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Impact of Opioid-Induced Constipation on Opioid Therapy Among Patients with Cancer: A Review

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Abstract

Constipation is a common problem as a result of medication (in particular opioids) for pain control, as well as disease, dietary and mobility factors, Opioids are very effective analgesics, frequently prescribed in cancer pain, despite proven analgesic efficacy, the use of opioids is commonly associated with frequently dose-limiting constipation that seriously impacts on patients' quality of life, almost all patients on opioids report constipation as the major side-effect. Therefore this article provides an integrative review about opioid –induced constipation from all aspects with focus on the prevention. Methods: An online search of science direct data base and PubMed and Google scholar. Based on the inclusion criteria 7 articles were selected and formed the basis for this review. Conclusion: Prevention of opioid- induced constipation, in general, is considered to be a more effective strategy than merely treating it when it occurs, It is widely advised that laxatives should be started concurrently with opioids, prevention of opioid induced constipation could lead to clinical and economic benefits, Effective prevention and treatment of opioid-induced constipation can improve pain management and quality of life for patients and their families; However, limited RCTs to determine the effectiveness of prophylactic management on the prevention of opioid-induced constipation.

Keywords

Opioid-Induced Constipation, Impact, Cancer, Prevention, Management

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1. Introduction

Constipation is a common problem as a result of medication (in particular opioids) for pain control, as well as disease, dietary and mobility factors. [1] Fredericks, Hollis, & Carrie Stricker, (2010) defines constipation as less than three defecations per week (or change from usual pattern), or the subjective symptom of difficult, infrequent, or incomplete passage of stool characterized by slowed gastrointestinal motility that occurs in up to 90% of patients with advanced cancer receiving opioids and can negatively impact pain management and quality of life [2].

Opioids are very effective analgesics, frequently prescribed in cancer pain [3]. Despite proven analgesic efficacy, the use of opioids is commonly associated with frequently dose-limiting constipation that seriously impacts on patients' quality of life [4].

Almost all patients on opioids report constipation as the major side-effect. A hospital survey showed that 87% of patients on strong opioids required the use of laxatives among patients using morphine 80% reported constipation [5].

When opiates bind to the opiate receptors in the GI tract, they interfere with peristalsis and the mucous secretion required for bowel movements [6, 7, 8, 9, 10, 11]. Use of exogenous opioids reduces peristalsis [10]. Which, together with reduced secretion, increased liquid reabsorption, and increased sphincter tone, leads to the formation of dry, hard

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stools which are difficult to pass [12]. As the induction of constipation by opioids is so predictable, Dutch pharmacotherapy guidelines advise starting a laxative simultaneously with an opioid [13]. At present, there are no data to support the use of opioid antagonists in place of regular rational laxative use in cancer patients with constipation on opioids, [14]. An opioid-receptor antagonist now licensed for the treatment of opioid-induced constipation in palliative care when response to usual laxative therapy is insufficient [1].

The impact of constipation on patients' quality of life is important, especially for cancer patients [15]. Whose quality of life is already significantly impaired by the illness itself, constipation has been deemed by cancer patients to be an even greater source of discomfort than the pain they suffered [16].

Prevention of opioid- induced constipation and bowel dysfunction in general, is considered to be a more effective strategy than merely treating it when it occurs. It is widely advised that laxatives should be started concurrently with opioids [4]. In addition to its negative impact on quality of life, persistent constipation may lead to serious medical squeal, including bowel obstruction and fecal impaction; may result in elevated use of prescription drugs and medical services; and may affect compliance with pain medications, further compromising pain management strategies [17]. The use of a prophylactic bowel regimen that includes a stimulant laxative and stool softener generally is accepted and should be initiated at the start of opioid therapy. Effective prevention and treatment of OBD reduce the risk of associated physiologic complications and can improve pain management and quality of life for patients and their families [2].

Therefore, the purpose of this paper is to provide an integrative review that reports on the science for determining the impact of opioid-induced constipation and prophylactic management for the prevention of opioid-induced constipation and its consequences, with focus on concurrent use of laxatives among cancer patients starting opioid therapy.

