REVIEW ARTICLE

Current concepts in the management of opioid-induced constipation

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ABSTRACT

Patients with chronic pain on daily opioid therapy are frequently burdened with symptoms of constipation. Opioid-induced constipation (OIC) contributes to an overall negative impact on the quality of life and may result in poor pain management outcomes. Laxative agents are crucial in opioid-related pain management. Following a careful assessment, a stepwise approach to OIC may provide comfort and relief to patients. This article reviews the pathophysiology, assessment, and pharmacological treatment of OIC. Novel approaches for OIC such as the peripheral opioid receptor antagonists and selective serotonin antagonists are also discussed.

INTRODUCTION

Opioid analgesics are the mainstay of cancer-related pain management and are also important in the treatment of chronic nonmalignant pain. Isolated as the active ingredient in opium in the early nineteenth century by Sertürner, morphine was first used as an analgesic agent for postoperative pain and an adjunct to general anesthesia.[1] Nearly 200 years later, the World Health Organization recognized opioids in their three-step ladder approach for effective cancer pain relief.[2] Despite the analgesic benefits of opioids, the side effects of sedation, confusion, nausea, constipation, etc, cause a significant burden on patients. Most side effects resolve over time, but constipation tends to persist throughout treatment.[3]

Constipation has been suggested to affect more than 40 percent of patients on chronic opioid therapy.[3] In fact, 81 percent of patients on daily opioid therapy reported constipation as the most prevalent side effect in the PROBE1 study.[3] Patients in the same study rated opioid-induced constipation (OIC) as the most severe side effect (48 percent), contributing to an overall negative impact on the quality of life.[3] As a result, some patients may discontinue or reduce their opioid dose because of its side effects, receiving suboptimal pain management. Uncontrolled constipation may lead to hemorrhoids, tenesmus, rectal pain, fecal impaction, pseudo-obstruction of the bowel, and the extremes of potential perforated viscus and even death.[4,5]

Having adequate knowledge of the recognition and treatment of OIC is essential for the opioid prescriber. The following review examines the pathophysiology, assessment, and pharmacological treatment of OIC. Novel approaches for OIC such as the peripheral opioid receptor antagonists and selective serotonin antagonists are also discussed.

PATHOPHYSIOLOGY

The control of motor and mucosal function of the gastrointestinal (GI) tract is primarily provided by the enteric nervous system (ENS), which is a complex array of neurons and ganglia organized around the myenteric and submucosal layers of the GI wall.[6,7] Intrinsic primary afferent neurons (IPANs) originate in the submucosal and myenteric plexuses and project into the mucosa, submucosa, and smooth muscle of the gut; their stimulation leads to simultaneous fluid and electrolyte secretion and smooth muscle contraction.[6,7] Mechanical (stretch or tension) and chemical stimulation of IPANs produces a series of reflexive actions facilitating smooth

muscle contraction via polarized circuits of excitatory and inhibitory motor neurons. Temporally and spatially arranged, these concerted actions of upstream longitudinal smooth muscle and downstream circular muscle contraction lead to propulsion of the food bolus through the GI tract. Intestinal pacemaker cells known as interstitial cells of Cajal modulate propulsion with "slow wave" propagated contractions.[7]

The autonomic nervous system also mediates GI function through extrinsic primary afferent neurons (EPANs) sensing heat, pain, and luminal volume. The parasympathetic arm, composed of EPANs of the vagus and pelvic nerves, modulates GI motility through vasodilatation and contractility. Conversely, thoracolumbar spinal nerves of the sympathetic system reduce GI blood flow, contractility, and motility.[7,8]

Additionally, many neurotransmitters are present in the ENS such as acetylcholine, vasoactive intestinal peptide (VIP), 5-hydroxytryptamine (5-HT), substance P, nitric oxide (NO), and endogenous opioid peptides (ie, enkephalins, endorphins, and dynorphins).[6,9] For instance, acetylcholine plays a pivotal role in stimulating GI contractility, whereas VIP participates in the modulation of smooth muscle relaxation and intestinal secretions.[7]

As exogenous opioids exert their effects on central nervous system (CNS) pain pathways, they interact with mu-, kappa-, and delta-opioid receptors in the GI tract, resulting in the undesirable effect of constipation. Investigations have demonstrated that opioids, both endogenous and exogenous, participate in the relaxation of longitudinal smooth muscle while stimulating circular muscle motility via pathways that include VIP and NO, thereby, decreasing peristalsis.[10,11] Additionally, opioids delay gastric emptying, inhibit bowel secretory activity, promote luminal fluid absorption, and reduce sphincter function.[6]

