Updates on the Management of Irritable Bowel Syndrome Management
Brooke Fidler, PharmD

Live Activity Handout
4 slides per page
Updates on the Management of Irritable Bowel Syndrome Management

ACTIVITY DESCRIPTION
According to the International Foundation for Functional Gastrointestinal Disorders irritable bowel syndrome (IBS) is the most common functional gastrointestinal disorder worldwide with an estimated prevalence rate of 10-15%. While most patients do not recognize the symptoms as IBS it is the most common disorder seen and diagnosed by gastroenterologists. In the United States between 2.4-3.5 million physician visits take place annually for symptoms related to IBS. While IBS appears to be more common among females approximately 35-40% of males may experience symptoms related to IBS as well. There are different types of IBS resulting in varying symptoms and treatments. This knowledge-based activity will educate pharmacists on the diagnosis and management of IBS, as well as the importance of counseling patients to adhere to lifestyle modifications and their treatment.

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:
- Define Irritable Bowel Syndrome (IBS) and its diagnostic criteria
- Recognize the pathophysiology and symptomatology of IBS
- Determine the risk factors and comorbidities related to IBS
- Identify effective elements of an appropriate drug therapy evaluation for IBS
- Recommend nonpharmacological measures to manage the symptoms of IBS when counseling patients

After completing this activity, the pharmacy technician will be able to:
- Define Irritable Bowel Syndrome (IBS) and its diagnostic criteria
- Recognize the pathophysiology and symptomatology of IBS
- Determine the risk factors and comorbidities related to IBS
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- Recommend nonpharmacological measures to manage the symptoms of IBS when counseling patients

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Brooke Fidler, PharmD

Associate Professor, LIU Pharmacy, Arnold & Marie Schwartz College of Pharmacy and Health Sciences

ABOUT THE AUTHOR
Dr. Brooke Fidler joined the faculty in 2000 as assistant professor of pharmacy practice. In 1999 Dr. Fidler completed a Pharm.D. at the University of Rhode Island and went on to complete a PGY-1 residency at URI the following year. Currently Dr. Fidler’s practice site is Kings Specialty Pharmacy where she precepts APPE students completing their MTM elective experience. At Kings Pharmacy Dr. Fidler is also the residency director for the PGY-1 Community Residency. Dr. Fidler’s primary didactic responsibilities including teaching and coordinating the physical assessment course at the college. Dr. Fidler has published in Pharmacy and Therapeutics Journal and Journal of Nurse Practitioners. She has also presented numerous webinars for Drug Store News and FreeCE related to community practice and nonprescription medications.

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UPDATES ON THE MANAGEMENT OF IRRITABLE BOWEL SYNDROME

1

LEARNING OBJECTIVES

• Define Irritable Bowel Syndrome (IBS) and its diagnostic criteria
• Recognize the pathophysiology and symptomatology of IBS
• Determine the risk factors and comorbidities related to IBS
• Identify effective elements of an appropriate drug therapy evaluation for IBS
• Recommend nonpharmacological measures to manage the symptoms of IBS when counseling patients

2

TYPES OF GASTROINTESTINAL (GI) DISORDERS

3

FUNCTIONAL GI DISORDERS (FGID) DEFINITION

4

• “Functional GI disorders are disorders of gut-brain interaction. It is a group of disorders classified by GI symptoms related to any combination of the following: motility disturbance, visceral hypersensitivity, altered mucosal and immune function, altered gut microbiota, and altered central nervous system processing.”
  • Motility disturbance- movement of food and waste through GI tract
  • Visceral hypersensitivity- heightened experience of pain
  • Altered immune function- changes in the gut’s immune defense
  • Altered gut microbiota- changes in gut bacteria
  • Altered CNS processing- changes in the signaling of messages between the gut and brain
  • “Syndrome based on symptoms that cluster together and the diagnosis is based on Rome criteria”

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ROME IV

- History of Rome Foundation
  - Mission is to improve the lives of people with FGIDs
  - Input from 117 experts representing 23 countries
- Rome IV defines 33 adult and 20 pediatric FGIDs
- Bowel Disorders
  - IBS with predominant constipation (IBS-C)
  - IBS with predominant diarrhea (IBS-D)
  - IBS with mixed bowel habits (IBS-M)
  - IBS unclassified (IBS-U)

