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Trajectory of Medication-induced Constipation

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Introduction

Constipation is a common problem among cancer patients and is believed to be among the most nurse-sensitive patient outcomes (Hoekstra, deVos, van Duijn, Schade & Bindels, 2006; McMillan & Rivera, 2009). Although it is very amenable to nursing intervention, constipation often goes unrecognized and untreated in oncology settings (McMillan, Tittle, Hagan & Laughlin, 2000; Miaskowski, 1995; Woolery et al, 2008; Woolery et al, 2006). A significant problem facing oncology nurses with regard to treating medication-induced constipation is the lack of research on which to base treatment decisions. Research in patients with cancer indicated self-reported prevalence to be between 43 and 58%, with mean intensity ranging between 5.2 and 6 on a 0 to 10 scale, demonstrating the significance of the problem (Hoekstra et al., 2006; McMillan & Rivera, 2009). However, these studies did not focus on opioids or other medications as a cause of constipation; thus, very little research has been conducted that can provide clear data on the prevalence and trajectory of medication-induced constipation (Thomas, Karver, Cooney, et al., 2008). The *purpose* of this study was to determine the severity and trajectory of constipation among cancer patients at risk for constipation due to either 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 cancer patients with opioid-induced or other types of constipation. Further, this expert group concluded that, in spite of the frequent occurrence of constipation in oncology patients, 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 among the elderly. It is estimated that the prevalence of constipation in the elderly varies and may be as high as 30%, is more common in women, persons from rural areas, blacks, those from lower socioeconomic levels, and persons residing in northern states

(Hsieh, 2005). In cancer settings it is likely to be even higher; studies have shown constipation to be common with prevalences ranging from 43 to 80% in cancer patients in intensive care units, veterans hospitals, and hospice home care (Hoekstra et al., 2006; McMillan, 2002; McMillan & Rivera, 2009; McMillan, Tittle, Hagan & Laughlin, 2000; Tittle & McMillan, 1994). However, the causes of constipation varied.

Five common causes of constipation in persons with cancer have been reported: 1) the cancer itself which can obstruct the bowel or affect the autonomic nervous system; 2) the disease effects such as dehydration, spinal cord compression, immobility, or changes in normal bowel habits; 3) previous laxative abuse; 4) cancer therapies including one of the vinca alkaloids; and 5) symptom management using one of the opioids or tricyclic antidepressives (Wilkes, Ungwersen & Barton-Burke, 2001).

Opioid-induced Constipation

Opioids are among the most common types of drugs used to treat cancer-related pain (Canty, 1994; Robinson et al, 2000). 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). In fact, because of this 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 this 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. This 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 (Wilkes et al, 2001; 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 persons receiving one of the vinca alkaloids for treatment of cancer (Lehne, 2007; McMillan & Williams, 1989; Wilkes et al, 2001).

Summary

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 cancer patients 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 review suggests that additional research is needed in all areas relating to management of constipation in persons with cancer including understanding the prevalence and trajectory.

This paper reports Phase I results of an NIH-funded clinical trial that was based on the Theory of Unpleasant Symptoms (TOUS). TOUS posits that symptoms are characterized by intensity, distress, timing and quality. Phase I of the study focused only on the intensity and distress of constipation over an 8 week period (timing). Quality is addressed in Phase II of the study which is still underway. Thus, the focus of this paper is the description of the trajectory and the intensity and distress of medication-induced constipation over eight weeks.

METHODS

Setting and Sample

The setting was an NCI-designated comprehensive cancer center that sees more than 6,600 new patients annually with a variety of cancers. The outpatient clinics have approximately 170,000 clinic visits annually. At the time of the study, there was no standard treatment or prevention protocol for constipation for patients receiving opioids or vinca alkaloids, so care providers in the cancer center could address this problem or not, as they chose.

To be *included* in the study, 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. They were adults over 18 years and able to consent, were alert, and able to read and understand English. Mental status was screened at accrual to insure patients had sufficient cognitive capacity to respond to self-report instruments.

Patients were *excluded*: if they had non-melanoma skin cancer, gynecologic or colorectal cancer as their primary diagnosis, or if they were excessively debilitated or deemed unlikely to survive for the eight weeks of data collection. Performance status was assessed using the Eastern Cooperative Oncology Group (ECOG) Performance Status Scale score (Oken, Creech Tormey, et al., 1982); a score of greater than 3 excluded the patient from the study. They also were excluded if they were unable to read and understand English; if they had an ostomy that changed bowel function; if they had a current peritoneal catheter; if they had 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 this did not occur in this sample.

Instruments

Short Portable Mental Status Questionnaire—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 to 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 8 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 ($r=.79$) was evaluated with a group of 340 patients with advanced cancer using an internal consistency approach; this supported reliability of the SPMSQ (McMillan, Small, Weitzner, Schonwetter, Tittle, Moody, & Haley, (2006).