Opioids demonstrate unique pharmacodynamics with associated receptor-binding profiles.[12] As a result, the degree of analgesia and adverse effects varies between opioids.[13] In a retrospective study comparing three long-acting opioids, patients receiving transdermal fentanyl developed less constipation than those receiving either controlled-release oxycodone or morphine.[14] However, a recent randomized, controlled trial found no benefit when comparing transdermal fentanyl, transdermal buprenorphine, and oral sustained-release hydromorphone with respect to constipation.[15] Methadone also appears to be less constipating when compared with morphine and hydromorphone.[16] In contrast, altering the route of morphine administration does not affect the rates of constipation.[13] Yet, higher opioid dose and persistent daily use of opioids are associated with an increased incidence of constipation.[17]

ASSESSMENT

Surveys have demonstrated a significant variability among healthcare providers and patients in defining constipation. Common terms for constipation used by patients are straining to have a bowel movement, hard stools, and infrequent stools.[18] Healthcare providers generally prefer to describe constipation based on stool frequency, less than three bowel movements weekly.[19] Outlined in the most recently revised Rome III Criteria in 2006 and summarized in Table 1, an expert panel formulated a consensus definition for constipation.[20]

Constipation affects between 2 and 28 percent of the general population.[19] Factors such as female gender, age >65 years, nonwhite ethnicity, and low socioeconomic status have been correlated to an increased risk for constipation.[19] Constipation may be classified as either primary or secondary in nature. Primary constipation is commonly a result of idiopathic, functional disorders of the colon and rectum categorized as normal-transit, slow-transit, and defecatory subtypes.[21,22] The more prevalent secondary constipation may be a product of multiple etiologies including adverse effects of medications (eg, opioids, anticholinergic agents, and calcium channel blockers), metabolic derangements, neurologic disorders, and mechanical obstruction, which are further outlined in Table 2.[19] Patients may experience constipation as a result of multiple, concurrent etiologies, and it may be difficult to isolate a single entity. Opioids can further aggravate constipation in patients with chronic constipation from other etiologies.

The initial evaluation should begin with a problem-focused history noting the duration of symptoms, stool frequency, and potential associated symptoms such as abdominal pain or distention. Furthermore, the character and quality of bowel movements should be elicited with identification of warning symptoms: hematochezia, change in stool caliber, weight loss, anemia, and family history of colorectal cancer or inflammatory bowel disease.[23] It is essential to review potential etiologies of

Table 1. Rome III criteria for functional constipation*
Rome III criteria
Loose stools are rarely present without laxative use and insufficient criteria for IBS.
Two or more of the following (fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis):
1. Fewer than three bowel movements per week
2. Straining in >1 of 4 defecations
3. Lumpy or hard stools in >1 of 4 defecations
4. Sensation of incomplete evacuation in >1 of 4 defecations
5. Sensation of anorectal obstruction or blockade in >1 of 4 defecations
6. Manual maneuvers (eg, digital evacuation and support of the pelvic floor) to facilitate a bowel movement in >1 of 4 defecations
*Source: Ref. 20.

secondary constipation as detailed in Table 2, including opioid use. Also, history of depression, inadequate dietary (fiber and fluid) intake, immobility, and laxative use should be assessed.[23]

Digital rectal examination should be performed as part of the recommended physical examination to evaluate for potential fecal impaction, stricture, rectal prolapse, or mass.[23] Additionally, it is recommended to observe for evidence of perianal fissures or external hemorrhoids. A careful abdominal examination should evaluate for distention, palpable hard stool, and tenderness.[19] Serum chemistries (ie, thyroid-stimulating hormone, serum calcium, etc) can be obtained if electrolyte imbalance or thyroid disease is suspected. Abdominal radiographs can be obtained if there is a suspicion of bowel obstruction or fecal impaction. Colonoscopy is indicated if malignancy is being considered.[23]

