Level of Fatigue in Women Receiving Dose-Dense Versus Standard Chemotherapy for Breast Cancer: A Pilot Study

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Purpose/Objectives: To determine whether women receiving dose-dense chemotherapy for breast cancer experience different levels of fatigue than women receiving standard chemotherapy regimens for the disease.

Design: Quasi-experimental pilot study.

Setting: Private physicians' offices in California.

Sample: 15 women with stage I, II, or III breast cancer receiving dose-dense or standard chemotherapy. The average female participant was 48 years old ($\bar{X}$ = 48.3), was married (80%), and had a college degree (73%).

Methods: The revised Piper Fatigue Scale was completed by patients at three different times: pretreatment, three days after their cycle 1 chemotherapy dose, and three days after their cycle 2 chemotherapy dose. Patients returned completed surveys by mail.

Main Research Variables: Fatigue levels associated with chemotherapy.

Findings: Pretreatment total fatigue scores were not significantly different in the dose-dense and standard chemotherapy groups. Total fatigue scores were significantly higher in the dose-dense group at the cycle 1 and 2 time points. Fatigue scores were significantly higher in women who had undergone a mastectomy, were working, were HER2 positive, and had a tumor size larger than 2 cm.

Conclusions: Dose-dense chemotherapy resulted in significantly greater fatigue.

Implications for Nursing: Nurses should educate women receiving dose-dense chemotherapy as part of informed consent and assist them in preparing and planning for fatigue. Information about which patients are more likely to experience significant fatigue allows nurses to judge the frequency with which they need to assess and manage fatigue to improve patient outcomes.

Key Points . . .

- ➤ Dose-dense chemotherapy has an intertreatment interval shorter than standard chemotherapy.
- ➤ Women receiving dose-dense chemotherapy may experience higher levels of fatigue than are expected with standard chemotherapy.
- ➤ Poor prognostic factor selection bias, demographic differences, and use of pegfilgrastim in women receiving dose-dense chemotherapy may be causes of higher fatigue scores.

Breast cancer is the most common cancer in women, with an estimated 212,920 new cases and 40,970 deaths predicted for 2006 (American Cancer Society, 2006). Adjuvant chemotherapy following surgical intervention is a commonly prescribed treatment modality, even for women diagnosed with stage I or II disease. For women undergoing treatment for breast cancer, fatigue has been reported to be the most common and problematic side effect of treatment (Longman, Braden, & Mishel, 1997). Jacobsen et al. (1999) found that slightly more than 90% of women receiving adjuvant chemotherapy reported fatigue. Since 2003, clinical trials have shown a benefit in disease-free survival as well as overall survival for patients with breast cancer when dose-dense chemotherapy is used in the adjuvant setting (Citron et al., 2003). No study has determined how dose-dense chemotherapy affects fatigue levels.

Literature Review

Fatigue

Many definitions for fatigue exist, but most note that fatigue is a complex concept that is multidimensional and multicausal (de Jong, Courtens, Abu-Saad, & Schouten, 2002). Fatigue also has been defined as a subjective feeling of tiredness influenced by circadian rhythm (Piper, Lindsey, & Dodd, 1987). Definitions suggest that the nature of cancer-related fatigue is somehow different than fatigue experienced in everyday life. Although everyone experiences fatigue on a daily basis as a protective mechanism, fatigue that becomes constant, unusual, or excessive loses its protective function and can lead to an aversion to activity (Piper et al., 1987). Cancer-related fatigue is more

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severe and disruptive than fatigue experienced in everyday life (Cella, Lai, Chang, Peterman, & Slavin, 2002), and it prevents patients from having a normal life (Curt et al., 2000).

Studies that examined levels of fatigue based on type of drug regimen have yielded inconsistent results. At least one study has shown no difference in fatigue based on drug regimen (Green, Nail, Fieler, Dudgeon, & Jones, 1994). However, studies also have shown that doxorubicin-containing regimens may cause increased fatigue after the first cycle of chemotherapy (Berger, 1998; de Jong, Candel, Schouten, Abu-Saad, & Courtens, 2004). Berger also found that mean activity levels determined by wrist actigraph measurements were lower in those receiving doxorubicin-containing regimens. Another difference may occur in 28-day versus 21-day regimens in which midcycle fatigue levels are higher for patients receiving 28-day regimens (Berger). In 28-day regimens, cyclophosphamide is taken orally for 14 days, or up to midcycle, versus an IV bolus of cyclophosphamide on day 1 in 21-day regimens, possibly accounting for higher midcycle fatigue scores.

