RESEARCH ARTICLE

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# Constipation Severity and Quality of Life among Patients with Cancer Who Received Prophylactic Laxatives: Quasi-Experimental Study

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## Abstract

**Background:** Prophylactic laxatives were associated with decreasing the incidence of Opioid-induced constipation among patients with cancer. This study aims to evaluate the effectiveness of early prophylactic laxatives therapy on the severity of constipation and quality of life among patients with cancer receiving opioids. **Methods:** Using a quasi-experimental design with 64 patients assigned to control group and 66 patients assigned to intervention group. The final sample was composed from 112 patients (57 in control group and 55 in intervention group), who were selected from an oncology clinic. Patients in the intervention group have received prophylactical laxatives The intervention included an oral colonic stimulant laxative (i.e., Bisacodyl, Dose= 3 tab/ day and/or Senna 6.8 mg twice daily) and an oral colonic osmotic laxative (i.e., Lactulose, Dose = 15 ml three times per day). Patients in the control group continue to receive their routine care without laxatives. **Results:** Patients in the intervention group have reported a significant reduction in the severity of constipation symptoms at eight weeks post the intervention ($p < 0.001$). Furthermore, the patients in the intervention group have revealed a significant improvement in their quality of life (QoL) ($p< 0.001$). **Conclusions:** Patients with cancer need to use the first line of laxatives as prophylactic alongside with opioids to minimize the severity of Opioid-induced constipation symptoms and to enhance the QoL.

**Keywords:** Cancer- constipation- quality of life- prophylactic laxatives

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## Introduction

Cancer is considered one of the most common health problems worldwide (Dascălu et al., 2022; Siegel et al., 2015). Many studies have shown that patients with cancer usually suffer from pain and need to use opioids (Azizoddin et al., 2021; Chou et al., 2009; Mercadante, 2014; Mohammad and Ahmad, 2019). Despite the analgesic effects of opioids, these drugs have many adverse effects, such as constipation, loss of appetite, vomiting, urinary alterations, and may cause an alteration in cognitive ability (Daoust et al., 2020; Els et al., 2017). Constipation caused by opioid therapy is considered as one of the most common bothering symptoms among patients with cancer (Larkin et al., 2018; Mesía et al., 2019); and it is considered by many patients as more severe than cancer pain itself (Dhingra et al., 2013; Larkin et al., 2018). The reported incidence of opioid-induced constipation (OIC) in the previous studies was varied from 22% to 81% based on the study sample size (Abramowitz et al., 2013; Ducrotté et al., 2017).

Opioid-induced constipation has a negative impact on patients' quality of life (QoL) and comfort level (Bell et al., 2009; Varrassi et al., 2021). Around 38% - 95% of patients with cancer with OIC have reported poor (QoL) (Abramowitz et al., 2013; Al-Daken and Ahmad, 2018; Panchal et al., 2007; Veiga et al., 2018). Moreover, several studies showed that about 35% of patients decreased their adherence to opioid medication to avoid OIC (Andresen et al., 2018; Bell et al., 2009). Some patients decrease or discontinue opioid medication to minimize constipation, thus, weakening the analgesic effect and impaired QoL (Christensen et al., 2016). As a result, OIC management became difficult and did not reach patient satisfaction (Ahmad et al., 2010; LoCasale et al., 2016; Varrassi et al., 2021).

There are two broad strategies to prevent and manage OIC, including pharmacological and/or non-pharmacological approaches (De Giorgio et al., 2021). The strategies to avoid OIC are considered more effective than treating constipation when it occurs. A combination of pharmacological and non-pharmacological approaches was used to manage OIC (Manchikanti et al., 2012). The recent recommendations published by the European consensus regarding OIC management suggest that when starting opioid management for pain in the palliative

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care setting, the physicians should start and continue a prophylactic treatment of laxatives (Farmer et al., 2019). In a recent study, prophylactic laxatives were associated with decreasing OIC incidence among patients with cancer (Harada et al., 2021).

