

Cancer Constipation

Clinical summary of the ONS Guidelines™ for opioid-induced and non-opioid-related cancer constipation

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Constipation is a prevalent and distressing symptom affecting people with cancer. It may be a chronic condition, or it may be caused by the effects of the disease, its treatment, or the side effects of symptom management, including the use of opioids. These evidence-based guidelines can assist clinicians in the decision-making process, guiding patients to effective interventions to decrease the incidence and severity of constipation.

THIS DOCUMENT ACTS AS THE CLINICAL SUMMARY component of the ONS Guidelines™ for the management of opioid-induced and non-opioid-related constipation in adult patients with cancer (Rogers et al., 2020) and the systematic review for the synthesis of evidence on the topic (Ginex et al., 2020). The ONS Guidelines for management of opioid-induced and non-opioid-related cancer constipation have been developed by a panel of oncology healthcare providers after rigorous systematic review of high-quality randomized clinical trials designed to establish the evidence-based efficacy of prevention of and interventions to manage constipation in adults with cancer. Sources of evidence have been divided into pharmacologic and non-pharmacologic interventions (such as acupuncture or lifestyle education). The GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) approach was used to assess the certainty of the evidence and make the constipation management recommendations presented in this clinical summary.

Guideline Questions and Target Audience

What is the evidence regarding lifestyle, pharmacologic, and nonpharmacologic approaches that can be used to manage opioid-induced and non-opioid-related constipation? Where are the gaps in the evidence regarding constipation in cancer care? This guideline is intended for a target audience of clinicians caring for patients with cancer who experience constipation, as well as policymakers, patients, and caregivers.

How the Guideline Was Developed

This guideline was developed by an interprofessional panel of healthcare providers, including a gastroenterologist, a dietitian, nurses, a methods expert, and patient representation. The panel prioritized clinical questions related to the management of constipation in patients with cancer and patient-important outcomes identified as critical for decision making. A systematic review and meta-analysis of the literature was conducted to inform the clinical questions. The GRADE approach was used to assess the certainty of the evidence and provide a foundation for recommendations (Guyatt et al., 2011).

KEYWORDS

constipation; opioid-induced constipation; acupuncture; evidence-based guidelines

Why the Guideline Matters

For patients with cancer, constipation can be a common but distressing symptom. McMillan et al. (2013) found that 43% to 58% of patients with cancer experienced constipation. Multiple factors lead to this high risk. Opioids prescribed for pain and symptom management are a common cause. Constipation is associated with select medications prescribed in cancer treatment, such as vinca alkaloids, and those prescribed to control side effects, as seen with select antiemetics. Tumor or disease directly affecting the gastrointestinal tract may lead to constipation. Patients may have preexisting or chronic constipation or comorbidities, and treatment may result in constipation. In addition, factors such as dehydration, inactivity, or poor fiber intake may contribute to constipation in patients with cancer.

An individual's experience with constipation may range from a mild annoyance to a life-threatening impaction. Cost estimates for management of severe constipation range from \$500 to more than \$2,300 per person per month (Hjalte et al, 2010; Sommers et al., 2015). Assessing those at risk for constipation, taking preventive measures, or treating the symptom early will improve the patient's experience while decreasing healthcare costs.

Clinical Practice Recommendations

Assessment of Constipation

Constipation is most often assessed through patient interview. Healthcare providers can help patients build awareness of their normal pattern of elimination, including frequency, time of day, and stool characteristics (e.g., color, consistency, odor). Healthcare providers should instruct patients to report significant changes in their normal patterns, as well as any associated symptoms (e.g., abdominal pain, cramping, gas, nausea, vomiting, bleeding, rectal pressure) (Bohnenkamp & LeBaron, 2010). Standard assessment tools are available for constipation and are used in research studies on constipation (Wickham, 2016).

Prevention of Constipation

The ONS Guidelines panel recommends lifestyle education for all individuals at risk for constipation (Rogers et al., 2020). Nurses should review the treatments or medications placing patients at higher risk for constipation and discuss preventive steps to follow. It is important to include a discussion of mobility and explore methods to increase activity. Encourage a diet high in fiber and hydration with at least two liters of caffeine-free fluids daily (Bohnenkamp & LeBaron, 2010; Rogers et al., 2020). Some individuals may benefit from consultation with a dietitian.

Interventions for Opioid-Induced Constipation

The ONS Guidelines panel suggests initiation of a bowel regimen in addition to lifestyle education for the prevention and treatment of opioid-induced constipation in adults (Rogers et al., 2020). The type of bowel regimen is at the discretion of the

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healthcare team, but an initial treatment with senna, bisacodyl, or another stimulant laxative is commonly included, with a stool softener to be added if needed (Wickham, 2017). Some patients may prefer to forgo prophylaxis with a bowel regimen because of pill burden, cost, or other personal or treatment factors.

