



Paul Gauguin. *Breton Landscape - Fields by the Sea (Le Pouldu)*, 1889. Oil on canvas.

The advent of constipation in a patient with cancer is a common and significant event that impairs quality of life.

Assessing and Managing Opiate-Induced Constipation in Adults With Cancer

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Introduction

Constipation, a common problem among persons receiving opiates for treatment of pain, is often underassessed and undertreated by both physicians and nurses, leaving many patients to grapple with this problem alone.¹⁻⁵ Because patients often do not understand the mechanism that is causing the constipation, self-treatment may not be effective. Narcotic-induced constipation is a problem caused by the treatment provided by healthcare professionals and thus is a problem that should be addressed by them.

Prevalence

Limited studies of prevalence of constipation have been conducted on healthy persons and on persons with cancer. The prevalence in the general population is believed to be approximately 2%. Among the elderly in long-term care facilities, the prevalence of constipation ranges between 40% and 50%. Although the overall prevalence of consti-

pation among persons with cancer is unknown, some studies have investigated patients receiving hospice care and who are receiving active curative treatment. The range of prevalence in hospitalized patients receiving cancer treatment varies from 70% to 100%.²⁻⁴ Studies of patients with advanced cancer who are receiving hospice care show that the prevalence of constipation ranges between 23% and 84%.^{2,3,5-9} A series of studies⁹⁻¹¹ conducted in a large Florida hospice evaluated opiate-induced constipation and found that 40% to 64% of hospice patients with cancer have been found to have constipation. However, the number was lower when the data were obtained from a chart audit (40%)⁹ and higher when the researchers prospectively interviewed patients about their symptoms (63% to 64%).^{10,11} Walsh⁶ found constipation to be the most common side effect of morphine among 688 hospice patients, with a prevalence of 48%. The finding of constipation is relevant because studies have shown that it is negatively related to overall quality of life ($r = -.38, P < .001$).¹²

Defining Constipation

A significant problem in assessing constipation has been the variety of definitions used by patients and healthcare providers. Some patients believe they are constipated if they do not have a bowel movement every day. Other patients expect to have only 3 bowel movements per

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week, so if they have 3, they believe they are not constipated — and in both cases these patients may (or may not) be correct. One of the largest studies of bowel function ever conducted was reported in 1965.¹³ Of the 1,055 persons included in the study, 99% reported bowel movements in the range of 3 per day to 3 per week. Any number outside of this range was considered by these researchers to be abnormal. However, with such a wide range of normal, it is easy to see how misleading it would be to characterize a person as constipated solely on the basis of the daily number of bowel movements.

Others have attempted to define constipation by looking at more than just frequency of bowel movements. Table 1 lists 22 defining characteristics of constipation resulting from a study of 300 healthy adults by McShane and McLane in 1985.¹⁴ The Constipation Assessment Scale, first published in 1989, presents 8 characteristic symptoms and allows the patient to self-report on a valid and reliable scale.⁴ These symptoms are also presented in Table 1.

An acceptable definition of constipation for clinical practice would be the following: *a decrease in the frequency of passage of formed stools and characterized by stools that are hard and difficult to pass.* This definition suggests four characteristics that may be presented in the acronym DISH: difficult to pass, infrequent compared to normal, smaller than normal, and hard.

Etiologies

Although opiates are a common cause of constipation in persons with cancer, there are many other potential causes as well. Constipation may be classified into one of three types: primary, secondary, or iatrogenically induced (Table 2).¹⁵ Opiate-induced constipation falls under the third category.

Primary or simple constipation results from extrinsic factors that affect bowel function, such as inadequate dietary fiber, inadequate fluid intake, decreased physical activity, and inadequate time or privacy for defecation.¹⁵ Any or all of these factors may lead to decreased bowel motility and increased transit time for fecal material, which causes fluid to be reabsorbed and stools to be dry and hard. Patients with advanced cancer are already at risk for many of these factors and therefore are candidates for problems with constipation even before narcotics are administered.

Secondary constipation results from pathologic changes. Examples that may be seen in persons with cancer include partial intestinal obstruction, spinal cord compression at a level that affects bowel function, and metabolic effects of hypercalcemia and hypokalemia.¹⁵ Diabetes can cause neuropathy that results in constipation.¹⁷ Patients with cancer may have other problems as well; concomitant conditions that may occur in persons with cancer and contribute to constipation are listed in Table 2.¹⁸

Iatrogenically induced constipation is caused by administration of pharmacologic agents. Although narcotics are chief offenders in the cancer setting, a host of other drugs also may be implicated.¹⁵ Examples of these are listed in Table 2.