Fatigue patterns appear to remain stable throughout each successive treatment, during which fatigue intensity does not vary significantly from cycle to cycle. During each cycle, a pattern exists in which fatigue levels appear to peak sometime in the first two to five days after treatment and then gradually decline. This peak-trough or roller-coaster pattern was found by Berger (1998) when fatigue scores measured 48 hours after treatment for breast cancer were higher than at the cycle midpoint and overall mean physical activity and rhythmic fluctuations measured by wrist actigraphs were lowest at day three. The roller-coaster pattern of fatigue also was seen in women receiving adjuvant chemotherapy when fatigue peaked sometime prior to or at cycle midpoint (Jacobsen et al., 1999). Fatigue patterns also have been studied in various chemotherapy regimens and tumor types using daily diary entries. High levels of fatigue were found during the first four to five days after treatment (Richardson, Ream, & Wilson-Barnett, 1998).

Various patient- and disease-related factors have been studied for their effects on fatigue in women with breast cancer. Disease stage and tumor size are disease-related factors that have not previously been shown to have a relationship to fatigue (Hann et al., 1999; Hwang, Chang, Rue, & Kasimis, 2003; Jacobsen et al., 1999; Mast, 1998). Menopausal symptoms, mastectomy, and lymph node–positive disease have inconsistently shown a relationship to higher fatigue levels (Berger, 1998; Bower et al., 2000; de Jong et al., 2004; Hann et al.; Jacobsen et al.; Tchen et al., 2003). Work status and educational level have not been linked to increased fatigue (Bower et al.; Hann et al.), although other demographic variables such as age and marital status have been inconsistently linked to fatigue. In studies that have found a relationship between fatigue and age, all suggest that younger women are more likely to experience fatigue (Bower et al.; Mast; Woo, Dibble, Piper, Keating, & Weiss, 1998). Finally, divorced women may experience higher levels of fatigue than single women or those living with a partner (de Jong et al., 2004). However, this finding also is inconsistent because Hann et al. did not find a difference in fatigue and marital status.

Dose Density

Interest in dose-dense chemotherapy arose based on the Gompertzian model. Described by Hudis and Norton (2004), the model shows that doubling time is not constant in the Gompertzian growth tumor. Small tumors will grow rapidly, almost exponentially, but tumor growth slows as tumor size increases. Eventually, a plateau is reached at which growth no longer takes place and cell mitosis equals cell apoptosis. Unfortunately, the plateau is thought to be reached long after the tumor burden becomes lethal. Chemotherapy kills a fraction (log-kill) of cells with each exposure. In subclinical tumors, such as in the adjuvant breast cancer setting, tumor growth would be rapid. Chemotherapy, in the adjuvant breast cancer setting, administered at a time interval equal to or greater than the time interval for tumor regrowth would yield suboptimal tumor reduction. Therefore, the concept of dose-dense chemotherapy is to deliver full-dose chemotherapy at time intervals shorter than those needed for tumor regrowth while still maintaining acceptable and tolerable levels of toxicity.

In clinical practice, dose density is the administration of chemotherapy with an intertreatment interval that is shorter than standard chemotherapy regimens currently used. Important to this concept is the ability to maintain dose strength while shortening the intertreatment interval. Commonly used standard adjuvant chemotherapy regimens for breast cancer include doxorubicin and cyclophosphamide (AC) alone or followed by paclitaxel (AC-T) administered every 21 days; cyclophosphamide, methotrexate, and fluorouracil (CMF); or cyclophosphamide, doxorubicin (or epirubicin), and fluorouracil (CAF, CEF) administered on 28-day treatment cycles. In 21-day cycles, all chemotherapy is administered via IV on day 1 of the cycle, followed by a rest period on days 2–20. In the 28-day CMF, CAF, and CEF cycles, cyclophosphamide is administered orally on days 1–14 and the remaining chemotherapy drugs are administered via IV on days 1 and 8, followed by a rest period on days 15–27. The dose-dense regimen supported by the work of Citron et al. (2003) is AC-T administered at full drug dosage levels on a 14-day treatment cycle.

