Time to Get Moving – Options for Chronic Idiopathic Constipation
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Live Activity Handout
2 slides per page
Time to Get Moving – Options for Chronic Idiopathic Constipation

ACTIVITY DESCRIPTION
Many people have a difficult time with bowel movements. Because so many patients self-treat the condition, estimates of the number of Americans that suffer from chronic idiopathic constipation vary widely but the National Institute of Health estimates that 42 million people are afflicted with constipation. 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 CIC, pharmacists must be prepared to educate patients regarding the pharmacologic options available to relieve this frustrating and costly condition.

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:
• Describe the impact and economic burden of CIC in the U.S.
• Review the FDA approved pharmacologic treatment options for CIC beyond laxatives, to include novel targets, efficacy data, primary contraindications, and adverse effects
• Outline the pharmacist’s role 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:
• Describe the impact and economic burden of CIC in the U.S
• Identify first line treatments for constipation
• Recognize prescription medications available to treat constipation not adequately treated by laxatives and dietary measures

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Universal Activity No.: 0798-0000-17-113-L01-P
Credits: 1.0 contact hour (0.1 CEU)

Release Date: 7/5/2017
freeCE Expiration Date: 7/5/2020
ACPE Expiration Date: 7/5/2020

ACTIVITY TYPE
Knowledge-Based Live Webinar

FINANCIAL SUPPORT BY
Synergy Pharmaceuticals Inc.
ABOUT THE AUTHOR
Dr. Tammie Lee Demler received her Doctor of Pharmacy, Master of Business Administration, and Bachelor of Science degrees at the State University of New York (SUNY) at Buffalo. Dr. Demler is a Board-Certified Psychiatric Pharmacist and is currently the Director of Pharmacy Services and Pharmacy residency training at the New York State Office of Mental Health (OMH) at the Buffalo Psychiatric Center. She holds numerous adjunct academic appointments, including Clinical Associate Professor for SUNY Buffalo School of Pharmacy and Pharmaceutical Sciences, Clinical Assistant Professor at SUNY School of Medicine Department of Psychiatry, D’Youville College School of Pharmacy, University of Florida School of Pharmacy, and Clinical Instructor for the Erie County >Community College’s Pharmacy Technician Certification Program (PTCB). Dr. Demler collaborates with both the National Association of the Boards of Pharmacy (NABP) and the Board of Pharmaceutical Specialties (BPS) to develop board examinations that establish the minimum competencies expected for new practitioners to practice in an ever changing clinical environment. Prior to embarking on her academic and institutional career, Dr. Demler’s clinical practice focused on ambulatory care in community pharmacy. Dr. Demler has authored and co-authored numerous original research articles and expert reviews for printmedia. She is a regular contributor to U.S. Pharmacist Pharmacist’s Letter. Dr. Demler is an author for the American College of Clinical Pharmacy’s Ambulatory Care Self-Assessment and has also has provided expert pharmacotherapeutic consultation for other books such as the Side Effects of Drugs: Annual Volume 36 and Clinical Consult to Psychiatric Nursing for Advanced Practice. In March 2017, she is publishing her own book Pharmacotherapeutics for Advanced Nursing Practice, and is planning a companion text for Physician Assistants hopefully in 2018.

She has presented medication continuing education programs internationally and nationally, and is an Academic Educator for the New York State Medicaid Prescriber Education program sponsored by the New York Department of Health. Dr. Demler served as President of both the Pharmacists Society of the State of New York and the Pharmacists Association of Western New York.

Dr. Demler is also a local media personality, hosting her own weekly TV talk show as well as a weekly community affairs radio segment. She has won a number of prestigious national, state, and local awards acknowledging both her professional and community-based contributions.