Eastern Cooperative Oncology Group (ECOG) Performance Status Scale—The ECOG is a measure of functional status that is widely used in oncology settings to assess patient functioning. It is scored on a scale from 0 (normal) to 5 (dead). ECOG scores were used to determine patient eligibility for the study. Patients with scores higher (worse) than 3 were excluded (Oken et al., 1982).

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

Constipation Assessment Scale—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 no problem (0), some problem (1), or severe problem (2). Total scores may range from 0 (no constipation) to 16 (worst possible constipation). Validity was supported in an earlier study (McMillan & Williams, 1989) by significant difference between patients known to be at risk due to vinca alkaloids or opioids and a group of apparently healthy adults ($p=.0001$). A further 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 previously. The significant difference between these two groups ($p<.01$) 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 ($r=.70$ to $.78$) were acceptable for such a short scale. Test-retest with brief delay provided strong evidence of reliability ($r=.98$) (McMillan & Williams, 1989).

Laxative Interview—At each contact, patients were asked if they have used any form of laxative (oral, suppository, enema) during the past week. All doses were recorded by the

RAs on a laxative interview form as number of days a laxative was used and types of laxatives.

Memorial Symptom Assessment Scale (MSAS)—The 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; 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 to 4 scale with 4 being the greatest bother. Intensity also is asked on a 0 to 4 scale, with 4 being the greatest intensity or severity. Validity and reliability data for the MSAS have been strong when the tool was used with persons 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 persons with cancer (.83–.88) (Porteney, Thaler, Kornblith et al, 1994).

Demographic Data Form—Standard demographic data were collected to allow description of the sample. Data included: age, gender, marital status, race/ethnicity, education, and cancer diagnosis. In addition, the chart was reviewed to determine the ECOG Performance Status Score, and the Charlson Co-morbidity Score. Cancer stage was not recorded because these 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 Cancer Center, the proposal was approved by the Institutional Review Board for the University.

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 research assistants (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 RA’s could ask the questions over the telephone while the patients were looking at the items on the instruments.

Baseline Data Collection—During this initial contact, patients were interviewed to collect demographic data. The CAS, the MSAS, and the Laxative Interview were administered. Following the interview, the chart was reviewed.

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 past 24 hours and any laxatives or stool softeners taken. These diaries were not taken by the RAs but were used solely by the patients.

Follow-up Data—Patients were contacted via telephone at one week intervals for data collection. During these telephone contacts, patients responded to the items on the CAS and the laxative interview. They completed the items on the MSAS during the interviews weeks 4 and 8. At the end of the study, the chart again was reviewed to determine what changes in dose of medication (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 have been removed from the study and their attending physicians notified. However, no patients became impacted during the course of the study. After the week eight 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 SAS Proc Mixed (Littell, Milliken, Stroup, Wolfinger & Schabenberger, 2006). There are a number of advantages of this procedure over traditional repeated measures ANOVA, including the ability to include persons 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 over 2 years in an attempt to get 240 patients with complete data. The sample of patients providing baseline data was divided into three sub-groups: patients receiving opioids (n=255), those receiving vinca alkaloids (n=95) and those receiving both (n=50). Although complete CAS data was available over eight weeks on 271 patients (67.5%), the breakdown was not equal; the largest group (n=255) at baseline was the opioid group. There were many fewer patients in the opioid plus vinca population, and we 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), had slightly more women (55%) than men, and the majority (85.5%) were married and white/non-Hispanic (85.5%) (Table 1). Years of education ranged from 5 to 21, with a mean of 13.6 (SD=2.5). The most common primary sites of cancer according to the medical record were lymphoma (24.5%), lung (18.3%), breast (16.3%) and leukemia (10.3%) (Table 1).

Review of medical records indicated that the patients had some performance deficits based on their ECOG Performance Status Scale scores (Table 2) which varied from 0 to 3; patients with scores greater than 3 were excluded. Slightly less than half of patients (48%) had some co-morbidities in addition to their cancers with Charlson scores of 1 and 2 being most common (40%). Patients in the opioid only group (mean=.94) had significantly more co-morbidities ($p=.021$) than the vinca only group (mean = .61). The majority of patients in the study (n=305) were receiving opioids (76.2%) either with or without vinca alkaloids. The weekly dose of opioid is reported in morphine equivalents which, at baseline, ranged from

none to 19,320 mg per week with a mean of 1,042 mg (SD=1839). Mean weekly doses fluctuated during the eight weeks of the study (Table 3). A small subset could not report the amount of opioid taken during the week, so that data is missing from the table.