The most significant study of dose-dense chemotherapy was done by Citron et al. (2003). In their study, 2,005 women with axillary node–positive breast cancer were randomly assigned to receive adjuvant chemotherapy with one of four regimens: (a) sequential doxorubicin for four doses, followed by paclitaxel for four doses, followed by cyclophosphamide for four doses (Ax4→Tx4→Cx4) with doses every three weeks; (b) sequential Ax4→Tx4→Cx4 with doses every two weeks (dose dense) and filgrastim support; (c) concurrent AC-T with doses every three weeks; and (d) concurrent AC-T with doses every two weeks (dose dense) and filgrastim support. Drug dosage was standardized for all regimens. A statistically significant increase in disease-free and overall survival was found for the dose-dense regimens, and no difference was found between sequential versus concurrent regimens.

Toxicities studied in the dose-dense regimens were tolerable and similar to the three-week regimens. The exceptions were a statistically significant increase in the frequency of grade 4 granulocytopenia in the three-week regimens and that a significant number of patients in the dose-dense AC-T regimen required at least one red blood cell transfusion. The two-week regimens included filgrastim support, which could account for the lower frequency of grade 4 granulocytopenia. Unfortunately, information regarding the incidence and severity of fatigue was not included in the study.

Additional studies of dose-dense chemotherapy in breast cancer provide limited information on fatigue. The difficulty

in assessing the role of dose density on fatigue in the studies is that other variables such as differences in drugs or dose intensity (higher drug dose) also were introduced. In one study, dose density as well as drug regimen varied because women were randomized to receive either dose-dense doxorubicin plus docetaxel every two weeks or standard AC followed by docetaxel (von Minckwitz et al., 2005). World Health Organization grades 3 and 4 fatigue were experienced by 28% of women receiving the dose-dense regimen, versus 22% on the standard regimen. Two additional studies including fatigue measures found that women receiving a dose-dense, dose-intense regimen had significantly worse fatigue scores compared to those receiving a standard chemotherapy regimen (Bottomley et al., 2005; Fairclough, Fetting, Cella, Wonson, & Moinpour, 1999). Because the regimens in these two studies were dose dense and dose intense, the fatigue levels experienced were likely a result of both factors and determining how dose density contributed to fatigue levels would be difficult.

Based on previous studies of adjuvant chemotherapy for breast cancer, factors such as drug regimen, treatment schedule, and drug dosage may affect the level of fatigue experienced by patients with breast cancer receiving chemotherapy. The Gomperztian model predicts that dose-dense chemotherapy may be an effective strategy to improve survival in breast cancer as well as other solid tumors. Citron et al. (2003) showed clinical support for the model, with significant improvement in disease-free and overall survival rates reported for dose-dense adjuvant chemotherapy in patients with breast cancer. However, women choosing to undergo a dose-dense chemotherapy regimen must understand treatment toxicity in addition to survival data. To date, no study has effectively addressed the level of fatigue that women can expect to experience with dose-dense chemotherapy. Therefore, the purpose of this pilot study was to determine whether women receiving dose-dense chemotherapy for breast cancer experience a level of fatigue that differs from those receiving standard regimens.

Conceptual Framework

Piper's Integrated Fatigue Model (IFM) (Piper et al., 1987) was the conceptual framework used in the present study. The IFM has been recognized and was chosen for its multidimensional perspective of fatigue. The model identifies 14 factors or patterns that influence fatigue. Fatigue is manifested objectively or subjectively. The relationship between the two manifestations is thought to be complex (Stone, Richards, & Hardy, 1998). Piper et al. (1987) reported that, because the relationship is not known, the best way to measure fatigue is by a person's own experience or by subjective measures. The subjective manifestations of fatigue have been categorized into four subdimensions: physical (sensory), mental (cognitive/mood), emotional (affective), and the effect on activities of daily living (behavioral/severity).

Methods

Sample and Setting

The present study used a quasi-experimental design to compare the levels of fatigue in two groups of women undergoing chemotherapy for breast cancer. Fatigue was measured in women receiving dose-dense AC-T or one of four standard regimens. Women were recruited from three private physicians' offices and infusion centers in California during a six-week period of time.

Women who qualified for the study were 18 years of age or older; able to speak, read, and write English; diagnosed with stage I, II, or III breast cancer; and receiving dose-dense chemotherapy or a standard regimen. Exclusionary criteria included prior chemotherapy and prior or current radiotherapy.