DEFINITION

- A relapsing disorder of the bowel function resulting in constipation and/or diarrhea plus abdominal pain
- A gut-brain disorder due to disturbances of the large and small intestine (gut) motility which are regulated by the brain
- Patients with IBS may experience additional symptoms or comorbidities
- Once referred to as spastic colon, nervous colon and spastic bowel

BACKGROUND

- Most common FGID worldwide ranging between 10-15%
- Estimated 2.4-3.5 million annual physician visits in the US related to IBS symptoms
- Direct (medical) and indirect (loss of work days) costs approximately $21 billion annually
  - Twice as many days off from work for people with IBS
- Second most common reason for loss of work days after the common cold
- More commonly reported in female than male population (60-65% vs. 35-40%)
- Can occur at any age but peak ages are 25-54 years
**BACKGROUND**

- Risk for developing IBS is twice as high if a relative has IBS
- People with IBS stated they experience symptoms an average of 8.1 days per month
- Two-thirds of people with IBS report reduced activity levels
- No increase in mortality compared to general population
- Only an estimated 1 in 4 people seek medical attention

✓ **Pharmacy plays an important role in counseling on nonprescription and prescription medications, physician referral when necessary and encouraging lifestyle changes**

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**PATHOPHYSIOLOGY**

- The exact cause of IBS is not completely understood
- Possibilities...
  - Alteration of intestinal muscle contraction
  - Abnormalities with the nerves in the gut
  - Intestinal inflammation
  - Recent bacterial or viral infection
  - Psychological (anxiety, stress, depression)
  - Genetic disposition
  - Immunological changes
  - Diet
  - Hormones
  - Visceral hypersensitivity
  - Alteration in gut serotonin
  - Gut-brain dysregulation
  - Changes in gut microbiota (gut flora)

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**PATHOPHYSIOLOGY**

- Communication or biochemical signaling between the gut and the central nervous system is known as the gut-brain axis
- Recent research shows that the gut microbiota plays an important role in the signaling pathways which led to the concept of the microbiota-gut-brain (MGB) axis
- Bidirectional signaling (i.e., gut microbiota can affect brain activity and brain activity can alter the development of gut microbiota composition)
- Gut microbiota is made up of more than 1000 species of bacteria

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**PATHOPHYSIOLOGY**

- The number and types of species is determined by the individual person, diet, genetics, environmental factors and the specific area of the GI tract
- Appropriate balance or eubiosis of gut microbiota influences immune function, nutrition, metabolism and the body’s physiology
- Disruption or dysbiosis may be linked to bowel disorders, obesity, cancer, psychological disorders and pain²
- Gut microbiota composition can be altered due to changes in lifestyle, diet, stress, medical procedures, medications
**MICROBIOTA-GUT-BRAIN AXIS**

- Healthy status
  - Healthy CNS function
  - Normal gut physiology
  - Physiological levels of inflammatory cytokines
  - Normal gut microbiota

- Stress/disease
  - Alterations in behaviour, cognition, emotion, perception
  - Abnormal gut function
  - Increased levels of inflammatory cytokines
  - Intestinal dysbiosis

- Chronic disease
  - Bowel diseases
  - Cancerous transitions
  - Obesity
  - Gut microbiota balance
  - Host physiology
  - Inflammation
  - Immune function

- Healthy "organ"

**GUT MICROBIOTA AND IBS**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Microbial association*</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBS</td>
<td>Increased: Firmicutes:Bacteroidetes ratio, Ruminococcus, Coriobacterium, Gemmigerfaecalis (pIBS), Haemophilus influenzae (pIBS) Decreased: Bifidobacterium, Faecalibacterium, Bacteroides</td>
<td>Ohashi et al. [2012], Jeffery et al. [2012b], Rajilić-Stojanovic et al. [2011], Saulnier et al. [2011]</td>
</tr>
</tbody>
</table>

