

Selected Readings Focusing on Constipation in Cancer Patients

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Mancini I, Bruera E. Constipation in advanced cancer patients. *Support Care Cancer*. 1998;6(4):356-364.

Published 6 years ago, this comprehensive article provides a clear outline for assessing and managing patients with advanced cancer and constipation, especially those related to opioid therapy. The authors called for randomized clinical trials between different laxatives and/or prokinetic agents in cancer patients and validation of different clinical assessment tools for constipation. Unfortunately, little progress has occurred in either of these areas. There is still a large void in the type of information needed to institute true evidence-based prophylaxis and management guidelines.

Hajek P, Gillison F, McRobbie H. Stopping smoking can cause constipation. *Addiction*. 2003;98(11):1563-1567.

Many cancers are caused by smoking, and many patients with cancer smoke. Constipation is noted occasionally as a possible tobacco withdrawal symptom, but no systematic data have been published on this issue. Smokers' clinic patients provided ratings of their level of constipation on three occasions prior to their quit date, and then weekly after they stopped smoking. All of the 1,067 participants maintained at least 1 week of continuous abstinence and provided usable data. The three precessation ratings of constipation were stable. After cessation of smoking, the ratings increased significantly. In 514 patients who maintained continuous abstinence for 4 weeks and provided complete data, constipation peaked at 2 weeks but remained elevated over the whole period. The net proportion of patients affected was 17%, including 9% who were symptom-free at baseline and became very or extremely constipated. In patients using nicotine replacement, the increase in constipation, although significant, was less than in patients on bupropion. Clinicians treating smokers need to be aware of a possibility that 1 in 6 quitters develops constipation and that the problem can be severe in about 1 in 11. Descriptions of tobacco withdrawal syndrome should include constipation.

McMillan SC, Moody LE. Hospice patient and caregiver congruence in reporting patients' symptom intensity. *Cancer Nurs*. 2003;26(2):113-118.

The surprising result from this evaluation of symptom intensity in patients with advanced cancer in hospice

home care was that there was significant overestimation of the severity of pain, dyspnea, and constipation by family caregivers compared with that reported by the patients themselves. Since we often must depend on family caregivers for symptom assessment, health professionals need to give the family caregivers the tools and training to optimize their assessment capabilities and skills. Development and utilization of a generally accepted simple scale for constipation would assist this endeavor.

Robinson CB, Fritch M, Hullett L, et al. Development of a protocol to prevent opioid-induced constipation in patients with cancer: a research utilization project. *Clin J Oncol Nurs*. 2000;4(2):79-84.

Opioids are the major class of analgesics used in the management of moderate to severe cancer pain, and constipation is a common side effect of opioid administration. Through the efforts of a nursing research utilization committee, a protocol to prevent opioid-induced constipation in patients with cancer was developed and implemented. The algorithm includes cancer patients beginning opioid pain medication and those who are already taking opioids who are constipated.

Smith S. Evidence-based management of constipation in the oncology patient. *Eur J Oncol Nurs*. 2001;5(1):18-25.

Constipation is suffered by over 50% of cancer patients and is regarded as one of the most distressing symptoms causing both physical and emotional distress. Their study led to the development of evidence-based drug guidelines to be used in the prevention of constipation and acute/chronic constipation to ensure that patients receive the best treatment possible. Not truly evidenced-based because of the lack of pertinent data, the guidelines were based on a survey (30% return) of UK Cancer Centers and the local institutions' policies. The guidelines include both acute and chronic constipation, but many of the drugs mentioned are those used in the UK rather than in the United States.

Yuan C. Clinical status of methylnaltrexone, a new agent to prevent and manage opioid-induced side effects. *J Support Oncol*. 2004;2(2):111-122.

Significant progress has been made over the past several decades in understanding the mechanisms of action

of opioid compounds; however, these advances have yielded few new treatments for the bowel dysfunction caused by opioids. Previously available opioid receptor blockers such as naloxone block both the beneficial pain relief of opioids and their side effects. Methylnaltrexone, however, does not cross the human blood-brain barrier and thus has the potential of blocking the undesired effects of opioids (peripheral receptors) while sparing analgesia (CNS receptors). This article reviews encouraging data from IV, SC, and oral administration in healthy subjects and in chronic opioid users. Transient abdominal cramping and flatulence were the most common adverse effects. Large-scale clinical trials are in progress.

Bennett M, Cresswell H. Factors influencing constipation in advanced cancer patients: a prospective study of opioid dose, dantron dose and physical functioning. *Palliat Med.* 2003;17:418-422.

This study highlights the importance of opioid therapy to bowel functioning in patients with advanced cancer, but it suggests little relationship between opioid dose and bowel score. The authors emphasize that patients may be no more constipated using a strong opioid than using a weak opioid. Incidentally, dantron is an over-the-counter stimulant laxative (anthraquinone) in the same class as senna and cascara. It was taken off the market in the United States in 1999 because of carcinogenicity at high doses in animals. No human cancers occurred.

Radbruch L, Sabatowski R, Loick G, et al. Constipation and the use of laxatives: a comparison between transdermal fentanyl and oral morphine. *Palliat Med.* 2000;14(2):111-119.

This was a study of constipation and the use of laxatives in patients with chronic cancer pain who were treated with two different analgesic regimens. Transdermal fentanyl was associated with a significantly lower use of laxatives compared to oral morphine. The difference in the degree of constipation between the two analgesic regimens should be confirmed in a randomized double-blind study that takes into account both constipation and use of laxatives.

Cleveland MV, Flavin DP, Ruben RA, et al. New polyethylene glycol laxative for treatment of constipation in adults: a randomized, double-blind, placebo-controlled study. *South Med J.* 2001;94(5):478-481.

Daily therapy with 17 g of polyethylene glycol (PEG) laxative for 14 days resulted in a significant improvement in bowel movement frequency in constipated patients relative to placebo by the second week of treatment.

Imanishi N, Iwaoka K, Koshio H, et al. New thiazole derivatives as potent and selective 5-hydroxytryptamine 3 5-HT₃ receptor agonists for the treatment of

constipation. *Bioorg Med Chem.* 2003;11(7):1493-1502.

In this series, 10f (YM-31636) showed high affinity and selectivity for the cloned human 5-HT₃ receptor; furthermore, it showed potent and selective 5-HT₃ receptor agonistic activity. YM-31636 was examined for its effects on defecation in animals, thus evaluating the compound as an agent against constipation. This article describes no human data, so it is not of immediate practical value for clinicians who treat patients with constipation. However, the preclinical studies reported demonstrate the range of approaches that are being taken to develop new and clinically useful agents to promote laxation.