Several tools have been developed for assessing constipation-related symptoms. They include the Gastrointestinal Symptom Rating Scale (GSRS), the Patient Assessment of Constipation Symptom (PAC-SYM) questionnaire, the Elderly Bowel Symptom Questionnaire (EBSQ), and the Bowel Function Index (BFI).[5] The GSRS is a 15-item survey designed to assess both upper and lower GI symptoms as they relate to irritable bowel syndrome and peptic ulcer disease.[24] Specifically designed for the geriatric population, the EBSQ is a 56-item questionnaire assessing overall GI functions including general health habits and medication history (ie, laxative therapy).[25] The BFI is a 3-item validated tool evaluating perception of constipation among chronic pain patients.[26] The PAC-SYM questionnaire is a simple, 12-item survey encompassing a triad of abdominal, rectal, and stool symptoms, as represented in Table 3. Symptom severity is rated on a 5-point Likert Scale (0 = absence of symptom to 4 = very severe). As the PAC-SYM assessment is succinct, it was studied in patients with chronic pain on opioid therapy and found to be both reliable and valid in assessing the presence and severity of OIC.[27]

MANAGEMENT

OIC is a form of secondary constipation that is chronic in nature and relative to the length of time opioids are administered. As a result, diligent observation and effective management of constipation are vital skills that healthcare providers must acquire to assist their patients on daily opioid therapy.[4]

Presently, OIC lacks specific guidelines for its management; therefore, the general approach to chronic constipation is often followed, emphasizing maintenance of a regular bowel movement every 1 to 2 days.[2] Recommendations begin with nonpharmacological management: increasing dietary fiber and fluid intake as well as activity level.[23] These interventions are usually insufficient to prevent or treat OIC. Therefore, a standard laxative regimen is recommended to all patients on chronic opioid therapy. Table 4 provides the laxative agents commonly used in the management of OIC. Initial therapy with a stimulant agent such as a sennoside is appropriate,

Table 2. Etiology of secondary constipation*
Medications
Calcium channel blockers (eg, verapamil)
μ-Opioid agonists (eg, loperamide, morphine, and fentanyl)
Anticholinergic agents (eg, antispasmodics, antipsychotics, tricyclic antidepressants, and antiparkinsonian drugs)
Anticonvulsants (eg, phenobarbital, carbamazepine, and phenytoin)
Antacids
5-Hydroxytryptamine$_3$ antagonists (eg, alosetron)
Iron supplements
Nonsteroidal anti-inflammatory agents (eg, ibuprofen)
Diuretics (eg, furosemide)
Antineoplastic agents (eg, vinca derivatives)
Metabolic and endocrinological disorders
Diabetes mellitus
Hypothyroidism
Hyperthyroidism
Hypokalemia
Hypercalcemia
Pregnancy
Pheochromocytoma
Panhypopituitarism
Porphyria
Heavy metal poisoning (eg, lead, mercury, and arsenic)
Neurologic and myopathic disorders
Progressive systemic sclerosis
Amyloidosis
Dermatomyositis
Multiple sclerosis
Parkinsonism
Spinal cord injury
Autonomic neuropathy
Chagas' disease
Intestinal pseudo-obstruction
Stroke
Shy-Drager syndrome
Mechanical obstruction
Colon cancer
Rectocele or sigmoidocele
Stricture
Extrinsic compression
Anal stenosis
*Source: Ref. 19(p225).

titrating upward as needed.[2] Addition of a detergent laxative like docusate sodium may be beneficial for selective patients with symptoms of hard, dry stools. If a stimulant laxative is ineffective despite upward titration, then coadministration of an osmotic laxative should be initiated. Rectal laxative agents including suppositories or enemas are indicated if fecal impaction is present.[2] Alternative recommendations include careful consideration toward opioid dose reduction or switching to an alternative opioid. Currently, opioid receptor antagonists such as alvimopan and methylnaltrexone have select criteria for use; they may be appropriate for consideration in refractory OIC as rescue therapy.[9]

Bulk-forming laxatives

Bulk-forming laxatives are derived from either natural plant polysaccharides (eg, psyllium and methylcellulose) or synthetic agents (eg, calcium polycarbophil), which pass undigested in the GI tract. They exert their effect by absorbing water, increasing fecal mass, and stool frequency. The most common adverse effects include abdominal distention and flatulence. Adequate water intake is necessary when using these agents. Bulk-forming agents are not recommended for patients unable to meet adequate daily fluid intake such as those with advanced illness and poor functional status for concerns regarding risk of worsening of constipation and fecal impaction.[28] It is widely believed that these agents alone are not sufficient to treat OIC due to lack of bowel stimulatory effect.

