Chemotherapy-Induced Vomiting in Women Treated for Breast Cancer

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Purpose/Objectives: To describe the incidence and intensity of vomiting in women receiving chemotherapy treatment for breast cancer since the advent of 5-HT_3 antagonists.

Design: Longitudinal, descriptive.

Setting: 7 outpatient oncology clinics situated in hospitals, 5 outpatient oncology clinics associated with major teaching universities, 27 private outpatient oncology practices, and 1 outpatient clinic located in a county hospital.

Sample: Typical participants (N = 303) were 51.9 years, Caucasian (79%), married or partnered (65%), born U.S. citizens (93%), heterosexual (96%), living with someone (84%), and high school graduates (82%).

Methods: Baseline and poststudy questionnaires and a daily diary of vomiting through two cycles of chemotherapy (approximately two months) were used to collect data.

Main Research Variable: Vomiting experience.

Findings: The worst vomiting occurs three days after having chemotherapy for breast cancer. The types of oral antiemetics ordered for home use were changed between the two cycles of the study only 8% (n = 24) of the time. No demographic factors were associated with acute vomiting at times 1 or 2; younger age ($r = -0.16$; $p = 0.012$) was associated with more vomiting. Delayed vomiting was associated with age and body mass index, and younger, heavier women experienced more vomiting. Minority women (n = 55) reported significantly more delayed vomiting than did Caucasian women ($\bar{X} = 6.56$ versus 2.82; $t = 2.02$; $p < 0.05$).

Conclusions: Vomiting continues to be a significant problem for some women receiving chemotherapy for breast cancer.

Implications for Nursing: Oncology nurses can use the results from this study to provide anticipatory guidance for patients undergoing chemotherapy for breast cancer and to support efforts to provide appropriate symptom management for these women.

Key Points . . .

- Chemotherapy-induced acute vomiting continues to be a problem for approximately 15% of women treated for breast cancer despite the advent of 5-HT_3 antagonists.
- Medications rarely are changed between cycles of chemotherapy even though better antiemetic control is needed.
- Delayed chemotherapy-induced vomiting affects more than a third of women undergoing treatment for breast cancer.
- Minority women experience delayed chemotherapy-induced vomiting significantly more frequently than Caucasian women.

An estimated 211,300 women were diagnosed with breast cancer in 2003, 32% of all new female cancer cases in that year (American Cancer Society, 2003). Many of these women received chemotherapy. Two of the side effects of chemotherapy, nausea and vomiting, remain a major worry for patients who are undergoing treatment for breast cancer. The positive relationship between breast cancer survival and the completion of a full course of chemotherapy demonstrates the necessity for adherence to the treatment plan. Research has documented that some patients experiencing postchemotherapy nausea and vomiting have withdrawn from seemingly beneficial treatment (Fessele, 1996; Osoba et al., 1997), and 10%–50% of patients may refuse or delay chemotherapy treatments because of fears about nausea and vomiting (Pendergrass, 1998).

Vomiting is a physical protective reaction to the ingestion of toxins resulting in the expulsion of gastric contents through the mouth. Vomiting during chemotherapy is distinguished as either anticipatory and acute, occurring within 24 hours of initial administration, or delayed, occurring after 24 hours. Researchers have theorized that the physiologic causes of acute and delayed vomiting differ because the pharmacologic agents that are effective in acute vomiting are not as effective with delayed vomiting (Kris, Roila, De Mulder, & Marty, 1998; Maisano et al., 2000). Chemotherapy-induced vomiting is an area that requires better understanding and treatment and, therefore, was the focus of this study.

Chemotherapy for breast cancer consists of the following standard chemotherapy regimens: cyclophosphamide, methotrexate, and 5-fluorouracil and cyclophosphamide and

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doxorubicin, with or without 5-fluorouracil and with or without paclitaxel. Although these are considered mildly to moderately emetogenic regimens, they have been associated with a significant amount of nausea and vomiting (Goodman, 1997; Greene, Nail, Fieler, Dudgeon, & Jones, 1994; Stewart, 1996). Despite the advent of new medications, specifically 5-HT_3 antagonists, acute vomiting appears to persist in 10%–25% of women receiving chemotherapy treatment for breast cancer (Uyl-de Groot, Wait, & Buijt, 2000). Delayed chemotherapy-induced vomiting is associated particularly with cyclophosphamide and doxorubicin, with an incidence of 33%–67% (American Cancer Society & National Comprehensive Care Network, 2001; Kris et al., 1998). Nausea and vomiting are a symptom cluster that has been studied together for decades. The current study's authors have chosen to deconstruct them to better understand each as a separate side effect, both in their acute and delayed phases (see Dibble, Israel, Nussey, Casey, & Luce, 2003).