2. Methods

Articles were retrieved for review via a combination of computer and manual searches of selected constipation and cancer-related publications. A comprehensive, and extensive online database search of Science Direct Database, PubMed, Nursing Ovid / Ovid, Springer Link (Springer Online Database), HINARI/WHO Database, and Google scholar was conducted for opioid-induced constipation, keywords used were "opioid-induced constipation" "impact" "cancer" "prevention" "management" in multiple combination.

The review utilized 7 articles despite extensive search which met the inclusion criteria. The inclusion criteria were: 1. it investigated opioid-induced constipation 2. It investigated impact rather than management of opioid-induced constipation 3. It is written in English language. Based on this inclusion criteria a total of 7 articles published from 2006 to 2011 were selected and formed the basis for this review. The earliest study included was published in 2006. Most articles were published in nursing journals. Studies included in this review focused on the prevention rather than management of opioid-induced constipation, This integrative research review composed from 7 studies were quantitative and descriptive studies. The sample sizes in the seven studies in this review ranged from 58 to 23,313 adult patients.

3. Results

Descriptions of included studies in the review displayed through table in (Appendix No. 1).

Evidence shows that the long-term use of opioids for chronic pain can lead to improvements in patients' QoL [18, 19]. However, the side effects of opioid therapy, mainly constipation, are likely to limit this benefit [20, 21, 22, 23]. Attempts have been made to quantify the impact of OBD on health-related QoL. The Patient Reports of Opioid-related Bothersome Effects survey – a web-based cross-sectional survey of 161 chronic pain patients in the USA taking oral opioids and generally using laxatives – was conducted to characterize the prevalence, frequency and severity of OBD symptoms, and their impact on QoL and activities of daily living (ADL). Participants were asked to identify any GI side effects they had experienced during opioid treatment, and rate the impact of each symptom on QoL and ADL on a five-point scale. The most common side effect was constipation, with 85–95% and 74–92% of these constipated patients reporting some degree of negative impact on QoL and ADL, respectively [20].

To evaluate the cost of managing constipation in patients taking opioids in a specialist palliative care inpatient unit, a retrospective review of the medical records of 58 patients (70 admissions) who died during a six-month period was undertaken to identify prescribing patterns for opioids and oral laxatives and tasks associated with managing constipation in these patients. A prospective time and motion study also was undertaken, whereby staff recorded the time and resources required to perform each task. These data were then applied to the actual frequency recorded in the retrospective review to calculate the direct cost of managing constipation in those 70 admissions during that six-month period. There was no discernable pattern in oral laxative

prescribing. The mean cost of managing constipation was £29.81 (48.74 USD) per admission, with staff time accounting for 85%of the cost. The most time-consuming activity was staff discussion about bowel management, which occurred at least once daily for doctors and twice for nurses and involved up to eight members of staff at a time. The cost of managing constipation is skewed in that it costs £30 (49 USD) or less in 71%of admissions but exceeded £100 (163 USD) in 5%. In the latter group, earlier and/or more effective intervention for constipation could lead to clinical and economic benefits [24]. In an attempt to quantify the potential impact of constipation on health care resource utilization in opioid-treated patients using real-world administrative data, the impact of constipation on resource utilization and associated costs compared with controls without constipation, patients with constipation had higher rates of concurrent use of ≥2 opioids, opioid discontinuation, opioid switching, nausea with vomiting, and respiratory depression. Compared with controls, more patients with constipation received inpatient, hospice, home health, laboratory, other outpatient, emergency, office visit, and nursing home care. Compared with controls, patients with constipation had substantially higher total costs [17]. Also in another study to estimate the prevalence of constipation concomitant to opioid treatment and related resource use and costs from the private payer perspective, using retrospective database analysis of 23,313 patients were classified as opioid-treated patients (2.2%) and 6678 of them had events related to constipation (29.0%). Compared with opioid-treated patients without constipation, total costs per month per patient were 261.18 BRL; the average cost per month for opioid-related constipation patients was 787.84 BRL, significantly higher than other patients. These results indicate that reducing opioid-induced constipation could lead to potential cost savings for the health care system [25].

