

Changes in Children's Reports of Symptom Occurrence and Severity During a Course of Myelosuppressive Chemotherapy

Journal of Pediatric Oncology Nursing
XX(X) 1-9
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DOI: 10.1177/1043454210377619
<http://jpon.sagepub.com>



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Abstract

The purposes of this study in children who underwent a cycle of myelosuppressive chemotherapy were to describe changes in symptom occurrence and severity during the chemotherapy cycle. Patients (N = 66) 10 to 18 years of age completed the Memorial Symptom Assessment Scale for 10- to 18-year-olds (MSAS 10-18) at the start of a chemotherapy cycle (T1) and weekly for the next 2 weeks (T2 and T3). More than 30% of children reported 10 or more symptoms at all 3 time points. Symptom occurrence trajectories were tested with multilevel logistic regression. In all, 6 symptoms (ie, fatigue, sadness, irritability, worrying, weight loss, sweating) showed a decreasing linear trend. Significant quadratic patterns of change were found for feeling drowsy, nausea, and vomiting. Changes in symptom severity over time were evaluated with multilevel negative binomial regression. No significant differences over time were found in any of the symptom severity scores on the MSAS. Children experienced a high number of symptoms at the initiation of a chemotherapy cycle that persisted over the subsequent 2 weeks.

Keywords

symptoms, pediatric, cancer, chemotherapy

Introduction

Current understanding of the childhood cancer disease and treatment-related symptoms is based on a limited amount of cross-sectional data (Collins et al., 2000; Collins et al., 2002; Enskär & von Essen, 2007, 2008; Hedström, Skolin, & von Essen, 2004; Tseng, Cleeland, Wang, & Lin, 2008; Woodgate & Degner, 2003; Yeh et al., 2008), and these symptoms have a significant negative impact on their quality of life (Ewing, King, & Smith, 2009; Hinds, 1990; Tseng et al., 2008). In a systematic review of 29 primarily cross-sectional studies that evaluated the symptom experience of children and adolescents with cancer (Baggott, Dodd, Kennedy, Marina, & Miaskowski, in press), only 4 studies were found that evaluated for changes in children's symptom experience over time (Baggott et al., in press; Hinds et al., 2000; Hinds, Quargnenti, & Wentz, 1992; Mulhern, Fairclough, Douglas, & Smith, 1994; Schneider & Workman, 1999).

In 3 of these studies (Hinds et al., 1992; Hinds et al., 2000; Mulhern et al., 1994), symptoms were evaluated at intervals of weeks or months. In the fourth study (Schneider & Workman, 1999), symptoms were evaluated prior to chemotherapy administration, at the end of the chemotherapy infusion, and 48 hours later. Because only total symptom scores were reported in these 4 studies, no data are available on changes in the occurrence and severity of individual symptoms over time. Therefore, it is difficult to determine which symptoms pose the most significant problems for children undergoing cancer chemotherapy.

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To design intervention studies, it is important to evaluate multiple dimensions of the symptom experience (ie, occurrence, severity) and to determine how these dimensions change within the context of cancer treatment. Given the paucity of longitudinal data on the symptom experience of children with cancer, the purposes of this study were to describe changes in symptom occurrence and severity over time (ie, prior to administration, 1 week after chemotherapy, and 2 weeks after chemotherapy) and describe the severity of the 31 symptoms that were evaluated at each time point in a sample of children who underwent a cycle of myelosuppressive chemotherapy. It was hypothesized that for the majority of the symptoms, occurrence rates and severity scores would be highest 1 week after the administration of chemotherapy.

Patients and Methods

Patients and Procedures

In this descriptive, longitudinal study, we administered self-report questionnaires to a convenience sample of children and adolescents with cancer (10 to 18 years of age) who were able to understand English or Spanish and give assent or consent to participate. Participants were receiving chemotherapy, either as their initial therapy or for relapsed or refractory disease; had received chemotherapy within the preceding 4 weeks; and were scheduled for additional myelosuppressive chemotherapy on the day of enrollment into the study.

Myelosuppressive chemotherapy refers to treatment that is expected to cause a significant drop in the absolute neutrophil count to less than 500 cells/ μ L, with subsequent blood count recovery expected to occur within 3 to 4 weeks. Similar chemotherapy regimens were targeted for selection among common diagnoses (eg, doxorubicin with cisplatin for osteosarcoma, cyclophosphamide with cytarabine for acute lymphoblastic leukemia). Some patients received additional chemotherapy in the interim between doses of myelosuppressive chemotherapy. Patients were excluded if they were receiving concurrent radiation therapy. Patients were recruited from 3 pediatric oncology settings in the San Francisco Bay area.