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Introduction and Key Messages

Educational Objectives Pharmacists:

• Describe the impact and economic burden of CIC in the United States
• Review the FDA approved pharmacologic treatment options for CIC beyond laxatives, to include novel targets, efficacy data, primary contraindications, and adverse effects
• Outline the pharmacist’s role in identifying inadequately treated patients and providing patient counseling regarding prescription treatment options that will facilitate communication with the physician
Introduction and Key Messages

Educational Objectives Pharmacy Technicians:

- Describe the impact and economic burden of CIC in the United States
- Identify first line treatments for constipation
- Recognize prescription medications available to treat constipation not adequately treated by laxatives and dietary measures

Definitions Rome III Criteria for Chronic Constipation

- Does not meet criteria for IBS, rarely (almost never) has loose stools without the use of laxatives, and meets two or more of the following criteria:
  - Fewer than three bowel movements per week.
  - Hard or lumpy stools more than 25% of the time
  - Straining with defecation more than 25% of the time.
  - Sensation of incomplete evacuation more than 25% of the time.
  - Manual maneuvers necessary to facilitate defecation more than 25% of the time.
  - Sensation of anorectal obstruction more than 25% of the time.

Definitions

**Constipation-summarized**
- Usually defined as having hard bowel movements fewer than 3 times per week (highly individualized and benchmarked on that “normally” experienced)

**Chronic**
- Otherwise known as “long-lasting”
- Per Rome III: 3 days per month for last 3 months with onset at least 6 months

**Idiopathic**
- This means that the cause is **unknown**

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The Impact and Economic Burden of CIC

**It is common**
- Many people have a difficult time with bowel movements
- National Institute of Health estimates that 42 million people are afflicted with constipation.

**It is costly**
- It is estimated that $400 million dollars that are spent annually on laxatives
- Accounts for 2.5 million physician visits annually in the U.S.

**It is not benign**
- Many patients self-treat the condition
- Consequences to this self-management and long term unresolved issue?
- How do we address frustrated patients who feel there are no options?

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What We Do Know....

What are common “known” reasons for constipation?
• Drug induced
• Decreased mobility
• Dehydration
• Dietary
• Pregnancy
• Medical conditions

Primary Medical Conditions With Secondary Symptoms

• Endocrine and metabolic: diabetes and hypothyroidism
• Neurologic: Parkinson’s disease, multiple sclerosis, stroke, spinal cord injury
• Bowel: IBS, anal fissures, strictures
• Psychiatric: eating disorders, depression
• Other: post surgical
What Is Expected as Early Intervention

Diet and lifestyle changes

• Increase fiber intake
• Exercise most days of the week
• Make time and respond to your body’s triggers! Do not ignore the urge to have a bowel movement

Pharmacologic Options
For What We Know...

Laxatives
• Fiber supplements
• Stimulants
• Osmotic agents
• Lubricants
• Stool softeners
• Enemas and suppositories
Pharmacologic Options for What We Know...

**Fiber supplements**
- Natural or synthetic polysaccharides or cellulose derivatives
- Increase stool mass by absorbing water
- More evidence supporting insoluble fiber for constipation intervention

**Universal Prescribing Alerts to avoid in patients with:**
- Appendicitis
- Esophageal stricture or perforation
- Dysphagia
- GI obstruction or ileus
- Unexplained abdominal pain


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Pharmacologic Options for What We Know...

**Fiber supplements**
- Methylcellulose
- Psyllium
  - Has best data among these agents (most studied)
  - Undergoes bacterial fermentation in the colon that causes gas and bloating and powder can be gritty when mixed with liquid)
- Malt soup extract
- Wheat dextrin

Pharmacologic Options for What We Know...

**Stimulant Laxatives**
- Alter electrolyte transport, increase water uptake and motor activity
- May cause electrolyte imbalance, GI discomfort and hepatic toxicity
- Senna has been associated with apoptosis of cells in large intestine, though current evidence does not correlate this to an increased rate of colon cancer
- May work best when combined with bulk-forming agents (caution risk of overuse)

**Universal Prescribing Alerts to avoid in patients with:**
- Diarrhea or loose stools
- Abdominal pain or dysphagia
- GI obstruction or bleeding
- Hemorrhoids

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**Stimulant Laxatives**

Bisacodyl usual dose:
- 5 to 15 mg PO per day
- 10 mg suppository or enema once daily

Usual oral tablet dose:
- Sennosides 8.6 to 17.2mg once or twice daily (MDD: 34.4mg sennosides)
- Available in liquid also
Pharmacologic Options for What We Know...

