Trajectory of Medication-Induced Constipation in Patients With Cancer

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Constipation is a common problem among patients with cancer and is believed to be among the most nurse-sensitive patient outcomes (Hoekstra, de Vos, van Duijn, Schadé, & Bindels, 2006; McMillan & Rivera, 2009). Although very amenable to nursing intervention, constipation often goes unrecognized and untreated in oncology settings (McMillan, Tittle, Hagan, & Laughlin, 2000; Miaskowski, 1995; Woolery et al., 2006, 2008). A significant problem facing oncology nurses in treating medication-induced constipation is the lack of research on which to base treatment decisions. Research in patients with cancer indicates self-reported prevalence to be 43%–58%, with mean intensity ranging from 5.2–6 on a scale from 0 (none) to 10 (worst), demonstrating the significance of the problem (Hoekstra et al., 2006; McMillan & Rivera, 2009). However, those studies did not focus on opioids or other medications as a cause of constipation; therefore, very little research has been conducted that can provide clear data on the prevalence and trajectory of medication-induced constipation (Thomas et al., 2008). The purpose of this study was to determine the severity and trajectory of constipation among patients with cancer at risk for constipation from opioids and/or vinca alkaloids and to evaluate the levels and relationships between constipation intensity and distress.

Background

A systematic review of the literature related to opioid-induced constipation was undertaken by a team of clinical and research experts assembled by the Oncology Nursing Society. The goal was to develop evidence-based guidelines (Woolery et al., 2008). The results showed few intervention studies including patients with cancer with opioid-induced or other types of constipation. In addition, the expert group concluded that, in spite of the frequent occurrence of

Purpose/Objectives: To determine the severity and trajectory of constipation among patients with cancer from opioids and/or vinca alkaloids.

Design: Exploratory, descriptive.

Setting: Moffitt Cancer Center, a National Cancer Institute–designated comprehensive cancer center in Tampa, FL.

Sample: 400 patients at risk for developing medication-induced constipation from opioids, vinca alkaloids, or both.

Methods: Patients' baseline data included the Constipation Assessment Scale (CAS), the constipation item from the Memorial Symptom Assessment Scale (MSAS) for intensity and distress, and the laxative interview. Following the interview, the medical chart was reviewed for clinical and demographic data. Patients were asked about constipation (CAS) and laxatives consumed (laxative interview) during eight weekly telephone calls.

Main Research Variables: Constipation presence, intensity, and distress.

Findings: At baseline, 63% of patients reported some level of constipation. During the eight weeks, constipation fluctuated with scores ranging from 0–16, with the opioid-only group showing a small but statistically significant decrease in intensity. Constipation intensity and distress on the MSAS were significantly correlated (r = 0.76; p = 0.000).

Conclusions: The majority of the sample reported constipation that ranged from mild to severe, persisted over time, and caused symptom distress. Therefore, healthcare providers in the cancer center likely were neither adequately managing the medication-induced constipation nor apparently teaching patients to manage it themselves.

Implications for Nursing: National Comprehensive Cancer Network guidelines support the importance of managing medication-induced constipation. However, guidelines are not being followed in many cases; therefore, more focus is needed on constipation in clinical and educational settings as well as more research.

Knowledge Translation: Patients receiving opioids and vinca alkaloids are at risk of constipation. Currently, medication-induced constipation is poorly managed. Managing constipation may lessen symptom distress, thereby improving quality of life in these patients.

constipation in patients with cancer, research is limited and oncology nurses do not adequately assess or manage constipation.

Prevalence and Causes of Constipation

Constipation occurs most frequently among older adults and accounts for a large portion of outpatient visits in this population. The prevalence of constipation in older adults varies, but may be as high as 30% and is believed to be more common in women, rural populations, Blacks, those from lower socioeconomic levels, and residents of northern states (Hsieh, 2005). In cancer settings, constipation is likely to be even higher; studies have shown constipation to be common, with prevalences ranging from 43%–80% in patients with cancer in intensive care units, veterans hospitals, and hospice home care (Hoekstra et al., 2006; McMillan, 2002; McMillan & Rivera, 2009; McMillan et al., 2000; Tittle & McMillan, 1994). However, the causes of constipation varied.

