<table>
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<tr>
<th>Program Name:</th>
<th><strong>Role of Antispasmodics in the Self-Treatment of Abdominal Cramping and Pain</strong></th>
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<tr>
<td>Planning Committee:</td>
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<td>Accreditation Information:</td>
<td>This version of the program is unaccredited and intended for informational purposes only. An accredited version is available online at <a href="http://www.rxBriefCase.com">www.rxBriefCase.com</a> until February 11, 2018.</td>
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<td>This case study is supported by an educational grant from Sanofi Pasteur Canada.</td>
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Learning Objectives

Upon successful completion of this continuing education lesson, the pharmacist will be better able to:

- Explain a functional gastrointestinal disorder to a patient;
- Discuss the epidemiology of abdominal pain and cramping;
- Assess a patient for “red-flag” circumstances that would prompt referral to a physician for further assessment;
- Review the role of non-pharmacological interventions in reducing GI symptoms; and,
- Discuss the role of antispasmodics for the self-medication of abdominal cramping and pain.
Meet our Patient Lynn S.

Lynn S., a 28-year-old female, approaches the pharmacy counter to see if you have a recommendation to help her. After breakfast this morning she developed some abdominal pain and is feeling very uncomfortable.

When you ask her about the pain, she says she feels bloated, with tightening and knotting pain. When you ask her to describe her level of pain on a scale from 0 to 10 (where 0 means no pain, and 10 is the worst pain she has experienced) she rates the pain a 7.

She is concerned as she has a major presentation to give at work and the cramping and pain are going to make it very difficult for her to present. She has had this before and has taken ibuprofen and calcium carbonate. Although the ibuprofen provided some relief of pain, it caused an upset stomach. The calcium carbonate did very little and neither product helped to reduce the abdominal cramping.

She wants to know if there are any products that can quickly improve how she is feeling.
Introduction
Abdominal pain, bloating, cramping, diarrhea and constipation are commonly seen in clinical pharmacy practice. These symptoms cause significant discomfort and can impair a patient’s ability to perform their daily activities. Pharmacists are commonly asked to recommend products to reduce symptoms or even to cure their conditions.

Some pharmacists may be concerned that a patient’s symptoms could be precipitated by an organic condition (e.g., peptic ulcer disease, inflammatory bowel disease, bowel infections and cancer) or structural abnormality (e.g., hiatal or inguinal hernia). For a large portion of patients with abdominal pain and cramping, the cause of the condition is not known. Functional gastrointestinal (GI) disorders are non-structural and non-organic in nature. Unlike structural conditions that can often be cured by medical interventions (e.g., surgery), many functional conditions have treatments that are directed at the specific GI symptoms.¹ Community pharmacists are positioned very well to assess patients and recommend treatments for the GI symptoms associated with functional GI disorders.

Functional GI disorders are believed to be caused through a link between the brain, the central nervous system (CNS) and the gut.¹ In certain patients, environmental factors such as stress or a psychological state can make them more susceptible to gut dysfunction such as abnormal motility, altered mucosal immunity or visceral hypersensitivity. Unlike those for other GI conditions, therapies for functional conditions target the patient’s specific symptoms.¹ One of the most common functional GI disorders is irritable bowel syndrome (IBS).

Pharmacists are frequently presented with patients experiencing symptoms of functional GI disorders. By discussing the patient’s symptoms and assessing the patient for “red flag” symptoms, pharmacists can help to ensure that their patients are managed satisfactorily.
Pathophysiology
The exact cause of functional GI disorders is unknown. It is not uncommon that at times these can be precipitated by an infection of the gastrointestinal tract or food poisoning and then classified as post infectious IBS. The symptoms are believed to be caused by both gut physiologic factors as well as a complex interaction between the brain/CNS and the gut. Some of the common pathophysiologic features of functional GI disorders are reviewed in Table 1.

<table>
<thead>
<tr>
<th>Table 1 – Pathophysiological Features of Functional GI Disorders</th>
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<tr>
<td><strong>Genetic Predisposition and Family Environment</strong></td>
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<td><strong>Psychosocial Factors</strong></td>
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<td><strong>Abnormal Motility</strong></td>
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<td><strong>Visceral Hypersensitivity</strong></td>
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</table>
| Inflammation                                                                 | • Increased inflammation in the enteric mucosa or neural plexuses may contribute to symptom development  
                                  • Approximately 1/3 of patients with IBS or dyspepsia describe that their symptoms began after an acute enteric infection and up 25% of patients presenting with an acute enteric infection will go on to develop IBS-like or dyspeptic symptoms |
| Bacterial Flora                                                              | • Growing interest in the role of altered bacterial flora contributing to the development of IBS |
| Brain-Gut Interactions                                                       | • Extrinsic factors (vision, smell) or enteroreceptive information (emotion, thought) are capable of affecting GI sensation, motility, secretion and inflammation  
                                  • Increased reactivity to stress  
                                  • Neuropeptides and receptors present in both the CNS and the gut could play a key role in the pathophysiology and can be potential therapeutic targets |

**Clinical Fact:**

There are currently 28 adult functional GI disorders in the Rome III classification system.²
This system was developed by the Rome Foundation to classify – by clinical symptoms -- disorders of the digestive system in which symptoms cannot be explained by the presence of structural or tissue abnormality.¹ The most recent revision of the criteria, the Rome III criteria, were published in 2006 in book form, and in a shorter journal supplement in Gastroenterology. Pharmacists interested in reading more on the Rome III classification are referred to the Rome Foundation website.
Some of the most common functional GI symptoms are functional dysphagia, functional dyspepsia, irritable bowel syndrome, functional constipation, functional diarrhea and functional abdominal pain.
Test Your Current Knowledge

Based on your current knowledge, please select the proper answer for each of the following questions.