**BRAIN-GUT-SEROTONIN PATHOPHYSIOLOGY**

- The gut is comprised of the enteric nervous system which can perform functions independent of the brain
- The enterochromaffin cells in the gut lining produces 95% of serotonin (5-HT) in the body
- Certain gut microbes stimulate gut cells to produce more serotonin or may produce serotonin on their own
- Alterations in serotonin signaling can result in increased serotonin levels and changes in bowel motility, fluid secretion by the intestines and heightened sensitivity to pain
- Seven 5-HT subtypes with 5-HT2, 5-HT3 and 5-HT4 found in the CNS and gut

**VISCERAL HYPERSENSITIVITY**

- The enteric nervous system releases a number of neuropeptides including serotonin and opioid peptides
- Opioid peptides interact with opioid receptors in the gut controlling motility and secretion
- Principle opioid receptors include the mu, kappa and delta opioid receptors
- Animal studies show that these opioid receptors directly inhibit intestinal muscle activity and also affect the brain which can impact GI function
SYMPTOMS

- Abdominal pain
- Change in bowel habits (i.e., diarrhea and/or constipation)
- Relief of pain with bowel movement
- Symptomatic flares or periods of remission
- Bloating
- Urgency
- Sensation of incomplete passing of stools
- Increase in symptoms during women’s menstrual cycle
- Other GI symptoms (i.e., acid reflux, belching, dysphagia, fullness after eating, nausea)

"RED FLAG" SYMPTOMS

- Weight loss
- Nighttime symptoms
- Rectal bleeding
- Anemia
- Fever
- Elevated white blood count
- Unexplained vomiting
- Difficulty swallowing
- Persistent pain not relieved by flatulence or bowel movement
- Family history of colon cancer, IBD, etc

COMORBIDITIES

- Fibromyalgia
  - As many as 60% of patients with IBS have FM and 70% of patients with FM have IBS
  - Both associated with chronic pain, stress, anxiety and depression
- Chronic fatigue syndrome
  - Both share similar pathophysiology
- GERD
  - Similar trigger foods
- Mental health disorders
  - 60% of patients have anxiety, 20% of patients have depression and 20% have other psychological disorders

RISK FACTORS

- Female gender
- Age <50 years
- Family history
- Eating habits
- Smoking
- Mental health issues
- History of abuse
- Medications
COMPLICATIONS

- No increase in mortality
- Poor quality of life
- Mental health issues
- Hemorrhoids

<table>
<thead>
<tr>
<th>Irritable Bowel Syndrome (IBS)</th>
<th>Chronic Idiopathic Constipation (CIC)</th>
<th>Inflammatory Bowel Disease (IBD)</th>
<th>Celiac Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>• FGID</td>
<td>• FGID</td>
<td>• Structural GI Disorder</td>
<td>• Autoimmune</td>
</tr>
<tr>
<td>• Must meet Rome IV criteria</td>
<td>• Same symptoms as IBS-C, but must not meet the Rome IV criteria</td>
<td>• Includes Crohn’s disease and Ulcerative Colitis</td>
<td>• Attacks the gluten in the digestive system</td>
</tr>
<tr>
<td>• Constipation and/or diarrhea and abdominal pain</td>
<td>• &lt;3 bowel movements a week</td>
<td>• Chronic swelling of the intestines</td>
<td>• Damages the tissues of the intestines</td>
</tr>
<tr>
<td>• Gut-brain dysfunction</td>
<td>• Symptoms present for at least 3 months</td>
<td>• Frequent diarrhea</td>
<td>• Constipation and/or foul smelling diarrhea</td>
</tr>
<tr>
<td>• Does not lead to serious complications</td>
<td>• Onset at least six months prior to diagnosis</td>
<td>• Immune system related resulting in inflammation</td>
<td>• Can lead to complications (malnutrition, colon cancer)</td>
</tr>
</tbody>
</table>

DIAGNOSIS CRITERIA

- Rome III 2006
  - Recurrent abdominal pain or discomfort at least 3 days/month in the last 3 months, associated with ≥ 2 of the following
    * Improvement in defecation
    * Onset associated with a change in frequency of stool
    * Onset associated with a change in form (appearance) of stool
- Rome IV 2016
  - Recurrent abdominal pain at least one day per week, on average in the last 3 months, associated with ≥ 2 of the following
    * Related to defecation
    * Associated with a change in frequency of stool
    * Associated with a change in form (appearance) of stool