Seventy-five percent of patients who experience vomiting within the first 24 hours after receiving chemotherapy are likely to experience delayed vomiting as well (Italian Group for Antiemetic Research, 1999). Twenty-five percent of those who do escape nausea and vomiting within the first 24 hours also will develop delayed vomiting (Italian Group for Antiemetic Research, 2000). Treating acute vomiting therefore is seen as an important component in preventing delayed vomiting. Chemotherapy induces acute vomiting through direct or indirect stimulation of the chemoreceptor trigger zone (CTZ) and vomiting center. The CTZ is located outside of the blood-brain barrier and, therefore, can be stimulated directly by cytotoxic agents in the bloodstream or cerebrospinal fluid (Pendergrass, 1998). The CTZ stimulates the vomiting center through key receptors: serotonin (5-HT_3), dopamine, and neurokinin (Oettle & Riess, 2001). The CTZ also can be stimulated by enterochromaffin cells on the gastrointestinal mucosa that, when assaulted by cytotoxic agents, release 5-HT_3, which binds to 5-HT_3 receptors along the gastrointestinal tract, vagus nerve, and, ultimately, the CTZ, which then sends a signal to the vomiting center (American Cancer Society & National Comprehensive Care Network, 2001; Dicato, 1996). The stimulation of enterochromaffin cells and resultant release of 5-HT_3 largely is responsible for acute chemotherapy-induced nausea and vomiting (Maisano et al., 2000). Understanding this chain of events and role of neurotransmitters is important in choosing a medication to treat acute vomiting. Because the pathways mediating delayed vomiting are believed to be different from acute vomiting and are not well understood, an effective medication regimen that targets delayed vomiting has not been found.

The most effective medications used to treat chemotherapy-induced acute vomiting are aimed at blocking the neurotransmitters mentioned that ultimately stimulate the vomiting center: 5-HT_3, dopamine, and neurokinin. These medications include 5-HT_3 receptor antagonists, such as ondansetron, granisetron, and tropisetron, and dopamine-receptor antagonists, such as metoclopramide and alizapride, and are most effective if given prior to initiation of treatment. They can be used alone or in combination with a corticosteroid such as dexamethasone (Oettle & Reiss, 2001; Pendergrass, 1998). The combination of a 5-HT_3 receptor antagonist and a corticosteroid, especially dexamethasone, is considered the "gold standard" in treating acute vomiting with moderately to highly emetogenic doses of cyclophosphamide (Bartlett & Koczwara, 2002; Clavel, Soukop, & Greenstreet, 1993; Oettle & Reiss; Stewart, 1996). For patients receiving moderately emetogenic regimens, the 5-HT_3 receptor antagonists alone do not appear to be effective in controlling delayed vomiting, leaving a 22%–89% incidence of delayed nausea and emesis (Italian Group for Antiemetic Research, 2000; Uyl-de Groot et al., 2000).

The initial studies of the 5-HT_3 receptor antagonists, their interpretation by clinicians, and the observation of women as they undergo chemotherapy would suggest that acute vomiting almost has been eliminated from the acute side affects associated with chemotherapy administration with control rates of 75%–90% (Uyl-de Groot et al., 2000). Unfortunately, the concerns of 33%–67% of women receiving moderately emetogenic chemotherapy who continue to experience vomiting after this acute period are not being addressed effectively (Kris et al., 1998). Therefore, the purpose of the current study was to describe the acute and delayed vomiting experience and intensity in women undergoing chemotherapy for breast cancer since the advent of the 5-HT_3 receptor antagonists.

Methods

Design

The design for this multisite research was a longitudinal descriptive study over two cycles of chemotherapy. A cycle of chemotherapy for women with breast cancer usually ranges from 21–28 days.

Sample and Setting

The settings for this study conducted from July 1999 through December 2000 consisted of 40 sites throughout the United States, including 7 outpatient oncology clinics situated in hospitals, 5 outpatient oncology clinics associated with major teaching universities, 27 private outpatient oncology practices, and 1 outpatient clinic located in a county hospital. The sites were located in the western, eastern, and midwestern United States and one site in Virginia. The sites were a combination of urban and rural. The eligibility criteria included (a) receiving any vomiting-inducing chemotherapy regimen in the treatment of breast cancer, (b) the ability to communicate (verbally and in writing) in English, and (c) the willingness to participate in the study. Of the 353 eligible women who were approached to participate, 50 women refused. The most common reason patients gave for refusal to participate was feeling overwhelmed.

Instruments

Patient information questionnaire: Demographic information collected included age, education, partnership status, ethnicity, employment status, and income. This tool has been used successfully to collect demographic data in previous work.

Disease and treatment questionnaire: Information gathered from the medical record included diagnostic information, treatment regimen, chemotherapy dosages, and antiemetics ordered. This tool has been used successfully to collect treatment data in previous work.

A daily log consisted of the three-item vomiting experience subscale from **Rhodes Index of Nausea, Vomiting, and Retching (INVR).** This scale has established reliability and validity (Rhodes, Watson, & Johnson, 1984; Rhodes, Watson, Johnson, Madsen, & Beck, 1987). Items from this subscale were summed. Subscale scores could range from 0–12 with a

higher number reflecting a more severe vomiting experience. In addition, the log also provided a place for each person to record any interventions used for nausea and vomiting control. Ratings were done on a daily basis, before bedtime.