1. Worldwide, what percent of the population is affected by the Irritable bowel syndrome?
   a. Less than 1%
   b. 7% to 10%
   c. Greater than 15%

2. Based on data from the United States, approximately what percent of patients with abdominal pain and cramping report that these symptoms cause them major distress?
   a. 7%
   b. 26%
   c. 36%

3. How does the impact of IBS on health-related quality of life compare with the impact of other chronic diseases?
   a. It is less than that of other chronic diseases.
   b. It is comparable to that of other chronic diseases.
   c. It is greater than that of other chronic diseases.
**Epidemiology**

Abdominal pain and discomfort, bloating and altered bowel habits (constipation, diarrhea or both) are common lower GI dysmotility and sensory symptoms and are characteristic of irritable bowel syndrome (IBS). The prevalence rate of IBS ranges from 1% to more than 20%. Using criteria for IBS as defined by the American College of Gastroenterology Task Force on Irritable Bowel Syndrome, it is estimated that close to 7-10% of people worldwide suffer from IBS.

An international study assessed the number of patients with abdominal pain and cramping in nine countries during a 12 month period. They found this condition was highly prevalent and reported in 46% of survey respondents in Mexico and only 10% of respondents in Japan. Although Canada was not assessed directly, 24% of respondents in the United States and 31% of respondents in the United Kingdom indicated they experienced abdominal cramping and pain over the past year. When the data from the United States were further evaluated it was found that:

- 61% of respondents had these symptoms at least once per week
- 41% had severe abdominal symptoms
- 36% reported major distress due to abdominal symptoms
- 52% of respondents took medications for these symptoms at least once per week resulting in a significant effect on the duration of the episode.

A Canadian survey of 689 women who had GI symptoms (abdominal pain, abdominal discomfort, bloating, constipation or constipation with occasional diarrhea) found:

- 78.1% experienced two or more GI symptoms
- Abdominal pain was the most bothersome and most severe
- Over 90% of women reported abdominal pain and discomfort at least once per month and over 65% had these symptoms at least once per week
- 13.2% of respondents missed work or school and 28.8% were less productive over the last 3 months
- 63.8% of women were receiving treatment for these symptoms with the majority being non-prescription products. The most common agents used are:
- Antacids (32.2% of respondents) – Most commonly used OTC products
- Omeprazole (14.3% of respondents) – Most commonly used prescription product

[Note: As of July 17, 2015, omeprazole was marketed in Ontario OTC by Laboratoire Riva Inc. It may currently be marketed OTC by other companies and in other Provinces.]

- The frequency of use of treatment increased with the severity of the symptoms

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**Clinical Practice Tip:**

A Canadian survey found that almost 1 in 5 patients with GI symptoms take herbal or alternative medications.³ It is important for pharmacists to screen patients who present with GI symptoms for these products. It is imperative that pharmacists phrase their questions in a non-judgmental manner to ensure that patients feel comfortable revealing which herbal or alternative medications they may be taking. Questions such as “You’re not taking natural products to treat your symptoms, are you?” can discourage a patient from disclosing their alternative medication use. However, statements and/or questions such as, “It is important that I know all of the medications you are taking so I can help you deal with your symptoms” or “Could you tell me what prescription or non-prescription medications you may be using to help relieve your symptoms?” encourages patients to disclose without fear of ridicule or judgment.
The Impact of Functional GI Disorders

Although some patients and clinicians may view GI symptoms as a minor nuisance, patients with functional GI disorders often experience emotional distress, a perceived lack of validation and an unsatisfactory experience with healthcare providers. Patients with functional GI disorders (such as IBS) have similar experiences to patients who live with other chronic conditions of uncertain etiology and ambiguous diagnostic criteria. These chronic illnesses are characterized by long-term courses, unpredictable symptom episodes and disabling effects that are often accompanied by social stigma, isolation and treatments that are not effective.

Patients with IBS repeatedly experience unpredictable symptoms of discomfort or pain and altered bowel habits, accompanied by emotional distress over the lack of control of symptoms. Patients commonly report personal sacrifices as they struggle to accommodate GI symptoms. Anticipation and worry over when and where the next symptom episode will occur, imposes limitations on planning and on daily activities.

Clinical Practice Fact:

Although some GI symptoms may be viewed as minor, studies have demonstrated that several functional GI disorders are associated with an impaired health-related quality of life (HRQoL) that is comparable to other chronic conditions.
Clinical Practice Tip:

Pharmacists must NOT underestimate nor trivialize the impact of GI symptoms on a patient's life. Although a pharmacist may not believe the GI symptoms are serious following assessment, he/she can use reflective listening skills to demonstrate empathy and exhibit appreciation for the effect the symptoms may be having on the patient's quality of life. For instance, the pharmacist can say, “I hear your frustration. It must be difficult having to deal with stomach pain and cramping on a weekly basis. Would it be ok if we discussed non-prescription options that may help relieve your symptoms?”