Between February 2008 and February 2009, a total of 73 patients were approached to participate, and 66 provided assent or consent (response rate of 91.4%). The primary reason for refusal was that patients were not interested in completing questionnaires. Data were collected weekly over a 3-week period. Of the 66 patients who enrolled in the study, 56 (85%) had complete data for all 3 study time points.

The study was approved by the Human Subjects Committee at the University of California, San Francisco, and

at each of the study sites. Patients' parents or guardians and patients who were 18 years of age signed written, informed consents. Patients aged 10 to 17 (85%) gave either written or verbal assent as per each institution's guidelines.

During the enrollment visit, prior to the administration of the cycle of chemotherapy (T1), children completed the Memorial Symptom Assessment Scale for 10-to-18-year olds (MSAS 10-18) (Collins et al., 2000). In addition, they completed the Karnofsky Performance Status (KPS) scale (Karnofsky & Burchenal, 1949) and a weekly data form to capture other data not uniformly included in the medical record (eg, number of hospitalizations, fever). Children were asked to respond to each question based on their experiences during the week prior to chemotherapy administration. The study questionnaires were repeated weekly for 2 additional weeks (ie, during the week when symptoms might be the most severe or T2 and during nadir or T3). Children received support from the research assistants to complete the study questionnaires as needed in person (if the patients were hospitalized or had clinic appointments) or via telephone. The instruments were translated from English to Spanish using forward and backward translation procedures (Acquadro, Conway, Girouard, & Mear, 2004). Patients' medical records were reviewed for disease and treatment information. The children were given a \$50 gift card to compensate them for their time.

Instruments

The revised version of the MSAS 10-18 assesses 31 symptoms on 3 dimensions. If patients reported the occurrence of a symptom over the previous week, they rated the symptom's frequency (1, *almost never*; 2, *sometimes*; 3, *a lot*; 4, *almost always*), severity (1, *slight*; 2, *moderate*; 3, *severe*; 4, *very severe*), and distress (0, *not at all*; 1, *a little bit*; 2, *somewhat*; 3, *quite a bit*; 4, *very much*) using Likert scales. Data on the patients' occurrence and severity ratings are presented in this article in Table 2. The MSAS 10-18 was chosen because it is a multidimensional inventory that evaluates 31 symptoms, yet can be completed in less than 15 minutes and has established validity and reliability (Collins et al., 2000). Cronbach's α coefficients for the MSAS 10-18 in this sample at T1 were 0.82, 0.77, and 0.63 for the total scale and physical and psychological subscales, respectively.

Positive responses for occurrence of each symptom were summed to determine the total number of symptoms experienced by each patient. Mean symptom severity scores were calculated in 2 ways. In a manner similar to previously published research (Kim et al., 2009; Portenoy et al., 1994), if the patient indicated that he or she "did

not have” the symptom, a 0 was used in the calculation of the symptom severity score in order to determine the mean symptom severity score for each symptom for the entire sample. In addition, to evaluate the severity of symptoms in those patients who reported the occurrence of each symptom, the percentage of patients who experienced slight, moderate, or severe/very severe symptoms was calculated at each time point.

The KPS scale was used to assess patients’ functional status. KPS scores range from 0 (*dead*) to 100 (*normal function*) in 10-point increments (Karnofsky & Burchenal, 1949). The KPS has well-established validity and reliability in adults (Firat, Bousamra, Gore, & Byhardt, 2002; Mor, Laliberte, Morris, & Wiemann, 1984; Schaafsma & Osoba, 1994; Schag, Heinrich, & Ganz, 1984) and has been used in pediatric studies (Forinder, Lof, & Winiarski, 2006; Jalali et al., 2008; Tseng et al., 2008; Williams, Schmideskamp, Ridder, & Williams, 2006).