Five common causes of constipation in people with cancer have been reported to include the cancer itself, which can obstruct the bowel or affect the autonomic nervous system; disease effects such as dehydration, spinal cord compression, immobility, or changes in normal bowel habits; previous laxative abuse; cancer therapies including one of the vinca alkaloids; and symptom management using one of the opioids or tricyclic antidepressants (Wilkes, Ingwersen, & Barton-Burke, 2001).

Opioid-Induced Constipation

Opioids are among the most common types of drugs used to treat cancer-related pain (Canty, 1994; Lehne, 2007). Opioids bind with receptors in the enteric nervous system, specifically in the myenteric plexus, decreasing stimulation of the required propulsive contractions in the bowel (Canty, 1994). Research also identified opioid-induced delayed gastric emptying as well as increased bowel transit time and decrease in water in the bowel (Canty, 1994; Murphy, Sutton, Prescott, & Murphy, 1997), resulting in slowing of peristalsis and a decreased urge to defecate (Cameron, 1992; Glare & Lickiss, 1992; Levy, 1991; Thomas et al., 2008). In fact, because of that effect on the bowel, opioids were used for treatment of diarrhea long before they were used for analgesia (Lehne, 2007). Studies that show a relationship between pain intensity and constipation support that finding. For example, in a sample of 178 hospice patients with cancer (McMillan & Small, 2002), the relationship between pain intensity and constipation intensity was significant.

One study of opioid-induced constipation was reported in 2008 (Thomas et al., 2008). That study of subcutaneously administered methylnaltrexone in hospice patients showed its effectiveness in treating constipation in patients with advanced disease, slightly more than half of whom had cancer as their primary diagnosis.

Vinca Alkaloid–Induced Constipation

The vinca alkaloids are derived from the periwinkle plant, *vinca rosea*, hence the name. All of the drugs in this class cause constipation (Lehne, 2007). Although the mechanism is not clear, it may be related to the peripheral neuropathy that also commonly occurs. Regardless of the mechanism, previous research has confirmed the likelihood of constipation in patients receiving one of the vinca alkaloids for treatment of cancer (Lehne, 2007; Wilkes et al., 2001).

Given the frequent occurrence in oncology populations, relatively little research has been conducted focusing on medication-induced constipation. The little current research that has been done with patients with cancer is primarily cross-sectional and descriptive in nature and suggests that nurses in oncology settings do not adequately assess or manage constipation (McMillan et al., 2000). This lack of current research suggests that additional research is needed in all areas relating to management of constipation in patients with cancer, including understanding the prevalence and trajectory.

The current article reports phase I results of a National Institutes of Health–funded clinical trial that was based on the Theory of Unpleasant Symptoms. That theory posits that symptoms are characterized by intensity, distress, timing, and quality (Lenz, Pugh, Milligan, Gift, & Suppe, 1997). Phase I of the study focused only on the intensity and distress of constipation during an eight-week period (timing). Quality is addressed in phase II of the study, which is still underway. Therefore, the focus of this article is the description of the trajectory, intensity, and distress of medication-induced constipation during an eight-week period.

Methods

Setting and Sample

The setting was an National Cancer Institute–designated comprehensive cancer center in Tampa, FL, that sees more than 6,600 new patients annually with a variety of cancers. The outpatient clinics have about 170,000 clinic visits annually. At the time of the study, no standard treatment or prevention protocol existed for constipation for patients receiving opioids or vinca alkaloids, so care providers in the cancer center could choose to address this problem or not.

To be included, patients on opioids had to be on stable doses for two days before the beginning of the study. Patients receiving vinca alkaloids had to have at least two scheduled doses of the vinca alkaloid medication

remaining at the time of accrual to allow study over time. Participants had to be aged 18 years or older, able to consent, alert, and able to read and understand English. Mental status was screened at accrual to ensure patients had sufficient cognitive capacity to respond to self-report instruments.