IBS CLASSIFICATIONS

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Stool Type 1 &amp; 2</th>
<th>Stool Type 6 &amp; 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBS-C</td>
<td>&gt;25%</td>
<td>&lt;25%</td>
</tr>
<tr>
<td>IBS-D</td>
<td>&lt;25%</td>
<td>&gt;25%</td>
</tr>
<tr>
<td>IBS-M</td>
<td>&gt;25%</td>
<td>&gt;25%</td>
</tr>
<tr>
<td>IBS-U</td>
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</tr>
</tbody>
</table>

*Meets diagnostic criteria for IBS but bowel habits cannot be categorized into the 3 subtypes

Bristol Form Stool Scale

- Based on days with abnormal bowel habits
- At least 4 days of abnormal bowel habits
- Off medications used to treat bowel habits abnormalities
**DIAGNOSIS**

- Diagnosis is based on clinical symptoms/diagnostic criteria and classification is based on bowel habits
- Testing is not warranted for patients who meet diagnostic criteria and <50 years of age
- There is limited diagnostic testing to distinguish IBS from other GI conditions
- No clinical biomarker to confirm or rule out IBS
- IBS-Detect® which confirms post-infectious IBS-D and IBS-M to determine treatment with antibiotics
- Patient demographics and “red flag” symptoms may guide additional testing
  - CBC, C-reactive protein, celiac disease, colonoscopy for patients ≥50 years of age, stool sample, psychological assessment

**PATIENT ASSESSMENT**

- Identify triggers such as diet, stress or hormones
- Assess for physical comorbidities (fibromyalgia)
- Assess for psychological comorbidities (stress, anxiety, depression)
- How symptoms impact quality of life
- Pain scale

**VALIDATED MEASURES OF IBS SYMPTOMS**

- Functional Bowel Disorder Severity Index (FBDSI)
  - Amount of pain present at visit today
  - A diagnosis of functional abdominal pain syndrome
  - Number of physician visits in the previous 6 months
  - <36 mild; 37-110 moderate; ≥111 severe
- IBS Symptom Severity Scale (IBS-SSS)
  - Evaluates the intensity of IBS symptoms during a 10-day period
  - Abdominal pain, distension, stool frequency, stool consistency and impact on daily activities
  - Scored on a visual analog scale 0-100 on each 5 areas

**SEVERITY OF IBS**

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>Mid (40%)</th>
<th>Moderate (30%)</th>
<th>Severe (20%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychometric index</td>
<td>FBDSI ≥36</td>
<td>FBDSI 37-110</td>
<td>FBDSI ≥111</td>
</tr>
<tr>
<td>Physiological factors</td>
<td>Primary bowel dysfunction</td>
<td>Slow distention and CNS pain-dysregulation</td>
<td>Primary CNS pain dysregulation</td>
</tr>
<tr>
<td>Psychosocial difficulties</td>
<td>None or mild psychosocial distress</td>
<td>Moderate psychosocial distress</td>
<td>Severe-High psychosocial distress, Cohen’s conventional, above norm</td>
</tr>
<tr>
<td>Sex</td>
<td>Male = woman</td>
<td>Female = man</td>
<td>Female = man</td>
</tr>
<tr>
<td>Age</td>
<td>Older = younger</td>
<td>Medium = young</td>
<td>Younger = older</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>Low (1-2)</td>
<td>Medium (4-6)</td>
<td>High (7-10)</td>
</tr>
<tr>
<td>Number of other symptoms</td>
<td>Low (1-2)</td>
<td>Medium (4-6)</td>
<td>High (7-10)</td>
</tr>
<tr>
<td>Health-related quality of life</td>
<td>Low (1-2)</td>
<td>Medium (4-6)</td>
<td>High (7-10)</td>
</tr>
<tr>
<td>Health care use</td>
<td>Low (1-2)</td>
<td>Medium (4-6)</td>
<td>High (7-10)</td>
</tr>
<tr>
<td>Workability</td>
<td>Normal = 15 days</td>
<td>Normal (15-50 days)</td>
<td>Very poor (100 days)</td>
</tr>
</tbody>
</table>

**NOTE:** Based on Drossman et al. 1997. FBDSI, Functional Bowel Disorder Severity Index; IBS-SSS, IBS Symptom Severity Index.
**IBS: MANAGEMENT**