Analytic Methods

Data were analyzed using SPSS for Windows version 15.0 (SPSS Inc, Chicago, IL) and STATA for Windows version 10.1 (StataCorp, College Station, TX). Descriptive statistics were generated on the sample characteristics and symptom occurrence and severity data. Because symptom characteristics did not differ significantly by study site or language, data were analyzed for the entire sample. Adjustments were not made for missing data. Therefore, the cohort for each analysis was dependent on the largest set of available data. One-way repeated measures analysis of variance (ANOVA) was used to evaluate for differences over time in the total number of symptoms and mean total symptom severity scores. Changes in individual symptom occurrence rates over time were evaluated with an individual multilevel logistic regression analysis, which generated an odds ratio (OR) for each symptom. Changes in individual symptom severity scores over time, with zeros included, were evaluated with multilevel negative binomial regression. Predicted effects were calculated on the original scale for the MSAS severity ratings, based on the estimate of the linear predictor suggested by Hardin (J. W. Hardin, STATA Corp, personal communication, October 10, 2008). A *P* value of <.05 was considered statistically significant.

Results

Demographic and Clinical Characteristics

The demographic and clinical characteristics of the patients (*N* = 66) are summarized in Table 1. The majority of the children were male (51.5%), a member of a racial/

Table 1. Demographic and Clinical Characteristics of the Sample (*N* = 66)

Age (years)	
Mean (SD)	14.8 (2.8)
Range	10-18
Median	15.3
Karnofsky Performance Status Scores time 1	
Mean (SD)	85.0 (17.5)
Range	30-100
Median	90
Time since diagnosis (months)	
Mean (SD)	16.3 (32.5)
Range	0.5-140
Median	3.3
Gender	
Male	34 (51.5%)
Female	32 (48.5%)
Ethnicity ^a	
White	25 (37.9%)
Hispanic	24 (36.4%)
Mixed race	7 (10.6%)
Asian	6 (9.1%)
Black or African American	2 (3.0%)
Native Hawaiian or other Pacific Islander	1 (1.5%)
American Indian or Alaska Native	1 (1.5%)
Diagnoses	
Acute lymphoblastic leukemia	15 (22.7%)
Osteosarcoma	10 (15.2%)
Other solid tumors	8 (12.1%)
Ewing sarcoma	7 (10.6%)
Non-Hodgkin’s lymphoma	7 (10.6%)
Central nervous system tumors	5 (7.6%)
Rhabdomyosarcoma	5 (7.6%)
Acute myeloid leukemia	4 (6.1%)
Hodgkin’s disease	3 (4.5%)
Other leukemia	2 (3.0%)
Chemotherapy administered inpatient	
Yes	43 (65.2%)
No	23 (34.8%)
Number of relapses	
0	50 (75.7%)
1	10 (15.2%)
≥2	6 (9.1%)

Abbreviation: SD, standard deviation.

^aRace/ethnicity reported by parents.

ethnic minority (62.1%), with a mean age of 15 years, and an average KPS score of 85.0 (standard deviation = 17.5). Children were diagnosed with a wide range of cancers. The majority were receiving their initial treatment (75.7%) in the inpatient setting (65.2%).

Mean Number and Severity of Symptoms Over a Cycle of Chemotherapy

The mean number of symptoms and total mean symptom severity scores for the 31 symptoms (with zeros included) at each of the 3 time points are listed in Table 2. The one-way ANOVA demonstrated significant differences over time in the mean total number of symptoms [$F(2, 112) = 10.08$; $P < .001$] and in the mean total symptom severity score [$F(2, 112) = 4.62$; $P = .01$]. Post hoc contrasts

Table 2. Mean Number of Symptoms and Mean Total Symptom Severity Scores Over Time (n = 57)

	Mean	SD	Statistic
Symptom total			$F(2, 112) = 10.08; P < .001$
T1	10.6	5.3	$T1 > T3; P = .005$
T2	10.7	4.3	$T2 > T3; P < .001$
T3	8.4	4.8	
Symptom severity			$F(2, 112) = 4.62; P = .01$
T1	0.7	0.4	
T2	0.7	0.4	$T2 > T3; P = .02$
T3	0.6	0.4	

Abbreviation: SD, standard deviation.

demonstrated that the patients reported a significantly higher number of symptoms at T1 and T2 compared with T3 (both $P < .005$) and that the mean total symptom severity score was significantly higher at T2 compared with T3 ($P = .02$). The number of symptoms with occurrence rates of $>30\%$ was 19 at T1, 18 at T2, and 10 at T3.