Patients were excluded if they had nonmelanoma skin, gynecologic, or colorectal cancer as their primary diagnosis, or any other condition that might affect bowel function, or if they were excessively debilitated or deemed unlikely to survive for the eight weeks of data collection. Performance status and cognitive function also were assessed to determine eligibility. In addition, patients were excluded if they had an ostomy, if they had a current peritoneal catheter, if they had abdominal surgery within the past six weeks, if they were currently having radiation therapy to the abdomen, if they had a history of chronic bowel disease—a disease process suggestive of mechanical obstruction (tumor or adhesion)—or reported chronic laxative use prior to cancer onset. For ethical reasons, patients were to be excluded from the study and referred for evaluation and treatment if they appeared to have an impaction at the time baseline data were collected; however, that did not occur in this sample.

Instruments

The **Short Portable Mental Status Questionnaire (SPMSQ)** is a simple 10-item dichotomously scored test of remote memory, knowledge of current events, and mathematical ability with total scores ranging from 0–10 (Pfeiffer, 1975). Because the data were self-reported by patients, the SPMSQ was used as a screening instrument for cognitive impairment including memory loss; patients with scores less than eight were excluded from the study. Validity has been demonstrated for the SPMSQ by its ability to detect moderate to severe cognitive impairment (Pfeiffer, 1975; Zarit & Zarit, 1998). Reliability (r = 0.79) was evaluated with a group of 340 patients with advanced cancer using an internal consistency approach, which supported reliability of the SPMSQ (McMillan et al., 2006).

The **Eastern Cooperative Oncology Group (ECOG) Performance Status Scale** is a measure of functional status widely used in oncology settings to assess patient functioning (Oken et al., 1982). The scale ranges from 0 (normal) to 5 (dead). ECOG scores were used to determine patient eligibility for the study. Patients with scores higher (worse) than three were excluded (Oken et al., 1982).

The **Charlson Comorbidity Index (CCI)** was used to determine the number of other conditions that might be occurring in the patients with cancer; comorbidities are weighted according to their seriousness. Although the CCI includes cancer as one of the comorbidities, this item was deleted from the form for this study because all patients had cancer, consistent with the intent of the scale developers (Charlson, Pompei, Ales, & MacKenzie, 1987). However, if the patients had metastatic disease, that Charlson weighted score was added into the total, which increased the patients' total comorbidity score. Weights for comorbidities range from 1 (i.e., myocardial infarction, heart failure) to 6 (i.e., metastatic disease or AIDS); therefore, scores could range from 0–35, although having every possible comorbidity seems very unlikely. Scores are reported by the scale developers as up to five or greater than five; scores in the current sample ranged from 0–7. Evidence of predictive validity was provided by a strong significant association with patient mortality (Charlson et al., 1987).

The **Constipation Assessment Scale (CAS)** is an eight-item, three-point summated rating scale that measures the presence (score greater than 0 on items) and intensity of constipation. Each item is rated by the patient as 0 (no problem), 1 (some problem), or 2 (severe problem). Total scores may range from 0 (no constipation) to 16 (worst possible constipation). Validity was supported in an earlier study (McMillan & Williams, 1989) by the significant difference between patients known to be at risk because of vinca alkaloids or opioids and a group of apparently healthy adults (p = 0.0001). An additional analysis compared the CAS scores of the patients receiving significant doses of morphine with the CAS scores of patients who had received vinca alkaloids three weeks prior. The significant difference between those two groups (p < 0.01) supported the sensitivity of the CAS to differentiate between moderate and severe symptoms of constipation. Reliability was evaluated using both internal consistency and stability over time approaches. Alpha coefficients (r = 0.7–0.78) were acceptable for such a short scale. Test-retest with brief delay provided strong evidence of reliability (r = 0.98) (McMillan & Williams, 1989).

At each contact, patients were asked if they had used any form of laxative (e.g., oral, suppository, enema) during the previous week. All doses were recorded by the research assistants (RAs) on a **laxative interview form** as the number of days a laxative was used and types of laxatives.