- 2014 ACG Guidelines on the Management of IBS (currently being updated with the Rome IV criteria)
- Education
- Nonpharmacological
  - Exercise
  - Dietary changes
  - Psychological management
- Pharmacological
  - Nonprescription and prescription
  - Treatment determined by IBS classification
- Follow-up

**EDUCATION**

- Use lay language
- Twelve steps for an effective patient-physician relationship (Rome IV)
- Patient friendly references
  - www.mayoclinic.com
  - www.imtablebowelsyndrome.net
  - www.aboutibs.org
  - www.patient.gi.org
  - www.niddk.nih.gov

**EXERCISE**

- First-line approach regardless of classification
- Limited research on IBS and exercise but studies show moderate exercise (30 min 5 days/week) decreases stress
- Maintains overall health, helps with IBS-C and stress-induced IBS
- Increased physical activity
  - Cardiovascular exercise, yoga, Tai chi, meditation, walking
- Avoid exercise within an hour before or after eating
- Choose exercise you enjoy
- Choose a time of day you can stick to
- Avoid intense exercise if IBS-D

**MANAGEMENT CONSIDERATIONS**

- Severity
- Symptoms
- Classification of IBS
- Impact on quality of life
- Patient preference on treatment
- Patient goals and expectations
- Previous treatment
- Psychological comorbidities

✓ No cure but goal is to improve quality of life and symptoms
✓ Management needs to be individualized
**DIETARY MANAGEMENT**

- Foods do not cause IBS but they can trigger an IBS flare
- Dietary plan needs to individualized based on trigger foods and IBS classification
- Design a well-balanced diet
- Maintain appropriate amount of fluid intake
- Key tips
  - Eat smaller meals more frequently
  - Avoid individual trigger foods (gassy, greasy, fried, spicy, high fat)
  - Avoid individual trigger beverages (milk, alcohol, soda)
  - Keep a food and symptom journal

**FODMAP CLINICAL STUDIES**

- Staudacher, J Nutrition 2012
  - 41 patients with IBS randomized to a low-FODMAP diet vs. regular diet; 68% of FODMAP group reported control of IBS symptoms vs 23% in regular diet group (p=0.005)
  - Meta-analysis of 6 RCTs and 16 NonRCTs included; low-FODMAP groups showed improvement in IBS SSS scores, QOL scores, abdominal pain, bloating and overall symptoms
- Schumann. Nutrition 2018
  - Meta-analysis of 9 RCTs and a total of 595 subjects; the FODMAP diet improved GI symptoms (p=0.0001), abdominal pain (p=0.008) and QOL (p=0.007)
- ACG recommendations (weak)
  - FODMAP diets have promise but require more long-term research

**DIETARY MANAGEMENT**

- Low-FODMAP diet
  - Fermentable, Oligo-saccharides, Di-saccharides, Mono-saccharides And Polyols
  - Focuses on carbohydrates that can exacerbate IBS symptoms
  - Reduce over 6-8 weeks and then slowly introduce them back to see which foods are triggers
- Gluten free diet
  - Beneficial for those with IBS and wheat allergy or celiac disease
- Lactose free diet
  - For those with IBS and lactose intolerance

**PSYCHOLOGICAL MANAGEMENT**

- Choice of therapy based on patient needs and therapist expertise
  - Cognitive behavioral therapy (CBT)
  - Relaxation therapy
  - Hypnotherapy
  - Biofeedback
- Although exact mechanism is unclear 20 clinical trials showed benefit in relieving IBS symptoms
- ACG recommendations (weak)
  - CBT and hypnotherapy can be recommended for some patients
  - Can be time intensive and expensive for patients and require a skilled therapist
**PROBIOTICS, PREBIOTICS AND SYNBIOTICS**

- **Probiotics** are foods or supplements that contain living microorganisms intended to maintain or improve the “good” bacteria (gut microbiota) in the body.
- **Prebiotics** are foods that act as food for the microbiota with the intention of improving the balance of the microorganisms.
- **Synbiotics** are foods or supplements that combine the probiotic and the prebiotic.