Constipation Trajectory

Constipation using the CAS was assessed weekly for eight weeks. Most patients (68.5%) completed all 8 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 to 16, and patients in this study used the full range. At baseline, 147 of the patients had no symptoms of constipation, leaving more than 63% of patients with uncontrolled constipation, with 20% having moderate to severe constipation. Forty-three percent reported mild symptoms of constipation (mean scores 2 to 5) at baseline. A small number of patients was already receiving laxatives or stool softeners at baseline (11%). Mean scores across all three patient groups from week to week ranged from a low of 2.3 to a high of 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 (Table 4).

The opioid group exhibited statistically significant decreases in CAS scores over time, but the other two groups did not. These changes are presented in Table 5 and 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 paper.

Constipation intensity and distress were assessed using the MSAS 0 to 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, CAS, and constipation intensity and distress from the MSAS. The ECOG Performance Status scores were weakly but significantly correlated ($r=.18$; $P<.001$) 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 ($r=.50$, $p=.001$) and distress ($r=.43$, $p=.001$) as assessed by the MSAS. The strongest relationship was found between constipation intensity and constipation distress ($r=.76$; $p=.000$).

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 over the 8 weeks of data collection. It should be noted that there was much missing data (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 constipation due to 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 eight. However, this difference was small and was due to 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 even though these nurses were careful not to recommend that patients take anything additional. It is likely that as a result of the weekly data collection, some of the patients became more aware of their constipation and began focusing on its treatment while others did not. Thus, 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 health care professionals (Schulman-Green, et al., 2012); perhaps with more systematic assessment and support from the nurses and physicians in the cancer center, these patients would be able to avoid medication-induced constipation altogether. However, this issue deserves further study with a specific focus on self-care management.

Constipation scores assessed over 8 weeks using the CAS varied widely but used the full range of possible CAS scores from 0 to 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; this finding supports earlier research (McMillan & Williams, 1989) in which patients receiving vinca alkaloids had less intense symptoms of constipation. Interestingly, the group receiving both opioids and vinca alkaloids had slightly lower scores than the patients receiving opioids only, suggesting there was not a cumulative effect as might have been expected. This may be a reflection of the general condition of the patients. That is, 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, thus, having somewhat less pain and needing lower opioid doses. However, further study is needed to confirm this finding.

It should be noted that attrition over the eight weeks of the study was relatively high ranging from 23% to 37% in the three groups as illustrated in the CAS data (Table 4). The highest attrition was in the opioid-only group; some became too debilitated to continue and a few died. This finding might be expected given that the patients receiving only opioids were probably the ones with the most advanced cancers.

Relationships Among Variables

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 thus more variance than the MSAS scores which were assessed on 0 to 4 scales. In addition, instead of one question about constipation, the CAS asks about 8 common indicators of constipation such as less frequent or smaller stools or difficulty passing stools. Thus, although measuring related variables, these scales may be not measuring constipation in exactly the same way. These relationships between scales, however, do further support the validity of the CAS as a measure of constipation.

As might be expected, constipation intensity was strongly related to constipation distress ($r=.76$; $p=.000$) in the MSAS data; however, the relationship was far from a perfect one. This relationship demonstrates that while there is a relationship between these two variables, they do not represent the same variable. Thus, it is important to assess both of them. While nurses need to track constipation severity so they can see the impact of laxatives and teaching patients about self care, they also need to know the degree to which this troublesome problem is distressing or bothersome to the patients. In a previous symptom study, constipation was shown to be more distressing than other symptoms, including both pain and shortness of breath (McMillan & Rivera, 2009); thus it deserves attention.

While CAS scores were significantly correlated with ECOG Performance Status Scale scores, the relationship was weak ($r=.18$; $p=.000$). This 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. This 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 as one way to decrease constipation (Wilkes et al., 2001). We 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.

Sample

At baseline, the sample size for the opioid group was very good ($n=255$) and the vinca alkaloid group ($n=95$) was a reasonable size, although 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. However, statistical comparison of the three groups was not the primary purpose of this study; rather, the purpose was to look at trends, and this was quite possible with these sample sizes. A limitation of the study was that all patients came from one 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 cancer patients in the U.S. The cancer diagnoses did not completely reflect the general cancer population. While lung and breast cancer are very common in the U.S., lymphoma and leukemia, the most prevalent cancers in this sample, are less so (ACS, 2012). The mix of cancers was pre-determined, to some

extent, by the focus on vinca alkaloids which are not used to treat all cancers. Thus, 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 3 were more debilitated and were excluded from the study. Although this 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 co-morbidities based on the chart review; this probably contributed to their performance deficits.