Effects of Opiates

Opiates affect bowel function in a variety of ways. First, opiates delay gastric emptying by producing gastroparesis secondary to spasm in the antropyloric region. This action appears to stem from the central nervous system and be dopamine mediated. Opiates also delay stool transit through the small bowel, thus increasing transit time.¹⁹ This effect is greatest in the jejunum and is related to an

increase in nonpropulsive contractions. Colonic transit time also is increased. The basis for this physiologic response to opiates was studied in the 1940s, before the days of the modern institutional review board and protection of human subjects. Researchers administered varying doses of morphine and hydromorphone to healthy male volunteers and studied the responses of the ileum and colon. The drugs significantly increased the amount of time needed for fecal material to move through by interfering with normal tone and contractility. While *segmental* motor tone and contractility were increased, *longitudinal propulsive peristalsis* was decreased.

Table 1. — Defining Characteristics of Constipation From Two Prospective Studies

McShane and McLane (1985) ¹⁴		McMillan and Williams (1989) ⁴
Abdominal distention	Inability to pass stool	Abdominal distention/bloating
Abdominal growling	Increased abdominal pressure	Change in gas passed
Abdominal mass	Indigestion	Less frequent bowel movements
Abdominal pain	Oozing liquid stool	Oozing liquid stool
Blood with stool	Rectal fullness	Rectal fullness or pressure
Change in abdominal size	Rectal mass	Rectal pain at bowel movement
Change in flatus	Rectal pain with stool	Smaller volume of stool
Change in frequency	Rectal pressure	Urge but inability to pass stool
Decreased appetite	Smaller volume of stool	
Dry, hard stool	Straining at stool	
Headache	Swollen rectal veins	

Adapted from McMillan SC. Assessing and managing narcotic-induced constipation in adults with cancer. *Cancer Control*. 1999;6(2):198-204.

Churning motions occurred in some cases but without adequate propulsive activity. The change in peristalsis began to occur 5 to 25 minutes after the administration of the opiate, depending on the amount of the dose.²⁰

Opiates also may cause the patient to experience a decreased urge to defecate. The constipating effect of morphine was confirmed in 1989 by a group of patients receiving at least 30 mg of morphine per day; evaluation showed that 100% of these patients were constipated.⁴ In summary, opiates decrease peristalsis and increase stool transit time, drying out the stool and causing constipation. The effect is immediate and is dose related. Treatment of narcotic-induced constipation should be based on an understanding of this physiologic response to opiates.

Assessing Constipation

Because managing constipation requires a complete understanding of the origins of the problem, complete assessment is critical. However, most patients are attuned to self-management of constipation and may not think to mention it to a healthcare provider. Thus, patients at risk must be asked specifically about their bowel function. If a patient is receiving opiate analgesics, he or she will have a problem with constipation. However, there may be other complicating factors that need attention.²¹

In spite of an obvious need to assess patients for constipation, research suggests that this assessment is

often overlooked. In a sample of 90 veteran inpatients with cancer pain, 72 (80%) had symptoms of constipation. However, evidence of any assessment for constipation was found in only 10 (14%) of these charts.²² A group of 44 patients with cancer who were in either an intensive care unit (ICU) or a surgical unit in a medical center were assessed for constipation. In the ICU, 70% reported symptoms of constipation to researchers, but no charts had any documentation about this problem. Among the 24 surgical patients, 17 (71%) had symptoms of constipation, but it was reported in only four of the charts.³ Constipation will continue to be poorly managed until healthcare professionals begin to take its assessment and documentation seriously.

History

On the patient's history, the essential information to obtain includes: (1) daily activity level, including participation in regular exercise, (2) food preferences and dislikes, (3) amount of fiber and fluid intake, (4) ability to chew and swallow, (5) current medications, including over-the-counter drugs (Table 2), (6) underlying medical problems (Table 2), and (7) recent changes in stool or bowel habits, eg, pain with stool, change in pattern or size of stool, diarrhea alternating with constipation accompanied by abdominal pain or discomfort, bright red blood or black tarry appearance of stools (ask for time of last bowel movement). In addition, a change in

mental status with confusion and increased agitation, elevated temperature, incontinence, and unexplained falls may sometimes be the only presenting symptoms of constipation in the elderly; therefore, maintain a high index of suspicion.