For adults experiencing opioid-induced constipation, the ONS Guidelines panel recommends initial treatment with osmotic (e.g., polyethylene glycol [PEG], magnesium citrate) or stimulant (e.g., senna, bisacodyl) laxatives in addition to lifestyle education (Rogers et al., 2020). Research on specific bowel regimens is not available, so the regimen is at the discretion of the healthcare team. One example in the literature suggests initial treatment with senna, and then adding lactulose or PEG if no bowel movement occurs after 24–48 hours (Wickham, 2017).

For persistent opioid-induced constipation that has not responded to a bowel regimen, the ONS Guidelines panel suggests treatment with a peripherally acting mu-opioid receptor antagonist (PAMORA) (i.e., methylnaltrexone, naldemedine, or naloxegol) in addition to the existing bowel regimen. For those unable to take other forms of PAMORAs, subcutaneous methylnaltrexone may present an effective option (Rogers et al., 2020).

Interventions for Non–Opioid-Related Constipation

Constipation can occur during and after cancer treatment. The ONS Guidelines panel considered non–opioid-related constipation to be from any cause other than opioids, such as medications (e.g., antiemetics), decreased oral intake, or changes in activity levels. In adult patients with cancer who have non–opioid-related constipation, treatment with osmotic or stimulant laxatives in addition to lifestyle education is recommended (Rogers et al., 2020). The healthcare team should work with the patient to determine a bowel regimen that meets their individual needs.

Interventions Without Sufficient Evidence

In adult patients with cancer who have opioid-induced constipation, the use of prucalopride, linaclotide, and lubiprostone are recommended by the ONS Guidelines panel only in the context

TABLE 1.
SUMMARY OF RECOMMENDATIONS: ONS GUIDELINES™ FOR OPIOID-INDUCED AND NON-OPIOID-RELATED CANCER CONSTIPATION

RECOMMENDATION	STRENGTH OF RECOMMENDATION	CERTAINTY OF EVIDENCE
Opioid-induced constipation		
The ONS Guidelines panel recommends that, before starting an opioid regimen, patients with cancer have a clear understanding of constipation prophylaxis lifestyle education of increased fiber, water intake, and exercise.	Good practice statement	–
Among adult patients with cancer who are receiving opioids, the ONS Guidelines panel suggests either prophylactic bowel regimen with laxatives and lifestyle education or lifestyle education alone for prevention of constipation. Remarks: Patients who place a higher value on avoidance of constipation may prefer to start on a prophylactic regimen; however, patients who place a higher value on avoiding undue costs, taking pills, or undue harms (diarrhea) may prefer to not start on a bowel regimen prophylactically.	Conditional	Low
Among adult patients with cancer, the ONS Guidelines panel recommends osmotic or stimulant laxatives and lifestyle education rather than lifestyle education alone for treatment of opioid-induced constipation.	Strong	Moderate
Among adult patients with cancer, the ONS Guidelines panel suggests osmotic PEG and lifestyle education rather than lifestyle education alone for opioid-induced constipation.	Conditional	Low
Opioid-induced constipation; have not responded to a bowel regimen		
Among adult patients with cancer who have opioid-induced constipation and have not responded to a bowel regimen, the ONS Guidelines panel suggests methylnaltrexone and a bowel regimen rather than a bowel regimen alone for treatment. Remarks: Subcutaneous methylnaltrexone may present an additional option for patients who are unable to take other forms of PAMORAs.	Conditional	Very low
Among adult patients with cancer who have opioid-induced constipation, the ONS Guidelines panel recommends naldemedine and a bowel regimen rather than a bowel regimen alone for treatment.	Strong	Moderate
Among adult patients with cancer, the ONS Guidelines panel suggests naloxegol and a bowel regimen rather than a bowel regimen alone for opioid-induced constipation.	Conditional	Very low
Among adult patients with cancer, the ONS Guidelines panel recommends prucalopride for treatment of opioid-induced constipation only in the context of a clinical trial.	No recommendation; knowledge gap	–
Among adult patients with cancer, the ONS Guidelines panel recommends lubiprostone for opioid-induced constipation only in the context of a clinical trial.	No recommendation; knowledge gap	–
Among adult patients with cancer, the ONS Guidelines panel recommends linaclotide for opioid-induced constipation only in the context of a clinical trial.	No recommendation; knowledge gap	–
Non-opioid-related constipation in patients with cancer		
Among adult patients with cancer, the ONS Guidelines panel suggests osmotic or stimulant laxatives and lifestyle education over lifestyle education alone for constipation. Remarks: Patients with a higher tolerance of constipation symptoms or duration or who place a greater value on avoiding laxatives may not wish to use osmotic or stimulant laxatives.	Conditional	Moderate
Among adult patients with cancer, the ONS Guidelines panel recommends the use of acupuncture for constipation only in the context of a clinical trial.	No recommendation; knowledge gap	–
Among adult patients with cancer, the ONS Guidelines panel recommends the use of electroacupuncture for constipation only in the context of a clinical trial.	No recommendation; knowledge gap	–
ONS—Oncology Nursing Society; PAMORA—peripherally acting mu-opioid receptor antagonist; PEG—polyethylene glycol Note. PAMORAs should only be considered after a patient has not responded to a bowel regimen.		