Although just over half of the patients (52%) had no co-morbidities on the Charlson Index, many did, and some as high as indexes of 7. In this sample, we found a significant difference ($p=.021$) between the opioid-only and the vinca-only groups in the expected direction, providing additional support for the validity of this index with patients who have varied cancer types.

Patients receiving opioids varied greatly in the doses they were receiving. Only a few were receiving the very high doses; the weekly doses of the remainder of patients varied widely with half of patients receiving 500 mg or less morphine equivalent doses per week and 75% receiving less than 1200 mg per week. It should be noted that the patients receiving the highest doses were averaging about 115 mg per hour; while high, this 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, sometime severe constipation that, untreated, may be putting the patient at risk for other more serious complications such as intestinal obstruction. In addition, constipation that is more severe is likely to cause significant symptom distress in cancer patients. 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; thus, 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. It appears that simply asking patients about their constipation might have led to some clinically insignificant improvements. If nurses caring for these patients were helping patients to focus on this problem, it is likely that the problem could be managed completely. The fact that nurses do not appear to be managing medication-induced constipation may indicate that it is not emphasized during their educational programs. The problem might decrease if nursing educators in both schools of nursing and in continuing education settings would increase the focus on this pervasive problem.

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

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Figure 1.
Trajectory of Constipation Over 8 Weeks

Table 1Frequency and Percent of Patients^a by Demographic Variable

Variable	Frequency	Percent
Men	180	45
Women	220	55
Marital Status		
Married	261	65.3
Single	68	17.0
Divorced	52	13.0
Widowed	19	4.8
Race/Ethnicity		
White/non-Hispanic	342	85.5
Hispanic/White	27	6.8
Black/non-Hispanic	23	5.8
Asian/Pacific Islander	2	0.5
Black/Hispanic	1	0.3
Other	5	1.3
Education		
Less than HS Graduate	36	9.0
High School Graduate	143	35.9
Some College	118	29.6
College Graduate	56	14.1
Graduate School	43	10.8
Missing data	4	1.0
Site of Primary Cancer		
Lymphoma	98	24.5
Lung	73	18.3
Breast	65	16.3
Leukemia	41	10.3
Invasive skin (melanoma & Basal cell)	19	4.8
Multiple myeloma	17	4.3
Prostate/Testicular	15	3.8
Pancreas	12	3.0
Sarcoma	11	2.8
Head and Neck	10	2.5
Gastrointestinal (Bile duct, Esophagus, Gall Bladder & Stomach)	4	1.0
Other	33	8.3

^aN=400

Table 2

Frequency and Percent of Patients^a by Clinical Variables: Performance Status Score, Presence of Pain, Cause of Pain, and Co-morbidity Score

Variable	Frequency	Percent
ECOG Performance Status Score		
0	121	30.3
1	226	56.5
2	45	11.3
3	7	1.8
Missing data	1	<1
Pain		
Yes	314	78.5
No	86	21.5
Cause of Pain		
Cancer	164	41.0
Non-cancer	53	13.3
Cancer and non-cancer	89	22.3
Unknown	8	<1
No pain	86	21.5
Charlson Co-morbidity Score		
0	208	52.0
1	110	27.5
2	50	12.5
3	18	4.5
4	7	1.8
5	1	<1
6	3	<1
7	2	<1
Missing data	1	<1

^aN=400

Table 3

Ranges, Means and Standard Deviations for Weekly Morphine Equivalents in Opioid and Opioid plus Vinca Groups^a

Week	N	Range	Mean	SD
1	268	0–19,320	1042.8	1893
2	237	0–17,640	986.7	1802
3	221	0–17,640	954.0	1764
4	211	0–17,640	977.8	1792
5	199	0–17,640	999.3	1802
6	191	0–17,640	933.7	1716
7	189	0–17,640	935.1	1688
8	189	0–14,490	914.8	1517

^a
n=305;

data missing for 37 patients

Table 4
Means, Standard Deviations and Ranges of CAS Scores by Week for the Three Study Groups^a

Week	Opioids				Vinca Alkaloids				Both Vinca+ Opioid			
	N	Mean	SD	Range	N	Mean	SD	Range	N	Mean	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	0-16	86	1.5	1.7	0-10	45	3.1	3.2	0-10
4	185	3.0	3.0	0-13	82	2.0	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	0-12
6	168	2.8	2.9	0-14	76	2.0	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	3.0	3.1	0-14	72	1.9	2.6	0-14	38	2.5	2.9	0-10

^aN=400

Table 5

Estimate of changes in CAS Scores over time.

Estimate	Overall (n = 400)	Opioids (n = 255)	Vinca Alkaloids (n = 95)	Both (n = 50)
Intercept	3.19***	3.79***	1.85***	2.72***
Time	-.26***	-.45***	.06	.05
Time*Time	.02*	.05***	-.01	-.02