Physical Examination

A complete physical examination is performed when constipation is suspected. This examination includes oral, abdominal, and anorectal examinations.²¹

Oral Examination: Dentition should be checked to ensure adequacy of chewing, and the oral cavity should be examined for lesions or tumors that could interfere with chewing, tasting, or swallowing. Not uncommonly, ill-fitting dentures make chewing so difficult or uncomfortable that the elderly patient takes the path of least resistance and eats only soft foods that require no chewing, such as custards, but also contain no fiber and thus contribute to primary constipation.

Table 2. — Etiologies of Constipation

Primary	Secondary	Iatrogenically Induced
Due to:	Due to:	Due to drugs including:
Lack of fiber, exercise, fluid, or time and privacy for defecating	Parkinson's disease*	Antacids
	Intestinal obstruction	Anticholinergics
	Volvulus	Antihistamines
	Adhesions	Barium sulfate
	Stroke	Calcium channel blockers
	Hypercalcemia	Drugs for Parkinsonism*
	Hypokalemia	5HT3 antagonists
	Diverticulosis	Ganglionic blockers
	Spinal cord compression	Hypotensives
	Rectocele	Iron supplements
	Multiple sclerosis	Monoamine oxidase inhibitors
	Diabetes	Opiates
	Hypothyroidism	Psychotherapeutic drugs
	Chronic renal failure	Tricyclic antidepressants
		Vinca alkaloids**
* Controversy remains about whether constipation is caused by drugs for Parkinsonism, the disease itself, or both.		
** In one study, ¹⁶ 100% of patients receiving vinblastine, a vinca alkaloid, became constipated and one had paralytic ileus.		
Adapted from McMillan SC. Assessing and managing narcotic-induced constipation in adults with cancer. <i>Cancer Control</i> . 1999;6(2):198-204.		

Abdominal Examination: The patient should empty the bladder before the examination begins. *Inspection:* Begin by looking for bloating, distention, or bulges. When distention is noted, consider the possibility of obesity, fluid, flatus, or tumor. If these are ruled out, then the possibility of feces must be considered. *Auscultation:* Listen for hyperactive bowel sounds or absent bowel sounds. If no bowel sounds are readily heard, listen continuously for five minutes before establishing the absence of bowel sounds. Absent bowel sounds may indicate paralytic ileus, whereas increased bowel sounds may indicate impending diarrhea. *Percussion:* Gas in the colon produces tympany. Dullness is present over intestinal fluid and feces. *Palpation:* Light palpation can detect abdominal tenderness and muscular resistance associated with chronic constipation. When abdominal pain occurs on coughing or with light palpation and/or when rebound tenderness is detected, peritoneal inflammation is suspected. Deep palpation may be used to detect abdominal masses including a sausage-like mass of fecal material in the left colon. A feces-filled colon is suggestive of constipation.

Anorectal Examination: A digital rectal examination may reveal a stool-filled rectum, suggesting constipation. Endoscopic examination of the anus and rectum can reveal not only an impacted fecal mass, but also fissures, hemorrhoids, ulceration, or rectal ulcers. Look also for the presence of blood or for alterations of the vascular pattern that might indicate ischemic proctitis.

Follow-up Evaluation

A history and physical examination conducted by a physician, nurse practitioner, or physician's assistant are necessary for the initial diagnosis of constipation. However, ongoing assessment also is necessary to monitor the effect of treatment. For this purpose, the Constipation Assessment Scale (CAS) was developed. It is an easy-to-read, 8-item, self-report tool that is clinically useful in a variety of settings.^{2-4,23} The CAS is valid and reliable, and it takes approximately two minutes to complete.⁴ The 8 items focus on the symptoms of constipation that are most universal (Table 1). The patient is asked to rate each symptom as "no problem" (0), "some problem" (1), or "severe prob-

lem" (2). Item scores are added together for a total that may range from 0 (no constipation) to 16 (worst possible constipation). Readability is at approximately the sixth-grade level, so most patients can read and understand the CAS. A series of these CAS assessments completed over a period of days or weeks provides an ongoing standardized assessment of the cancer patient's constipation.

Preventing Constipation

The approach to preventing constipation should be related to the patient's risk factors. Assessment of these factors should place the patient's risk into one of the three categories described earlier: primary, secondary, or iatrogenically induced constipation.

Primary Constipation

If the patient is at risk for primary constipation because of eating habits or lack of exercise or other lifestyle factors, it is useful to attempt lifestyle changes. However, in debilitated or anorectic cancer patients, increasing fiber and exercise may not be feasible alternatives. For patients who are well enough to cooperate, prevention strategies for primary constipation include the following.^{24,25}

Increased dietary fiber: Fiber holds water in the stool, making it heavier and faster. It also may increase flatus.