Detergent laxatives

Detergent laxatives such as docusate act as surfactants, reducing surface tension and producing softened, lubricated stools.[9] The use of docusate may be tailored to constipated patients experiencing symptoms of hard, dry stools in addition to increased fluid intake and an additional laxative agent.[28] Docusate has been approved by the Food and Drug Administration (FDA) for the relief of occasional constipation. The role of detergent laxatives in OIC has not been fully established. A recent study reviewed the efficacy of docusate in combination with a sennoside-based bowel protocol in patients with cancer. This study concluded that docusate offered no benefit in alleviating constipation or reducing burdensome abdominal cramps.[29]

Table 3. PAC-SYM questionnaire*	
How severe have each of these symptoms been in the last 2 weeks?	
Abdominal symptoms	Discomfort in your stomach
	Pain in your stomach
	Bloating in your stomach
	Stomach cramps
Rectal symptoms	Painful bowel movements
	Rectal burning during or after a bowel movement
	Rectal bleeding or tearing during or after a bowel movement
Stool symptoms	Incomplete bowel movement, like you did not finish
	Bowel movements that were too hard
	Bowel movements that were too small
	Straining or squeezing to try to pass bowel movements
	Feeling like you had to pass a bowel movement but you could not, "false alarm"
*Source: Ref. 27.	

Stimulant laxatives

Stimulant laxatives offered in the United States include the sennosides and bisacodyl that belong to the broader anthracene and diphenol groups, respectively. Stimulants reduce sodium and water reabsorption as well as promote ionic transport of sodium, calcium, and chloride into the lumen. Additionally, sennosides exert their effects on the myenteric plexus with consequent smooth muscle contraction, directly promoting peristalsis.[28] Sennosides were evaluated with and without coadministration of docusate in a hospital-based bowel protocol of oncology patients, 80 percent receiving oral opioids. Sennosides alone induced laxation more effectively than in combination with docusate.[29] Abdominal cramps are a common adverse effect of stimulant laxatives. Chronic use of sennosides may lead to hyperpigmented mucosa known as melanosis coli, a benign and reversible condition, as well as hypokalemia and refractory constipation.[9]

Osmotic laxatives

Various osmotic laxatives are available for the relief of constipation. These hyperosmolar solutions establish a gradient between the intestinal lumen and bowel wall that leads to water retention in the lumen. The subclass of salts includes the magnesium salts (eg, magnesium citrate and magnesium hydroxide) and sodium salts (eg, sodium biphosphate). They are safe and effective in relieving the symptoms of constipation. With a propensity for electrolyte abnormalities and fluid overload, hyperosmolar salts should be avoided in patients with congestive heart failure and renal insufficiency.[9]

Saccharines are the second subclass of osmotic laxatives, with lactulose and sorbitol being the most commonly used. They are metabolized by bacterial flora in the GI tract into short-chain fatty acids (eg, lactate, acetate, propionate, and butyrate). The resulting acidic environment stimulates smooth muscle peristalsis, accelerating colon transit time, whereas the increased hyperosmolarity contributes to intracolonic water retention.[30] The metabolic process also produces significant amounts of gas leading to the common side effects of flatulence, abdominal distention, and cramps.[28]

Polyethylene glycol (PEG) 3350 is of the macrogol subclass of hyperosmolar agents. Following oral administration, this electrolyte solution retains its original character without metabolic breakdown,

