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Update on the Management of Chronic Constipation

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INTRODUCTION

Constipation is a common symptom that affects up to 27% of the North American population.¹ Constipation is prevalent in people aged 65 and older, and the rate of constipation in women is twice that of men in all age groups.^{2,3} Constipation has been shown to diminish quality of life and has a substantial direct (i.e., health care utilization) and indirect (i.e., work absenteeism) socioeconomic impact.^{4,5,6} Constipation has many causes and is often a sign of serious undiagnosed diseases. Although constipation is frequently identified as functional or idiopathic, patients with constipation need to be thoroughly assessed and counselled.^{6,7} Constipation can lead to serious complications such as malnutrition, fecal impaction, fecal incontinence, colonic dilation and even perforation of the colon.⁸

DEFINITION

Constipation has different meanings to patients versus physicians. A patient's perception of constipation may include not only the objective

observation of infrequent bowel movements, but also subjective complaints of straining with defecation, incomplete evacuation, abdominal bloating or pain, hard or small stools, or a need for digital manipulation to enable defecation. In recently published expert recommendations, the American College of Gastroenterology Chronic Constipation Task Force characterized chronic constipation as "unsatisfactory defecation that results from infrequent stool, difficult stool passage or both."⁹ In an effort to standardize the definition of chronic constipation for research purposes, the Rome Committees have developed three iterations of consensus definitions. The Rome III criteria for functional bowel disorders are used in research and, to a lesser extent, in clinical practice. Because the definition of constipation can be subjective, this committee has recommended an operational definition of chronic functional constipation in adults (Table 1).¹⁰ These criteria include signs and symptoms that patients frequently describe,

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STATEMENT OF OBJECTIVES

Pharmacists who successfully complete this lesson will be able to:

1. Understand the etiology and pathophysiology of chronic constipation in adults and children.
2. Identify the Rome III criteria in the definition of chronic idiopathic constipation.
3. Understand what is involved in the evaluation of chronic idiopathic constipation.
4. Describe the risks and benefits in the management strategies, both non-pharmacological and pharmacological, for chronic idiopathic constipation.
5. Identify key issues in counseling patients on the safety and effectiveness of over-the-counter (OTC) products and non-pharmacologic approaches for constipation.

INSTRUCTIONS

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TABLE 1: Rome III diagnostic criteria¹⁰

Criteria fulfilled for the last three months, with symptom onset at least six months prior to diagnosis with ≥ 2 of the following symptoms:

- Straining (dyschezia) during $\geq 25\%$ of defecations
- Lumpy or hard stools in $\geq 25\%$ of defecations
- Sensation of incomplete evacuation for $\geq 25\%$ of defecations
- Sensation of anorectal obstruction/blockage for $\geq 25\%$ of defecations
- Manual maneuvers to facilitate $\geq 25\%$ of defecations
- < 3 defecations per week

Loose stools rarely present without the use of laxatives
Insufficient criteria for irritable bowel syndrome

TABLE 2: Secondary causes of constipation¹¹⁻¹⁷

Endocrine: Hypothyroidism, diabetes

Metabolic: Hypercalcemia, hypokalemia

Neurologic: Parkinson's disease, multiple sclerosis, spinal cord lesions, muscular dystrophies, stroke, autonomic neuropathy

Non-Neurologic: Systemic sclerosis, chronic renal failure

Psychological: Depression, dementia, eating disorders

TABLE 3: Drugs associated with constipation¹¹

Cation-containing agents: aluminum, calcium, iron, bismuth, barium

Analgesics

- Nonsteroidal anti-inflammatory drugs
- Opioids and related narcotics

Anticholinergic agents

- Anti-Parkinson's agents
- Antipsychotic and neuroleptic agents
- Antidepressants (e.g., tricyclics and SSRIs)

Anticonvulsants (e.g., phenytoin)

Antihypertensive agents

- Calcium channel antagonists (verapamil>diltiazem>dihydropyridines)
- Central alpha-adrenergic agonists
- Diuretics

Chemotherapeutic agents (e.g., vinca alkaloids)

Resins (e.g., sodium polystyrene sulfates)

such as straining, lumpy or hard stools, incomplete evacuation, anorectal obstruction or blockage and the use of manual maneuvers to facilitate evacuation, as well as infrequency of defecations (i.e., less than three per week).