The **exit questionnaire** packet included a series of questions about other things (besides medication) that the participant may have tried to alleviate chemotherapy-induced vomiting, and three evaluation questions.

Procedures

Institutional review board approval of the protocol was obtained for each institution participating in this study. Potential participants were approached about the study by the research assistants in the waiting room, by their physician, or by their nurse. After consenting to take part in the study, participants completed the baseline data collection and were taught how to complete the daily logs. All women received their usual antiemetics as prescribed by their physicians and recorded their usage on a daily basis. The participants recorded in their daily log for two cycles of chemotherapy. Women receiving chemotherapy on a weekly basis were asked to complete their logs for three weeks per log.

To exit the study, participants were scheduled to arrive 30 minutes early on the first day of their next chemotherapy cycle (after completing data for two cycles of chemotherapy) to complete the exit questionnaire. In addition, nurses reviewed the patients' medical records to obtain information about their cancer diagnosis, antiemetic prescription, and current, previous, and known future treatment modalities. All participants who completed the study were paid $10 to thank them for their time.

Data Analysis

SPSS® statistical software package (SPSS Inc., Chicago, IL) and SAS® (SAS Institute Inc., Cary, NC) were used for data analysis. Data were double entered into SPSS, and discrepancies between the files were resolved to ensure the accuracy of the data entered. Descriptive statistics were generated related to sample characteristics and other variables of interest. Repeated measures analysis of variance (ANOVA) was used to answer the research questions. With this analysis strategy, participants serve as their own controls, so that the variability caused by the individual differences is eliminated from the error term (Dawson-Saunders & Trapp, 1994). This analysis technique is quite robust with small sample sizes and statistical assumption violations. In addition, a Delayed Vomiting Scale (DVS) was created by adding the three-item vomiting subscale of the INVR for days 1–10 after chemotherapy administration (day 0). Scores on the DVS could range from 0–120. Because of the small sample size, the researchers did not attempt to explore differences resulting from setting or types of treatment. Other statistical tests used were t tests, paired t tests, chi square, McNemar, and ANOVA.

Results

Typical participants (N = 303) were 51.9 years old (SD = 11.0), Caucasian (79%), married or partnered (65%), not on disability (86%), unemployed (52%), born U.S. citizens (93%), heterosexual (96%), not living alone (84%), and had an annual personal income of more than $20,000 (58%). The average education for these participants was 13.9 years (SD = 2.9); 56% had more than a high school education. The average body mass index (BMI = a ratio of weight to height) for these women was 28.3 kg/m^2 (SD = 6.1 kg/m^2); 30% of the women had a BMI from 25–30, which reflects being overweight; and 35% of the women had a BMI of greater than 30, which indicates obesity. Most (60%) of the women had experienced morning sickness with a pregnancy, 24% had a history of seasickness, 20% had a history of car sickness, and 22% had a history of nausea with stress (see Table 1).

Table 1. Demographic Characteristics

Characteristic	n	%
Age (years)		
$\bar{X}$ (SD) = 51.9 (11.0)	–	–
Range = 28–86	–	–
Education (years)		
$\bar{X}$ (SD) = 13.9 (2.9)	–	–
Range = 7–23	–	–
Body mass index (kg/m^2)		
$\bar{X}$ (SD) = 28.3 (6.1)	–	–
Range = 15.5–40.4	–	–
Ethnicity		
Caucasian	239	79
Other	62	21
Sexual orientation		
Heterosexual	272	96
Other	12	4
Employed		
Yes	145	48
No	155	52
Born a U.S. citizen		
Yes	281	93
No	22	7
Retired		
Yes	66	22
No	234	78
Disabled		
Yes	41	14
No	259	86
Income		
< $20,000	106	42
$20,000–$39,999	79	32
> $40,000	65	26
Relationship status		
Married or partnered	196	65
Other	105	35
Lives alone		
Yes	48	16
No	253	84
History of car sickness		
Yes	62	20
No	240	80
History of seasickness		
Yes	72	24
No	229	76
History of nausea with stress		
Yes	67	22
No	235	78
History of morning sickness		
Yes	181	60
No	121	40

N = 303

Note. Because some data are missing for some variables, the n values may not equal the total N.

The average time since diagnosis for these women was 2.64 months (SD = 9.28 months, range = 0.07–139.6 months). Included in these statistics are two women who had recurrent disease. Excluding those two women resulted in an average time since diagnosis for the sample of 1.93 months (SD = 1.87) or approximately two months. Most participants had a surgical biopsy (64%) to determine that they had infiltrating ductal breast cancer (80%). Most (62%) of the women did not have a mastectomy. Multiple lymph nodes were examined in 241 women (80%), and 12% of the women had a sentinel node biopsy. Positive nodes were reported in 46% (n = 123) of the participants. Radiation therapy had been completed or was concurrent with their chemotherapy in 7% of the sample, and 61% (n = 171) were planning radiation therapy after finishing their chemotherapy (see Table 2).