Table 4. Laxatives commonly used in the management of opioid-induced constipation.[4,9,22]			
Laxative agent	**Dose/route**	**Onset, h**	**Comments**
Bulk-forming laxatives			
Psyllium (Metamucil)	3.4 g (powder) po daily in 8 oz of water or juice	12-72	May lead to impaction in patients unable to meet proper fluid intake and activity level.
Methylcellulose (Citrucel)	2 g (powder) po daily in 8 oz of water or juice		
Calcium polycarbophil (Fibercon)	625 mg caplets, take two caplets po daily		
Detergent laxatives			
Docusate sodium (Colace)	100 mg tablets, titrate up to two tablets (200 mg) po daily	24-48	Select use for patients with hard, dry stools in concert with another laxative.
Stimulant laxatives			
Senna (Senokot)	8.6 mg tablets, titrate up to eight tablets (68.8 mg) po daily	8-14	May produce abdominal cramps.
Bisacodyl (Dulcolax)	5 mg tablets, titrate up to six tablets (30 mg) po daily; 10 mg suppository pr daily prn		
Osmotic laxatives			
Salt osmotics		12-48	
Magnesium citrate (Evac-Q-Mag)	150-300 mL po daily as needed		May produce diarrhea.
Magnesium hydroxide (Milk of Magnesia)	15-30 mL po daily to bid		Salt osmotics may produce electrolyte disturbances.
Sodium biphosphate (Phospho-Soda)	10-20 mL diluted in 12 oz of water as needed		
Saccharine osmotics			
Lactulose (Chronulac)	15-30 mL po daily to bid		Saccharine osmotics may produce bloating and cramps.
Sorbitol (Cystosol)	15-30 mL po daily to bid		
Glycerin suppository	1 suppository pr prn		
Macrogol osmotics			
Polyethylene glycol 3350 (MiraLax)	17 g (powder) po daily in 8 oz of water or juice		Macrogol osmotics may produce diarrhea.
Peripheral μ-opioid antagonists			
Alvimopan (Entereg)	0.5 mg po bid	1-4	Select use for patients with refractory constipation
Methylnaltrexone (Relistor)	5-10 mg subcutaneous qod		

and thus, intraluminal pH is preserved and gas byproducts are not formed.[9] PEG 3350 is an effective laxative for patients with secondary constipation related to medications (ie, opioids).[31] In critically ill patients receiving opiates, PEG 3350 was more effective than lactulose in laxation induction.[32]

Rectal laxatives

Although seldom required for patients maintaining a routine bowel regimen, alternative therapies for patients with OIC refractory to oral agents include suppositories and enemas.[2,9,28] Prior to administration, careful evaluation must be undertaken to exclude potential fecal impaction.[2,28] Suppositories such as bisacodyl and glycerol are safe and effective preparations when combined with an oral laxative in the management of constipation; bisacodyl stimulates contractility from the transverse colon to rectum and glycerol acts as a softener.[28] Enemas of varying types have also been used with success for relief of fecal impaction.[2,28] Saline and oil retention enemas are preferred over phosphate and soapsuds enemas as they cause less mucosal irritation.[33]

Selective chloride channel activators

Lubiprostone was approved by the FDA in 2006 for chronic functional constipation in adults.[34] It acts as a selective chloride channel stimulator in the apical membrane of the GI epithelium, increasing intestinal chloride secretion and thereby fluid secretion in the gut. This facilitates bowel transit and increases stool frequency.[8] The common side effects of lubiprostone are dose dependent and include nausea, headache, and diarrhea.[35] The role of lubiprostone in the management of OIC has not yet been established.

Opioid antagonists

A novel approach to OIC refractory to routine laxative therapy targets peripheral opioid receptors of the ENS, thereby reversing constipating effects of opioids.[9]

Centrally acting opioid antagonists, such as naloxone, are potential agents to reverse OIC; however, there is concern for systemic absorption leading to antagonism of CNS effects, which include symptoms of withdrawal and pain crisis in patients on chronic opioid therapy. Previous studies have revealed the efficacy of naloxone in inducing laxation but with great variability in reversal of CNS effects.[9] However, a recent randomized, double-blind, placebo-controlled trial of 202 patients with chronic pain on stable doses of oral sustained-release oxycodone found that coadministration of oral naloxone at a 2:1 ratio (oxycodone/naloxone) was effective in improving laxation without reversing analgesia or producing symptoms of withdrawal.[36] Concurrently, an investigation of a combined prolonged-release oxycodone and naloxone formulation demonstrated improvement in pain scores and laxation when compared with prolonged-release oxycodone alone.[37] With respect to parenteral opiate use, oral naloxone was simultaneously administered to intensive care unit patients receiving sedation/analgesia with continuous fentanyl infusion to assess a therapeutic approach to OIC; the mean fentanyl dose, sedation scores, pain scores, and vital signs remained unchanged while successfully inducing laxation.[38]

Fashioned from alkyl derivatives of their centrally acting counterparts, the peripherally acting μ-opioid receptor (PAM-OR) antagonists include alvimopan and methylnaltrexone. They do not cross the blood-brain barrier, thus avoiding unwanted reversal of opioid CNS effects.[9]