According to the above definition, constipation associated with irritable bowel syndrome (IBS) should be ruled out.¹⁰ About 10%-20% of the world's adults and adolescents describe symptoms consistent with IBS, with most North American studies reporting a predominance among women. Patients with IBS typically suffer from diarrhea-predominant IBS, constipation-predominant IBS, or mixed IBS with alternating bowel patterns.¹⁰ Expert opinion indicates that symptoms of chronic constipation frequently overlaps with

IBS. IBS is defined as the presence of clinically important abdominal discomfort associated with constipation symptoms; patients with constipation may report minimal bloating or discomfort, thereby creating a spectrum between chronic constipation and IBS.

EPIDEMIOLOGY

It is difficult to estimate the incidence of this common disorder because of the widespread availability of OTC therapies. The overwhelming majority of patients self-medicate when they initially develop symptoms of constipation, making it difficult to track these individuals at the time they initially experience the problem. A survey of Canadians 18 years of age or older, estimated the

prevalence of functional constipation to be 14.9%—according to the Rome criteria.¹¹ Of all the subjects with Rome-defined functional constipation, 26.3% reported using prescribed or OTC medication in the past three months for their constipation.¹¹

RISK FACTORS

In general, constipation demonstrates a progressive increase in prevalence with increasing age, and this increase is particularly acute after the age of 65. Elderly patients are prone to suffer from constipation for a variety of reasons. These include a low activity level, changes in diet, presence of various diseases, use of drugs that cause constipation and low fluid intake.

The prevalence of constipation in cancer patients is up to 78%; the cause is from primary or metastatic bowel tumors and from chronic opioid use.¹²

Constipation affects up to 30% of women in late pregnancy. Causes include the use of calcium and iron supplements, high levels of circulating progesterone, and the effect of the gravid uterus pushing on the colon.¹³

PATHOGENESIS

Constipation is a symptom of many diseases. When constipation is due to another disease, it is referred to as secondary chronic constipation (Table 2).¹⁴⁻²⁰ Use of specific drugs can also lead to secondary chronic constipation (Table 3).¹⁴

When there is no known underlying disorder, chronic constipation is termed primary or idiopathic. Although idiopathic chronic constipation has many potential causes, it is usually classified into three categories based on differences in pathophysiology: *normal-transit constipation*, *dyssynergic defecation* and *slow-transit constipation*.^{21,22}

Normal-transit constipation, or *functional constipation*, is the most common form of idiopathic chronic constipation, with an estimated prevalence of 60%. In patients with normal-transit constipation, the stool passes through the colon at a normal pace and defecation frequency is normal. However, patients perceive difficulty with evacuation or the presence of hard stools.²¹

Dyssynergic defecation affects about 25% of patients with idiopathic constipation and is commonly due to a failure of the pelvic floor or external anal sphincter to relax when one attempts to defecate.²³ This can result from anal pain associated with the passage of hard stool, anal fissure, hemorrhoids, incorrect toilet training or psychosexual troubles.²¹

Slow-transit constipation accounts for about 15% of idiopathic chronic constipation cases and

is characterized by the delayed emptying of the proximal colon with fewer high-amplitude peristaltic contractions.²¹ It can also be associated with the loss of neurons from the enteric nervous system and/or chronic outlet obstruction.²¹

The majority of individuals with constipation do not have an identifiable cause to explain their symptoms. However, it is important to distinguish functional constipation from other disorders that can be associated with altered bowel habits. The patient's medical history and a physical exam frequently provide much of the necessary diagnostic information to determine the cause of constipation. It is particularly important to distinguish recent change in bowel habits (i.e. within the last 3-6 months) from chronic constipation, as the former is more likely to be due to one of the causes in Tables 2 or 3.

EVALUATION

PHYSICAL EXAMINATION

Most chronically constipated individuals do not require an extensive diagnostic evaluation. In order to identify disorders or risk factors that might be associated with constipation, the initial assessment should incorporate a careful review of the patient's medical history and an examination. A recent or persistent change of bowel habits should prompt further evaluation for any of the causes listed in Tables 2-3. Constipation may be secondary to metabolic disorders (e.g., hypothyroidism), myopathies (e.g., amyloidosis), neurological diseases (e.g., Parkinson's disease) or medications (e.g., opiates). Therefore, numerous diagnostic tests such as complete blood count, thyroid function tests, serum calcium and structural tests (see below under diagnostic studies) have been recommended to exclude secondary causes of constipation. Although these tests are recommended, "no data exists to strictly evaluate and define the tests that need to be done."²⁴

Weight loss of greater than 5%, blood in stool, severe and persistent constipation that is unresponsive to treatment, and new onset/worsening in elderly patients constitute "alarm symptoms" which require careful evaluation. Patients with these symptoms must be referred to the physician for thorough evaluation.