Changes in Symptom Occurrence Rates Over a Cycle of Chemotherapy

Symptom occurrence rates at each time point are listed in Table 3. Significant linear decreases in occurrence rates over time were noted for 6 symptoms. For each week, the odds of reporting fatigue were approximately 0.6 times lower ($OR = 0.58; P < .05$) than the previous week. Similar patterns were noted for feeling sad ($OR = 0.48; P < .01$), weight loss ($OR = 0.54; P < .01$), feeling irritable ($OR = 0.57; P < .05$), worrying ($OR = 0.58; P < .05$), and sweating ($OR = 0.59; P < .05$). Quadratic change was evaluated for 4 symptoms for which occurrence rates increased from T1 to T2, then decreased from T2 to T3. Significant quadratic change over time was noted for 3 of these symptoms. The significant quadratic effect indicates that the odds of reporting drowsiness, nausea, and vomiting increased from T1 to T2, then decreased from T2 to T3 ($OR = 0.44, 0.17, 0.38; P < .05$, respectively).

Changes in Symptom Severity Scores Over a Cycle of Chemotherapy

Using multilevel negative binomial regression analyses, no significant changes in symptom severity scores over time were found for any of the 31 symptoms when severity ratings for all patients were included in the analysis (ie, when a severity rating of zero was used in the analyses; data not shown).

However, to provide information on changes in the severity of individual symptoms during a cycle of chemotherapy, the percentage of patients who reported mild,

moderate, or severe/very severe levels of each symptom are illustrated in Figures 1A to 1D. Statistical analyses were not conducted for these severity ratings because valid estimates could not be obtained for some of the symptoms due to of the relatively small number of patients who reported a particular symptom at each time point. These percentages need to be placed within the context of the total number of patients who reported each symptom at each time point.

Discussion

To our knowledge, this study is the first to report changes in symptom occurrence and severity in a sample of children and adolescents over a cycle of cancer chemotherapy. Consistent with previous studies that used the MSAS 10-18 (Collins et al., 2000; Yeh et al., 2008), more than 30% of the children reported 10 or more symptoms at all 3 time points. Our a priori hypothesis that symptom occurrence rates would be highest in the week following chemotherapy administration (T2) was only partially supported in that the total number of symptoms reported by these patients was higher prior to the initiation of chemotherapy and in the week following chemotherapy compared to 2 weeks after treatment. In addition, when each of the symptoms was evaluated, the only occurrence rates that followed a significant pattern of increasing and decreasing rates over time were for drowsiness, nausea, and vomiting.

An important finding from this study is that although the mean number of symptoms decreased over time, patients reported between 8 and 11 symptoms across the 3 time points, which is similar to previous reports (Collins et al., 2000; Yeh et al., 2008). A surprising finding from this study is that the mean number of symptoms was higher prior to the administration of chemotherapy than 2 weeks after chemotherapy when many children were experiencing blood count nadirs. The higher number of symptoms prior to chemotherapy administration may be attributed to the higher occurrence rates for feeling sad (43.8%), irritability (41.5%), and worrying (40.6%). In addition, for these 3 symptoms, the majority of the patients reported severity scores in the moderate to very severe range. The higher rates of occurrence as well as the high severity scores for these 3 symptoms may be partially explained by patients' concern for anticipated symptoms and/or an impending hospitalization or lengthy clinic visit for chemotherapy. In a qualitative study, Hedström and colleagues described numerous distressing events that adolescent cancer patients shared when queried about being admitted to the inpatient setting (Hedström et al., 2004). Patients' emotional distress and physical symptoms are described as interrelated. Woodgate reported that adolescents with cancer experience a physical and mental

Table 3. Changes in Symptom Occurrence Rates During a Cycle of Chemotherapy (CTX)