Alvimopan is an oral PAM-OR antagonist that is presently FDA approved for laxation induction in patients with postoperative ileus following bowel resection.[9] Recommended dosing for patients undergoing bowel resection is 12 mg given 30 minutes to 5 hours prior to surgery and subsequent dosing of 12 mg twice a day (bid) postoperatively for a maximum of 15 doses.[39] Further investigations exploring its utility in managing refractory OIC in patients on chronic opioid therapy have been promising. A large randomized, double-blinded, placebo-controlled study of 522 patients with chronic non-cancer pain on daily morphine and criteria for OIC noted statistically and clinically significant improvements in spontaneous laxation, bowel symptoms, and quality of life. Alvimopan produced a mean spontaneous bowel movement frequency of 3.4 to 4.3 per week when compared with 1.7 per week in the placebo group. Dose finding during the study reported 0.5 mg bid of alvimopan as safe and effective. Common side effects of abdominal pain and diarrhea were reported as mild and comparable with placebo.[40] In a study investigating long-term safety alvimopan has been associated with an

increased risk of cardiovascular events including myocardial infarction. It is therefore recommended for short-term use only.[39]

The PAM-OR antagonist, methylnaltrexone, is administered via the subcutaneous route, and it received the FDA's approval in 2008 for OIC refractory to laxative therapy in patients with advanced illness receiving palliative care.[9] Recent randomized, controlled trials have demonstrated its efficacy in patients with terminal illness on daily opioid therapy with OIC refractory to routine laxative therapy.[41,42] Additionally, a dose of ≥5 mg (0.15 mg/kg) subcutaneous every other day provided safe and prompt laxation, often within 4 hours of administration. It is recommended by the manufacturer that if there is no response with respect to laxation induction after three doses, it should be discontinued. Adverse events included abdominal pain, flatulence, and vomiting; these were rated as mild to moderate and were comparable with placebo.[42]

A systematic review and meta-analysis of opioid antagonists conducted in 2008 examined both central and peripheral opioid antagonists when compared with routine laxative therapy. The search involved MEDLINE, EMBASE, and Cochrane databases, yielding 22 randomized, controlled trials. Both methylnaltrexone and alvimopan provided effective reversal of OIC symptoms, and alvimopan additionally contributed to safe relief of postoperative ileus. Central acting opioid antagonists, such as naloxone, had insufficient data to provide recommendations on their safety and efficacy related to OIC.[43] Continued research is warranted to assess long-term safety and efficacy of opioid antagonists, as well as their appropriate role in therapy (ie, preventive versus rescue therapy).[9,43]

Selective serotonin agonists

Serotonin (5-HT) receptors of the ENS are involved in the mediation of reflexes controlling GI motility, secretion, and perception of visceral pain.[44] Previous research demonstrated that stimulation of 5-HT4 receptors improves symptoms of chronic constipation.[44] Tegaserod, a partial 5-HT4 receptor agonist, was approved by the FDA for chronic constipation and constipation-related irritable bowel syndrome, but removed from the market in 2007 because of an increased incidence of cardiovascular side effects including myocardial infarction, stroke, and unstable angina.

Prucalopride, a highly selective 5-HT4 receptor agonist with strong enterokinetic activity, is being investigated for the management of severe constipation. A phase II, double-blinded, placebo-controlled trial of 196 patients with OIC demonstrated that prucalopride significantly improved patient-rated severity of constipation and effectiveness of treatment versus placebo.[45]

Ghrelin receptor agonists

The peptide hormone ghrelin, primarily secreted by the stomach in anticipation of a meal, has an important effect on energy metabolism and GI motility. It induces hunger contractions in the fasting state and acts to stimulate gastric emptying postprandially.[46] The use of Ghrelin receptor agonists is being investigated for the treatment of GI motility disorders. A recent experimental study in mice demonstrated the effects of oral Ghrelin receptor agonists on stimulation of upper GI motility and normalization of GI motility in opioid-induced dysmotility.[47]

SUMMARY

Constipation is a clinically significant problem that negatively impacts the quality of life of patients on chronic opioid therapy. Having adequate knowledge of the recognition and treatment of this condition is an essential skill for the opioid prescriber. A thorough medical history, physical examination, and identification of contributing etiologic factors are important elements of patient assessment. The routine administration of laxatives is always necessary. The use of stimulant agents (with or without docusate) followed by the coadministration of osmotic agents is widely recommended. Peripherally acting opioid antagonists are a targeted approach to manage OIC. These agents may be appropriate for cases refractory to a standard laxative regimen. Emerging therapies such as the serotonin agonists and the ghrelin receptor agonists will add to the therapeutic armamentarium for this condition.

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