The **Memorial Symptom Assessment Scale (MSAS)** was used to obtain data about constipation intensity and distress at baseline, week 4, and week 8. The MSAS was designed to differentiate among intensity and distress from symptoms and has 33 items reflecting symptoms commonly associated with cancer (Portenoy et al., 1994); only constipation data are reported here. Distress is defined in the scale as how much the symptom "distressed or bothered" the patient on a 0–4 scale, with four being the greatest bother. Intensity also is assessed on a 0–4 scale, with four being the greatest intensity or

severity. Validity and reliability data for the MSAS have been strong when the tool was used with people receiving active cancer therapy. Factor analysis confirmed the scale structure. Validity was further supported by high correlations with clinical status and quality of life. Alpha reliabilities have been high in people with cancer (0.83–0.88) (Portenoy et al., 1994).

Standard demographic data were collected to allow description of the sample. Data included age, gender, marital status, race or ethnicity, education, and cancer diagnosis. In addition, the chart was reviewed at baseline to determine the ECOG Performance Status Scale score and the CCI. Cancer stage was not recorded because those data were considered to be unreliable; patients in the cancer center are not restaged after their original diagnosis so, for many patients, their current stage was unknown.

Procedures

After approval was received from the Scientific Review Committee of the Moffitt Cancer Center, the proposal was approved by the institutional review board of the University of South Florida in Tampa.

Accrual: Patients in the outpatient clinics who were referred by the physicians or primary nurses were screened using the computerized data system, and patients who met study criteria were invited to participate in the study by trained RAs. After consent, baseline assessment was conducted during that regular outpatient visit. Contact information was collected so that follow-up assessments could be conducted via telephone. Patients were given a packet of information including the questionnaires to keep by the telephone at home so the RAs could ask the questions over the telephone while the patients were looking at the items on the instruments.

Baseline data collection: During the initial contact, patients were interviewed to collect demographic data. The CAS, MSAS, and laxative interview were administered. Following the interview, the chart was reviewed, as well.

To help patients with remembering details of their bowel function, patients in all groups were given a laxative diary to use to help them keep up with their bowel function during the study. The laxative diary asked the patient to record, once each day at the same time of day, the number of bowel movements during the previous 24 hours and any laxatives or stool softeners taken. The diaries were not taken by the RAs but were used solely by the patients as a memory aid.

Follow-up data: Patients were contacted via telephone at one-week intervals for data collection. During those telephone contacts, patients responded to the items on the CAS and the laxative interview. They completed the items on the MSAS during the interviews at weeks 4 and 8. At the end of the study, the chart again was reviewed

to determine what changes in medication dose (opioid or vinca alkaloid) had occurred and whether any laxatives had been ordered or suggested to patients. Patients who were found (or suspected) to have fecal impactions during the course of the study were to be removed from the study and their attending physicians notified. However, no patients became impacted during the course of the study. After the week 8 data collection, the patients were thanked for their participation in the study.

Data Analysis

Demographic data were analyzed using descriptive statistics. Relationships among variables were evaluated using a series of Pearson correlations and linear regression. Finally, changes in the CAS scores were analyzed in random effects models, using the SAS MIXED procedure (Littell, Milliken, Stroup, Wolfinger, & Schabenberger, 2006). The procedure has a number of advantages over traditional repeated-measures analysis of variance, including the ability to include people who have not contributed complete data across all of the follow-up occasions, as well as to allow for variations in the exact timing of the follow-ups (Singer & Willett, 2003).

Results

Sample

A sample of 400 patients was accrued during a two-year period in an attempt to get 240 patients with complete data. The sample of patients providing baseline data was divided into three subgroups: patients receiving opioids (n = 255), those receiving vinca alkaloids (n = 95), and those receiving both (n = 50). Although complete CAS data were available over eight weeks on 271 patients (68%), the breakdown was not equal; the largest group (n = 255) at baseline was the opioid group. Fewer patients were in the opioid plus vinca population, and the authors were not able to reach the goal of 80 patients with complete data in that group.