Most (76%) of the women were receiving doxorubicin and cyclophosphamide as their chemotherapy regimen. The average dose of doxorubicin was 102.7 mg and the average dose of cyclophosphamide was 993.2 mg. The dosages of chemotherapy were reduced between the two cycles of the study only 5% (n = 14) of the time. The most common IV antiemetics given during the administration of chemotherapy were dexamethazone (80%), ondansetron (49%), granisetron (24%), and dolasetron (17%). Numerous combinations and dosages were given pre- and postchemotherapy. No one combination or dosage emerged as the "right" treatment for controlling acute or delayed vomiting. The types of IV antiemetics were changed between the two cycles of the study only 6% (n = 18) of the time. The most common antiemetic ordered for home use was prochlorperazine (70%). The types of oral antiemetics ordered for home use were changed between the two cycles of the study only 8% (n = 24) of the time (see Table 3).

The pattern of acute and delayed vomiting as measured by the INVR vomiting subscale can be observed in Figure 1. The worst vomiting occurs the day of chemotherapy and for the next three days as measured by the INVR. Included in those statistics are those who did not experience vomiting on a particular day. Figure 2 details the percentage of participants who described any vomiting as measured by the vomiting subscale

Table 2. Diagnostics and Surgical Treatments Used

Characteristic	n	%
Time since diagnosis (months)[a]		
$\bar{X}$ (SD) = 1.93 (1.87)	–	–
Range = 0.07–19.4	–	–
Surgical biopsy		
Yes	193	64
No	108	36
Lumpectomy		
Yes	145	48
No	156	52
Mastectomy		
Yes	113	38
No	188	62
Lymph node dissection		
Yes	241	80
No	60	20
Sentinel node biopsy		
Yes	37	12
No	264	88
Positive nodes		
Yes	123	46
No	142	54
Type of breast cancer		
Infiltrating ductal	238	80
Infiltrating lobular	25	8
Other	35	12
Radiation therapy		
Yes	19	7
No	92	33
Planned after chemotherapy	171	61

N = 303

[a] Does not include two patients who had recurrence

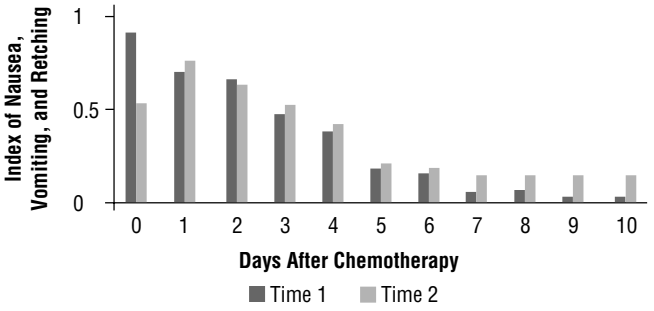
Note. Because some data are missing for some variables, the n values may not equal the total N. Because of rounding, percentages may not total 100.

Table 3. Chemotherapy Treatments Used

Treatment	n	%
Chemotherapy regimen		
Cyclophosphamide, methotrexate, and 5-fluorouracil	34	11
Cyclophosphamide and doxorubicin	228	76
Cyclophosphamide, doxorubicin, and 5-fluorouracil	5	2
Cyclophosphamide, doxorubicin, and paclitaxel	7	2
Other	28	9
Weekly chemotherapy		
Yes	23	7
No	277	93
Dosage of cyclophosphamide (mg) (n = 273)		
$\bar{X}$ (SD) = 993.2 (267.7)	–	–
Range = 90–1,888	–	–
Dosage of 5-fluorouracil (mg) (n = 41)		
$\bar{X}$ (SD) = 920.6 (232.2)	–	–
Range = 60–1,200	–	–
Dosage of doxorubicin (mg) (n = 258)		
$\bar{X}$ (SD) = 102.7 (16.9)	–	–
Range = 30–145	–	–
Dosage of chemotherapy decreased with next cycle		
Yes	14	5
No	285	95
IV antiemetics given		
Dexamethazone	241	80
Ondansetron	148	49
Granisetron	72	24
Dolasetron	51	17
Lorazepam	20	7
Diphenhydramine	7	2
Prochlorperazine	12	4
IV antiemetics changed with subsequent chemotherapy		
Yes	18	6
No	282	94
Oral antiemetics ordered		
Prochlorperazine	211	70
Ondansetron	113	38
Dexamethazone	68	23
Lorazepam	59	20
Granisetron	36	12
Phenergan	15	5
Diphenhydramine	15	5
Oral antiemetics changed with subsequent chemotherapy		
Yes	24	8
No	273	92

N = 303

Note. Because some data are missing for some variables and some patients received more than one antiemetic treatment, the n values may not equal the total N and percentages may not total 100.