Increased fluid intake: Water has to be available to be absorbed. The thirst mechanism may be diminished in elderly patients, and patients experiencing nausea may be unwilling to drink. However, they should keep up fluid intake because fiber without fluid can become hard and difficult to pass.

Adequate exercise: Activity helps the bowels to stay active.

Adequate time and privacy for toileting: Some patients are unable to defecate in a public bathroom and will wait until they get home. Likewise, hospitalized patients and residents in nursing homes who need help to toilet may find it difficult to defecate. Holding the stool in the large bowel allows the water to be reabsorbed, which causes the stool to be hard and difficult to pass. Patients should be taught to plan a time for good bowel hygiene.

Karam and Nies²⁶ reported use of a bowel management regimen for the elderly that included all of the required elements: fluids, exercises, fiber, and a regular toileting time. The program was implemented at three levels — mild, moderate, and aggressive.

The mild program included a minimum of 1,500 mL of fluid per day, abdominal and pelvic exercises, 1 oz of fiber supplement daily (Table 3), 5 to 15 minutes on the commode after each meal, and ambulation of at least 50 feet twice per day. These same elements were included in the moderate and aggressive programs, but the amount of

Table 3. — Recipe for Fiber Supplement

Ingredient	Amount
All-bran cereal	2 cups
Applesauce	2 cups
Prune juice	1 cup
Mix well and refrigerate.	
From McMillan SC. Assessing and managing narcotic-induced constipation in adults with cancer. <i>Cancer Control</i> . 1999;6(2):198-204.	

fiber supplement was increased to 2 oz and 3 oz per day, respectively. As a result of this protocol, laxative use was markedly decreased and spontaneous bowel movements significantly increased. This appears to be an effective prevention protocol in otherwise healthy elderly adults.

Secondary Constipation

Secondary constipation may not be as amenable to prevention as primary constipation. Because it is caused by concurrent diseases, there may be little available in the way of prevention.²⁷ The prevention protocol recommended for primary prevention may be effective in some cases, but in others, it may be necessary to treat the underlying disease or begin a constipation treatment program.

Iatrogenically Induced Constipation

Unfortunately, many of the treatments given to patients can cause constipation, and polypharmacy is a particular problem among elderly patients.²⁸ For example, one specialist may prescribe a calcium channel blocker and another may prescribe an antidepressant. Then cancer treatments are added, and another specialist may prescribe one of the vinca alkaloids and an opiate for pain. As drugs are added, the risk of constipation mounts.

When patients come into a cancer setting, the nurse may list current medications, but how is that list used? When taking the drug history, one should look for drugs that may cause constipation. If a patient reports taking one or more of these drugs, a careful assessment for constipation must be conducted. In a few cases, it may be possible to substitute a less constipating drug. However, this will not be possible in most cases, and ongoing management of constipation will become necessary. While it may be tempting to withhold opiates to avoid constipation, this leads to impaired quality of life; a better approach is to give the narcotic analgesic to manage the pain and then prevent or treat the resulting constipation appropriately.

Managing Opiate-Induced Constipation

The treatment of opiate-induced constipation should include, to whatever degree possible, the use of prevention strategies to avoid primary constipation. However, this alone will be insufficient for patients receiving opiates. Other strategies involve the use of various pharmacologic agents, given both orally and rectally, and enemas. The choice of strategy depends on the underlying cause of the constipation and its severity.

Several types of pharmacologic agents are available for treating constipation, including osmotic laxatives, emollient or lubricant cathartics, bulk cathartics, and stimulant cathartics.^{18,21}

Osmotic Laxatives

Two commonly used osmotic laxatives are the disaccharides and the saline cathartics. Disaccharides exert an osmotic effect because they are not absorbed or metabolized in the small bowel. This increases bulk via fermentation in the bowel. Unfortunately, the disaccharides may have the side effect of cramps, abdominal distention, and flatulence, which can be uncomfortable for the patient. In addition, disaccharides are usually in a liquid form and may not be palatable to patients. Examples are lactulose and sorbitol.^{18,21,29} Polyethylene glycol (PEG) without electrolytes is more concentrated than the PEG-electrolyte solutions that are used for bowel cleansing and may be better tolerated than lactulose or sorbitol.³⁰ Saline cathartics employ osmotic forces to pull fluid into the bowel to increase the weight of the stool and soften it. An example is Milk of Magnesia.^{18,21}

Emollient or Lubricant Cathartics

Emollient or lubricant cathartics soften stools. An example of this is docusate sodium (marketed as Surfak).^{18,21} Some older patients may have developed a habit of taking mineral oil as a lubricant, but this has a tendency to wash out fat-soluble vitamins. If the patient persists in using mineral oil, he or she should be instructed to avoid taking it at or near mealtimes. Glycerin suppositories also are a type of lubricant.