Instruments

The **demographic and disease information form** was developed by the investigator to collect common demographic data such as age, ethnicity, and employment as well as disease and treatment-related information such as tumor size, menopausal status, and type of chemotherapy. The revised **Piper Fatigue Scale (PFS)** was used to measure total fatigue as well as the four subjective dimensions of fatigue. Based on data collected from 382 breast cancer survivors, the revised PFS contains 22 11-point, numerical, adjective-wording scales designed to measure current levels of fatigue in four dimensions: behavioral/severity, affective meaning, sensory, and cognitive/mood (Piper et al., 1998; Wu & McSweeney, 2001). Each question was anchored by two words such as "mild" or "severe." Subjects answered questions by circling the number (0–10) that best described their current state. Reliability for the four subscales and total scale was well established with a Cronbach's alpha coefficient of 0.92–0.97 (Piper et al., 1998). The tool had been validated in additional studies with alphas ranging from 0.80 (Berger & Higginbotham, 2000) to 0.99 (Berger, 1998).

Construct validity for the four dimensions of fatigue was verified by principle axis factor analysis (Piper et al., 1998). Mock et al. (1997) reported that convergent validity was established by correlation with the Fatigue Symptom Checklist ($r = 0.55$) and the Profile of Mood States ($r = 0.42$). Generally accepted limitations of the revised PFS included psychometric testing in a study sample primarily composed of female breast cancer survivors that may have limited generalizability (Schwartz, 2002). In addition, response wording of the 22 numerical scales was in one direction only ("none" to "great deal" and "mild" to "severe"), which potentially could have lead to response sets (Piper et al., 1998).

Procedure

The study was approved by the human subjects review board at the authors' sponsoring university. Those identified as potential study participants were approached prior to or the day of their first scheduled chemotherapy treatment. Seventeen women were invited to participate; one woman declined participation, and one woman did not meet inclusion criteria because she had metastatic disease, leaving a sample size of 15. Signed informed consent and a medical record release were obtained from all participants. Fatigue data were collected using the revised PFS prior to or the day of chemotherapy cycle 1, three days following cycle 1 infusion, and three days following cycle 2 infusion. Time points two and three were chosen based on previous studies in which fatigue levels peaked two to five days following treatment (Berger, 1998; Richardson et al., 1998). Each patient was given the survey form with a stamped return envelope at the time of chemotherapy infusion for cycles 1 and 2 and

asked to complete the survey on the corresponding day and return it by mail. The demographic and disease information form was given to the patients with the cycle 1 revised PFS, and participants were asked to return both together by mail. Information missing from the demographic and disease form was collected by chart review whenever possible.

Data Analysis

Descriptive statistics were calculated for dose-dense and standard regimens for demographic and disease data. Descriptive statistics also were calculated for the overall fatigue score and subscale scores from the PFS. A two-tailed t test was used to compare raw fatigue scores between the two groups at the pretreatment, cycle 1, and cycle 2 time points to determine whether differences in fatigue scores existed. A two-tailed t test also was used on subscale scores at each time point to determine whether differences in the manifestations of fatigue were present between the two groups. A post hoc analysis was done to compare fatigue scores to disease and demographic groups.

Results

Sample

Fifteen women provided data for evaluation, with eight participants in the dose-dense group and seven in the standard group. All women in the dose-dense group received dose-dense AC-T. Six of seven women in the standard group received standard-dose AC with or without paclitaxel, and one woman received CMF. Demographic and disease characteristics are presented in Table 1. Marital status, employment status, type of surgery, HER2 status, and estrogen receptor status appeared to be similar between the two groups. The dose-dense group appeared more likely to have a higher educational status, stage II or III disease, lymph node–positive disease, and tumor size greater than 2 cm and more likely to be premenopausal. The standard chemotherapy group appeared more likely to have stage I disease, lymph node–negative disease, and a tumor size less than 2 cm. The most apparent differences between the dose-dense group and the standard group were in educational status (88% versus 57% with a college degree, respectively), disease stage (25% versus 71% with stage I disease, respectively), lymph node status (75% versus 14% lymph node–positive, respectively), and tumor size (25% versus 100% < 2 cm, respectively). Post hoc analysis of disease and demographic groups (see Table 2) showed that the independent factors of larger tumor size, positive HER2 status, mastectomy, and currently being employed predicted higher fatigue scores ($p \leq 0.001$) following cycle 1 chemotherapy.