The combined sample had a mean age of 54.9 years (SD = 12.3), and the mean years of education was 13.6 (SD = 2.5). The majority of participants were married and White non-Hispanic (see Table 1).

Review of medical records indicated that patients had some performance deficits based on their ECOG Performance Status Scale scores (see Table 2), which varied from 0–3; patients with scores greater than 3 were excluded. Forty-eight percent of participants had some comorbidities in addition to their cancers, with CCI scores of 1 and 2 being most common (40%). Patients in the opioid-only group ($\overline{X}$ = 0.94) had significantly more comorbidities (p = 0.021) than the vinca-only group ($\overline{X}$ = 0.61). The majority of patients in the study (n = 305) were receiving opioids (76%), either with or without

Table 1. Sample Characteristics (N = 400)

Characteristic	n	%
Gender		
Female	220	55
Male	180	45
Marital status		
Married	261	65
Single	68	17
Divorced	52	13
Widowed	19	5
Race or ethnicity		
White non-Hispanic	342	86
Hispanic White	27	7
Black non-Hispanic	23	6
Asian or Pacific Islander	2	< 1
Black Hispanic	1	< 1
Other	5	1
Education		
Less than high school graduate	36	9
High school graduate	143	36
Some college	118	30
College graduate	56	14
Graduate school	43	11
Missing data	4	1
Site of primary cancer		
Lymphoma	98	25
Lung	73	18
Breast	65	16
Leukemia	41	10
Invasive skin (melanoma or basal cell)	19	5
Multiple myeloma	17	4
Prostate or testicular	15	4
Pancreas	12	3
Sarcoma	11	3
Head and neck	10	3
Gastrointestinal[a]	4	1
Other	35	9

[a] Includes bile duct, esophagus, gall bladder, and stomach
Note. Because of rounding, not all percentages total 100.

vinca alkaloids. The weekly dose of opioids is reported in morphine equivalents, which, at baseline, ranged from 0–19,320 mg per week with a mean of 1,042 mg (SD = 1,839). Mean weekly doses fluctuated during the eight weeks of the study.

Constipation Trajectory

Constipation using the CAS was assessed weekly for eight weeks. Sixty-nine percent of patients completed all eight weeks of data collection, and 77% completed four or more weeks of data collection. Only 12% of patients dropped out of the study after week 1. CAS scores could range from 0–16, and patients in this study fit the full range. At baseline, 147 (37%) of the patients had no symptoms of constipation, leaving more than 63% of patients with uncontrolled constipation—20% with moderate-to-severe constipation. Forty-three percent reported mild symptoms of constipation (range = 2–5) at baseline. A small number of patients were receiving laxatives or

stool softeners already at baseline (11%). Mean scores across all three patient groups from week to week ranged from 2.3–3.1, but means were pulled down by the 37% of patients with no constipation. Means of the groups tended to decline over time and means in the opioid groups (opioids alone and with vinca alkaloids) tended to be higher than the vinca alkaloid group (see Table 3).

The opioid group exhibited statistically significant decreases in CAS scores over time, but the other two groups did not. Those changes are illustrated in Figure 1. Other medications that could potentially cause constipation also were recorded, but the resulting number was so great and the type so varied in these patients that it could not reasonably be analyzed for inclusion in this article. Constipation intensity and distress were assessed using the MSAS 0–4 scales. At baseline, mean constipation distress (2.4, SD = 1.3) was somewhat higher than constipation intensity (2.3, SD = 1.1).

Relationships Among Variables

Pearson correlations were calculated among baseline study variables, including the ECOG Performance Status Scale, CAS, and constipation intensity and distress from the MSAS. The ECOG Performance Status Scale scores were weak but significantly correlated ($r = 0.18$, $p < 0.001$), with both CAS scores indicating that patients with greater constipation were slightly more likely to have impaired performance status. Constipation as measured by the CAS at baseline was significantly correlated with constipation severity ($r = 0.5$, $p = 0.001$) and distress ($r = 0.43$, $p = 0.001$) as assessed by the MSAS. The strongest relationship was found between MSAS constipation intensity and constipation distress ($r = 0.76$, $p = 0.000$).