**Osmotic agents**

- Include saline agents, polyethylene glycol and sugars (poorly absorbed)
- Osmotic changes facilitate water retention in the intestinal lumen
- Patients at risk for electrolyte imbalance (i.e. renal failure) experience increased risk

**Universal Prescribing Alerts to avoid in patients with:**

- Diarrhea or loose stools
- Abdominal pain
- GI obstruction or bleeding

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Pharmacologic Options for What We Know...

**Osmotic agents**

- Glycerin
- Lactulose*
- Magnesium (citrate, hydroxide)
- Mineral oil (lubricant)
- Polyethylene glycol*
- Saline laxatives
- Sodium phosphates
- Sorbitol*
Pharmacologic Options for What We Know...

Stool Softeners
• Promote water uptake into stool as surface acting agent
• Little data demonstrating robust efficacy
• Psyllium generally considered “more effective”
• Fewer side effects than psyllium

Universal Prescribing Alerts to avoid in patients with:
• Prolonged use: when used for self-medication, do not use for longer than 7 days
• Abdominal pain, nausea, or vomiting is present

Docusate usual oral dose:
• Calcium and sodium formulations available (oral tabs, liquid capsule, oral liquid)
• 50 to 240 mg per day for calcium and 300 mg for sodium based capsules
• Rectal enema also available for use
• Ensure adequate fluid intake; mix oral liquid with milk or fruit juice
• Discontinue rectal use if rash develops or if there is resistance upon insertion
• Monitor: occasional rectal exams with impaired rectal function
The Impact and Economic Burden of CIC

People with CIC can experience the same symptoms as those with known causes:

- Less than 3 bowel movements a week
- Hard-to-pass bowel movements
- Bloating
- Straining
- Discomfort
- Not feeling empty after a bowel movement

Patients may describe being stuck in the bathroom without relief and are extremely frustrated.

What Does This all Mean?

**Education is needed**
- Improved patient counseling
- Enhanced provider knowledge of pharmacologic options beyond laxatives

**Clinical Decision making**
- Must consider “next steps” when traditional treatments fail
- What is failure?
- What should we do?
## Non-Pharmacologic Treatment Options for CIC

### Retraining pelvic muscles
- Biofeedback training to learn to relax and tighten the muscles in the pelvis.

### Surgery
- Chronic constipation is caused by a blockage, rectocele, anal fissure or stricture.

### Alternative medicine
- Not been well-studied
- Probiotics such as bifidobacterium or lactobacillus
- Fructooligosaccharide
- Acupuncture?

## Pharmacologic Treatment Options for CIC

### Beyond Laxatives...considerations
- Novel targets
- Efficacy data
- Primary contraindications
- Adverse effects
- Cost
Pharmacologic Treatment Options for CIC

**Beyond Laxatives**

**FDA approved:**

- Draw water into the intestines & speed movement of stool
  - Lubiprostone (Amitiza)
  - Linaclotide (Linzess)
  - Plecanatide (Trulance)

**Non-FDA approved:**

Other medications used “off-label” for side effects – may still be seen

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**Lubiprostone (Amitiza)**

**Generic Name:** Lubiprostone  
**Brand Name:** Amitiza  
**Mechanism of action:** bicyclic fatty acid, prostaglandin E1 (PGE 1) derivative  
**FDA approved indications for use 2006**  
- Chronic idiopathic constipation (CIC)  
- OIC with CNCP  
- Irritable bowel syndrome with constipation in adult women  

