
 - ↓ quantity, ↓ fat meals slow bowel movement



Non-pharmacologic Therapy



- Gradually increase dietary fiber intake (+ fluids)
 - Recommend 15 grams/day
- Physical activity
- Low fermentable oligo-, di-, and monosaccharides and polyols (FODMAP) diet
- Allow time to use the bathroom
- Mineral oil
- Peppermint oil
 - 0.2 to 0.4 mL PO (enteric-coated capsules) three times daily
- Cognitive behavioral therapy
- Dynamic psychotherapy
- Hypnotherapy
- Relaxation therapy



Pharmacologic Therapy



• Bulking agents

MOA: Increases intestinal mass with an emollient and reduces intraluminal rectosigmoid pressure

➤ May take 1-3 days to begin working

- Calcium polycarbophil (Fibercon®, Equalactin®)

Adults: Two caplets PO daily with 8 ounces of water, juice, milk, etc.; maximum of QID

- Psyllium hydrophilic mucilloid (Metamucil®)

Adults: 3.4 g PO up to TID dissolved in 8 ounces of water, juice, milk, etc.

Children (6+): ½ of adult dose up to 3 times a day

- Methylcellulose (Citrucel®, Celevac®)

Adults: Two caplets PO daily with 8 ounces of water, juice, milk, etc.; maximum of 12 caplets/ day

Children (6+): ½ of adult dose



Pharmacologic Therapy



• Laxatives

MOA: Increases motility, mucous secretion, and bowel evacuation

- Book: use not encouraged
- Guidelines: use only prn for shortest duration at smallest dose
- May take 2-4 days to begin working

• Bisacodyl (Dulcolax®, Fleet Bisacodyl®)

Adults: 5 to 15 mg PO once daily OR 10 mg suppository rectally once daily
Children (6 +): 5 mg PO once daily OR 5 mg suppository rectally once daily

• Polyethylene glycol (PEG) (Colyte®, MiraLax®)

Adults: 17 g PO per day dissolved in 4 to 8 ounces of water, juice, soda, coffee, or tea



Pharmacologic Therapy



• 5-HT₄ Agonists

MOA: Increases GI motility, decreases visceral sensation, increases gastrocolic reflex

- Only indicated in women
- Only indicated for severe IBS
- May take 1 week to begin working

• Tegaserod (Zelnorm®)

Adults: 2 mg or 6 mg PO twice daily 30 minutes prior to a meal with water

- Serious side effects: cardiovascular events (1 placebo vs. 13 tegaserod, N=7,031)
- Only available for emergency use in life-threatening situations



Pharmacologic Therapy



• Probiotics

- *Lactobacilli*
- *Bifidobacteria* (Align®, Activia®, VSL #3)



Pharmacologic Therapy



• Selective C-2 chloride channel activators

MOA: Promote chloride into intestine → sodium enters → water enters → increases GI motility

- Only indicated in women (for IBS-C)

• Lubiprostone (Amitiza®)

Adults: 8 mcg PO twice daily

- Common side effects: nausea and diarrhea
- Pregnancy category C: not recommended
- 30 day supply = ~\$350



Pharmacologic Therapy



• Guanylate Cyclase-C Agonists

MOA: Promote chloride and bicarbonate into intestine → sodium enters → water enters → increases GI motility

• Linaclotide (Linzess®)

Adults: 290 mcg PO once daily on an empty stomach

- Common side effect: diarrhea
- Pregnancy category C: not recommended
- 30 day supply = ~\$350

• Plecanatide (Trulance®)

Adults: 3 mg PO once daily with or without food

- Common side effect: diarrhea
- Pregnancy category: not assigned (not recommended)
- 30 day supply = ~\$360



Pharmacologic Therapy



• Selective serotonin reuptake inhibitors (SSRIs)

MOA: modulate perception of visceral pain and treat underlying comorbidities

• Paroxetine (Paxil®)

Adults (off-label): 10 mg/day PO in the morning; may titrate at intervals of at least 1 week to maintenance dose of 10-60 mg/day

• Sertraline (Zoloft®)

Adults (off-label): 25-50 mg/day PO; may titrate at intervals of at least 1 week to maximum maintenance dose of 200 mg/day

• Fluoxetine (Prozac®)

Adults (off-label): 10 mg/day PO; may titrate at intervals of at least 1 week to maintenance dose of 10-80 mg/day



Treatment Approach



A Note About the Mind/ Body Relationship...

Harvard Medical School researchers recently devised a strategy for testing volunteers' response to varying levels of therapeutic ritual, focused on IBS.