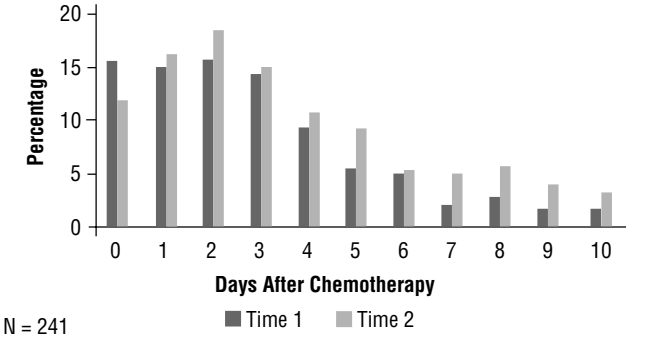
N = 241

Figure 1. Vomiting Over Time

of the INVR on a particular day for this sample. This figure reveals that less than one-fifth of the women undergoing treatment for breast cancer on any given day actually experienced vomiting after receiving chemotherapy, with the worst day being two days after the administration of chemotherapy. When the women who did not experience vomiting on a particular day are eliminated from the analyses, vomiting clearly is a significant problem for those who have it (see Figure 3).

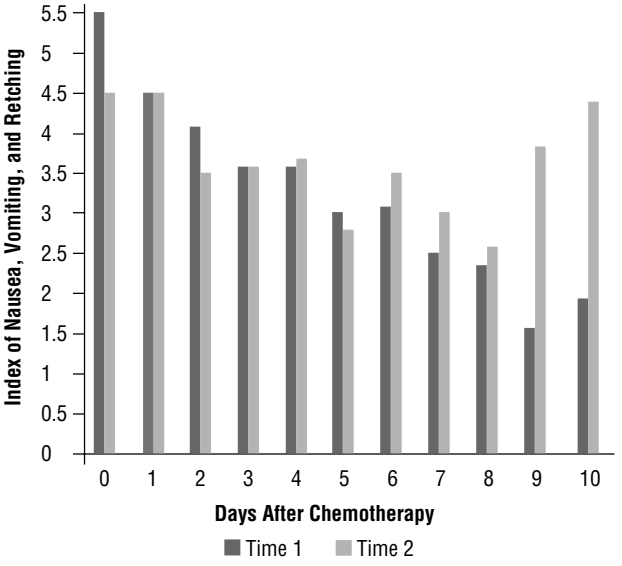
The average Acute Vomiting Score (AVS) was 0.82 (SD = 2.2) during the first data collection period and 0.55 (SD = 1.7) for the second data collection period. This difference was not statistically significant ($t = 1.66$, $p = 0.099$; $n = 255$). Using a McNemar test, significant ($p < 0.0001$) differences existed in the percentage of women with acute vomiting from the first to second data collection periods. Eighty-two percent (n = 216) of the sample had absolutely no acute vomiting during both time periods and 0.4% (n = 1) had acute vomiting during both time periods. Of the 223 women without acute vomiting at the first data collection period, seven (3%) developed acute vomiting with their next cycle. Of the 42 women with acute vomiting at the first data collection period, 41 (98%) did not have acute vomiting with their next cycle.

The mean DVS score for the women during the first data collection period was 2.8 (SD = 6.0), and the mean DVS score during the second data collection period was 3.5 (SD = 9.2). Again, these values were compared using a paired t test, and no significant differences existed in delayed vomiting between the two time periods ($t = 1.623$; $p = 0.106$; $n = 242$). In exploring the percentage of women who had absolutely no delayed vomiting, the authors found that 63% (n = 165) of the women did not have any delayed vomiting during the first data collection period and 64% (n = 161) did not have any delayed vomiting during the second data collection period. In comparing delayed vomiting at both time periods using a McNemar test, no significant differences existed in the percentage of women with delayed vomiting from the first to second data collection periods. Forty-eight percent (n = 116) of the sample had absolutely no delayed vomiting during both time periods, and 19% (n = 45) had delayed vomiting during both time periods. Of the 155 women without delayed vomiting at the first data collection period, 39 (25%) developed delayed vomiting with their next cycle. Of the 87 women with delayed vomiting during the first data collection period, 42 (48%) did not have delayed vomiting with their next cycle. These differences were not statistically significant ($p = 0.824$).



N = 241

Figure 2. Percentage of Sample With Vomiting Over Time



N = 241

Note. Includes only those reporting vomiting

Figure 3. Intensity of Vomiting Over Time

No demographic factors were associated with AVS scores at time 1. At time 2, age was associated with AVS ($r = –0.16$; $p = 0.012$); younger women had more acute vomiting. Education and BMI were not associated with AVS scores at either time period. No significant differences in AVS existed by ethnicity, relationship status, or living arrangement. No significant differences in AVS existed by history of nausea with stress, seasickness, or morning sickness. Women with a history of car sickness (n = 62) had more acute vomiting during the second time period ($t = 2.1$; $p < 0.04$) than those who did not get carsick. Significantly less acute vomiting was reported by women receiving 5-fluorouracil ($t = 2.84$; $p = 0.005$) during the second time period, whereas those receiving doxorubicin had more acute vomiting ($t = 4.07$; $p < 0.0001$) during the second time period. Those having their chemotherapy on a weekly basis reported less acute vomiting during the second time period than those on a more traditional 21- or 28-day cycle ($t = 4.95$; $p < 0.0001$). The women who received IV ondansetron with their chemotherapy had higher AVS scores during the second time period ($t = 1.98$; $p < 0.05$). No significant differences in AVS scores existed by any other IV antiemetic usage. Those who had their IV antiemetic changed did not have significantly higher AVS scores during either time period.