Revisit our Patient – Lynn

You ask Lynn more questions about her symptoms. She explains that the abdominal cramping and pain usually occur about 3-4 times per month. When she experiences an attack it occurs suddenly and will normally last about a day without any treatment before it gets better. She finds that the symptoms will normally occur during periods of high stress, around her menstrual cycle, when she gets little sleep or drinks too much coffee.

When you ask, she explains that she usually has abdominal pain, cramping and bloating. She finds that the pain usually improves when she has a bowel movement. Normally she has diarrhea and the pain improves. She is not experiencing any GI burning, nausea, vomiting or blood in the stools.

You feel that she has a functional GI disorder (possibly IBS) and decide to perform a brief assessment prior to making any recommendations.
Test Your Current Knowledge

Based on your current knowledge, please select the correct answer for each of the following questions.

1. Which of the following symptoms should be considered “red-flag” symptoms, alerting pharmacists to recommend that a patient consult a physician?
   a. Dysphagia
   b. Weight loss of > 3kg over 6 months
   c. Recent changes in symptoms
   d. All of the above

2. Which of the following medications commonly cause/causes abdominal pain and cramping?
   a. Dabigatran etexilate
   b. Metformin
   c. NSAIDs
   d. All of the above

3. Which of the following does not help improve IBS symptoms?
   a. Wheat bran
   b. Psyllium
   c. An antispasmodic agent

Managing a Patient Presenting with Abdominal Pain and Cramping

GI symptoms are common in the Canadian population. Pharmacists can play a key role in helping to select the most appropriate treatment option for a patient. This will normally involve a process of assessing the patient’s symptoms, determining if there are any “red-flag” circumstances, providing the necessary education, recommending non-pharmacological options and selecting an option for the patient’s symptoms. This process is reviewed in Figure 1.
Assessment of Patients with Abdominal Pain and Cramping

Many patients with functional GI disorders report unsatisfactory or unhelpful experiences with healthcare professionals. Many clinicians also share their patients’ frustration due to the poorly understood nature of many functional GI disorders and the lack of specific treatments. A strong patient-provider relationship is fundamental to the successful management of these conditions. Clinicians who offer patient-oriented care are more likely to empower the patient to properly manage these conditions. Improved patient-provider relationships have been shown to:

- Improve patient satisfaction
- Improve adherence to treatment
- Reduce symptoms
- Improve other health outcomes

Although many times the exact reason for a patient approaching the pharmacist will be clear (e.g., GI symptoms), at other times the exact reason for a patient discussing their symptoms may not be as apparent. With functional GI disorders
being chronic in nature, it is important for the provider to assess the primary reason(s) for the patient’s visit. Clinicians could consider asking the following question:

- “What is the main reason for your visit today?”

By understanding the primary reason for the visit, providers can address the main concern(s) of the patient. Several reasons for a patient’s visit are listed in Table 2. To help improve the relationship with patients, providers should take a variety of steps. These steps are reviewed in Table 3.

### Table 2 – Potential Reasons for a Patient with a Functional GI Disorder to Visit their Healthcare Provider

- **New factors that exacerbate symptoms**
  - Dietary changes, concurrent medical disorder, side effects from a new medication
- **Personal concern about a serious disease**
- **Environmental stressors**
  - Major loss, abuse history
- **Psychiatric comorbidity**
  - Depression, anxiety
- **Impairment in daily functioning**
  - Recent impairment in working or socializing

### Table 3 – Guidelines for Pharmacists in Evaluating and Managing Patients with Functional GI Disorders

1. Obtain a detailed patient history through a patient assessment
2. Determine how much the patient understands about his/her condition
   a. Consider asking “What do you think is causing your symptoms?”
3. Provide a thorough explanation of the disorder that takes the patient’s beliefs and concerns into consideration
   a. The Rome III diagnostic criteria for functional GI disorders can provide pharmacists the different characteristics for these disorders
4. Assess the impact of the symptoms on the patient’s daily life
   a. Consider asking, “What is the impact of your symptoms on your daily life?”

5. Identify and respond realistically to the patient’s expectations for improvement
   a. Consider asking “How do you feel I can help you?”
   b. Consider explaining that a cure for these conditions is generally unrealistic and most treatments are focused on reducing symptom severity and their impact on daily life.

6. When possible provide a link between stressors and symptoms that is consistent with the patient’s beliefs
   a. For example, “I understand that you feel that stress is not a major contributor to your cramping and pain, but the pain is so severe that it must be causing you a great deal of distress.”

7. Set treatment limits but acknowledge his/her symptoms
   a. For example, “I understand the severity of your pain, but pain medications such as narcotics are not recommended for your type of pain.”

8. Involve the patient in the treatment
   a. Consider asking, “Would it be ok if I suggested some different treatments for you to consider?”