Using regression analysis, morphine-equivalent weekly doses were not found to be a predictor of CAS scores at baseline, nor as a predictor of changes in CAS scores during the eight weeks of data collection. Much data was missing (37 missing cases) for the morphine-equivalent doses because some patients could not report how much they had taken in a week.

Discussion

The primary purpose of this study was to evaluate the course of constipation in patients known to be at risk for developing constipation from opioids and/or vinca alkaloids. The majority of patients (63%) had some level of constipation. The constipation mean scores in the total group were significantly lower from baseline to week 8. However, that difference was small and was from the change in the opioids-only group. Scores in the other two groups did not change significantly. Although the change in the opioid groups was so small that it was not clinically significant, it was statistically significant and

deserves scrutiny. Patients were keeping a laxative diary every day. When the RAs called the patients to ask about their constipation severity each week, they also asked about laxatives, thereby linking the two in the minds of the patients although the nurses were careful not to recommend that patients take anything additional. As a result of the weekly data collection, some of the patients likely became more aware of their constipation and began focusing on its treatment. Therefore, although no intervention was provided to this group of patients as part of this study, they experienced a minor but statistically significant improvement in their symptoms. The scores in week 5 began trending back up, so the effect of the telephone calls might have been wearing off. Although self-care was not a focus of this study, it appears that this issue might have been raised by the change in scores. Self-care management involves managing symptoms with the help and support of healthcare professionals (Schulman-Green et al., 2012); perhaps the patients would be able to avoid medication-induced constipation altogether with more systematic assessment and support from the nurses and physicians in the cancer center. However, the issue deserves additional study with a specific focus on self-care management.

Constipation scores assessed during eight weeks using the CAS varied widely but used the full range of possible CAS scores from 0–16, indicating some patients had very severe constipation. The two groups receiving the opioids tended to have more severe constipation than the group receiving only vinca alkaloids; that finding supports earlier research in which patients receiving vinca alkaloids had less intense symptoms of constipation (McMillan & Williams, 1989). Interestingly, the group receiving both opioids and vinca alkaloids had slightly lower scores than the patients receiving opioids only, suggesting a cumulative effect did not exist as might have been expected. That may be a reflection of the general condition of the patients; more severe pain generally tends to occur later in the course of the disease, and patients who are receiving chemotherapy may be earlier in their disease course, therefore having somewhat less pain and needing lower opioid doses. However, additional study is needed to confirm that finding.

Attrition during the eight weeks of the study was relatively high, ranging from 23%–37% in the three groups as illustrated in the CAS data. The highest attrition was in the opioid-only group; some became too debilitated to continue and a few died. That finding might be expected given that the patients receiving only opioids were probably the ones with the most advanced cancers.

Variable Correlations

Constipation scores on the MSAS (intensity and distress) and the CAS (intensity) were significantly correlated, but the correlations were moderate. The CAS had a wider range of scores (0–16) and therefore more variance than the MSAS scores, which were assessed on 0–4 scales. In addition, instead of one question about constipation, the CAS asks about eight common indicators of constipation, such as less frequent or smaller stools or difficulty passing stools. Therefore, although measuring related variables, the scales may be not measuring constipation in precisely the same way. Those relationships between scales, however, further support the validity of the CAS as a measure of constipation.