Symptom ^a	Time 1 (Prior to CTX, %)	Time 2 (1 Week After CTX, %)	Time 3 (2 Weeks After CTX, %)	Odds Ratio ^b	P Value
Lack of energy	75.8	70.5	57.4	0.58	.017
Hair loss	69.2	65.6	62.3	0.72	.219
Pain	62.1	68.9	52.5	0.77	.228
Feeling drowsy	49.2	57.4	36.7	0.71	.118
				0.44	.034
Nausea	47.0	80.3	50.0	1.10	.635
				0.17	<.001
Feeling sad	43.8	24.6	24.6	0.48	.008
Weight loss	43.1	29.5	23.0	0.54	.009
Feeling irritable	41.5	31.1	26.2	0.57	.030
Worrying	40.6	29.5	24.6	0.58	.031
Lack of appetite	40.6	55.7	41.0	1.01	.980
Difficulty sleeping	40.0	37.7	31.7	0.76	.217
Headache	40.0	37.7	37.7	0.95	.842
"I don't look like myself"	36.9	28.3	26.2	0.62	.089
Dry mouth	36.4	37.7	33.3	0.94	.803
Change in the way food tastes	35.4	42.6	21.3	0.54	.032
Feeling nervous	33.3	26.2	21.7	0.69	.104
Skin changes	32.3	34.4	23.0	0.74	.179
Sweating	31.3	26.2	16.4	0.59	.043
Constipation	30.8	23.0	18.0	0.65	.072
Dizziness	27.7	29.5	21.3	0.76	.292
Lack of concentration	27.3	31.1	24.6	0.87	.597
Numbness/tingling in hands/feet	27.7	24.6	20.0	0.69	.182
Cough	25.8	31.1	23.3	0.90	.672
Vomiting	25.0	45.9	34.4	1.33	.197
				0.38	.014
Diarrhea	25.0	14.8	26.2	1.04	.881
Mouth sores	21.9	19.7	23.0	1.10	.770
Itching	17.5	21.3	11.5	0.79	.351
				0.59	.211
Difficulty swallowing	16.9	18.0	19.7	1.21	.547
Dyspnea	14.1	9.8	9.8	0.69	.291
Swelling of arms/legs	9.2	6.6	4.9	0.54	.261
Problems with urination	4.6	4.9	3.3	0.84	.707

^aSymptoms in boldface had significant changes in occurrence rates over time.

^bWhen 2 odds ratios are listed for a symptom, the first value represents the linear change, and the second value represents the quadratic change.

vulnerability associated with their symptoms (Woodgate, 2005). In addition, most pediatric oncology patients have a history and physical examination at the start of each chemotherapy cycle. Recent discussions with the clinicians about the patients' disease and treatment status may have contributed to high occurrence rates of psychosocial symptoms at T1. Clinicians need to evaluate patients for these "invisible" symptoms prior to the initiation of a chemotherapy cycle and improve the delivery of multidisciplinary psychosocial support.

Fatigue had the highest occurrence rates at T1 and T2, with a significant linear decrease over time. In addition, at all 3 time points, the majority of patients reported fatigue severity scores in the moderate to severe/very severe range. Although our findings are consistent with previous cross-sectional studies (Ekti Genc & Conk, 2008; Hinds, Hockenberry, Gattuso, et al., 2007; Hinds, Hockenberry, Rai, et al., 2007; Hockenberry et al., 2003; Whitsett,

Gudmundsdottir, Davies, McCarthy, & Friedman, 2008), it is not clear why fatigue occurrence rates were higher at the initiation of chemotherapy, and this warrants evaluation in future studies. Additional research, using a multidimensional assessment tool, is needed to evaluate the physical as well as the psychosocial aspects of fatigue in pediatric oncology patients during chemotherapy.

Feeling drowsy had a significant quadratic pattern of change in its occurrence. This finding is consistent with the common practice of prescribing antiemetics with sedative effects during the week of chemotherapy administration. In addition, the high occurrence rates and severity of drowsiness may be partially explained by the fact that more than 30% of the patients reported difficulty sleeping across the entire cycle of chemotherapy (Hinds, Hockenberry, Rai, et al., 2007). Like drowsiness, the majority of the children reported sleep disturbance in the moderate to severe/very severe range.