Moreover, patients with cancer who suffer OIC had more severity of constipation when they do not receive laxatives as prophylaxes than those who underwent prophylaxes treatment (Ishihara et al., 2010). There were no clear stated guidelines in Jordan by the oncologist's physicians to prevent or manage OIC. However, some physicians prescribed laxatives for patients with cancer who received opioid-based on their routine practice rather than evidence-based practice. Thus, the purpose of the current study was to evaluate the effectiveness of early prophylactic laxatives therapy on the severity of constipation and QoL among patients with cancer receiving opioids.

*Research Questions*

This study was designed to answer the following questions: 1) What is the effect of prophylactic laxatives on constipation severity and QoL among patients with cancer who received prophylactic laxatives compared to those who did not? And 2) Is there a difference in the factor related to OIC among patients who received prophylactic laxatives and those who did not?

## Materials and Methods

*Design and sample*

This study has followed the quasi-experimental study trial. This study included 112 adult patients with cancer who were oriented and capable of participation. All patients were diagnosed with cancer such as breast, colorectal, and lung cancer. All of the participants were receiving opioids when they included in this study. The exclusion criteria were limited to those patients on an opioid antagonist, experiencing diarrhea or with an ileostomy, currently on simultaneous treatment with laxatives, and or in the terminal stage of cancer.

G-power software was used to estimate the sample size based on the two-tailed independent t-tests (Faul et al., 2007). The following criteria were considered: moderate effect size of 0.3, an alpha of 0.05, and a power of 0.8, a total number of 90 participants in the two groups were considered adequate. However, considering attrition, we enrolled 130 patients. Eighteen patients dropped out, and 112 completed the study (Figure 1).

*Setting*

This study was conducted in a single oncology out-patient clinic at the biggest governmental hospital in Jordan, where about 26% of patients with cancer are followed (Khatib and Nimri, 2022).