At time 1, age was associated with DVS ($r = -0.15$; $p = 0.014$) and at time 2, BMI was associated with DVS ($r = 0.125$, $p = 0.05$); younger, heavier women had more delayed vomiting. Education was not associated with DVS at either time period. No significant differences existed in DVS by relationship status or living alone. During the first time period, minority women (n = 55) reported significantly more delayed vomiting than did Caucasian women ($\overline{X} = 6.56$ versus 2.82; $t = 2.02$; $p < 0.05$). For those with a history of seasickness, car sickness, morning sickness, or nausea under stress, no significant differences in delayed vomiting existed during either time period. Significantly more delayed vomiting was reported by women receiving cyclophosphamide ($t = 3.11$; $p < 0.002$) during the second time period. Those receiving chemotherapy on a weekly basis did not report any less delayed vomiting than those on a more traditional 21- or 28-day cycle during either time period ($p = 0.194$; $p = 0.285$). No significant differences in DVS scores existed by any use of IV antiemetics. However, those who did not receive oral granisetron (n = 218) or dexamethazone (n = 184) for home use at time 2 had significantly more delayed vomiting than those who used granisetron (n = 29; $t = 3.13$; $p = 0.002$) or dexamethazone (n = 63, $t = 2.01$; $p < 0.046$). No significant differences in DVS scores existed in those who had their IV antiemetics changed during either time period. Other comparisons can be found in Table 4.

Discussion

The results of this study indicate that, in spite of the emergence of 5-HT_3 receptor antagonists that are considered the "gold standard" for chemotherapy-induced vomiting, acute and delayed vomiting continue to be a significant problem for some patients with breast cancer. Of particular interest is the indication that despite the clinical need for different antiemetic treatment between chemotherapy cycles, with specific IV and oral medications being more effective, few medication changes are made from one cycle to the next. This could be related to the false belief by patients that vomiting is a symptom that they must endure if they wish to seek treatment for their breast cancer or that clinicians are not aware of the prevalence of vomiting among their clients. In the second case, these data reaffirm that clinicians may believe the myth that nausea and vomiting are no longer a problem for chemotherapy recipients, a statement heard many times from oncology practices that were asked to participate in the authors' studies.

This study showed that a significantly greater number of minority women were affected by delayed vomiting than their Caucasian counterparts. Disparity in health care by ethnicity has received national attention for a number of years, resulting in the development of standards of culturally and linguistically competent care for healthcare workers in 2000 by the Office of Minority Health of the U.S. Department of Health and Human Services. To eliminate language as a barrier, participants in this study could read and write in English. In addition, no difference existed in antiemetics ordered or taken by Caucasian and minority women. Currently, healthcare workers and researchers are trained to address the needs of the cultural majority, Caucasians. This training presumes that African American, Asian, or Hispanic or Latina clients will report symptoms and seek appropriate medications or interventions. Pharmaceutical researchers exploring the effectiveness of medications also may rely heavily on results from Caucasian samples that may metabolize the medication differently than some minorities. Recent research into the liver enzyme cytochrome P450 2D6, which varies somewhat by ethnicity, suggests that the metabolism of many drugs can be affected (Kaiser et al., 2002). In addition, by examining effectiveness of an intervention on one group—Caucasians—a researcher ignores the potential effect that different food and lifestyle habits have on the manifestation of a symptom and interventions used to treat it. However, the current study's finding was not similar to that of African American and Caucasian patients with colon cancer. In a large, randomized, phase III trial of adjuvant chemotherapy for resected colon cancer, African Americans appeared to experience fewer side effects related to chemotherapy, including significantly lower rates of nausea and vomiting (McCollum et al., 2002). More studies need to be conducted to examine the effectiveness of antiemetics with diverse populations.

Research has documented that some patients experiencing postchemotherapy vomiting withdraw from seemingly beneficial treatment (Fessele, 1996; Osoba et al., 1997). This suggests a need for increased vigilance by clinicians who treat chemotherapy-induced vomiting. In addition to determining the incidence of vomiting in people currently receiving treatment, nurses may be able to anticipate those who are more likely to experience this symptom in the future by looking at available data. For instance, younger women had significantly more acute vomiting in their first cycle of chemotherapy and significantly more delayed vomiting in their second cycle. In addition, as with nausea (Dibble et al., 2003), women with a higher BMI had significantly more delayed vomiting than their smaller counterparts. Women with a history of carsickness had significantly more vomiting than those who did not experience motion sickness. Each of these factors could assist nurses in their approach to educating clients about what to expect regarding vomiting with the administration of chemotherapy to those diagnosed with breast cancer. In addition, oncology nurses can work with patients to plan the intensity of postchemotherapy antiemetic prophylaxis and treatment as well as surveillance strategies.