Urinary symptoms, including stress incontinence, may indicate pelvic floor weakness. A medication history, diet and any relevant social or psychological problems should always be explored.¹⁴

DIAGNOSTIC STUDIES

Laboratory studies and colorectal imaging are appropriate when constipation is persistent and fails to respond to conservative treatment, or when

a particular disorder is suspected. Flexible sigmoidoscopy and colonoscopy are excellent for identifying obstructive colonic lesions. An alternative examination is the barium enema and flexible sigmoidoscopy, a combination that can demonstrate potentially diagnostic features such as colonic dilatation and strictures.²⁰

If extracolonic and mechanical causes of constipation are excluded by laboratory studies and colorectal imaging, a complete physiologic evaluation may be warranted. Possible tests include ano-rectal manometry, defecography and colonic transit time studies. Anal manometry is performed to assess the condition of the anal sphincter, pelvic floor and associated nerves. Defecography and colonic transit studies are particularly useful in patients with intractable constipation or pelvic floor disorders.²⁵

MANAGEMENT

Treatment should be aimed at relieving constipation safely and effectively, to improve the patient's quality of life. In general, effective treatment of constipation consists of several strategies: (a) non-pharmacological approaches such as diet, exercise, and bowel habits; (b) pharmacological approaches, such as laxatives; and (c) surgery in selected circumstances (will not be discussed in this review).

GOAL OF TREATMENT

The goal for the treatment of constipation should include:

- Improvement of symptoms of constipation such as straining, sensation of incomplete evacuation or obstruction
- Improvement in the consistency of the stools (not hard or lumpy)
- Increasing the frequency of defecation to at least three times per week or more
- Improving the patient's quality of life

Non-Pharmacological Approaches

Non-pharmacological treatment includes educating the patient about the physiologic basis and characteristics of normal bowel patterns, diet, physical activity and concurrent therapy for other conditions that may predispose them to constipation (Table 3).

Patient education includes reassurance and an explanation about normal bowel habits. Ninety-five per cent of the general population has as many as three bowel movements per day or as few as three bowel movements per week.^{26,27} Some patients are able to establish regular bowel routine at the same time each day, such as in the morning when the colonic activity is the highest after breakfast. For other people, bowel pattern varies

significantly.

Increase in caloric intake in patients with low-calorie diets has been shown to improve colonic transit time but does not help pelvic floor dysfunction.¹⁴ Dietary fibre is important for the successful long-term management of constipation. In a study of institutionalized elderly subjects, dietary supplementation with 6-15 g of bran per day resulted in an increase in the number of bowel movements.²⁸ Foods high in fibre, such as wheat bran, fruits (especially blackberries and raspberries) and vegetables (such as beans, lentils, peas and squash) retain water; therefore, in those with high-fibre diets, the stool is softened and fecal bulk is increased.²⁹ The American Dietetic Association recommends a daily fibre intake of 25 to 30 g for adults.

Although there is no conclusive scientific evidence to support a correlation between an increased level of physical activity and improved symptoms of constipation, it is still recommended for these patients. Abdominal and pelvic floor muscle-strengthening exercises can provide the additional strength needed for defecation.¹⁴

When possible, medications that can cause constipation should be discontinued or replaced by others. In the case of patients with chronic pain, narcotic analgesics should be continued at a dosage that controls pain; however, this could necessitate the routine use of stimulant laxatives to prevent impaction. In patients with narcotic-induced constipation who have not passed a stool in more than three days, impaction should be ruled out before recommending pharmacologic treatment.

Pharmacological Approach

For many patients, a regular regimen of laxatives might be necessary. However, caution is advised because the long-term use of laxatives can potentially lead to adverse effects such as malabsorption, dehydration, electrolyte imbalances and fecal incontinence.