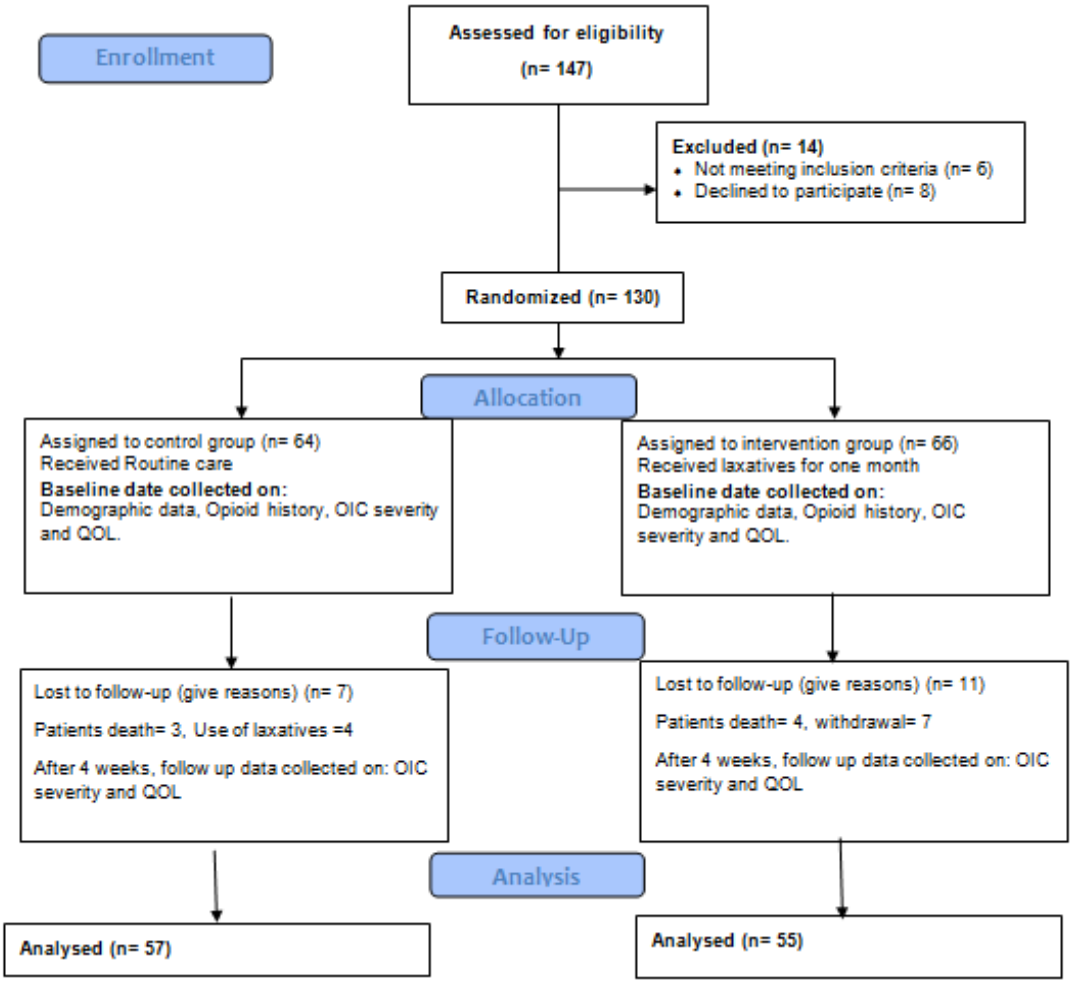


Figure 1. Data Collection Flowchart

*Instruments*

The questionnaire in the current study has three parts. The first part consists of socio-demographic and cancer-related information and collecting the essential data about constipation using the Confirmation of Constipation (CC) Scale. The CC scale was created according to the Rome III criteria (Drossman, 2006). This scale has criteria to define and confirm the diagnosis of constipation. Based on these criteria, patients considered constipated if they have at least two symptoms of the following: less than three defecations per week (and in at least 25% of the times), straining stools; lumpy or hard stool; feeling of incomplete evacuation or sensation of obstruction; need to manual remove stool, in addition to scarce signs and symptoms for irritable bowel syndrome. These symptoms have to be started at least six months before diagnosis and presented during the last three months. The final CC score would indicate constipation if the patients answered two or more of these criteria with "yes"; otherwise, they were considered non-constipated (Drossman, 2006).

The second part of the questionnaire was the Patient Assessment of Constipation Symptoms (PAC-SYM), consisting of 12- self-report items on a 5-point (0–4) Likert-type scale. It is a reliable and valid measure of the presence and severity of OIC symptoms with accepted Cronbach α Coefficient 0.80 (Frank et al., 1999). Responses with score 0 = absence of symptom, 1 = mild, 2 = moderate, 3 = severe and 4 = very severe symptom. The mean of the total scores for each patient was computed and extended from 0 to 4, where lower scores reflect low symptom severity. This measure had already been translated into the Arabic language. In this study, the Cronbach α Coefficient was 0.97, reflecting the excellent internal consistency of the instrument.

The third part was the Patient Assessment of Constipation Quality of Life (PAC-QoL) tool, which is a comprehensive and valid patient-reported measure used to assess the impact of constipation symptoms, and it had been a good internal consistency (Marquis et al., 2009). PAC-QoL scale consists of 28-items divided into four subscales about constipation-related worries and concerns (11 items), physical discomfort (4 items), psychosocial discomfort (8 items), and satisfaction (5 items). Each item is rated on a 5-point (0–4) Likert-type scale and the responses are scored as 0 = "Not at all" / "None of the time"; 1 = "Quite a bit" / "Most of the time"; 2 = "Moderately" / "Some of the time"; 3 = "A little bit" / "A little of the time" and 4 = "Extremely" / "All of the time". Scores of items 18, 25,26,27, and 28 were reversed. The mean of the total score for each participant was also calculated. It ranged from 0 to 4, where the lower score indicates better QoL. This tool was translated into the Arabic language using a back-translation technique. In the current study, Cronbach α Coefficient was 0.98, reflecting a good internal consistency of scales.

*The Intervention*

The intervention in this study was the prophylactic laxatives prescribed by oncologists. All invited oncologist have verbally agreed to participate in the study. The laxatives were prescribed for patients according to the constipation assessment and management algorithms that were developed by Cancer Care Ontario Symptom Management Group; and Winnipeg Regional Health Authority. This study used the recommended medications as the first line of treatment from both guidelines. The intervention included an oral colonic stimulant laxative (i.e., Bisacodyl, Dose= 3 tab/ day and/or Senna 6.8 mg twice daily) and an oral colonic osmotic laxative (i.e., Lactulose, Dose = 15 ml three times per day). At the same time, patients in control continue receiving their routine care as usual.