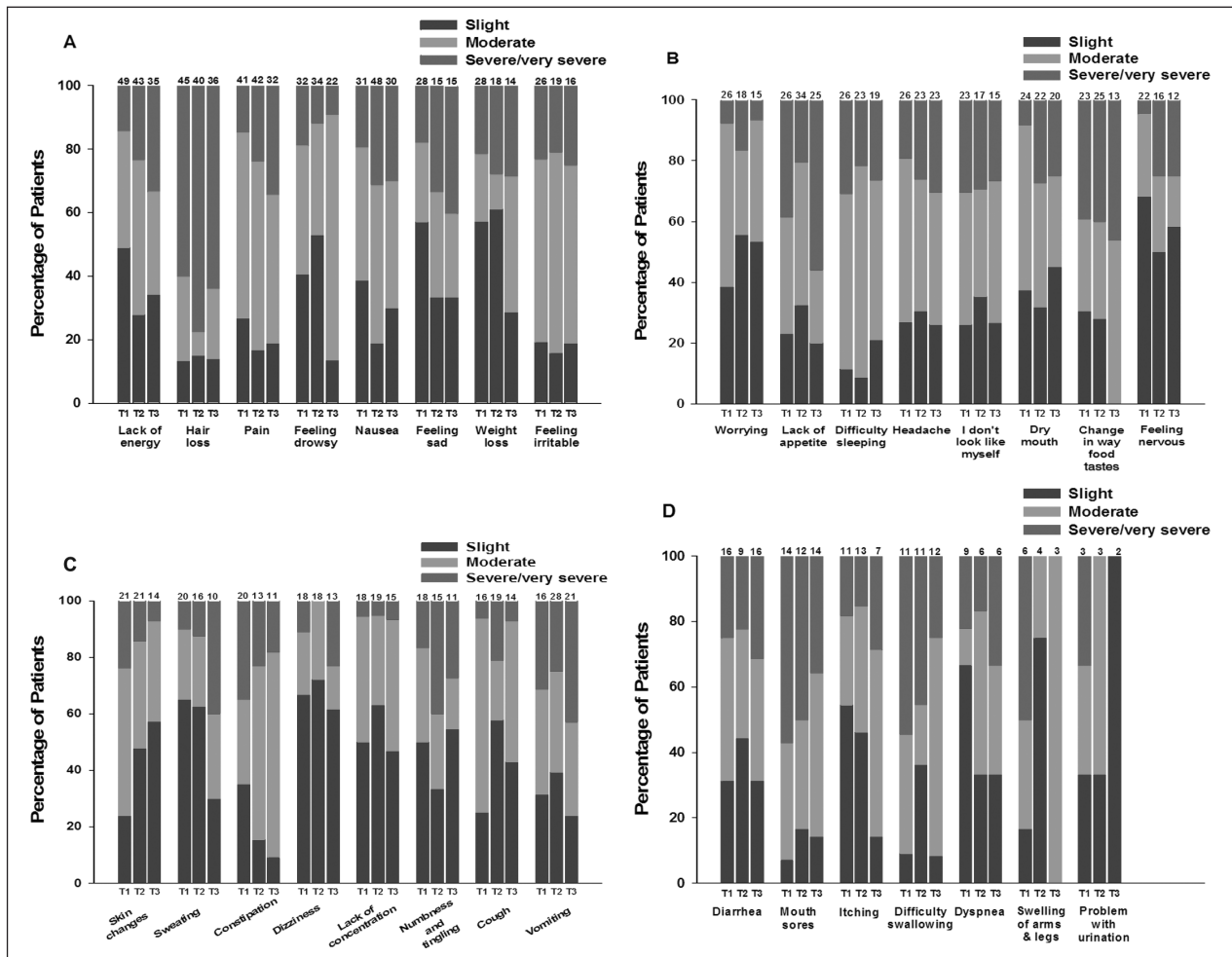


Figure 1. For each symptom on the Memorial Symptom Assessment Scale for 10- to 18-year-olds, of those patients who reported having the symptom, the percentage of patients who reported slight, moderate, or severe/very severe levels of symptoms that were prevalent in 42% to 76% of the patients (A), in 33% to 41% of the patients (B), in 25% to 32% of the patients (C), and in 5% to 25% of the patients (D) at each assessment. Numbers above the bars indicate the number of children who reported the occurrence of the symptom at each assessment.

As expected, a significant quadratic pattern of change was noted for nausea, with the occurrence of nausea being highest during the week of chemotherapy administration. However, rates of nausea were high at T1 (47.0%) and T3 (50.0%). Although a similar pattern was noted for vomiting, consistent with previous studies (Collins et al., 2000; Holdsworth, Raisch, & Frost, 2006; Rhodes, Watson, Johnson, Madsen, & Beck, 1987; Yeh et al., 2008), the occurrence rates for nausea were higher than those for vomiting. In addition, severity scores for vomiting were in the moderate to severe/very severe range. Although delayed nausea typically occurs 2 to 5 days after chemotherapy (Bloechl-Daum, Deuson, Mavros, Hansen, & Herrstedt, 2006; Grunberg et al., 2004; Holdsworth et al., 2006; Liau et al., 2005), 47% of patients in this study

reported nausea in the week prior to chemotherapy, which was approximately 2 to 3 weeks after the start of the prior cycle. This finding suggests that children may experience anticipatory nausea and vomiting, which warrants investigation in future studies.