9. Establish a long-term relationship with the patient in light of the chronic nature of these conditions
Screening for “Red-Flag” Symptoms

When presented with a patient with abdominal pain and cramping it is important to assess the patient for symptoms that are more commonly associated with organic causes. Table 4 lists symptoms and situations that dramatically increase the risk that the patient’s symptoms could be organic and more serious in nature. Patients presenting with these symptoms or circumstances should be referred to a physician for further assessment.

Many medications can cause abdominal pain. Pharmacists should consider screening a patient’s profile for common medications that could be causing or exacerbating the GI symptoms. Common examples are listed in Table 5.

Table 4 – Potential “Red-Flag” Symptoms/Circumstances with GI Concerns

| • Dysphagia (difficulty swallowing) |
| • Weight loss of > 3kg over 6 months |
| • Persistent vomiting |
| • Bleeding, hematemesis, melena (blood in vomit or black, tarry stools) |
| • Anemia |
| • Fever, chills |
| • Recent changes in symptoms |
| • New onset of symptoms after the age of 50 years |
| • Family history of colon cancer, inflammatory bowel disease or celiac disease |
| • Patients with poor clinical status |
| • Patients with high-risk disease states (e.g., ischemic heart disease, immunosuppression, renal insufficiency, etc.) |
| • Patients with a history of international travel – risk of parasitic infection |

Table 5 – Common Medications Associated with Abdominal Pain

| • Amiodarone |
| • Antibiotics |
| • Antineoplastics |
| • Dabigatran etexilate |
| • Iron supplements |
| • Metformin |
| • NSAIDs |
| • ASA |
| • Opioids |
| • SSRIs |
Patient Counselling and Education

For patients with mild symptoms, counselling and education may be the only treatment recommendation.\(^1\) This education focuses on providing key information about the disease and its treatment.\(^1\) Patients require reassurance that their providers have listened to their concerns and understand the severity of the experienced GI symptoms. It is important to stress that there is not a cure that will rid them of their condition.\(^1\) Patients should also be educated that without the presence of “red-flag” symptoms, it is unlikely that their symptoms are due to a life-threatening disease such as cancer.\(^1\) Providers should work to address a patient’s fears and concerns.\(^2\) Key counselling messages are listed in Table 6.

Clinical Practice Tip:

With IBS affecting a large number of Canadians, it is important that pharmacists are comfortable with current management approaches. The American College of Gastroenterology has published An Evidence-Based Systematic Review on the Management of Irritable Bowel Syndrome to help clinicians with IBS management. Some key recommendations from these guidelines are:\(^4\)

- Extensive diagnostic testing is unnecessary in patients with IBS symptoms who do not have alarm features. Diagnosis is made strictly based on symptoms
- Psyllium is moderately effective for IBS
- Wheat bran and corn bran are no more effective than placebo
- Polyethylene glycol (PEG) increases stool frequency but does NOT reduce abdominal pain
- Antispasmodics may provide short-term relief of abdominal pain/discomfort
- Loperamide is effective for diarrhea, and reducing stool frequency but NOT for reducing pain or bloating
- Probiotics are somewhat effective for reducing IBS symptoms
Tricyclic antidepressants and SSRIs are more effective than placebo for relieving global IBS symptoms and appear to reduce abdominal pain.

Psychological therapies are more effective than usual care in relieving global symptoms of IBS.

Table 6 – Key Counselling Messages for Patients with Functional GI Disorders

- Providers and patients must realize that symptoms are real and are caused by the GI tract being more sensitive to a variety of stimuli.
- For most patients, extensive laboratory testing and investigation is unnecessary as it does not improve outcomes and can negatively affect the patient’s quality of life.
- The pain can be the result of spasms and from an overly sensitive gut. This can result in GI symptoms such as nausea, vomiting, diarrhea.
- There is a strong link between psychological factors and the severity and type of GI symptoms experienced.* (you should stress to patient that this doesn’t mean symptoms are “not real” or “in their head” BUT that learning stress reduction techniques may help in addition to medications and dietary treatments*******)
- Psychological factors may alter symptom perception and addressing these factors can improve the patient’s sense of well-being and may help to reduce the severity of these symptoms.
- Diet and lifestyle changes may help to improve the condition.
- Current pharmacological choices are directed not at the condition but at the primary symptoms.

Clinical Practice Tip:

The key for pharmacists is to facilitate learning. Their role is not to identify the problem and provide the answer. Rather, the role is to ensure the patient is aware of possibilities and can make an informed choice. It is essential for pharmacists to avoid the “righting reflex” by staying away from phrases such as “But you need to...” or “You know what might happen if you don’t.” Instead pharmacists should explore with the patient what he/she feels is the problem and then, as a partnership, examine possible solutions.
Test Your Current Knowledge

Based on your current knowledge, please select the correct answer for each of the following questions.

1. Which of the following often helps relieve symptoms of mild IBS?
   a. Avoidance of foods to which a person is allergic
   b. Avoidance of trigger foods
   c. Avoidance of lactose

2. Which of the following, in general, is/are not helpful in relieving functional GI symptoms?
   a. High-fibre diets
   b. Reducing excessive caffeine intake
   c. Relaxation exercises
   d. Regular physical activity

3. Which laxative must be used with caution in patients with renal dysfunction?
   a. Psyllium
   b. Magnesium hydroxide
   c. Bisacodyl
   d. Sennoside

4. Antispasmodics should not be recommended for persons who have which of the following conditions?
   a. Glaucoma
   b. Urinary retention or obstruction
   c. Myasthenia gravis
   d. Tendency to cardiac arrhythmias
   e. Any of the above
Non-Pharmacological Options
For many conditions such as mild IBS, a healthy lifestyle and diet may help to improve GI symptoms.\(^1\) Interventions that are directed at reducing psychological stress (e.g., exercise, yoga, deep breathing, counselling) may also reduce the symptoms.