*Data collection procedure*

Data were collected between July and September 2019. As a first step, the principal investigator (PI) approached the responsible oncologist and nurses to inform them about the study purpose, protocol, and process. The PI directly approached the patients who showed an interest in the study to give them more details about the study project, possible interventions, and side effects (that was minimal). Patients were informed that the PI randomly assigned them into two groups. After answering all patients' questions, the interested participants were called after 24 hours to sign the consent form. After that, all consented patients were required to fill out the first part of the questionnaire about the socio-demographic information and CC scale. According to the CC scale results, only constipated patients were selected and asked to complete baseline data, including OIC severity and QoL. Participants were then randomly assigned by the PI to each group purely randomly for every assignment (group A= intervention group, group B = Control group). Since the estimated sample size was around 120, a quasi-experimental study technique was applied. All patients with even medical record numbers were allocated to group A (intervention), and patients with odd medical record numbers were allocated to group B (Control group) (Figure 1). The assigned oncologist prescribed prophylactic laxatives for patients in the intervention group, but patients in the control group continued their routine care without laxatives. Finally, after two months, follow-up data about OIC severity and QoL were collected from both groups. During the eight weeks, the PI called each one of the patients at least once per month to answer their questions and assure protocol adherence.

*Ethical considerations*

The relevant institutional review boards have approved this study. Full information about the study aim, intervention, possible side effects of laxative treatment, and requirements were given to the patients earlier signing the consent form. In addition, all participant questions were answered, and all study-related information was explained in the consent form. After the first meeting with patients, 24-hours were given for them to read and determine whether to enroll or not. Participants were informed to sign the consent form only after completely understanding all requirements and participation instructions. Moreover, continuing data about laxatives and possible side effects were made accessible at any time

through their oncologists. All patients were confirmed that they could freely withdraw from the study for any reason without any consequence on their medical or nursing care.

*Data analysis*

Data were analyzed using the Statistical Package for the Social Sciences version 25 software program(IBM, 2017). Descriptive and inferential analyses for the major study variables were performed. The mean and standard deviation were computed and rounded to two decimals for continuous variables. For categorical variables, the number and percentage distribution for each category were reported. Independent t-test was utilized to compare the differences in OIC severity and QoL for the intervention and control group. At the same time, a paired t-test was used to assess the difference between the baseline and two months post-intervention in OIC severity and QoL for each group. A Chi-square test was also used to compare the difference between intervention and control groups in constipation assessment factors.

## Results

*Socio-demographic data*

A total of 112 patients were included in the analysis (86.2% response rate). Fifty-five patients (49.1%) were enrolled in the intervention group and 57 (50.9%) in the control group. Including 62 female (55.4%) and 50 males (44. 6%). The mean age of participants in the intervention group was 55.8 years (SD = 11.7) and 51.7 (SD= 9.4) in the control group. In the intervention group, most participants were married and diagnosed with cancer within one year compared with the control group. One-quarter of participants had breast cancer, followed by lung and colorectal cancers. Tramal medication was prescribed for most patients (74.1%), and the majority of patients consumed opioids 1-2 times daily. One-third of participants had a palliative performance scale of less than 70%, reflecting the need for hospice care. No statistically significant difference was found at the baseline in socio-demographic and clinical variables between intervention group and control group (Table 1).

Table 1. Characteristics of Participants, Using Chi=Square Tests (N=112)