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**PROBIOTICS**

- IBS studies have shown a decrease in certain gut species including *Bifidobacteria, Lactobacilli, Bacteroides and Faecalcibacterium*.
- Alterations in gut microbiota may be linked to anxiety, depression, bloating, pain, abnormality in intestinal motility (diarrhea and/or constipation) → symptoms of IBS.
- Literature shows some specific probiotics may help with abdominal pain, bloating, reduce constipation, improve frequency and/or consistency of bowel movements and improve QOL.
- ACG recommendations (weak):
  - While the studies are small and there are variations in study design, dose, species and strains, probiotics are well tolerated and pose minimal to no serious side effects.
  - May be beneficial for some patients but cannot recommend specific species, preparations or strains due to conflicting evidence.

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**PREBIOTICS AND SYNBIOTICS**

- **Prebiotic**
  - Provide nutrients for mainly *bifidobacteria and lactobacilli*.
  - Belong to the group of non-digestible carbohydrates (FODMAPs).
  - Few studies have evaluated prebiotics in IBS.
- **Synbiotic**
  - Limited experience in the management of IBS.
- According to ACG there is insufficient evidence to recommend prebiotics or synbiotics in IBS.

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**PHARMACOLOGICAL MANAGEMENT OF IBS**

**IBS-D**
- Fiber supplements
- Loperamide
- Alosetron
- Rifaximin
- Eluxadoline

**IBS-C**
- Fiber supplements
- Laxatives
- Tegaserod
- Lubiprostone
- Linaclootide
- Plecanatide
**IBS-D AND IBS-C: FIBER SUPPLEMENTS**

- May be more beneficial for IBS-C
- Most studies utilizing fiber did not state which IBS subtype
- Can cause bloating and abdominal pain
- Gradually increase dietary fiber till 22-38 grams per day (depending on age and gender) plus water
- Trial and error depending on improvement or worsening of symptoms
- Although weak, ACG recommends psyllium as first line

<table>
<thead>
<tr>
<th>IBS Symptoms</th>
<th>Fiber Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower abdominal pain</td>
<td>Methycellulose or Psyllium</td>
</tr>
<tr>
<td>Upper abdominal pain</td>
<td>Oatmeal, Oat bran, or Psyllium</td>
</tr>
<tr>
<td>Constipation</td>
<td>Methycellulose or Psyllium</td>
</tr>
<tr>
<td>Incomplete evacuation</td>
<td>Methycellulose or Psyllium</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Psyllium or Oligofructose</td>
</tr>
<tr>
<td>Excessive gas</td>
<td>Methycellulose or Polycarbophil</td>
</tr>
</tbody>
</table>

**TREATMENT OF IBS-D**

- Fiber supplements
  - Psyllium to firm loose stools
  - Drink with at least 8oz of water
  - Do not take for more than 7 days
- Imodium® (Loperamide)
  - μ-opioid receptor agonist that decreases peristalsis, prolongs gut transit time and reduces fluid secretion in the intestine
  - An effective antidiarrheal but insufficient evidence for its use in IBS-D or improvement of overall IBS symptoms
  - Used frequently as first-line therapy as treatment and prevention
  - 4mg after first bowel movement then 2mg after each loose stool. No more than 8mg/day
  - Do not take for more than 2 days

**IBS-D: LOTRONEX® (ALOSETRON) FEBRUARY 2000**

- A selective serotonin 5-HT₃ antagonist that inhibits serotonin from binding to 5-HT₃ receptors to decreased GI motility and abdominal pain
- Approved only for women with severe IBS-D who have symptoms lasting longer than 6 months, rules out abnormalities of the GI tract and no response to conventional therapy
- Starting dose is 0.5mg twice a day and may increase to 1mg twice a day after 4 weeks
- Discontinue medication if no response after 4 weeks
- BBW of ischemic colitis and severe complications of constipation
- Was removed from the market November 2000 and reintroduced in 2002

**IBS-D: XIFAXAN® (RIFAXIMIN) 2004**

- Antibacterial indicated for the treated of IBS-D in adults
- 550mg three times a day with or without food for 14 days and can retreat up to two times if symptoms reoccur
- Studies show benefit in relieving symptoms of bloating, diarrhea and abdominal pain although symptoms may resume
- ACG provides a strong recommendation for minimally absorbed antibiotics for short term use
- Long term use rifaximin is unknown
**IBS-D: VIBERZI® (ELUXADOLINE) 2015**