Although 60% of patients with IBS believe that food exacerbates their symptoms, there is no correlation between foods that patients identify as a cause of their IBS symptoms and the results of food allergy testing.\(^4\) Patients should be encouraged to avoid nutritionally depleted diets and have regular, unhurried meals.\(^11\) Avoiding lactose fails to improve symptoms but avoiding excessive fructose and artificial sweeteners such as sorbitol or mannitol may help to improve diarrhea, bloating, cramping and flatulence.\(^11\) Common food and lifestyle recommendations are listed in Table 7.

**Clinical Practice Tip:**
Each patient with functional GI disorders has slightly different food triggers. Patients should be encouraged to keep a food diary to document the possible link between different foods and GI symptoms. Pharmacists can download a Food and Symptom Diary to provide to their patients. With this diary, the patient can mark down the different foods that they consume and any possible reactions. Although it is labour-intensive, it is one of the most effective methods of identifying food triggers.
Table 7 – Lifestyle Recommendations for Patients with Functional GI Disorders$^{4,11,12}$

- Encourage a healthy diet based on Canada’s Food Guide to Healthy Eating.
- Avoid food fads, excessive caffeine and alcohol intake.
- Many of the treatment recommendations from alternative practitioners have no proven efficacy. Some of the diets recommended by these practitioners are not nutritionally sound.
- Stress management and relaxation exercises can reduce many GI symptoms.
- Although increase in dietary fibre is a common recommendation for patients with IBS, there is very little data to support its use. Psyllium is the exception and is moderately effective for IBS symptoms.$^4$
- Avoidance of food triggers. Each patient has unique triggers and avoidance of all potential triggers is NOT recommended. Common food triggers include:
  - Dairy products
  - Cereals (wheat, oats, corn)
  - Citrus fruit
  - Potatoes
  - Caffeinated drinks
  - Fat
  - Alcohol
  - Simple sugar alternatives (e.g., fructose, lactose, sorbitol)
  - An excess or insufficient intake of dietary fibre
- Regular physical activity can reduce psychological symptoms and improve general well-being. Pharmacists should be encouraging the recommendations in Canada’s Physical Activity Guide.
**Revisit our Patient – Lynn**

You recommend to Lynn to start a food diary to look for particular triggers for her symptoms. With her symptoms commonly occurring during periods of stress (e.g., presentation at work), you recommend that she try different relaxation exercises to see if they help to reduce the number of episodes of GI symptoms.

Lynn says she will try the food diary and stress reduction but she wonders if you could select a specific treatment to help her today. When you ask, she states that the most troubling symptoms are her abdominal pain and cramping.

**Selecting the Optimal Non-Prescription Option for Patients**

In patients with GI symptoms that are interfering with their daily routine, medications can be considered. The choice of medication will depend on the predominant symptoms. In practical terms, pharmacists should ask about the symptoms and direct their recommendation at the medication(s) that target the patient’s specific symptoms. There is no one single drug that has been shown to be beneficial for all patients with functional GI disorders such as IBS.

The different OTC treatment options are dependent on the patient’s symptom presentation. The most common symptoms in patients with IBS that can be self-managed include constipation, diarrhea, abdominal cramping and pain.
Constipation

Psyllium has been found to be moderately effective for managing IBS. There is very little evidence to support the use of laxatives in patients with IBS. Magnesium-based laxatives, senna, bisacodyl, polyethylene glycol and lactulose are OTC options for pharmacists to consider. Patients should be reminded that some of these agents (e.g. lactulose) may worsen abdominal cramping and pain and if this occurs a change in dose or an alternative laxative could be considered. Different laxatives are listed in table 8. Linaclotide, which is available in Canada only on prescription, is mentioned here because it is sold OTC in the United States; it is a prosecretory 14-amino acid peptide indicated for the treatment of IBS with constipation or chronic idiopathic constipation.

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<tr>
<th>Product</th>
<th>Dose</th>
<th>Adverse Effects</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Psyllium (Bulk-forming laxative)</td>
<td>3.4 grams BID with meals and gradually titrate to 12-20 grams/day as tolerated</td>
<td>Abdominal pain, bloating, flatulence, cramping</td>
<td>Must take with adequate fluid</td>
</tr>
<tr>
<td>Lactulose (Osmotic laxative)</td>
<td>15-60 mL per day in 1 or 2 divided doses</td>
<td>Flatulence, abdominal cramps, diarrhea, bloating</td>
<td>No significant drug interactions, but taste could be an issue</td>
</tr>
<tr>
<td>Polyethylene glycol (PEG) (Osmotic laxative)</td>
<td>17 grams daily</td>
<td>Nausea, bloating, cramping, flatulence, diarrhea</td>
<td>Usually better tolerated than lactulose</td>
</tr>
<tr>
<td>Magnesium hydroxide (Osmotic laxative)</td>
<td>15-30 mL once or twice daily</td>
<td>Diarrhea and risk of hypermagnesemia in patients with renal dysfunction</td>
<td>Avoid in patients with impaired renal function</td>
</tr>
<tr>
<td>Bisacodyl (Stimulant laxative)</td>
<td>5-10 mg orally daily at bedtime</td>
<td>Abdominal cramping, GI upset</td>
<td>Stimulates peristalsis</td>
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10 mg rectally daily