As might be expected, constipation intensity was strongly related to constipation distress (r = 0.76, p = 0.000) in the MSAS data; however, the relationship was far from perfect. That demonstrates that although a relationship exists between those two variables, they do not represent the same variable. Therefore, assessing both of them is important. Although nurses need to track constipation severity so they can see the effect of laxatives and teach patients about self-care, they also need to know the degree to which this troublesome problem is distressing or bothersome to patients. In a previous symptom study, constipation was shown to

Table 2. Clinical Characteristics (N = 400)

Characteristic	n	%
ECOG Performance Status Scale score		
0	121	30
1	226	57
2	45	11
3	7	2
Missing data	1	< 1
Pain		
Yes	314	79
No	86	22
Cause of pain		
Cancer	164	41
Noncancer	53	13
Cancer and noncancer	89	22
Unknown	8	< 1
No pain	86	22
Charlson Comorbidity Index score		
0	208	52
1	110	28
2	50	13
3	18	5
4	7	2
5	1	< 1
6	3	< 1
7	2	< 1
Missing data	1	< 1

ECOG—Eastern Cooperative Oncology Group

Note. ECOG Performance Status Scale measures functional status on a scale ranging from 0 (normal) to 5 (dead).

Note. Charlson Comorbidity Index is used to determine the number of comoridities affecting patients. Scores can range from 0–35, with comoridities weighted by seriousness.

Note. Because of rounding, not all percentages total 100.

be more distressing than other symptoms, including pain and shortness of breath (McMillan & Rivera, 2009); therefore, it deserves attention.

Although CAS scores were significantly correlated with ECOG Performance Status Scale scores, the relationship was weak (r = 0.18, p = 0.000). That finding seems to suggest that patients with constipation are slightly more likely to have interference with function. However, it also should be noted, based on the very weak correlations, that patients with constipation apparently are able to maintain their functional status to some degree. That supports the idea that patients with cancer may be able to increase their activity, and those who can should be encouraged to be active and drink adequate fluids to decrease constipation (Wilkes et al., 2001). The authors did not collect data about what other things patients might have been doing to manage the constipation on their own. Future studies should include such data.

Limitations

At baseline, the sample size for the opioid group was adequate for the purposes of the study (n = 255) and the vinca alkaloid group (n = 95) was a reasonable size; however, the group receiving both (n = 50) was remarkably smaller than the other two and phase I ended before additional patients receiving vinca alkaloids could be accrued. Nevertheless, statistical comparison of the three groups was not the primary purpose of this study; rather, the purpose was to look at trends, which was quite possible with those sample sizes. One limitation of the study was that all patients came from the same comprehensive cancer center in one geographic area. The breakdown of patients by gender and ethnicity was representative of the population at this cancer center but may not be representative of all patients with cancer in the United States. The cancer diagnoses did not completely reflect the general cancer population. Although lung and breast cancer are very common in the United States, lymphoma and leukemia, the most prevalent cancers in this sample, are less so (American Cancer Society, 2012). The mix of cancers was predetermined, to some extent, by the focus on vinca alkaloids, which are not used to treat all cancers. Therefore, these results may not be completely generalizable to all cancer populations.

The ECOG Performance Status Scale scores varied widely, with some patients having no deficits (0) and others having significant deficits (3) in performance. Patients with scores higher than three were more debilitated and were excluded from the study. Although that exclusion criterion was designed to decrease attrition, it also biased the results to some unknown degree in favor of higher-functioning patients. Almost half had comorbidities based on the chart review, which probably contributed to their performance deficits.

Although 52% of the patients had no comorbidities on the CCI, many did, and some as high as indexes of seven. Significant differences (p = 0.021) were found between the opioid-only and the vinca-only groups in the expected direction, providing additional support for the validity of that index with patients who have varied cancer types.

Patients receiving opioids varied greatly in the doses they were receiving. Only a few were receiving very high doses; the weekly doses of the remainder of patients varied widely, with 50% of patients receiving 500 mg or less morphine-equivalent doses per week and 75% receiving less than 1,200 mg per week. It should be

Table 3. Means, Standard Deviations, and Ranges of CAS Scores by Week for the Three Study Groups (N = 400)