of a clinical trial (Rogers et al., 2020). These medications have not been widely studied in the population of patients with cancer to support a recommendation.

There is insufficient evidence to support the use of acupuncture or electroacupuncture combined with lifestyle education for non-opioid-related constipation, and these treatments should be reserved for use within clinical trials (Rogers et al., 2020). Refer to Table 1 for a summary of the guideline recommendations.

Implications for Nursing

Nurses can play a key role in the prevention and management of constipation in adult patients with cancer. After assessment of patients at risk, nurses can incorporate preventive education and lifestyle initiatives to minimize this symptom. Prompt treatment of constipation will help to improve patient comfort and outcomes. Nurses can teach patients and caregivers when to notify the healthcare team if symptoms are not alleviated.

Conclusion

A number of factors place patients with cancer at high risk for constipation. It may be a side effect of their disease or treatment or experienced as a chronic condition. This clinical summary provides evidence-based strategies for prevention and management of this distressing symptom.

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IMPLICATIONS FOR PRACTICE

- Control constipation using these evidence-based guidelines that have been developed to guide clinicians to effective measures.
- Provide lifestyle education regarding constipation prevention and treatment to adult patients with cancer at risk for or experiencing constipation.
- Recommend a bowel regimen for prophylaxis and treatment of constipation.

REFERENCES

- Bohnenkamp, S., & LeBaron, V.T. (2010). Management of constipation in patients with cancer. *Journal of the Advanced Practitioner in Oncology*, 1(3), 211–217. <https://doi.org/10.6004/jadpro.2010.1.3.7>
- Ginex, P.K., Hanson, B.J., Lefebvre, K.B., Lin, Y., Moriarty, K.A., Maloney, C., . . . Morgan, R.L. (2020). Management of opioid-induced and non-opioid-related constipation in patients with cancer: Systematic review and meta-analysis. *Oncology Nursing Forum*, 47(6), E211–E224. <https://doi.org/10.1188/20.ONF.E211-E224>
- Guyatt, G.H., Oxman, A.D., Akl, E.A., Kunz, R., Vist, G., Brozek, J., . . . deBeer, H. (2011). GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *Journal of Clinical Epidemiology*, 64(4), 383–394. <https://doi.org/10.1016/j.jclinepi.2010.04.026>
- Hjalte, F., Berggren, A.C., Bergendahl, H., & Hjortsberg, C. (2010). The direct and indirect costs of opioid-induced constipation. *Journal of Pain and Symptom Management*, 40(5), 696–703. <https://doi.org/10.1016/j.jpainsymman.2010.02.019>
- McMillan, S.C., Toftagen, C., Small, B., Karver, S., & Craig, D. (2013). Trajectory of medication-induced constipation in patients with cancer. *Oncology Nursing Forum*, 40(3), E92–E100. <https://doi.org/10.1188/13.ONF.E92-E100>
- Rogers, B., Ginex, P., Anbari, A., Hanson, B., LeFebvre, K.B., Lopez, R., . . . Morgan, R.L. (2020). ONS Guidelines™ for opioid-induced and non-opioid-related cancer constipation. *Oncology Nursing Forum*, 47(6), 671–691. <https://doi.org/10.1188/20.ONF.671-691>
- Sommers, T., Corban, C., Sengupta, N., Jones, M., Cheng, V., Bollom, A., . . . Lembo, A. (2015). Emergency department burden of constipation in the United States from 2006 to 2011. *American Journal of Gastroenterology*, 110(4), 572–579. <https://doi.org/10.1038/ajg.2015.64>
- Wickham, R.J. (2016). Assessment of constipation in patients with cancer. *Journal of the Advanced Practitioner in Oncology*, 7(4), 457–462. <https://doi.org/10.6004/jadpro.2016.7.4.8>
- Wickham, R.J. (2017). Managing constipation in adults with cancer. *Journal of the Advanced Practitioner in Oncology*, 8(2), 149–161. <https://doi.org/10.6004/jadpro.2017.8.2.3>