Sennoside (Stimulant laxative) 16.2 to 32.4 mg (2-4 tablets at bedtime) Abdominal cramping, GI upset Stimulates peristalsis and long-term daily use may cause melanosis coli

Maximum 8/day

Diarrhea

Loperamide has been found to be effective for helping to reduce diarrhea, stool frequency and for improving stool consistency.\(^4\) It has been found to be no more effective than placebo at reducing pain, bloating or global symptoms of IBS.\(^4\) It may actually worsen nighttime abdominal pain and therefore should only be used by patients with painless diarrhea.\(^{12}\) The dosing of loperamide in IBS is listed in Table 9.

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<th>Product</th>
<th>Dose</th>
<th>Adverse Effects</th>
<th>Notes</th>
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<tr>
<td>Loperamide</td>
<td>2-4 mg up to QID</td>
<td>Abdominal cramps, drowsiness, dry mouth, nausea, vomiting and skin rash</td>
<td>May cause constipation and worsen abdominal cramping and should not be used if there is bloody diarrhea or if the patient has a fever</td>
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Abdominal Pain and Cramping

Treatment of abdominal pain associated with cramping focuses on relieving symptoms rather than curing the disease. Management strategies should be offered as these symptoms can have a significant effect on the patient’s daily life. An international survey of women with IBS found that the average patient experiences 5.4 attacks per month. These attacks had a median duration of 2.8 hours and a median pain intensity score of 7 (on a scale from 0 to 10). The majority of pain attacks (63%) interfered with work and/or daily activities.

An international survey evaluated the treatment of abdominal cramping and pain across different countries worldwide. The majority of respondents from the Americas (approximately 90%) used medications to help control these symptoms. OTC medications were taken much more than prescription medications and most took the medication on demand to relieve the pain episode. The treatment used varied depending on the region. In Latin America, antispasmodics are clearly favoured by over half of the patients with abdominal pain and cramping. In areas such as the United States and the United Kingdom, analgesics were the drugs of choice. In the United States, antispasmodic agents are not available OTC and treatments such as antacids, laxatives and proton pump inhibitors are commonly used for abdominal pain but there is very little rationale to support the use of these drugs.

Role of Antispasmodics in Abdominal Pain and Cramping

Altered gastrointestinal motility is believed to play a role in the change in bowel habits of some patients with functional GI disorders. This intestinal motility is the target of current antispasmodic agents. There are two antispasmodics that can be purchased in Canada without a prescription; hyoscine butylbromide and dicyclomine hydrochloride. These agents have a long history of use; for example, hyoscine butylbromide has been used for over 50 years in Canada as an antispasmodic.
Mechanism of Action

These agents have a high affinity for muscarinic receptors located on the smooth-muscle cells of the GI tract. Their anticholinergic action exerts a smooth muscle relaxing/spasmolytic effect. This blockade of muscarinic receptors in the GI tract is the basis for the efficacy of these drugs in the treatment of abdominal pain secondary to cramping. When they are taken orally they are able to directly affect the muscarinic receptors in the GI tract.

When explaining these products to patients, consider describing them as medications that specifically target the spasm in the gut. By relaxing these muscles, the medication helps to reduce the pain associated with abdominal cramping.

Systemic Absorption

Hyoscine butylbromide is chemically modified to contain a quaternary ammonium compound to limit the systemic absorption of the medication. This structure also reduces its ability to penetrate the blood-brain barrier and for this reason it is generally well-tolerated.

Efficacy

The role of antispasmodics in the treatment of abdominal pain and cramping has been evaluated in a number of systematic reviews and meta-analyses. One meta-analysis evaluated data from 23 randomized clinical trials using all antispasmodics in IBS and found that the use of antispasmodics led to 56% of patients achieving a significant global improvement in symptoms even with a high placebo effect (38%). The percentage of patients with pain improvement was 41% with placebo and 53% with antispasmodics. This trial found that there was no significant difference in the adverse effects reported between the placebo and antispasmodic group.
Clinical Practice Tip:

When counselling patients with IBS on antispasmodic use, pharmacists may want to provide them with some information on the number of patients needed to treat with antispasmodics to improve different aspects of IBS. These include:\(^{20}\)

- Number of patients needed to treat for improvement of abdominal pain is 5
- Number needed to treat for improvement in global assessment is 4
- Number needed to treat for improvement in symptom score is 3

Another meta-analysis that reviewed the use of all antispasmodics in patients with IBS found that the number needed to treat (NNT) to prevent symptoms from persisting in one patient was 3.5.\(^{18}\) This same meta-analysis found that antispasmodics are very well-tolerated compared to placebo and the number needed to harm with antispasmodics was 17.5.\(^{18}\) In other words, 17.5 people would need to be treated with antispasmodics for a patient to be harmed from these agents that would not otherwise be harmed.\(^{18}\) Current IBS clinical practice guidelines recommend the use of antispasmodics for short-term relief of abdominal pain and discomfort from IBS.\(^{4}\)