| | Intervention (n=55) Frequency (%) | Control (n= 57) Frequency (%) | p-value |
|---|---|---|---|
| Age (mean ± SD) | 55.8 (11.7) | 51.7 (9.39) | 0.093 |
| Gender | | | 0.192 |
| Male | 34 (61.8) | 16 (28.1) | |
| Female | 21 (38.2) | 41 (71.9) | |
| Marital status | | | 0.356 |
| Married | 45 (81.8) | 44 (77.2) | |
| Unmarried | 10 (18.2) | 13 (22.8) | |
| Cancer primary site | | | 0.075 |
| Lung | 13 (23.6) | 9 (15.8) | |
| Colorectal | 11 (20) | 9 (15.8) | |
| Breast | 15 (27.3) | 13 (22.8) | |
| Brain | 2 (3.6) | 7 (12.3) | |
| Lymphoma | 3 (5.5) | 6 (10.5) | |
| Uterus and ovarian | 3 (5.5) | 6 (10.5) | |
| Prostate | 8 (14.5) | 7 (12.3) | |
| Duration of cancer diagnosis | | | 0.366 |
| ≤ One year | 33 (60) | 37 (64.9) | |
| > One year | 22 40) | 20 (35.1) | |
| Palliative Performance Scale | | | 0.554 |
| ≤ 40 | 1 (1.8) | 1 (1.8) | |
| 50-70 | 15 (27.3) | 21 (36.8) | |
| > 70 | 39 (70.9) | 35 (61.4) | |
| Cancer Therapy | | | 0.165 |
| Medication only | 11 (20) | 26 (45.6) | |
| Medication and adjuvant therapy | 44 (80) | 31 (54.4) | |
| Opioids Therapy | | | 0.294 |
| Tramadol | 39 (70.9) | 44 (77.2) | |
| Morphine | 16 (29.1) | 13 (22.8) | |
| Opioids Frequency | | | 0.064 |
| Once | 34 (61.8) | 22 (38.6) | |
| Twice | 19 (34.6) | 31 (61.4) | |
| 3 times or more | 2 (3.6) | 4 (7) | |

*Assessment of opioid-induced constipation*

At the baseline, all participants were assessed for OIC according to ROME III criteria (Drossman, 2006). The results revealed that most of the patients were classified as constipated (n= 86, 76.8%), while the remaining were considered non-constipated. Most of patients in intervention group (n=48, 87.3%) and control group (n=38, 66.7%) were constipated. Based on ROME III criteria, Chi-square test revealed a non-significant difference in all constipation criteria at the baseline except the feeling of straining with at least 25% of stools (Table 2). The results shows that most patients had bowel movements after two days but with non-significant difference at the time of the last bowel movement between both groups. The majority of patients had adequate privacy during defecation but not significantly differ in availability of privacy between both groups. Furthermore, in both groups, at least 25% of the daily time, there is a non-significant difference in patients feeling a lumpy/hard stool and patient need for assistance in defecation, sense of incomplete defecation, and the need to remove the stool manually. The frequency of defecation per week was also not significantly different in both groups. The intervention group had less than three times per week and more than three times among patients in the control group. On the other hand, a significant difference was found between both groups in patient reported straining feeling during defecation ($\chi^2$= 7.94, p = 0.007).

*Constipation severity*

The constipation severity at baseline was not significantly different among patients in the intervention group compared with the control group. After 8-weeks of implementing the intervention, a significant difference was found between the intervention group (Mean=12.4,

Table 2. Comparison between the Two Groups at the Baseline for Constipation (Chi-Square Test)

| Bowel movements | Intervention group | Control group | p-value |
|---|---|---|---|
| Last bowel movement | | | |
| ≤ 2 days | 15 (27.3%) | 19 (33.3%) | 0.541 |
| > 2 days | 40 (72.7%) | 38 (66.7%) | |
| Privacy during defecation | | | |
| Present | 50 (90.9%) | 49 (86%) | 0.302 |
| Not present | 5 (9.1%) | 8 (14%) | |
| Need help for defecation | | | |
| Yes | 16 (29.1%) | 16 (28.1%) | 0.535 |
| No | 39 (70.9%) | 41 (71.9%) | |
| Defecated less than 3 times/week | | | |
| Yes | 33 (60%) | 27 (47.4%) | 0.191 |
| No | 22 (40%) | 30 (52.6%) | |
| Straining with at least 25% of stools | | | |
| Yes | 23 (41.8%) | 10 (17.5%) | 0.007 |
| No | 32 (58.2%) | 47 (82.5%) | |
| Lumpy and hard stool at least 25% of the time | | | |
| Yes | 47 (85.4%) | 40 (70.2%) | 0.07 |
| No | 8 (14.6%) | 17 (29.8%) | |
| Incomplete evacuation or sensation of blockage for at least 25% of stools | | | |
| Yes | 45 (81.8%) | 47 (82.5%) | 0.562 |
| No | 10 (18.2%) | 10 (17.5%) | |
| Need to manually remove stool at least 25% of the time | | | |
| Yes | 2 (3.6%) | 0 | 0.239 |
| No | 53 (96.4%) | 57 (100%) | |

Standard Deviation=9.26) and control group (Mean =20.1, Standard Deviation =8.01) ($p < 0.001$). Furthermore, the intervention group (Mean =50.4, Standard Deviation =17.5) and control group (Mean =39.8, Standard Deviation =17.9) ($p = 0.002$) (Table 3).