Table 1. Participant Demographics

Characteristic	Dose Dense (n = 8)		Standard (n = 7)	
Age (years)				
$\bar{X}$	48.0		48.5	
SD	10.1		14.5	
Range	31–62		35–74	
Characteristic	**n**	**%**	**n**	**%**
Marital status				
Married	7	88	5	71
Single	–	–	1	14
Divorced	1	12	1	14
Education				
High school diploma	1	12	3	41
College degree	7	88	4	57
Employment				
Working	3	37	2	29
Stage				
I	2	25	5	71
II	4	50	2	29
III	2	25	–	–
Surgery				
Mastectomy	3	38	2	29
Lumpectomy	5	63	5	71
Menopausal				
Pre	2	25	5	71
Post	3	38	1	14
Peri	3	38	1	14
Lymph node status				
Positive	6	75	1	14
Negative	2	25	6	86
Tumor size (cm)				
< 2	2	25	7	100
2–5	5	63	–	–
> 5	1	12	–	–
HER2 status				
Negative	5	63	5	71
Positive	2	25	–	–
Missing data	1	12	2	29
Estrogen receptor status				
Negative	4	50	4	57
Positive	4	50	3	43
Progesterone receptor status				
Negative	4	50	2	29
Positive	2	25	4	57
Missing data	2	25	1	14

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

Fatigue Scores

Mean fatigue scores for the dose-dense and standard groups are listed in Table 3. The pretreatment total ($t = 1.32$, $p = 0.18$) and behavioral/severity, affective meaning, and sensory subscale scores (see Table 4) for the PFS did not significantly differ between the two groups. However, pretreatment cognitive/mood subscale scores were significantly higher in the dose-dense group ($t = -2.10$, $p = 0.04$). Cognitive/mood subscale scores also were higher for the dose-dense group at cycle 1 ($t = 2.36$, $p = 0.02$) but not at cycle 2 ($t = 1.48$, $p = 0.15$). A statistical significance was found in cycle 1 and cycle 2 total fatigue scores, with the dose-dense group having higher fatigue scores than the standard group at both time measurements ($t = 6.12$, $p \leq 0.001$ and $t = 3.77$, $p \leq 0.001$, respectively). Affective meaning, sensory, and cognitive/mood subscale scores were increased significantly in the dose-dense group at cycle 1 only. Behavioral/severity was the only subscale score significantly higher in the dose-dense group at cycle 1 and cycle 2 ($t = 4.43$, $p \leq 0.001$ and $t = 3.68$, $p \leq 0.001$, respectively).

Discussion

The findings showed significantly higher total fatigue scores among patients receiving dose-dense versus stan-

Table 2. Comparison of Demographic and Disease Groups to Fatigue Score

Characteristic	$\bar{X}$	SD	t	p
Lymph node status			–1.247	0.213
Positive	4.94	2.603		
Negative	5.34	3.134		
Tumor size (cm)			3.342	< 0.001
< 2	4.59	3.057		
> 2	5.66	2.621		
HER2 status			10.37	< 0.001
Positive	8.14	1.754		
Negative	4.76	2.621		
Age of patient (years)			–1.55	0.122
< 50	5.42	3.247		
≥ 50	4.93	2.426		
Currently working			3.461	< 0.001
Working	5.90	2.531		
Not working	4.78	3.009		
Surgery type			4.279	< 0.001
Mastectomy	6.20	2.359		
Lumpectomy	4.62	3.531		

dard chemotherapy for breast cancer in cycle 1 and cycle 2 fatigue scores. With the exception of the cognitive/mood subscale, pretreatment total fatigue scores were not significantly different. Therefore, women who received dose-dense chemotherapy experienced more fatigue than women who received standard chemotherapy regimens. The subjective manifestations of increased fatigue, as measured by subscale scores, varied between measurement points. The exception was behavioral/severity, in which the subscale score, designed to measure the effect of fatigue on activities of daily living, was significantly worse for the dose-dense group at cycles 1 and 2. Of interest was that a difference in total and all subscale fatigue scores existed at cycle 1, because chemotherapy drugs administered at cycle 1 would have been the same for patients receiving dose-dense AC-T or standard AC-T (14 of 15 patients) in the current study. The two groups did not diverge in their chemotherapy schedules until after cycle 1.

A possible explanation for the significant difference in fatigue scores at cycle 1 might be pegfilgrastim. Administration of filgrastim or pegfilgrastim is standard to dose-dense AC-T chemotherapy regimens to support white blood cell counts and maintain the every-two-weeks schedule. In the present study, all women in the dose-dense group received pegfilgrastim the day following chemotherapy. Pegfilgrastim would have been the primary treatment difference, because only one woman in the standard group received pegfilgrastim. No studies have investigated the relationship between pegfilgrastim and fatigue. However, a number of studies have found a positive correlation between pain and fatigue (Hwang et al., 2003; Jacobsen et al., 1999), and bone pain is a commonly known side effect of pegfilgrastim therapy. In a retrospective study by Kubista et al. (2003), the incidence of bone pain varied from 14%–29%. The mean number of days to onset of bone pain after pegfilgrastim administration was 3.2–5.8 days, with the shortest mean time to onset seen at cycle 1. The findings suggest that some of the women in the dose-dense group may have experienced bone pain prior to completing the cycle 1 PFS. Citron et al. (2003) did not report that a statistical difference in pain, myalgias, or arthralgia existed between dose-dense and standard groups. The timing of the measurement was not reported but may be an important factor, because bone pain caused by filgrastim therapy used in the study has been shown to have a mean duration of one to two days (Kubista et al.).