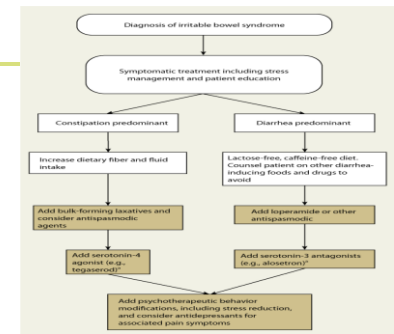
Volunteers were placed randomly in one of three groups:

1. One group was simply put on a waiting list; researchers know that some patients get better just because they sign up for a trial.
2. Another group received placebo treatment from a clinician who declined to engage in small talk.
3. Volunteers in the third group got the same sham treatment from a clinician who asked them questions about symptoms, outlined the causes of IBS, and displayed optimism about their condition.

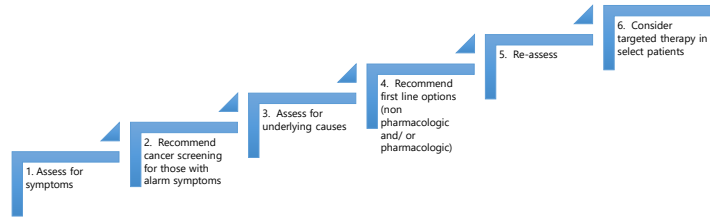
The health of the third group improved the most. In fact, they received as much relief as those taking the top prescription drugs for IBS.



Treatment Approach



Treatment Approach



References

- Pharmacotherapy: A Pathophysiologic Approach, Joseph T. DiPiro, et.al., 8th Edition.
Chapter 43: Diarrhea, Constipation, and Irritable Bowel Syndrome
- Treatment of constipation in adults. Pharmacists Letter.
- An evidence-based position statement on the management of irritable bowel syndrome. *Am J Gastroenterol.* 2009 Jan;104 (Suppl 1):S1
(PDF version)

Questions?

Ashish Advani, PharmD
ashish@inpharmd.com

Exam Questions:

1. To prevent constipation, IBS patients should be advised to include ____ of fiber in their daily diet.

- A. 10–15 g
- B. 30–35 g
- C. 50–55 g
- D. 100–110 g

2. Which of the following is appropriate for management of constipation + pain in a male patient with refractory irritable bowel syndrome (IBS-C)?

- A. Amitiza® (lubiprostone)
- B. Elavil® (amitriptyline)
- C. Immodium® (loperamide)
- D. Trulance® (plecanatide)

3. Which of the following statements about irritable bowel syndrome (IBS-C) is true?

- A. It affects up to 80% of adults worldwide
- B. It is equally prevalent in both men and women
- C. It is characterized by abdominal pain, disturbed defecation, and bloating
- D. It is known to be of viral origin

4. Which of the following statements about constipation is true?

- A. Lack of daily bowel movements leads to buildup of toxic substances.
- B. Genetic factors, psychosocial nature, and environmental factors all play a role in development of chronic idiopathic constipation (CIC).
- C. Normal healthy subjects pass at least 6 stools per week.
- D. It should be treated initially with castor oil.

5. Products such as psyllium, methylcellulose, and polycarbophil are known as _____.

- A. Stimulant laxatives
- B. Bulk forming agents
- C. Cathartics
- D. Lubricants

6. The Rome Criteria _____.

- A. Assesses mucus in stools
- B. Assesses abdominal distension
- C. Is useful to diagnose irritable bowel syndrome (IBS)
- D. Is useful to diagnose opioid-induced constipation

7. True or false? Decreased bowel movement frequency, changes in stool size or consistency, straining, sensation of incomplete evacuation, and inability to defecate at will are all symptoms of constipation.

- A. True
- B. False

8. Which of the following are treatment options for constipation predominant irritable bowel syndrome (IBS-C) or chronic idiopathic constipation (CIC) unresolved by fiber and OTC laxatives?

- A. Selective C-2 chloride channel activators
- B. Docusate sodium
- C. Guanylate Cyclase-C Agonists
- D. A and C
- E. A, B, and C

9. Which of the following medications is matched to the appropriate dose and schedule for a 36 year-old female with IBS-C?

- a. linaclotide (Linzess) 145 mcg once daily with the first meal (the lower dosing)
- b. plecanatide (Trulance) 3 mg once daily
- c. lubiprostone (Amitiza) 24 mcg twice daily (the higher dosing)
- d. naloxegol (Movantik) 25 mg once daily

10. What is most appropriate for JM, a 35 year old female who returns to your pharmacy with only 2 bowel movements per week for two weeks after following your recommendation of slowly increasing fiber/fluids and taking a dose of Miralax every day?

- a. counsel JM to increase fiber even more
- b. counsel JM to use an enema for relief and keep an extra on hand for next time she needs one
- c. educate JM on agents like plecanatide, linaclotide, and lubiprostone and refer her to a prescriber for further management
- d. educate JM on the Rome Criteria for diagnosing IBS and continue to try OTC options for constipation relief