- A mu-opioid receptor agonist (and delta opioid receptor antagonist and a kappa opioid receptor agonist) which reduces abdominal pain and reduces diarrhea
- Indicated for adults in the treatment of IBS-D
- 100mg twice a day with food
- 75mg twice a day with food in patients who cannot tolerate 100mg, mild/moderate hepatic impairment and taking OATP1B1 inhibitors (gemfibrozil, cyclosporine, some statins, some antibiotics and some antiretrovirals)
- Contraindicated in patients without a gallbladder or known or suspected biliary duct obstruction, or sphincter of Oddi disease or dysfunction

**IBS-C: LAXATIVES**

- Stimulant laxatives
  - Works to produce a bowel movement by inducing fluid secretion and peristalsis by the large intestine
  - Bisacodyl (Dulcolax®) and sennosides (Senna®)
- Osmotic laxatives
  - Increase the amount of water that is secreted by the intestines helping to pass stool
  - PEG (Miralax®)
- Key points
  - 7 day time limit without supervision of provider
  - Can cause cramping, abdominal pain and diarrhea
  - Does not appear to help abdominal pain
  - Weak recommendation by ACG

**IBS-C: ZELNORM® (TEGASEROD) 2002**

- A 5-HT₄ agonist approved in 2002 for IBS-C to enhance GI secretion and increase GI motility
- Removed from the market in March 2007 due to increase risk of cardiovascular events (stroke, heart attack and unstable angina
- July 2007 FDA allows restricted use of tegaserod for life-threatening situations only or situations requiring hospitalization
- Authorization denial if
  - History of CV disease
  - Diabetes
  - Hyperlipidemia
  - >55 years of age
  - Smoking
  - Obesity
  - Mental health issues

**IBS-C: AMITIZA® (LUBIPROSTONE) 2006**

- Chloride channel activator indicated for the treatment of IBS-C in women ≥18 years of age
- Works by increasing intestinal fluid secretion and intestinal motility
- 8mcg twice a day with food and water and if severe hepatic impairment the dose is 8mcg once daily
- Contraindicated in patients with mechanical GI obstruction
- Discontinue if patient experiences severe diarrhea
- May cause hypotension and dyspnea after first dose
- ACG provides a strong recommendation for lubiprostone and recommends additional studies in men
IBS-C: LINZESS® (LINACLOTIDE) 2012

- A guanylate cyclase-C agonist that works locally on the intestinal tissue to accelerate GI transit time, increase intestinal fluid and reduce abdominal pain
- Indicated for the treatment of IBS-C in adults ≥ 18 years of age
- BBW for patients <6 years old and between 6-18 years of age; animal studies showed deaths related to dehydration within 24 hours of administration
- 290 mcg once daily given on an empty stomach at least 30 minutes before the first meal
- If patient experiences severe diarrhea discontinue medication and hydrate

IBS-C: TRULANCE® (PLECANATIDE) 2017

- A guanylate cyclase-C agonist indicated for IBS-C in adults ≥ 18 years of age
- Same mechanism and BBW as Linzess®
- 3mg once daily with or without food
- If patient experiences severe diarrhea discontinue medication and hydrate

TREATMENT OF IBS-M AND IBS-U

- Target individual and most bothersome symptoms
- Continue to re-evaluate based on symptoms
- Limited literature on mixed IBS subtype
- ‘pseudo’ IBS-M due to use of laxatives, antidiarrheals or side effects of medications
- Implement changes to diet and exercise habits
- Psychological management, if applicable

ABDOMINAL PAIN

- May be add on therapy for all subtypes
- Antispasmodics
- Antidepressants
- Peppermint oil
**ANTISPASMODICS**

- Hyoscymine, dicyclomine, phenobarbital/hyoscymine/atropine/scopolamine
- Short-term relief only and long-term efficacy is unknown
- Limited by anticholinergic side effects
- Variations in results among the studies
- ACG provides a weak recommendation due to low level of evidence