The occurrence of pain (52.5% to 68.9%) and headache (37.7% to 40.0%) were common and persisted throughout the chemotherapy cycle. In addition, severity ratings for both symptoms were in the moderate to severe/very severe range for the majority of children at all 3 assessments. A variety of factors may contribute to pain and headache, including invasive procedures (eg, lumbar punctures), anemia, the use of hematopoietic growth factors, and the underlying malignancy. Previous research on children's pain during cancer treatment has been

limited to cross-sectional studies (Ljungman, Gordh, Sorensen, & Kreuger, 1999, 2000; Miser, Dothage, Wesley, & Miser, 1987; Van Cleve et al., 2004; Zernikow et al., 2006). Future prospective evaluations that include the use of daily electronic diary assessments may help determine the causes, characteristics, and impact of pain during chemotherapy.

Anorexia was a common, severe, and persistent symptom across the entire cycle of chemotherapy. However, reports of weight loss decreased over the chemotherapy cycle. Although children are weighed at the start of a chemotherapy cycle, at the other 2 assessments, children often stated that they were unaware of their current weight. These findings suggest that more objective assessments of weight are warranted, given the high occurrence rates for anorexia across the entire chemotherapy cycle.

Hair loss was reported by more than 60% of the children at all 3 time points. However, research staff noted higher rates of alopecia than reported by patients. This finding is consistent with previous reports (Collins et al., 2000). In fact, Collins revised this item on the MSAS 10-18 to read "less hair than usual" (J. J. Collins, written communication, May 2007). In this study, research staff asked patients to rate their hair loss compared with before cancer treatment started. However, some patients in this study with complete alopecia responded "no" to this item. Additional revision of this item is warranted.

No significant changes over time in individual symptom severity scores were noted when these scores were analyzed for the entire sample (ie, a zero was included in the mean score when a symptom was not reported). In addition, all the scores were below 1 (ie, slight). However, given the relatively small sample and differences in symptom occurrence rates over time (see Table 3), valid estimates of changes in each symptom's severity scores over time for children who had the symptom could not be calculated. Because of this limitation, the statistical evaluation of changes in each symptom's severity score over time, for those patients who reported the symptom at one or more times, was not performed in the current study. However, as illustrated in Figures 1A to 1D, a descriptive analysis was done for each symptom at each time point to provide information on the percentage of patients who reported mild, moderate, or severe/very severe symptom severity scores. Based on these descriptive analyses, the most severe symptoms among the patients who reported them were hair loss, pain, irritability, anorexia, difficulty sleeping, headache, alterations in self-perception, taste changes, constipation, mouth sores, and difficulty swallowing. As seen in Figures 1A to 1D, approximately 80% of patients who experienced these symptoms rated them in the moderate to severe/very severe range across all

3 time points. In contrast, patients reported much lower severity scores for sweating, dizziness, difficulty concentrating, and feeling nervous. These findings may be useful to guide the prioritization of symptom management intervention studies.

Several study limitations need to be acknowledged. The small sample size limited our ability to evaluate changes in symptom severity scores over time. In addition, the patients were heterogeneous with respect to diagnoses and treatments. More specific patterns of symptom trajectories might be found if patients with similar cancer diagnoses were evaluated. In addition, a more precise evaluation of the trajectories of symptom occurrence and severity would be obtained if patients were followed for multiple cycles of chemotherapy. Finally, a 1-week recall period was used. Some patients commented that their symptom experiences were extremely variable during a given week. More frequent symptom assessments using electronic symptom diaries would provide more precise estimates of changes in symptom occurrence and severity.

Despite these limitations, this study is the first to report the trajectory of multiple symptoms that children experienced during a cycle of chemotherapy. Although the occurrence of these symptoms peaked as hypothesized during the week following chemotherapy administration, the children in this study reported a high number of symptoms across the entire cycle of chemotherapy. A high emotional symptom burden was apparent as the patients started a chemotherapy cycle. Findings from this study suggest that intervention studies are needed to improve psychosocial support and self-care or dependent care for these symptoms.

Declaration of Conflicting Interests

No author has a direct interest, particularly any financial interest, in the subject matter discussed.

Funding

Research supported by National Institute of Nursing Research (NR010600); American Cancer Society Doctoral Degree Scholarship in Cancer Nursing; Betty Irene Moore Doctoral Fellowship in Nursing; and Oncology Nursing Foundation Doctoral Scholarship in Nursing.

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