There are five basic groups of laxatives: bulk, osmotic, saline, emollient/lubricant and stimulant (Table 4). Few trials have compared the efficacy of the different types of laxatives; however, the data that are available show no statistically significant difference between treatments.³⁰ Therefore, a careful evaluation of the patient's signs and symptoms would help the pharmacist in determining which laxative would be most appropriate to recommend.

BULK-FORMING LAXATIVES

Several OTC fibre supplements (or bulk-forming laxatives) are available. Psyllium, polycarbophil and methylcellulose all increase water content

TABLE 4: Medications recommended for constipation

TYPE	GENERIC NAME	TRADE NAME	DOSAGE	SIDE-EFFECTS	TIME TO ONSET OF ACTION	COMMENTS
Fibre	Bran		1 cup/d	Bloating, flatulence, iron and calcium malabsorption	1–3 days	Increases stool bulk, decreases colonic transit time, increases GI motility. Inappropriate for fluid-restricted patients or patients with dysphagia, esophageal strictures or partial obstruction and/or fecal impaction. Do not take within 2h of other medication or the effect of the other medication may be reduced.
	Psyllium	Metamucil® Prodiem®	1 tbsp daily to t.i.d.	Bloating, flatulence	1–3 days	
Hyperosmolar	Lactulose	Laxilose®	15–30 mL daily to t.i.d.	Sweet tasting, transient abdominal cramps, flatulence	24–48 hours	Nonabsorbable disaccharides metabolized by colonic bacteria into acetic acid. Many patients find sweet taste intolerable.
	Polyethylene Glycol	Colyte® GoLyteLy®	4 L over 6–12 hrs	Nausea, bloating, abdominal cramps and vomiting	0.5–1 hour	Commonly used prior to colonoscopy.
	Glycerin Suppository		1 supp q.d.	Rectal irritation	0.5–1 hour	Evacuation induced by local rectal stimulation.
Stool softener (emollient)	Docusate Sodium	Colace® Soflax®	100 mg b.i.d.	Ineffective for treatment of constipation; may be useful in prevention	12–72 hours	Stimulates cells to secrete water, NaCl into lumen. Evidence poor regarding efficacy of stool softeners; most useful to soften hard stools; no documented laxative action.
	Docusate Calcium	Surfak®	240 mg b.i.d.			
Lubricant	Mineral Oil		15–45 ml daily	Lipid pneumonia, malabsorption of fat-soluble vitamins, dehydration, incontinence	6–8 hours	Stool lubricant. Not recommended for periods greater than one week.
Saline Laxatives	Magnesium	Milk of Magnesia®	15–30 ml daily to t.i.d.	Magnesium toxicity, dehydration, abdominal cramps, incontinence	0.5–3 hours	Fluid osmotically drawn into small bowel lumen. Not recommended for patients with cardiac or renal disease.
	Sodium Phosphate Oral	Fleet Phospho-Soda®	5–15 mL daily; 45 mL for lavage	Hyperphosphatemia		Not recommended for sodium-restricted patients. Often used as a cathartic prior to surgery or GI procedures (45 mL).
	Magnesium Citrate	Citro-Mag®	300 mL for lavage	Hypermagnesia		Often used as a cathartic prior to surgery or GI procedures.
Stimulants	Bisacodyl	Dulcolax®	5–10 mg p.o. daily or	Incontinence, hypokalemia, abdominal cramps	6–12 hours	Electrolyte transport altered by increased intraluminal fluids; myenteric plexus stimulated; motility increased.
			10 mg suppositories 3 times/week– daily	Rectal burning with suppositories	0.5–1 hour	Do not take within one hour of antacids.
	Anthraquinones (senna, cascara)	Senokot®	2–4 tabs p.o. daily to b.i.d.	Malabsorption, abdominal cramps, dehydration, Melanosis coli	6–12 hours	May discolour urine red to pink or brown to black.
Enemas	Mineral Oil Retention	Fleet® Enema Mineral Oil	100–250ml per rectum	Incontinence, mechanical trauma	5–15 min	Stool softened and lubricated.
	Tap Water		500 ml per rectum	Mechanical trauma, fluid overload	5–15 min	Evacuation induced by distended colon; mechanical lavage.
	Phosphate Enema	Fleet®	1 unit per rectum	Accumulated damage to rectal mucosa, hyperphosphatemia, mechanical trauma	5–15 min	Avoid in patients with cardiac disease, renal dysfunction or pre-existing electrolyte abnormalities.
	Soapsuds Enema		1.5 L per rectum	Mucosal irritation, fluid overload	2–15 min	
µ-opioid receptor antagonists	Methylnaltrexone	Relistor®	Dose: weight-based: 38 to <62 kg: 8 mg q2days 62 to 114kg: 12 mg q2days All other weights (i.e., <38 kg or >114 kg): 0.15 mg/kg q2days	Abdominal pain, flatulence, nausea	30 min	Consider discontinuing treatment if no response after 4 doses (1 week). For patients with severe renal impairment (creatinine clearance less than 30 mL/min), the dose should be reduced by one-half.