Week	Opioids				Vinca Alkaloids				Opioids and Vinca Alkaloids			
	N	$\overline{X}$	SD	Range	N	$\overline{X}$	SD	Range	N	$\overline{X}$	SD	Range
1	255	3.8	3.2	0–14	95	1.6	1.8	0–9	50	2.6	2.4	0–8
2	216	3.4	3.1	0–13	89	2.4	3.1	0–12	46	2.9	2.9	0–9
3	202	3.1	3	0–16	86	1.5	1.7	0–10	45	3.1	3.2	0–10
4	185	3	3	0–13	82	2	2.7	0–11	41	2.7	2.7	0–10
5	175	2.8	2.7	0–12	75	2.1	2.5	0–11	38	3.1	3	0–12
6	168	2.8	2.9	0–14	76	2	2.7	0–13	38	2.6	2.8	0–10
7	167	2.7	2.9	0–14	72	1.4	2.1	0–10	37	2.1	2.7	0–11
8	161	3	3.1	0–14	72	1.9	2.6	0–14	38	2.5	2.9	0–10

CAS—Constipation Assessment Scale

Note. CAS scores indicate the presence and intensity of constipation. Total scores range from 0 (no constipation) to 16 (worst possible constipation).
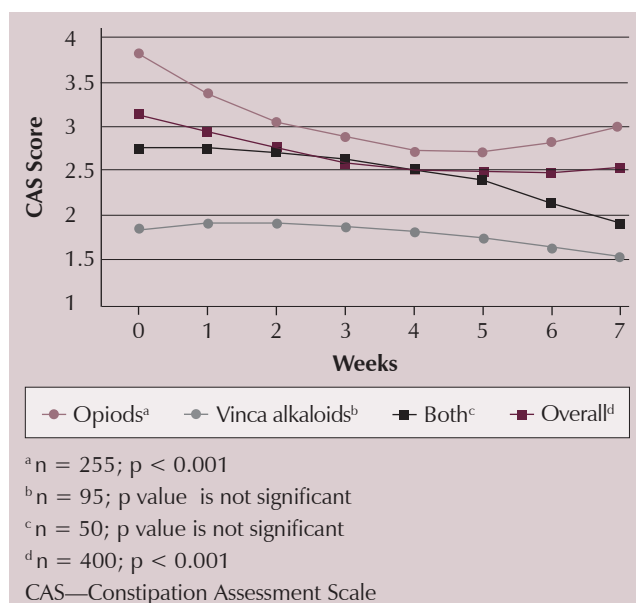
Figure 1. Trajectory of Constipation Over Eight Weeks

[a] n = 255; p < 0.001
[b] n = 95; p value is not significant
[c] n = 50; p value is not significant
[d] n = 400; p < 0.001
CAS—Constipation Assessment Scale

noted that the patients receiving the highest doses were averaging about 115 mg per hour; although high, that dose, when broken down in this way, may not seem unreasonable to oncology nurses who routinely work in palliative care settings.

Conclusions and Implications for Nursing

Patients receiving opioids and those receiving vinca alkaloids are at risk for medication-induced constipation, sometimes severe constipation that, untreated, may be putting them at risk for other more serious complications such as intestinal obstruction. In addition, more severe constipation is likely to cause significant symptom distress in patients with cancer. Given that a focus of oncology nursing is improving the quality of life of patients with cancer, managing constipation to decrease distress seems like an important way for oncology nurses to have a noticeable impact on these patients. The weak relationship between functional status and symptoms seems to suggest that patients may be able to continue to be active even with significant symptoms; therefore, nurses should encourage activity as one way to help decrease the impact of medication-induced constipation. Constipation is a readily treatable problem when it receives the attention it deserves. Simply asking patients about their constipation may lead to some clinically insignificant improvements. If nurses help patients to focus on this problem, the problem likely could be managed completely. The fact that nurses do not appear to be managing medication-induced constipation may indicate a lack of emphasis during their educational programs. The problem might decrease if nursing educators in schools of nursing and continuing education settings would increase the focus on this pervasive problem.

Based on the results of this study, it appears that additional study of medication-induced constipation in patients with cancer is in order. First, intervention studies are needed and may include the impact of a self-care component, consistent assessment, and attention by healthcare providers, as well as whether patients are consistently able to increase activity, fluids, and fiber in their diets. In addition, a study is needed focusing on the cumulative impact of the many and varied medications taken by patients that might contribute to constipation symptoms.

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