One trial evaluated the use of oral hyoscine butylbromide tablets in patients with recurrent episodes of self-reported gastric or intestinal spasm-like pain.\(^{21}\) This study involved patients documenting their pain score on a 10 cm visual analog scale (VAS). Hyoscine butylbromide was found to decrease pain intensity by 20% within 30 minutes and by 59% at 180 minutes.\(^{21}\) Another trial investigated the use of hyoscine butylbromide in combination with acetaminophen (10mg/500 mg TID) for patients with recurrent crampy abdominal pain.\(^{22}\) In this trial, both hyoscine butylbromide and the combination with acetaminophen were found to be comparable in reducing VAS pain intensity.\(^{22}\)
Clinical Practice Tip:
In a survey of patients with abdominal cramping and pain, the most important feature of a treatment reported was fast-acting and was followed by long-lasting action. Pharmacists should consider these features when selecting different treatment regimens.

Adverse Effects
Antispasmodics that can be purchased without a prescription are generally well-tolerated. Although the most commonly listed adverse effects are anticholinergic in nature, the incidence is low due to minimal systemic absorption of these agents. The most common adverse effects reported include dry mouth, dyshidrosis, blurred vision, tachycardia and urinary retention.

Interactions with Other Medications
Antispasmodics that can be purchased without a prescription should be used with caution with other medications that can cause anticholinergic adverse effects. Common agents with anticholinergic adverse effects include tricyclic antidepressants, antihistamines, quinidine and disopyramide. Hyoscine should be used with caution in patients using β-blockers due to the increased tachycardic effects.

These agents could be safely used with other common medications used to treat GI symptoms. They can be used with analgesics (e.g., acetaminophen), anti-diarrhea medications (e.g., loperamide) or medications for constipation. The primary role of antispasmodics is to target the abdominal cramping and pain. Other agents can target the other GI symptoms.

Bottom Line
Antispasmodics have an extensive history in Canada. These agents were found to target the smooth muscle spasm of the gastrointestinal tract of some patients with functional GI disorders and to be effective at reducing abdominal cramping and pain. They are generally well-tolerated and most anticholinergic adverse effects are minimal due to low absorption. They should be used with caution in
patients currently using other anticholinergic medications but can be used with other medications used to treat functional GI disorders. Key information on hyoscine and dicyclomine are listed in table 10.

Pharmacists may find it advisable to recommend that patients initiate either agent at a low dose, according to the dosages given in table 10, with advice to increase the dose if required.

<p>| <strong>Table 10 – Hyoscine and Dicyclomine Key Information</strong>&lt;sup&gt;12,13,23&lt;/sup&gt; |</p>
<table>
<thead>
<tr>
<th><strong>Product</strong></th>
<th><strong>Dose</strong></th>
<th><strong>Adverse Effects</strong></th>
<th><strong>Notes</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyoscine butylbromide</td>
<td>10-20 mg per day up to a maximum of 60 mg per day (commonly used 1 tablet 3 to 5 times daily) In prolonged illness which requires repeated dosing, one 10-mg tablet 3 to 5 times daily is recommended</td>
<td>Dry mouth, dyshidrosis, visual accommodation disorders, mydriasis, increased intraocular pressure, tachycardia, dyspnea, urinary retention</td>
<td>Contraindicated in patients with myasthenia gravis, megacolon, glaucoma, or obstructive prostatic hypertrophy.</td>
</tr>
<tr>
<td>Dicyclomine hydrochloride</td>
<td>10-20 mg TID-QID PRN</td>
<td>Dry mouth, dizziness, blurred vision, nausea, light-headedness, drowsiness, weakness, nervousness</td>
<td>Avoid in patients with gastrointestinal or urinary obstruction, paralytic ileus and intestinal atony, severe ulcerative colitis, myasthenia gravis, reflux esophagitis, glaucoma, unstable cardiovascular</td>
</tr>
</tbody>
</table>
status in acute haemorrhage.

Caution in patients with prostate enlargement, hiatal hernia with reflux esophagitis, autonomic neuropathy, hepatic or renal disease, hyperthyroidism, hypertension, coronary heart disease, congestive heart failure, cardiac tachyarrhythmia.

Revisit our Patient - Lynn

You discuss with Lynn that analgesics such as acetaminophen could be used for her pain but do not target the cramping and an antispasmodic could reduce cramping and the associated pain. You explain that antispasmodics relax cramping muscles or muscle spasm and can help to reduce the associated pain. She has never tried an antispasmodic before and would like to see if this option will work for her current attack.

You recommend that she look for methods to reduce her current stress level and encourage her to use a food diary to help identify potential triggers of her attacks. Lastly you encourage her to discuss her condition with her family physician to ensure that she is informed about her symptoms and the different treatment options she has tried.
Role of the Pharmacist

Many patients in clinical practice suffer from functional GI disorders. These conditions can cause the patient significant distress and can impair the patient’s daily life. Most guidelines advise clinicians to promote a healthy diet and lifestyle and to direct different pharmacological options at the primary GI symptoms experienced by the patient. Antispasmodics have demonstrated efficacy for both abdominal pain and cramping and addresses the major concern of patients with these symptoms.