and bulk volume of the stool to decrease colonic transit time, increase stool weight and improve stool consistency. Each dose of a bulk-forming laxative should be administered with at least 250 mL of water or juice to prevent fecal impaction and/or esophageal obstruction. Therefore, these agents would be inappropriate to use in fluid-restricted patients or patients with dysphagia and esophageal strictures. These supplements are generally well tolerated but may cause some flatulence and bloating at the start of therapy, which can be minimized by starting with a low dose, and increasing it gradually.³¹ It is important that these agents are not taken within two hours of other medications or the effect of the other medication may be reduced. These agents are best suited for patients with normal or slow transit constipation. The onset of action of fibre supplements is approximately one to three days and the usual doses are shown in Table 4.

HYPEROSMOTIC LAXATIVES

Osmotic laxatives include unabsorbed mono and disaccharides such as lactulose and sorbitol. These are poorly absorbed sugars that are hydrolyzed by coliform bacteria to form low-molecular organic acids. These organic acids draw fluid into the lumen and stimulate peristalsis.^{30,31} These agents usually produce soft, formed stool within 24-48 hours, but may also produce abdominal cramping, bloating and flatulence.^{32,33}

Glycerin suppositories can also act osmotically and have a much quicker onset of action of about 30-60 minutes. Glycerin suppositories may, however, cause rectal irritation when used chronically.

Other hyperosmolar agents such as polyethylene glycol (PEG) are commonly used prior to colonoscopy since they will, in most cases, completely empty out the colon. As a gastrointestinal lavage agent, PEG is usually dispensed as a powder (to be reconstituted with water) or the 4L jug as a solution. The recommended dose is 240 mL every 10 minutes and lavage is usually complete after consuming 3-4 litres. These agents, however, can cause abdominal cramping and bloating.

There are five randomized controlled trials comparing PEG (at a smaller dose) to placebo for chronic constipation. The trials used PEG solution at a dose of 17.5 g in 250 mL once to twice daily with improved stool frequency. Although the trials were well done, numbers were small and the incidence of diarrhea ranged from 2-40%.⁹ This dosing strategy is not an approved indication for PEG, however, it may be helpful in the more difficult cases of constipation.

SALINE LAXATIVES

Magnesium-containing products are the most common saline laxatives. Magnesium salts draw fluid osmotically into the lumen of the small bowel and colon, thus inducing wall contractions.³⁴ Magnesium ions are also believed to stimulate the release of cholecystokinin, a hormonal stimulant of intestinal secretion, and of prostaglandins, which are modulators of intestinal motility.³⁴ The onset of action of these agents is approximately 0.5-3 hours. The use of magnesium citrate is generally restricted to bowel cleansing before investigative or surgical procedures. The laxative dose of magnesium citrate for constipation is one-quarter to one-half the evacuant dose. It is important to recognize that these laxatives may lead to electrolyte imbalances and should be avoided in individuals with renal and cardiac impairment.

EMOLLIENT/LUBRICANT LAXATIVES

Emollients, or stool softeners, soften the stool by reducing surface tension, thus permitting penetration of the fecal mass by intestinal fluids. Docusate sodium or docusate calcium have not been shown to provide much benefit, although they may be worth a trial in preventing hard stools from forming.¹⁴ The onset of action of these agents is about 12-72 hours. Their most useful role is when excessive straining is hazardous; for example, in patients with unstable angina or postoperative states. They have no documented laxative effect and should be restricted to patients with mild constipation.