Bulk Cathartics

Bulk cathartics increase mass and soften stools. Several over-the-counter bulk cathartics are available. An example is psyllium,²⁴ marketed as Metamucil.

Stimulant Cathartics

Stimulant cathartics promote intestinal motility, which is the action that opiates suppress. These are available for both oral and rectal administration. Examples include the senna-based products such as Senokot and the stimulant bisacodyl marketed as Dulcolax. These can cause some cramping and may be unacceptable to patients for that reason.^{18,21} This effect may be diminished by spreading the dose out over the day, perhaps giving small doses with each meal and a slightly larger dose at bedtime. In addition, it should be noted that the cause of the narcotic-induced constipation, the analgesic, also should decrease the impact of cramping in this population of patients, thereby making it somewhat less problematic.

A comparative study of the efficacy of lactulose and senna was conducted using terminal cancer patients (n = 91).³¹ Both laxatives were found to be equally effective in treating narcotic-induced constipation, but senna was recommended because of its lower cost compared with lactulose.

Prostaglandins/Prokinetic Drugs

Prostaglandins work by changing water and electrolyte absorption in the intestines. It also is believed that the laxative effect may be due to the motor effect of prostaglandins, but this is not yet clear. Researchers found that misoprostol, marketed as Cytotec, increased the weight and frequency of stools and shortened colonic transit time in patients with severe chronic constipation.³² Cisapride, an agent that stimulates the upper gastrointestinal tract, is useful in patients with spinal cord injury or Parkinson's disease.²⁷ Colchicine, used to treat gouty arthritis, is useful in treatment of chronic constipation.³⁵ No studies on the effectiveness of these drugs for opioid-induced constipation have been reported.

Naloxone

Orally administered naloxone is an opioid-antagonist that has the ability to antagonize the gastrointestinal effects of opioids. For this reason, it has been studied as a treatment for opioid-induced constipation. In low and slowly escalating doses, naloxone has been shown to have a laxative effect. However, adverse reactions including withdrawal and return of pain have been demonstrated at varying dose levels. Thus naloxone is not recommended for routine use and its use should be avoided in outpatients.³⁴⁻³⁶

Peripheral Opioid Receptor Antagonists

Methylnaltrexone is an investigational laxative that affects the peripheral opioid receptor sites. It reverses the peripheral effects of opioids without affecting analgesia or precipitating symptoms of withdrawal.³⁷ This drug has been effective with refractory opioid-induced constipation, providing results within 4 hours,³⁷ but it is not commercially available.

Combination Agents

Some of these pharmacologic agents are available in combinations. For example, senna, a stimulant, is combined with docusate sodium, a stool softener, and sold as Senokot-S. This particular combination is recommended for narcotic-induced constipation because it helps to overcome the specific problems caused by narcotics. Because opiates are known to decrease longitudinal propulsive contractions that help to move stool downward and because they also allow stool to remain in the colon where it dries out and becomes hard, this combination seems ideal. The mechanism of action of senna is stimulation of longitudinal peristalsis (the action that opiates interfere with), and docusate sodium helps to soften stools that have become dry and hard.²¹ The effect of opiates on bowel function is so consistent that some experts

recommend administering senna and docusate sodium on a scheduled basis rather than when necessary.³⁸ An individualized program that includes careful follow-up evaluation should be developed for each patient.

Enemas

Although both nurses and patients dislike them, enemas sometimes are unavoidable. If the patient has a fecal impaction, an enema may be the only way to break up hardened fecal matter and wash it out. However, once the impaction has been removed, enemas should be used sparingly since they tend to wash out the normal mucus in the colon that provides lubrication for stools. Therefore, enemas should be considered an extreme measure rather than part of routine treatment.¹⁸⁻²¹

Conclusions

Constipation is common in patients with cancer because of their many risk factors, and in a cancer patient receiving opiates, constipation is almost guaranteed. Unfortunately, this potentially serious problem is often overlooked and under-managed. Although constipation may seem like a minor complication when compared to a life-threatening disease such as cancer, it can become a major detriment to quality of life if it is not well managed.

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