**ANTIDEPRESSANTS**

- SSRIs (fluoxetine, citalopram, paroxetine)
  - Literature search showed conflicting data among the 3 SSRIs with most studies lasting only 12 weeks
- Tricyclic antidepressants (amitriptyline, desipramine)
  - More evidence available with TCAs
  - Metaanalysis of 7 RCTs showed TCAs to significantly (p<0.0001) improve abdominal pain scores
- Low dose of antidepressants is suggested
- ACG provides a weak recommendation and does not provide guidance on which antidepressant

**PEPPERMINT OIL**

- Data suggest benefit for relaxing smooth muscle and improving pain sensations in IBS
- Dosing range from 187-225mg three times a day
- Studies did not differentiate IBS subtype
- Minimal adverse events with heartburn being most common
- Long-term efficacy is unknown
- Symptoms of abdominal pain resumed after peppermint oil was discontinued
- ACG provides weak recommendation due to limited evidence

**TREATMENT OF BLOATING**

- Simethicone (i.e., Gas-X, Mylcon)
- Alpha-galactosidase enzyme (i.e., Beano)
- Limited evidence available for strong recommendations
- Dietary changes should be first-line
- Managing overall symptoms of all IBS subtypes can help to alleviate bloating
**CLINICAL TRIALS**

- Elobixbat
  - Approved in Japan in January 2018 for CIC
  - Inhibitor of the ileal bile acid transporter (IBAT)
  - Works to inhibit uptake of bile acids thereby accelerating intestinal passage and softening stool
  - Ongoing clinical trials for use in IBS-C
- Ondansetron
  - 5-HT₃ receptor antagonist
  - Clinical trials ongoing for use in IBS-D
  - Preliminary results showed relief of IBS symptoms, reduced bowel movement frequency and urgency and reduced symptoms of bloating

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**GENERAL MANAGEMENT GUIDELINES BASED ON SEVERITY**

<table>
<thead>
<tr>
<th>Mild IBS</th>
<th>Moderate IBS</th>
<th>Severe IBS</th>
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</thead>
<tbody>
<tr>
<td>Dietary and lifestyle changes</td>
<td>See Mild IBS recommendations PLUS</td>
<td>See Mild IBS recommendations PLUS</td>
</tr>
<tr>
<td>Medication changes, if applicable</td>
<td>Pharmacotherapy during flares for moderate</td>
<td>Regular medication use focused on managing specific symptoms</td>
</tr>
<tr>
<td>Monitoring of symptoms</td>
<td>Daily use for moderate to severe</td>
<td>FOD treatment centers (multidisciplinary approach)</td>
</tr>
<tr>
<td>Psychological management</td>
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</tbody>
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**ROLE OF THE PHARMACIST**

- Be aware of patients frequently purchasing antidiarrheals or laxatives
- Counsel on time frames for use of products 2 days for antidiarrheals and 7 days for laxatives
- When assessing the patient ask about abdominal pain, change in bowel habits, time frame of symptoms, dietary habits and medical history
- Identify patients with warning signs and refer to PCP when necessary
- Counsel on appropriate use of all prescription and nonprescription medications
- Educate on dietary and exercise modifications
- Provide recommendations on psychological management if applicable

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**TAKE HOME POINTS**

- IBS is a relapsing condition that is associated with abdominal pain and changes in bowel movements based on the 2016 Rome IV criteria
- Diagnosis is based on patient assessment, physical examination and testing only when ruling out other GI disorders
- Knowing the warning signs will help determine patient referral from community to their PCP or specialist
- Multidisciplinary treatment approach
  - Diet, exercise, psychological management, nonprescription medications and prescription medications
  - Treatment is based on IBS subtype and bothersome symptoms
TAKE HOME POINTS

- For all subtypes can consider probiotics, dietary or supplemental fiber, exercise, dietary changes or psychological management
- IBS-D
  - Loperamide (μ-opioid receptor agonist), alosetron (5-HT3 antagonist), rifaximin (antibacterial), eluxadoline (μ and kappa opioid receptor agonist and delta opioid receptor antagonist)
- IBS-C
  - Laxatives, tegaserod (5-HT4 agonist), lubiprostone (chloride channel activator), linaclotide and plecanatide (guanylate cyclase-C agonists)
- IBS-M and IBS-U treatment is based on individual symptoms
- Assess other bothersome symptoms and treat as necessary (antispasmodics, antidepressants, peppermint oil, simethicone)

REFERENCES