Mineral oil, when taken orally, lubricates the stool; but if aspirated, it can cause lipid pneumonia, which can be fatal.³⁵ In addition, the long-term use of mineral oil is associated with malabsorption of fat-soluble vitamins. In general, this agent should be avoided.

STIMULANT LAXATIVES

Several stimulant laxatives are present in common OTC preparations. These include diphenylmethane derivatives, such as bisacodyl, and anthraquinone derivatives, such as cascara and senna. All of these agents act by altering electrolyte transport in the colon, increasing intraluminal fluids and generating propulsive activity.³³ In order to avoid nocturnal incontinence, bedtime administration is recommended due to the delayed onset of action (6-12 hours). The most common side effects of these medications are cramping, abdominal pain and hypokalemia. The rectal administration of bisacodyl can cause rectal irritation or burning. It is thought that stimulant laxatives can cause "cathartic colon", leading to dependence.³⁶ The pathophysiology of this phenomenon is not proven and remains poorly understood. This eventually leads to a dependence on increasing doses of stimulant medication for

defecation.^{36,37} Bisacodyl effectiveness may decrease if taken at the same time as antacids (e.g., H₂ blockers, calcium carbonate). It is thought that the increase in pH of the gut may affect the enteric coating of the bisacodyl tablets.³⁸ This is a minor interaction, but it is an issue to consider if a patient is not responding to bisacodyl and is using antacids on a regular basis.

ENEMAS

Enemas are indicated in acute constipation, especially in the presence of fecal impaction. A properly administered enema will cleanse the distal colon within an hour. Enemas are used for cleansing the bowel before rectal examination and pre- and post-operatively to relieve fecal impaction. Warm tap water or saline enemas are preferable to soaps, which will likely irritate the colonic mucosa. Hypertonic phosphate enemas are most efficacious, but they can also be irritating. Furthermore, repeated use of phosphate enemas can cause electrolyte imbalances; the ions are potentially absorbed from the rectum, and other ions are lost in the ensuing evacuation. Mineral oil enemas should be used in patients with renal dysfunction since the phosphate enema (without mineral oil) can cause severe and life-threatening hyperphosphatemia.

SUPPOSITORIES

Rectal suppositories are less effective than enemas but are more acceptable to most patients. They can be used for evacuating the distal colon, but they are ineffective if the stool is dry and hard.

SPECIAL CONSIDERATIONS

INFANTS AND CHILDREN

The use of mineral oil, stimulants and enemas are not recommended for infants. Glycerin suppositories can be used for rectal disimpaction and lactulose can be used as stool softeners. In children greater than one year of age, magnesium hydroxide, mineral oil, and lactulose are considered to be safe and effective by the North American Society for Pediatric Gastroenterology and Nutrition. Senna and bisacodyl may be used as rescue medication when other agents have failed. Enemas can also be used for disimpaction in young children.³⁹

Parents and/or child care providers should always double check for the appropriate dosing of laxatives in infants and children.

PREGNANCY

Dietary supplements and bulk laxatives are the agents of choice in pregnant women. Osmotic laxatives and magnesium hydroxide are consid-

ered safe for intermittent use as second-line agents. Stimulant laxatives are reserved for when other agents have failed.⁴⁰

BREASTFEEDING

Cascara, magnesium sulfate and senna are the only laxatives that have been identified by the American Association of Pediatrics as "compatible" with breastfeeding; information on other laxatives in breastfeeding women is not available. Therefore, laxatives that are not absorbed, such as the bulk-forming and osmotic agents, are considered safe and used as first-line therapy.⁴¹

CANCER PATIENTS

Stimulant laxatives are the first choice of therapy in cancer patients, secondary to the fact that in most cases the constipation is secondary to the use of opioids. Bulk forming laxatives should not be used since this can lead to impaction. If the patient has not passed a stool in more than three days, the pharmacist should refer the patient to a physician to rule out impaction.⁴²

OPIOID-INDUCED CONSTIPATION

Opioid-induced constipation is predominantly mediated by gastrointestinal μ -opioid receptors.⁴³ Methylnaltrexone belongs to a new drug class with selective antagonism of the peripheral μ -opioid receptors and might help relieve opioid constipation while maintaining analgesia. In a recently published study,⁴⁴ patients with incurable cancer or other end-stage diseases received analgesia for greater than two weeks (patients received an average dose of 100 mg of morphine) and were randomized to receive subcutaneous methylnaltrexone or placebo. Subcutaneous methylnaltrexone rapidly induced laxation in patients with advanced illness and opioid-induced constipation, and treatment did not appear to affect analgesia or precipitate opioid withdrawal. The most common adverse effects were abdominal pain (28%), flatulence (13%) and nausea (11%).⁴⁴