Limitations

This study has a number of limitations. First, the sites used in the study may have been those where vomiting was a particular problem. The physicians who told the authors that their patients did not experience any vomiting may have been correct and what is demonstrated in this article is the experience of women who are not properly treated for this side effect. Second, the women were not followed for their entire chemotherapy experience, so the researchers do not know how many women eventually stopped treatment or whether the vomiting increased or decreased with subsequent cycles. The study did not have large enough samples of women in the various ethnic groups to perform the appropriate analyses to profile by ethnicity the women who had the most vomiting.

Summary

This study clearly illustrates that chemotherapy-induced vomiting, especially delayed vomiting, continues to be a problem for women undergoing moderately emetogenic treatment for breast cancer. Nurses also must remember that this study was completed before the aprepitant substance P/neurokinin 1 receptor antagonist was released. Although research into better medications is needed, so is research into the various complementary

Table 4. Comparison of Differences in Delayed Vomiting by Various Factors

	Time 1				Time 2			
Variable	$\bar{x}$	**SD**	**n**	**p**	$\bar{x}$	**SD**	**n**	**p**
History of car sickness	3.28	7.20	57	0.641	4.60	14.60	57	0.524
No history of car sickness	2.84	5.97	203		3.32	7.04	192	
History of seasickness	3.21	6.04	67	0.677	3.13	7.62	62	0.591
No history of seasickness	2.84	6.34	192		3.78	9.82	186	
History of sickness under stress	3.76	6.92	55	0.271	4.13	8.32	53	0.646
No history of sickness under stress	2.72	6.05	205		3.47	9.55	196	
History of morning sickness	2.99	5.68	151	0.872	3.29	6.85	146	0.552
No history of morning sickness	2.86	6.98	109		4.07	12.00	103	
Weekly chemotherapy	1.35	4.81	23	0.194	1.59	4.02	22	0.043
No weekly chemotherapy	3.13	6.38	235		3.82	9.66	226	
Ondansetron by IV	3.10	5.78	128	0.715	3.83	8.16	123	0.732
No ondansetron by IV	2.82	6.70	131		3.42	10.35	125	
Dexamethazone by IV	2.97	6.28	209	0.962	3.77	9.73	200	0.555
No dexamethazone by IV	2.92	6.22	50		3.02	7.35	48	
Lorazepam by IV	3.53	5.86	19	0.681	3.35	5.97	17	0.855
No lorazepam by IV	2.91	6.29	240		3.65	9.52	231	
Diphenhydramine by IV	1.33	2.80	6	0.521	5.14	13.60	7	0.663
No diphenhydramine by IV	3.00	6.31	253		3.58	9.19	241	
Granisetron by IV	3.46	8.14	63	0.547	4.87	13.61	60	0.376
No granisetron by IV	2.80	5.53	196		3.23	7.44	188	
Dolasetron by IV	2.40	4.56	43	0.417	2.14	6.12	44	0.119
No dolasetron by IV	3.07	6.54	216		3.95	9.85	204	
IV antiemetic change	5.60	5.26	15	0.092	5.69	9.59	16	0.339
No IV antiemetic change	2.79	6.30	243		3.40	9.23	231	
Prochlorperazine orally	2.92	6.00	188	0.889	3.10	7.22	179	0.340
No prochlorperazine orally	3.04	6.99	70		4.72	13.20	68	
Lorazepam orally	2.88	5.55	50	0.927	2.55	5.79	47	0.265
No lorazepam orally	2.97	6.44	208		3.78	9.88	200	
Promethazine orally	1.73	2.33	11	0.132	0.70	1.49	10	0.000
No promethazine orally	3.01	6.38	247		3.67	9.42	237	
Diphenhydramine orally	2.62	4.57	13	0.842	2.38	6.08	13	0.643
No diphenhydramine orally	2.97	6.35	245		3.61	9.40	234	
Granisetron orally	2.43	4.67	30	0.540	1.28	2.63	29	0.002
No granisetron orally	3.02	6.45	228		3.85	9.76	218	
Ondansetron orally	3.20	5.41	97	0.612	4.26	8.25	99	0.321
No ondansetron orally	2.81	6.74	161		3.07	9.86	148	
Dexamethazone orally	1.57	5.61	63	0.965	0.83	4.96	63	0.046
No dexamethazone orally	2.03	6.48	195		2.55	10.30	184	
Cyclophosphamide	3.11	6.41	236	0.069	3.86	9.70	225	0.002
No cyclophosphamide	1.44	3.94	25		1.20	2.81	25	
5-fluorouracil	2.49	5.60	37	0.629	3.15	7.02	33	0.713
No 5-fluorouracil	3.02	6.34	224		3.66	9.59	217	
Doxorubicin	3.07	6.35	223	0.449	3.66	9.59	216	0.725
No doxorubicin	2.24	5.49	38		3.18	7.06	34	
Cyclophosphamide and doxorubicin	18.84	17.68	195	0.262	20.25	21.51	186	0.183
Cyclophosphamide, methotrexate, and 5-fluorouracil	15.21	15.38	34		14.70	18.37	30	

N = 303

Note. Because some data are missing for some variables, the n values may not equal the total N.

therapies. This descriptive study demonstrates that existing medications are not being used as effectively as they could. Oncology nurses play an active role in the prevention and treatment of this unpleasant symptom of chemotherapy. Further research should evaluate the relationships among vomiting with and without nausea and specific antiemetic regimens, as well as age, BMI, ethnicity, and history of car sickness.