The results of the paired t-test revealed a significant

Table 3. Between Groups Analysis of Constipation Severity Pre-and Post-Intervention (Independ t Test)

| Study Groups | Severity of Constipation (pre-test) | | Severity of Constipation (post-test) | |
|---|---|---|---|---|
| | Mean (SD)^ | p-value | Mean (SD) | p-value |
| Intervention group | 21.4 (8.19) | | 12.4 (9.26) | |
| Control group | 19.9 (6.95) | 0.313 | 20.1 (8.01) | <0.001 |
| | QoL (pre-test) | | QoL (post-test) | |
| Intervention group | 40.8(21.9) | 0.629 | 50.4 (17.5) | 0.002 |
| Control group | 38.8 (21.7) | | 39.8 (17.9) | |

^SD, Standard Deviation

Table 4. Within-Group Analysis of the Severity of Constipation and QOL (Paired Sample t Test)

| | Severity of constipation | | |
|---|---|---|---|
| | Pre-intervention (Baseline) | Post-intervention | |
| | Mean (SD)^ | Mean (SD)^ | p-value |
| Intervention group | 22.9 (7.20) | 14.22 (8.98) | 0.001 |
| Control group | 18.4 (7.33) | 18.3 (9.47) | 0.952 |
| Quality of Life | | | |
| Intervention group | 33.3 (20.4) | 50.4 (18.3) | 0.014 |
| Control group | 46.4 (21.1) | 37.1 (18.7) | 0.152 |

^SD, Standard Deviation

difference among participants in the intervention group in constipation severity at baseline (Mean=22.9, Standard Deviation=7.20) compared with after 8-weeks of intervention (Mean=14.22, Standard Deviation=8.98) ($p < 0.01$). Furthermore, the patients QOL has improved significantly in the intervention group in the post-intervention measurement (Mean=50.4, Standard Deviation=18.3), while in the control group it was (Mean= 33.3, Standard Deviation=20.4), (p=.014). Furthermore, the control group did show any significant changes in both the severity of constipation and in the QOL (Table 4).

*Quality of life*

At the baseline, there was no difference in QoL between the study groups, however, the intervention group had a significantly better QoL than the control group. Patients in intervention group had significantly better QoL compared with patients in control group after the intervention ($t = 3.14$, $p < 0.05$). When comparing the change in QoL at baseline and after 8-weeks of the intervention, a significant better in QoL among patients in intervention group ($M = - 9.6$, $t = - 2.51$, $p = 0.015$) while the control group had no significant difference in QoL scores ($M = -0.579$, $t = -0.156$, $p > 0.05$).

## Discussion

The main finding of this study highlighted the importance of administering the prophylactic first line laxatives patients with cancer who had constipation (i.e., Bisacodyl, Dose= 3 tab/ day or Lactulose, Dose = 15 ml three times per day) concurrently with opioid medication. This intervention has decreased constipation severit. Most participants in both groups were constipated (76.8%) at baseline in this study. This finding is congruent with several other similar studies. (Fine et al., 2019) reported that patients with cancer treated with opioids and had constipation were more than twice as likely as those without constipation. In a previous study conducted among 520 patients with cancer who received opioids, 61.7% of patients reported constipation, and 85.7% of patients were considered constipated as physician evaluation (Abramowitz et al., 2013). Patients with cancer receiving opioid treatment with prophylactic laxatives had a 34% decrease in OIC compared to patients receiving opioid treatment without prophylactic laxatives (Ishihara et al., 2010). Therefore, the frequency of having OIC may be estimated to elevate among patients with cancer who do not receive laxatives concurrent with prescribed opioids. Strategies must be implemented in practice that prevents or manage OIC, such as harmless and effective first-line laxatives.