In a study undertaken on 2430 patients who had been taking opioids for over 6 months for chronic pain To characterize the impact of opioid-induced constipation (OIC) on healthcare resource use, work productivity, and health-related quality of life (HRQOL), showed that Participants with OIC reported significantly more physician visits, alternative care provider visits than those without OIC. Respondents with OIC also reported significantly greater time missed from work, impairment while working, overall work impairment, and activity impairment. HRQOL scores were significantly lower in the OIC group than those without OIC on both the physical and mental components [22].

Hjalte, Berggren, Bergendahl, Hjortsberg, (2010). Estimated the direct and indirect costs of OIC in a defined patient population during treatment with strong opioids in 197 patients treated with strong opioids over a six-month period, the total costs per patient-month for patients with severe constipation are significantly higher than those for patients with mild, moderate, or no constipation. Patients with severe constipation have the highest total costs, Euro (EUR) 1525 per patient-month, whereas patients with mild, moderate and no problems cost EUR 1196, EUR 1088, and EUR 1034, respectively [23].

4. Conclusion

Opioid analgesics are the cornerstone of pain management for moderate-to-severe cancer pain, commonly associated with frequently dose-limiting constipation that seriously impacts on patients' quality of life, Prevention of opioid-induced constipation, and bowel dysfunction in general, is considered to be a more effective strategy than merely treating it when it occurs and much easier, it is widely advised that laxatives should be started concurrently with opioids unless there is a clear indication not to do so, the use of prophylactic bowel regimen that includes a stimulant laxative and stool softener generally is accepted and should be initiated at the start of opioid therapy.

Adequate assessment, attention to detail and rational use of laxatives and other medications is the minimum that should be offered to this group of patients in helping to improve this distressing symptom.

Effective prevention and treatment of opioid-induced constipation could lead to clinical and economic benefits, and reduce the risk of associated physiologic complications and can improve pain management and quality of life for patients and their families.

Appendix

Table 1. Descriptions of included studies in the review.

Authors	Purpose	Sample size	Outcomes/ Findings	Methods
(Bell, Annunziata, leslie, 2009).	Characterize the impact of opioid-induced constipation (OIC) on healthcare resource use, work productivity, and health-related quality of life (HRQOL) in patients receiving chronic opioid therapy.	2430	OIC has negative impact on individuals' HRQOL and on society in terms of healthcare resource use and work productivity beyond that imposed by patients' pain conditions.	Internet questionnaires during the international National Health and Wellness Survey (NHWS) 2004 (descriptive correlational)

Authors	Purpose	Sample size	Outcomes/ Findings	Methods
(Bell, Milanova, Groove, Williamson, 2007).	Characterize the prevalence, frequency and severity of OBD Symptoms, and their impact on QoL and activities of daily living (ADL).	161	OBD symptoms impair quality of life and daily activities, regardless of frequency and duration of opioid treatment.	Web-based cross-sectional survey
(Candrilli, Davis, Iyer, 2009).	Quantify the potential impact of constipation on health care resource utilization in opioid-treated patients using real-world administrative data.	8836 who met all study inclusion criteria	The impact of constipation on resource utilization and associated costs compared with controls without constipation, patients with constipation had substantially higher total costs.	Retrospective
(Hjalte, Berggren, Bergendahl, Hjortsberg, 2010).	Estimate the direct and indirect costs of OIC in a defined patient population during treatment with strong opioids.	197	Opioid use is costly to society, and the costs vary with OIC severity. OIC is discomforting, affects the QoL of patients, and can limit an effective pain therapy.	Descriptive correlational
(Leslie, Bell, Annunziata, Freedman, 2006).	Determine the impact of opioid-induced constipation on Chronic pain management, work productivity, and patient health-related quality of life (HRQOL).	2137	Opioid-induced constipation compromises pain management and impacts patients' quality of life.	Web-based cross-sectional survey
(Takemoto et al., 2011).	Estimate the prevalence of constipation concomitant to opioid treatment and related resource use and costs from the private payer perspective.	23,313	Patients with constipation coincident with opioid treatment exhibited a significantly higher economic burden than did patients without the condition.	Retrospective database analysis
(Wee et al., 2010).	Evaluate the cost of managing constipation in patients taking opioids in a specialist Palliative care inpatient unit.	58	Earlier and/or more effective intervention for constipation could lead to clinical and economic benefits.	Retrospective and prospective

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