Table 3. Fatigue Scores

	Dose Dense			Standard		
Time	$\bar{X}$	SD	Range[a]	$\bar{X}$	SD	Range[a]
Pretreatment	1.9	2.1	0–8	2.2	2.0	0–8
Cycle 1	6.0	2.0	0–10	4.2	3.0	0–9
Cycle 2	6.4	1.5	0–10	5.2	3.1	0–9

[a] Possible range = 0–10

An alternative explanation for the differences in fatigue levels at cycle 1 may be a different tolerance of treatment between the two groups. Because treatment groups were not randomized, disease and demographic factors may have existed between the groups that affected tolerance to chemotherapy treatment. Poor prognostic factors, such as positive lymph nodes and larger tumor size, in addition to employment status and type of surgery were shown in this study to be associated with significantly higher fatigue scores. Patients with poorer prognostic factors in this study also were more likely to have received dose-dense chemotherapy. However, studies to date have not consistently found a relationship between demographic and disease variables and fatigue (Berger & Higginbotham, 2000; de Jong et al., 2004; Jacobsen et al., 1999; Tchen et al., 2003).

Additional studies with larger sample sizes and matched prognostic factors are needed to confirm the results of this pilot study. Investigations to determine how pretreatment demographic and prognostic disease factors affect dose-dense chemotherapy tolerance in a matched sample also would be of benefit. The role that pegfilgrastim may have played in fatigue level suggests an additional area for further study. Because the behavioral/severity dimension of fatigue was significantly worse for the dose-dense group at cycles 1 and 2, interventions targeted to this dimension of fatigue may be most helpful, as well as additional studies that address such interventions.

This pilot study shows a significant difference in fatigue scores between women treated with dose-dense versus standard chemotherapy for breast cancer. If the results were confirmed in larger studies and different settings, the implications would be significant. Certainly, at a minimum, the information would need to be included as part of the informed consent process when discussing treatment options that include dose-dense chemotherapy.

Limitations

Pretreatment fatigue scores did not appear to follow a normal distribution and, thus, the t test may not have had statistical power to determine differences in pretreatment scores. Treatment groups were not randomized, and physician selection bias may have affected pretreatment fatigue levels and patient therapy tolerance in each group. For example, patients with more aggressive disease or lower

Table 4. Dose-Dense and Standard Fatigue Score Comparisons

Fatigue Score	t	p
Pretreatment		
Total fatigue score	–1.32	0.18
Behavioral/severity	0.33	0.74
Affective meaning	1.05	0.29
Sensory	–1.49	0.14
Cognitive/mood	–2.10	0.04
Cycle 1		
Total fatigue score	6.12	< 0.001
Behavioral/severity	4.43	< 0.001
Affective meaning	2.69	0.01
Sensory	2.74	0.01
Cognitive/mood	2.36	0.02
Cycle 2		
Total fatigue score	3.77	< 0.001
Behavioral/severity	3.68	< 0.001
Affective meaning	0.41	0.69
Sensory	1.66	0.11
Cognitive/mood	1.48	0.15

performance status may have been more heavily weighted in one group, which was more likely to have contributed to fatigue levels. Strict uniformity was not present between or within treatment groups, and the differences could account for fatigue level. Finally, the sample size was too small for subset analysis. Most women in this pilot study were married and had a college education and may not be representative of the population.

Implications for Nursing

Nurses have a responsibility to discuss all treatment side effects and possible toxicities with patients under their care. Because fatigue is the most frequently reported and most distressing side effect of chemotherapy, preparing patients is critical in the informed consent process. Such discussions are vital in helping patients prepare, plan, and manage fatigue. National Comprehensive Cancer Network (2003) guidelines recommend that patients be screened for fatigue at the initial visit, at regular intervals, and as clinically indicated. An understanding of which patients are more likely to experience significant fatigue can assist nurses and other healthcare providers to assess and manage fatigue, thereby improving patient outcomes.

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