Methylnaltrexone is currently indicated for the treatment of opioid-induced constipation in patients with advanced illness, receiving palliative care. When response to laxatives has been insufficient, methylnaltrexone should be used as an adjunct therapy to induce a prompt bowel movement.⁴⁵ Methylnaltrexone does not affect the pharmacokinetics of drugs metabolized by cytochrome P450 (CYP) isozymes. The recommended dose of methylnaltrexone is 8 mg for patients weighing 38 to less than 62 kg or 12 mg for patients weighing 62–114 kg, given as subcutaneous injection every other day as needed. Patients whose weight falls outside these ranges should be dosed at 0.15 mg/kg/dose. Consider discon-

tinuing treatment in patients who fail to show an adequate response to methylnaltrexone after four doses (one week).⁴⁵

LONG-TERM USE OF LAXATIVES

Long-term use of stimulant laxatives has traditionally been discouraged based on tests linking long-term use to damage of the enteric nervous system in the myenteric plexus and smooth muscles of the colon. However, even when neurologic damage is present, there is no evidence to suggest that it is due to laxative use; it might be the result of the constipation. Many experts now believe that the risks of long-term stimulant use have been overemphasized and if used no more than three times weekly they are safe and effective.^{14,46}

COMPLICATIONS OF CHRONIC CONSTIPATION

Complications resulting from untreated or chronic constipation include fecal impaction, anal fissures, hemorrhoids and megacolon. More rare complications include intestinal perforation, volvulus, rectal bleeding and stercoral ulceration, which is pressure necrosis of the rectal or sigmoid mucosa due to a fecal mass.¹⁴

APPROACH TO MANAGEMENT

It is important to attain a full medication history from the patient, including laxatives used in the past, duration and frequency of use, and the efficacy of the agent used. This may help in the selection of therapy, education and monitoring for that patient. Fibre, with appropriate hydration, is the cornerstone of prophylaxis for constipation. It is also important for the successful long-term management of constipation in those patients able to drink sufficient fluids, ambulate regularly, and who do not have symptoms of obstruction or a history of megacolon, volvulus or recurrent fecal impaction. However, these agents should be avoided in patients with fluid restrictions such as dialysis patients, and patients with congestive heart failure.

For patients with chronic functional constipation, it is recommended to initiate a trial of fibre supplementation along with physical activity after meals in conjunction with a laxative such as lactulose. The dose should be gradually increased every 3-5 days. If the response is inadequate after a two to four week trial, the medication should be discontinued and treatment with magnesium-containing products should be tried next. If this regimen is still ineffective, then either an enema, a suppository, such as glycerin, or a stimulant laxative should be recommended.³² In some cases, the patient might require both a stimulant and osmotic laxative to prevent and treat constipa-

tion. Fecal impaction should be excluded before proceeding with the use of laxatives, especially in patients who have abdominal distention or who are frail or immobile.

PHARMACIST'S ROLE

Pharmacists play a key role in the management of constipation since most patients are likely to seek advice from their community pharmacist before seeking medical attention from a physician. Therefore, education about the physiologic basis and characteristics of normal bowel patterns, and diet and lifestyle evaluation are the first steps in evaluating the patient's concerns of constipation. It is important that the pharmacist appropriately evaluate the signs and symptoms of constipation to help the patient choose the most appropriate therapy. Patients who require drug therapy should receive advice on the expected onset of action of the laxative, as well as the usual side effects of the medication.

CONCLUSION

Constipation is a common problem and can sometimes have debilitating symptoms. Although usually benign, constipation can have devastating effects on the quality of life of patients. Management of constipation is highly individualized and it must be based on cause and the patient's overall medical condition. Pharmacists play a very important role as caregivers, patient advocates, and educators for patients who are using laxative products purchased at a pharmacy. They should aim to educate their patients about the wide range of normal bowel habits, the benefits of fibre, and the potentially deleterious effects of prolonged use of laxatives.