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References

American Cancer Society. (2003). *Cancer facts and figures, 2003.* Atlanta, GA: Author.

American Cancer Society & National Comprehensive Care Network. (2001). *Nausea and vomiting: Treatment guidelines for patients with cancer.* Atlanta, GA: American Cancer Society.

Bartlett, N., & Koczwara, B. (2002). Control of nausea and vomiting after chemotherapy: What is the evidence? *Internal Medicine Journal, 32,* 401–407.

Clavel, M., Soukop, M., & Greenstreet, Y.L.A. (1993). Improved control of emesis and quality of life with ondansetron in breast cancer. *Oncology, 50,* 180–185.

Dawson-Saunders, B., & Trapp, R.G. (1994). *Basic and clinical biostatistics.* Norwalk, CT: Appleton and Lange.

Dibble, S., Israel, J., Nussey, B., Casey, K., & Luce, J. (2003). Delayed chemotherapy-induced nausea in women treated for breast cancer. *Oncology Nursing Forum, 30,* E40–E47. Retrieved March 7, 2003, from http://www.ons.org/ONF/2003/March_April_03/E40-E47.pdf

Dicato, M. (1996). Mechanisms and management of nausea and emesis. *Oncology, 53*(Suppl. 1), 1–3.

Fessele, K.S. (1996). Managing the multiple causes of nausea and vomiting in the patient with cancer. *Oncology Nursing Forum, 23,* 1409–1415.

Goodman, M. (1997). Risk factors and antiemetic management of chemotherapy-induced nausea and vomiting. *Oncology Nursing Forum, 24,* 20–32.

Greene, D., Nail, L.M., Fieler, V.K., Dudgeon, D., & Jones, L.S. (1994). A comparison of patient-reported side effects among three chemotherapy regimens for breast cancer. *Cancer Practice, 2,* 57–62.

Italian Group for Antiemetic Research. (1999). Prevention of cisplatin-induced delayed emesis: Still unsatisfactory. *Supportive Care in Cancer, 8,* 229–232.

Italian Group for Antiemetic Research. (2000). Dexamethasone alone or in combination with ondansetron for the prevention of delayed nausea and vomiting induced by chemotherapy. *New England Journal of Medicine, 342,* 1554–1559.

Kaiser, R., Sezer, O., Papies, A., Bauer, S., Schelenz, C., Tremblay, P.B., et al. (2002). Patient-tailored antiemetic treatment with 5-hydroxytryptamine type 3 receptor antagonists according to cytochrome P-450 2D6 genotypes. *Journal of Clinical Oncology, 20,* 2805–2811.

Kris, M.G., Roila, F., De Mulder, P.H.M., & Marty, M. (1998). Delayed emesis following anticancer chemotherapy. *Supportive Care in Cancer, 6,* 228–232.

Maisano, R., Spadaro, P., Toscano, G., Caristi, N., Pergolizzi, S., & Salimbeni, V. (2000). Cisapride and dexamethasone in the prevention of delayed emesis after cisplatin administration. *Supportive Care in Cancer, 9,* 61–64.

McCollum, A.D., Catalano, P.J., Haller, D.G., Mayer, R.J., Macdonald, J.S., Benson, A.B., et al. (2002). Outcomes and toxicity in African American and Caucasian patients in a randomized adjuvant chemotherapy trial for colon cancer. *Journal of the National Cancer Institute, 94,* 1160–1167.

Oettle, H., & Riess, H. (2001). Treatment of chemotherapy-induced nausea and vomiting. *Journal of Cancer Research and Clinical Oncology, 127,* 340–345.

Osoba, D., Zee, B., Warr, D., Latrelle, J., Kaizer, L., & Pater, J. (1997). Effect of postchemotherapy nausea and vomiting on health-related quality of life. *Supportive Care in Cancer, 5,* 307–313.

Pendergrass, K.B. (1998). Options in the treatment of chemotherapy-induced emesis. *Cancer Practice, 6,* 276–281.

Rhodes, V.A., Watson, P.M., & Johnson, M.H. (1984). Development of reliable and valid measures of nausea and vomiting. *Cancer Nursing, 7,* 33–41.

Rhodes, V.A., Watson, P.M., Johnson, M.H., Madsen, R.W., & Beck, N.C. (1987). Patterns of nausea, vomiting, and distress in patients receiving antineoplastic drug protocols. *Oncology Nursing Forum, 14*(4), 35–44.

Stewart, A. (1996). Optimal control of cyclophosphamide-induced emesis. *Oncology, 53*(Suppl. 1), 32–38.

Uyl-de Groot, C.A., Wait, S., & Buijt, I. (2000). Economics and health-related quality of life in antiemetic therapy: Recommendations for trial design. *European Journal of Cancer, 36,* 1522–1535.

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