**Usual oral dose for CIC:**  
- 24 mcg twice daily
Lubiprostone (Amitiza)

**Clinical pearls and precautions**

- IBS with constipation has a lower dose requirement; refer to PI
- Avoid use in patients with severe diarrhea
- May cause dyspnea & chest tightness after the first dose
- Nausea may occur; administer with food
- Not approved for use in males with IBS with constipation

**Contraindications:**

- Known or suspected mechanical bowel obstruction and who may be at higher risk or have suggestive symptoms

Linaclotide (Linzess)

**Generic Name** Linaclotide  
**Brand Name** Linzess  
**Mechanism of action** guanylate cyclase-C (GC-C) agonist  
**FDA approved indications for use 2012 –new dose in 2017**

- Chronic idiopathic constipation  
- Irritable bowel syndrome with constipation  
- Dose varies based on indication for use and patient’s clinical status

**Usual oral dose for CIC:**

- 145 mcg once daily (new dose available 72 μg based on patient’s status)
Linaclotide (Linzess)

Clinical pearls and precautions
• Take dose 30 minutes prior to first meal of the day
• May cause diarrhea; patients should discontinue the medication if severe or persistent diarrhea occurs

Contraindications:
• Known or suspected mechanical gastrointestinal obstruction

Associated with:
• Not for use in populations of a certain age; refer to PI prior to use
• BBW for severe dehydration in pediatric populations
• Contraindicated in neonates, infants, and children up to 6 years of age and use avoided in pediatric patients 6 to 17 years of age

Plecanatide (Trulance)

Generic Name: Plecanatide
Brand Name: Trulance
Mechanism of action: guanylate cyclase-C agonist

FDA approved indications for use 2017
Chronic idiopathic constipation
Usual oral dose for CIC:
• 3 mg once per day without regard to food and may be given via NG
Plecanatide (Trulance)

Clinical pearls and precautions
- Safety and efficacy in children less than 18 years of age is unknown and may be harmful (BBW-contraindicated) in those younger than 6 years of age
- Not for patients with bowel blockage (intestinal obstruction).
- Diarrhea is the most common side effect and can sometimes be severe. May cause serious dehydration
- Med guides are required by FDA

Contraindications:
- Known or suspected gastrointestinal obstruction

Associated with:
- Not for use in populations of a certain age; refer to PI prior to use (BBW)

Plecanatide (Trulance) & Linaclotidte (Linzess)

Clinical pearls and precautions
- Same MOA
- Treatment differences noted in randomized placebo controlled trials
  - Linaclotide: treatment differences 11% & 8%
  - Plecanatide: treatment differences 17% & 10%
- Measured in CSBM* per week at baseline treatment weeks 12
  - Improved frequency, stool consistency and decreased straining reported
  - No comparative studies comparing both agents against each other
  - Both represent options for CIC
  - Linaclotide has additional IBS indication
  - Cost?

*CSBM=complete spontaneous bowel movements
What is the Pharmacist’s Role?

- Identify inadequately treated patients
  - Question patients who appear to be self medicating OTC
  - Use open ended questions
- Understand the burden of CIC on your patient
  - Consider stocking educational pamphlets encouraging patients to self report and that increase awareness and prevalence of this problem
- Provide patient counseling regarding prescription treatment options
  - Good news! Patients may have more options to choose from and to re-challenge pharmacologic interventions for this frustrating clinical condition
- Facilitate communication with the physician
  - Prescribers may not know about the new options, dosing and adverse effects

Key Counseling Points for Patients

- Remember diet and exercise still matter!
- Changes in bowel patterns should be reported to MD and appropriate screening and monitoring always apply (colon cancer, etc.)
- Remind female patients to report pregnancy or plans to become pregnant
- For newest agent that we are all least familiar with:
  - Patients should swallow tablets whole, however may crush if needed but should be mixed with applesauce or dissolved in water before swallowing
  - Store in original container with desiccant left in to keep dry
  - Polyester coil should be removed
- Circle back to “drug induced constipation”
Questions? - Thank You!