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QUESTIONS

Answer by return card, fax or online at www.pharmacygateway.ca, CE Online section, "More CCCEP-Approved" area.

1. Constipation is a common disorder that is estimated to be prevalent in approximately ____% of Canadians.
- 10%
 - 15%
 - 25%
 - 35%
2. Studies suggest that constipation is associated with ____.
- diminished health-related quality of life
 - increased health care utilization
 - work absenteeism
 - all of the above
3. Which of the following is not considered a common symptom of chronic constipation?
- straining
 - dysphagia
 - bloating
 - dyschezia
4. The prevalence of functional constipation in patients with idiopathic constipation is ____%.
- 9%
 - 29%
 - 60%
 - 75%
5. Current dietary guidelines recommend the consumption of ____ of fibre per day for adults.
- 20-25 g
 - 25-30 g
 - 30-45 g
 - 45-50 g
6. Oral hyperosmolar agents have an onset of action of ____.
- 2-3 hours
 - 4-8 hours
 - 12-24 hours
 - 1-2 days
7. Which laxative is safe to use in patients with chronic kidney disease?
- senna
 - Fleet enema
 - magnesium citrate
 - sodium phosphate
8. Which signs are considered red flags for the pharmacist to recommend that the patient seek medical attention.
- severe, persistent constipation that is unresponsive to treatment
 - vomiting and weight loss (greater than 5%)
 - blood in stool
 - severe constipation of recent onset/worsening in elderly patients
 - all of the above
9. Which laxative may discolor urine red to pink or brown to black?
- senna
 - docusate sodium
 - mineral oil
 - Milk of Magnesia
10. Which agent should not be taken within one hour of antacids?
- docusate calcium
 - senna
 - bisacodyl tablets
 - Milk of Magnesia

Continued on next page

QUESTIONS *continued...*Answer by return card, fax or online at www.pharmacygateway.ca, CE Online section, "More CCCEP-Approved" area.

- 11. JB is a hemodialysis patient at the local hospital. He has diabetes and is currently taking insulin. He also has well controlled hypertension (currently on a beta blocker, and ACE Inhibitor and calcium channel blocker). He has been complaining of constipation—difficulty passing stools, fewer bowel movements—over the past week. Which would be a reasonable first line treatment for this patient?**
- increased fluid and bran intake
 - lactulose
 - Fleet enema
 - Milk of Magnesia
- 12. Which disease state is not considered a secondary cause of constipation?**
- diabetes
 - Parkinson's disease
 - depression
 - chronic renal failure
 - none of the above
- 13. Which drugs are associated with causing constipation?**
- opioids
 - SSRIs
 - ACE inhibitors
 - a and b
 - all of the above
- 14. Constipation is more common in females compared to males.**
- true
 - false
- 15. What type of advice should be given to patients regarding constipation?**
- a discussion about the normal variation in frequency of bowel movements
 - non-pharmacological methods of treating and preventing constipation
 - expected onset of action of the laxative
 - usual side-effects of medication
 - all of the above
- 16. RB is a 58 year old female who was in your pharmacy two weeks ago asking for advice on constipation. You counseled her on diet and lifestyle management and at that time she bought a bottle of psyllium. She returns to your pharmacy complaining of severe constipation (no bowel movement in more than three days) and that she tried diet and lifestyle management, which did not work. She tried increasing her fluid intake and also tried using psyllium. What do you recommend?**
- Fleet enema
 - lactulose
 - magnesium citrate
 - refer to physician
 - sodium phosphate
- 17. Which is the most effective laxative?**
- bulk
 - saline
 - osmotic
 - stimulant
 - depends on the patient's symptoms
 - all of the above
- 18. Rectal Suppositories are more effective than enemas.**
- true
 - false
- 19. A properly administered enema will cleanse the distal colon within ____ hours.**
- 5–6
 - 3–4
 - 2
 - 1
- 20. Stimulant laxatives are commonly used to treat constipation. When is the best time to administer these agents?**
- morning
 - lunch
 - supper
 - bedtime
 - anytime

CE FACULTY: Update on the Management of Chronic Constipation**AUTHORS**

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REVIEWERS

All lessons are reviewed by pharmacists for accuracy, currency and relevance to current pharmacy practice.

This lesson is valid until December 11, 2011. Information about chronic constipation may change over the course of this time. Readers are responsible for determining the most current aspects of this topic.

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