The findings of this study showed a significant decrease in constipation severity at eight weeks post-intervention among the intervention group, where no improvement was noted in the control group. This indicates that using prophylactic laxatives effectively reduced the constipation incidence when starting opioid treatment. This result is congruent with another study finding conducted on critically ill patients to assess the effectiveness of prophylactic laxatives on constipation occurrence (Masri et al., 2010). Moreover, Müller-Lissner et al. (2017) analyzed data pooled from two randomized controlled trials, which evaluated the effect of either Bisacodyl (BIS) among 736 patients with chronic constipation, Sodium Picosulfate (SPS) among 468 patients, or placebo. The analysis from the two randomized controlled trials compared the patients in intervention group 468 (who received SPS/BIS); with control group 250 (who received placebo) showed that patients in the intervention group reported a notable increase in the number of spontaneous bowel movements over four weeks from baseline compared with the control group (Müller-Lissner et al., 2017).

In terms of QoL, patients with cancer who received prophylactic laxatives significantly improved QoL at eight weeks post-intervention compared with patients in the control group. This result is consistent with the results of previous studies (Müller-Lissner et al., 2017). It was shown that the overall score of QoL among patients in the intervention groups was significantly improved compared to a placebo group (47%, 14.5%, respectively) (Müller-Lissner et al., 2017). Further, a survey was conducted on a sample of patients with cancer from the UK, Canada, and Germany to evaluate the magnitude of OIC (Coyne et al., 2016). It was found that OIC was prevalent, and QoL was severely compromised. However, most patients acknowledged a reduction in OIC and improved QoL after the laxative therapy was initiated (Coyne et al., 2016).

Quality of life is more important in cancer care. Previous studies found a high incidence of cancer-related symptoms, including OIC, among Jordanian patients with cancer and poor QoL (Ahmad et al., 2015; Al Qadire and Al Khalaileh, 2014). However, prophylactic manners for treatment of OIC in patients with cancer would lead to improving QoL. On the other hand, using more than one laxative and prolonged consumption are associated with low QoL (Christensen et al., 2016). The findings of this study should be explained in light of the following limitations. First, study respondents were selected from a single setting. OIC examination and managing might be distinct from one setting to another, and thus, the generalization of the results might be limited.

*Implications*

The findings of the current study have several implications for practice. First, oncology nurses and others who work with patients with cancer should perform an early comprehensive evaluation of OIC as possible as it is one of the common and distressing symptoms. Second, nurses need to use their evaluation for patient status to advocate for using laxative as prophylactic in expectation of OIC development. Finally, nurses are in a distinctive position to advance OIC management as they have a significant role in the healthcare team and stay with patients for a long time. In the research field, educational programs for physicians and nurses about assessment, prevention, and management of OIC require to be verified for its effectiveness and practicability in bedside caring areas.

*Recommendations*

Using prophylactic laxatives concurrently with opioids could effectively improve adherence to the recommended strategies on the management of OIC. This can be reached through offering educational sessions and material for physicians and nurses about OIC assessment, prevention, and management. However, it is necessary to test such an intervention for effectiveness and feasibility in clinical practice settings. Furthermore, knowledgeable and aware healthcare providers are considered a main source of information for patients; accordingly, they must educate patients about the significance of laxative consumption in avoiding the incidence and the treatment of OIC. Patients would likely cooperate and follow the management plan if they experience decreasing therapeutic complications such as constipation.

In conclusion, this study assessed the impacts of prophylactic laxatives on constipation severity and QoL among patients with cancer. Besides severity, many patients with cancer have developed OIC and have a poor QoL. It can be concluded that the benefits of using prophylactic first-line laxatives together with opioids are extended to reduce the severity of OIC and enhance the QoL for patients with cancer. Therefore, prophylactic laxatives are advised to be prescribed once the opioid treatment is started.

## Author Contribution Statement

Dr. Alnaeem (draft the proposal, data collection, writing the first draft); Prof. Ahmad (Data analysis, writing, editing, submission, supervisoin)

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*How the ethical issue was handled (name the ethical committee that approved the research)*

The research committee at the School of Nursing/ University of Jordan.

*Availability of data*

Data available on request and by considering the confidentiality of the patients.

*Was the study registered in any registering dataset (for clinical trials, guideline, meta analysis)*

No.

*Any conflict of interest*

None.

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