As the profession continues to evolve into the management of minor ailments, pharmacists will have to be comfortable assessing patients and selecting optimal treatments for different conditions. The treatment of abdominal pain is a common condition that many patients self-manage with different non-prescription options. By providing education, counselling and the most appropriate pharmacological agent, pharmacists can help to ensure that patients with abdominal pain and cramping are optimally managed.
Key Learning Points

• Functional gastrointestinal disorders such as irritable bowel syndrome are highly prevalent in the Canadian population.
• The exact cause of these gastrointestinal symptoms is poorly understood but is thought to be multifactorial.
• Functional gastrointestinal disorders have a tremendous impact on the patient and can negatively affect his/her health related quality of life (HRQoL).
• Pharmacists should ask the patient their primary concern and direct treatment and education towards this concern.
• Patients with “red-flag” circumstances should be referred to a physician to rule out organic causes of the symptoms.
• Although there is little data to support any specific dietary intervention, patients should be encouraged to eat a balanced diet and to avoid foods which trigger their symptoms.
• Current treatment of functional gastrointestinal disorders is focused on the primary symptom complaint(s) of the patient.
• Antispasmodic therapy is effective and is a recommended treatment option for patients with abdominal pain and cramps.
• Pharmacists will continue to have an ever increasing role in the management of patients with functional GI disorders.
Post Test:
Joan W. is in to see you for a medication review. During the review, she asks if you have any specific recommendations for her irritable bowel syndrome. She mentions that she has tried a variety of different options and the response rates have not been optimal. Through your discussion, you realize her knowledge about this condition is less than optimal and you feel that she would benefit from some education.

1. You start by discussing the pathophysiology of functional gastrointestinal disorders. Which one of the following statements is TRUE?
   a. All patients with functional gastrointestinal disorders have a strong family history of these conditions.
   b. Only patients with functional gastrointestinal disorders have gastrointestinal symptoms induced by psychological stress.
   c. Extrinsic factors such as vision and smell can affect gastrointestinal sensation, motility and secretions.
   d. The majority of patients with IBS develop symptoms after an acute enteric infection.

2. She asks if IBS is common. What is the prevalence of IBS worldwide, according to criteria of the American College of Gastroenterology Task Force on Irritable Bowel Syndrome?
   a. 1-2%
   b. 7-10%
   c. 11-15%
   d. 16-25%

3. You explain that IBS is a functional GI disorder. Which of the following statements is TRUE?
   a. Functional GI disorders are commonly caused by conditions such as a gastric ulcer.
   b. Treatment for functional GI disorders is mainly directed at the symptoms.
   c. Most patients with functional GI disorders can be cured of their condition with proper treatment.
d. All of the above

4. Joan mentions that the symptoms have a significant impact on her life. Which of the following statements is TRUE?
   a. The negative impact of functional gastrointestinal disorders on health-related quality of life tends to be less than other chronic conditions.
   b. Although these conditions can cause significant pain they rarely cause a patient to be less productive at work.
   c. Patients with IBS often worry over when and where the next symptom attack will occur.
   d. Most treatments for functional gastrointestinal disorders are 100% effective for reducing symptoms.

5. You assess Joan for “red-flag” circumstances. Which of the following is NOT a “red-flag” circumstance in a patient presenting with abdominal pain and cramping?
   a. Dysphagia
   b. Hematemesis
   c. Occasional vomiting
   d. Weight loss > 3kg over 6 months

6. You assess Joan’s medications for a possible cause of GI symptoms. Which of the following medications has been linked to abdominal pain?
   a. Dabigatran
   b. Opioids
   c. Amiodarone
   d. All of the above

7. You decide to counsel Lynn regarding functional GI disorders. Which of the following statements is TRUE?
   a. Extensive laboratory testing is recommended in all patients presenting with GI symptoms.
   b. Diet and lifestyle changes do not help to reduce symptoms.
c. All patients with irritable bowel syndrome will respond to a standard regimen of medications.
d. Addressing psychological factors can help to reduce the severity of symptoms.

8. You start discussing the lifestyle management of GI disorders. Which of the following is NOT a common trigger of GI symptoms in patients with IBS?
a. Red meat
b. Citrus fruit
c. Potatoes
d. Cereals

9. Joan mentions that abdominal cramping and pain are her primary concerns with her IBS. You feel she is a good candidate for antispasmodic therapy. Which one of the following statements is FALSE?
a. Antispasmodic therapies are not highly absorbed by the gastrointestinal tract.
b. Antispasmodic therapies are effective at reducing pain and global IBS symptom assessment.
c. These medications are not contraindicated in patients using loperamide therapy.
d. Antispasmodics are associated with significant adverse effects.

10. You discuss the different options with Lynn and you feel that an antispasmodic is a good choice for her. Which of the following statements regarding antispasmodics is TRUE?
a. They are well-tolerated and the risk of anticholinergic side effects is low.
b. They should be used with caution in patients taking tricyclic antidepressants.
c. They have been shown to reduce pain due to intestinal spasms within 30 minutes.
d. All of the above
References:


