Growth Patterns and Gastrointestinal Symptoms in Pediatric Patients After Hematopoietic Stem Cell Transplantation

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Purpose/Objectives: To identify growth patterns and gastrointestinal (GI) symptoms in pediatric patients during the first four months after hematopoietic stem cell transplantation (HSCT) and to assess whether an association exists between acute graft-versus-host disease (GVHD) and growth pattern changes or GI symptoms.

Design: A prospective, longitudinal cohort design.

Setting: A tertiary children's hospital in a metropolitan area in the southern United States.

Sample: A convenience sample of 35 pediatric patients receiving allogeneic HSCT.

Methods: Anthropometric measurements were obtained and GI symptoms were surveyed in pediatric patients before HSCT and two and four months after HSCT.

Main Research Variables: GI symptoms, anthropometric measurements, and presence or absence of acute GVHD.

Findings: All anthropometric measurements showed a significant change over time; height showed an increase, and weight, skinfold triceps, and mid-arm circumference showed a decrease over the four-month measurement period. Eight GI symptoms were prevalent over the four months, and the mean severity and distress scores fluctuated minimally during that time. No statistically significant differences were noted in any of the anthropometric measurements or GI symptoms between pediatric patients with and without GVHD.

Conclusions: Pediatric patients in the study exhibited poor growth patterns during the four months after HSCT and experienced multiple GI symptoms before and after HSCT.

Implications for Nursing: Nurses should be aware of the importance of evaluating growth and symptom experience in all pediatric patients during HSCT recovery and assist in defining treatment plans that will optimize patient health.

Key Points . . .

- Pediatric patients are exposed to multiple conditions after hematopoietic stem cell transplantation (HSCT) that leave them susceptible to malnutrition, exhibited by poor growth and persistent gastrointestinal (GI) symptoms.
- Pediatric patients in this study experienced multiple GI symptoms and had a significant loss of adipose tissue, muscle mass, and weight four months after HSCT.
- Nurses should perform a thorough nutritional assessment on all pediatric patients recovering from HSCT to determine effective nursing interventions that optimize nutritional health and improve health and quality of life.

Children require adequate nutrition for normal growth, development, and good health. Pediatric patients with chronic illnesses have additional nutritional needs from the demands of their disease and treatment. Malnutrition in the pediatric oncology population occurs in 8%–32% of patients (Han-Markey, 2000). Malnourished pediatric patients are predisposed to poor disease outcomes, decreased immune function, decreased quality of life, and poor growth and development (Han-Markey). Pediatric patients undergoing hematopoietic stem cell transplantation (HSCT) are exposed to similar risks as the pediatric oncology group; however, limited research has been performed to evaluate their long-term nutritional issues. Pediatric patients are at risk for long-term malnutrition after HSCT from a variety of issues, including poor oral intake, drug toxicity, altered absorption, and increased metabolic demands as a result of medical complications such as graft-versus-host disease (GVHD) and infection (Muscaritoli, Grieco, Capria, Iori, & Rossi Fanelli, 2002; Sigley, 1998). The purpose of the current study was to identify growth patterns and gastrointestinal (GI) symptoms in pediatric patients during the four months after HSCT and to assess whether an association exists between acute GVHD and growth pattern changes or GI symptoms. The research focused on the growth patterns, the frequency and severity of GI symptoms, and whether an association exists between GVHD and growth pattern changes or GI symptoms four months after HSCT.

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Digital Object Identifier: 10.1188/08.ONF.443-448

Background

Two signs of poor nutrition are inadequate weight gain and delayed linear growth (Wood, 1990). Mid-arm circumference and skinfold triceps measurements are helpful in identifying changes in body stores and fat (Papadopoulou, 1998). Wood performed a retrospective chart review on 60 pediatric patients undergoing HSCT and found that 20% had increased weight and only 12% increased height six months after HSCT. Few studies of mid-arm circumference and skinfold triceps changes in pediatric patients after HSCT exist. Taskinen and Saarinen-Pihkala (1998), evaluating mid-arm circumference and skinfold thickness in relation to height velocity in 42 pediatric patients during the first year after HSCT, found that height velocity strongly correlated with mid-arm circumference ($r = 0.45$, $p = 0.04$) and height velocity moderately correlated with skinfold triceps measurements ($r = 0.36$, $p = 0.1$), validating the effectiveness of using mid-arm circumference and skinfold triceps measurements to assess growth changes in pediatric patients.

Nausea, vomiting, diarrhea, mucositis, and anorexia are well-known GI side effects of HSCT conditioning regimens; however, only one study has evaluated GI symptoms in pediatric patients after discharge from HSCT. Barker, Anderson, Sauve, and Butzner (2005) used a retrospective chart review to evaluate 132 pediatric patients who had undergone HSCT and identify GI complications 100 days after HSCT. Mucositis, vomiting, abdominal pain, and diarrhea were common side effects experienced. Lenssen et al. (1990) evaluated 192 patients, 65 younger than 18 years, for prevalence and descriptions of nutrition-related issues one year after HSCT and found that the most common reported symptom was oral sensitivity (23%). Other common GI symptoms included xerostomia, anorexia, reflux symptoms, and diarrhea. Monitoring GI symptoms after discharge is a vital part of nursing assessment because transplantation patients continue to experience significant GI symptoms one year after HSCT.

No studies have evaluated growth patterns or the frequency of GI symptoms in children with acute GVHD, but one study, Mattsson, Westin, Edlund, and Remberger (2006), evaluated 231 adult patients after HSCT and found that patients with poor oral intake before the GVHD diagnosis had a significantly higher incidence of grade III or IV acute GVHD.

Theoretical Framework

The University of California San Francisco (UCSF) Symptom Management Model provides a conceptual framework for research with symptom experience, symptom management strategies, and outcome components (Dodd et al., 2001). Symptom experience involves a patient's perception of the phenomenon and an evaluation of meaning in response to the symptom; symptom management strategies allow for positive or negative outcomes; and outcome encompasses the patient's functional and emotional status, quality of life, self-care, costs, morbidity, and mortality. The goal is to avoid a negative outcome from the symptom experience (Dodd et al.).

Methods

Design and Setting

This descriptive study used a prospective, longitudinal cohort design to identify the symptom experience of GI characteristics and the outcome of growth patterns of pediatric patients during the first four months of HSCT recovery. A tertiary children's hospital in a metropolitan area in the southern United States was used for the study. The pediatric teaching hospital is a full-care pediatric facility providing inpatient and outpatient care in more than 40 specialties and performing about 100 pediatric autologous and allogeneic HSCTs annually.

Sample

A convenience sample of 45 pediatric patients receiving an allogeneic HSCT from 2004–2006 was recruited for the study. Patients ranged in age from 2–18 years ($\bar{X} = 10$ years, SD = 4.7 years), most were Caucasian (42%) or Hispanic (40%), and the sample included an even mix of males (49%) and females (51%). Patients received HSCT for a variety of malignant and nonmalignant diseases and were eligible for recruitment if they spoke English or Spanish and received a matched or mismatched, related or unrelated, allogeneic HSCT.

Exclusion from the study occurred if a patient experienced disease relapse after HSCT, failed to engraft after HSCT, or did not complete the measurements at any time (see Figure 1). Ten patients were removed from the study because of failure to engraft (n = 1), relapse of disease or death (n = 3), and failure to complete the study questionnaire (n = 6), leaving 35 pediatric patients for study.

Instruments

The demographic data form was developed by the primary investigator to collect information before HSCT, such as age, gender, race, disease, and HSCT type. A second demographic data form was developed to collect information after HSCT, such as disease status, GVHD presence and type, and engraftment status. Anthropometric measurements included height, recorded in centimeters using a stadiometer (Holtain Ltd.), and weight, recorded in kilograms using a stand-on scale (Scale-Tronix). Arm circumference was measured in millimeters by wrapping a tape measure around the circumference at the midpoint of the upper right arm. Triceps skinfold was measured in millimeters and obtained using a caliper to determine the amount of subcutaneous tissue around the triceps muscle of the right arm at the same reference point as the arm circumference measurement. All were obtained by a consistent caregiver using the same equipment. Caregivers performed inter-rater reliability on arm circumference and triceps skinfold measurements on every sixth patient enrolled on the study for four readings with 95% accuracy.

The Memorial Symptom Assessment Scale (MSAS) (Collins et al., 2000), a 30-item, patient-rated instrument that evaluates physical, psychological, and global distress symptoms by asking the patient or parent for a "yes" or "no" (frequency) response, was used to evaluate common symptoms. If the statement held true for the patient's condition, he or she was asked to rate the symptom for severity and distress. Severity was measured on a four-point Likert scale ranging from 1 (not at all) to 4 (very severe). Distress was measured on a five-point Likert scale ranging from 1 (not at all) to 5 (very much). The physical portion of the instrument evaluated 10 GI symptoms used for study analysis, showing reliability and validity for use with patients aged 10–18 years (Collins et al.). Nineteen

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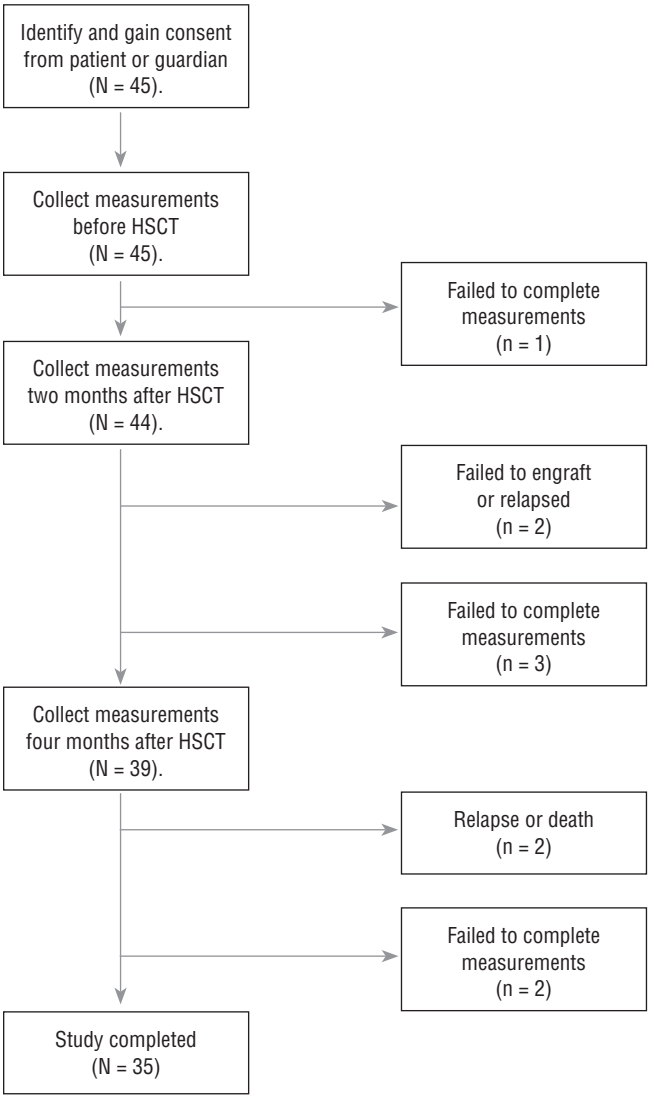

HSCT—hematopoietic stem cell transplantation

Figure 1. Progression of Pediatric Patients Through the Study

patients in the study were younger than 10 years; therefore, parents or guardians completed the questionnaire. Collins et al. established a Cronbach alpha of 0.87 for patient rating of physical symptoms, whereas Lobchuk and Degner (2002) established a Cronbach alpha of 0.84 for family caregiver's rating of physical symptoms. Convergent and discriminant validity of the instrument was confirmed with moderate correlations, 0.60 with the MSAS and the Revised Rand Mental Health Inventory distress scale and 0.65 with the MSAS and the Revised Rand Mental Health Inventory well-being scale (Portenoy et al., 1994). Validity of family caregiver ratings was determined with criterion-related validity of the physical symptoms, with results ranging from 0.22–0.70. Significant differences of symptom reporting by caregivers and patients occurred in 12 of the 32 symptoms items, with caregivers rating symptom experiences more severely than patients (Lobchuk & Degner). Of the 12 discrepant symptoms, only two were GI symptoms used in the current study.

Data Collection Procedures

Pediatric patients who met inclusion criteria and their parents were asked to join the study prior to admission for HSCT. After informed consent was obtained, the initial data were collected on the day of admission or the clinic visit prior to HSCT admission. The primary pediatric nurse practitioner completed the demographic data and anthropometric measurements, and the patient or the parent completed the MSAS. At two and four months after HSCT, demographic information and anthropometric measurements were recollected by the same pediatric nurse practitioner and the MSAS questionnaire was completed by the patient or same parent. Efforts were made to ensure data were not missing at each collection period. If two or fewer items on the MSAS scale were missing, in random order, the patient's data were used in the study; however, if three or more items on the MSAS scale or any growth measurements were missing from one collection time, the patient's data were not used.

Data Analysis

Information was entered in SPSS® 11.5 (SPSS Inc.) Repeated-measure analysis of variance was performed to evaluate anthropometric changes over time. Descriptive statistics, including frequencies and means, were used to analyze the GI symptom data. Differences in anthropometric measurements were evaluated between pediatric patients with and without GVHD using a t test. The frequency of GI symptoms was evaluated in pediatric patients with and without GVHD using chi square.

Results

Sample

Fifteen males and 20 females were among the sample that received HSCT for treatment of a variety of malignant and nonmalignant diseases (see Table 1). The majority received a bone marrow transplantation (10 males, 11 females). Sixteen of the participants were younger than 10 years and 19 were 10 years or older.

Growth Patterns

All anthropometric measurements showed a significant change over time, with height being the only measurement increasing at the four-month measurement period. Height showed a significant change over time, $\lambda = 0.546$, $F(2, 33) = 13.709$, $p < 0.001$, $\eta^2 = 0.454$, with the overall mean increasing 1.7 cm. Weight also showed a significant change over time, $\lambda = 0.604$, $F(2, 33) = 10.839$, $p < 0.001$, $\eta^2 = 0.396$; overall mean weight was 42.7 kg prior to HSCT and 39.8 kg four months after HSCT, a 2.9 kg loss. Skinfold triceps measurements showed a significant change, $\lambda = 0.790$, $F(2, 33) = 4.245$, $p < 0.05$, $\eta^2 = 0.210$, with overall mean decreasing from 15.2 mm before HSCT to 13.4 mm four months after HSCT, a 1.8 mm decline. Midarm circumference showed a significant change over time, $\lambda = 0.650$, $F(2, 33) = 8.621$, $p < 0.01$, $\eta^2 = 0.350$, starting at an overall mean of 23.3 mm before HSCT and decreasing to 21.9 mm four months after HSCT, a 1.4 mm decline.

Gastrointestinal Symptoms

Two of the 10 GI symptoms (difficulty swallowing and mouth sores) were not reported by any of the patients and are not listed in the results. The remaining eight GI symptoms

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Table 1. Disease by Gender and Age

Diagnosis	Male		Female		Total (N = 35)
	Younger Than 10 Years (N = 6)	10 Years or Older (N = 9)	Younger Than 10 Years (N = 13)	10 Years or Older (N = 7)	
Leukemia	4	6	8	3	21
Lymphoma	–	–	1	2	3
Myelodysplastic syndrome and monosomy 7	1	–	–	–	1
Hemophagocytic syndrome	–	–	1	–	1
Aplastic anemia	–	3	1	1	5
Fanconi anemia	–	–	1	–	1
Thalassemia	1	–	–	–	1
Sickle cell disease	–	–	1	–	1
Paroxysmal nocturnal hemoglobinuria	–	–	–	1	1

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were reported throughout the repeated measures (see Table 2). The mean severity ratings fluctuated minimally during the repeated measures and ranged from slight to moderate severity except for one severe rating two months after HSCT. The mean scores for distress caused from the reported GI symptoms also showed minimal change over time (see Figure 2).

Prior to HSCT, the most common GI symptom was a lack of appetite, with 14 patients reporting the symptom. Other frequently reported symptoms before HSCT were nausea (n = 10), dry mouth (n = 7), and diarrhea (n = 7). If present, diarrhea and perceived weight loss were rated as having slight severity, with the remaining existing GI symptoms rated as having moderate severity. Distress was rated as none to a little bit.

Symptom assessment two months after HSCT showed a high prevalence of all GI symptoms except constipation. Nausea was the most common, with 24 of 35 subjects reporting it. Other common symptoms included lack of appetite (n = 20), perceived weight loss (n = 18), vomiting (n = 16), and diarrhea (n = 16). Only one symptom, lack of appetite, was rated as severe, although a dry mouth and a lack of appetite coincided with higher distress levels.

Symptom assessment four months after HSCT showed lack of appetite to be the primary symptom (n = 12). Other common symptoms included diarrhea (n = 10), nausea (n = 8), and a change in taste (n = 8). Symptoms severity was primarily listed as slight, with three symptoms rated moderate. Distress also decreased, with three symptoms causing no distress and five symptoms causing a little distress.

Graft-Versus-Host Disease Associations

No statistically significant differences were noted in any of the anthropometric measurements or GI symptoms of pediatric patients with GVHD; however, the number of pediatric patients with GVHD may have been too small to detect a difference.

Discussion

Pediatric patients in the current study exhibited poor growth patterns during acute HSCT recovery. Decline in skinfold triceps measurements after HSCT represented a significant loss of adipose tissue, and the decrease in mid-arm circumference measurements showed a significant loss of muscle mass. Loss of fat and muscle mass is further illustrated by the children's significant weight loss over the four-month period. Although the mean height of the pediatric patients increased at an average rate for school-aged children, 1.7 cm height velocity over four months is significantly less than the average 2.3 cm height gain for toddlers and the average 3 cm height gain for preschoolers (Hockenberry & Wilson, 2007). Further studies on height should be performed on a long-term basis to assess growth changes for years after HSCT.

Table 2. Mean Severity and Distress Scores of Gastrointestinal Symptoms Over Time

Symptom	Before HSCT			Two Months After HSCT			Four Months After HSCT		
	n	$\bar{X}$ Severity	$\bar{X}$ Distress	n	$\bar{X}$ Severity	$\bar{X}$ Distress	n	$\bar{X}$ Severity	$\bar{X}$ Distress
Perceived weight loss	6	1.5	0.5	18	1.4	1.2	7	2.0	0.6
Constipation	4	1.8	1.5	2	1.0	1.0	–	–	–
Diarrhea	7	1.7	0.6	16	1.7	1.3	10	1.2	0.5
Nausea	10	1.7	1.2	24	1.7	1.3	8	1.6	1.1
Vomiting	3	1.6	1.3	16	1.6	1.3	3	1.3	1.0
Changes in taste	6	2.0	0.6	15	1.9	1.1	8	1.4	0.6
Dry mouth	7	1.6	1.4	15	2.1	1.6	7	1.1	0.9
Lack of appetite	14	1.6	1.0	20	2.6	1.6	12	1.8	1.2

N = 35

HSCT—hematopoietic stem cell transplantation

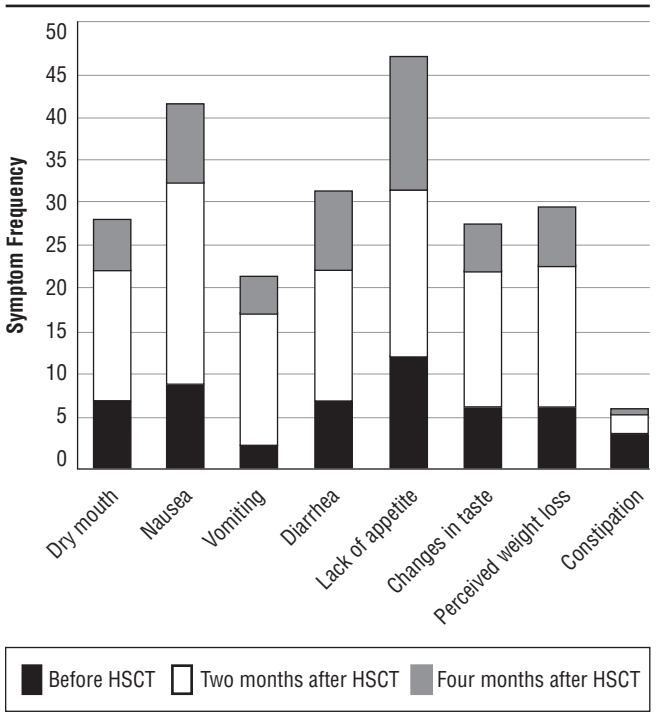

Figure 2. Gastrointestinal Symptom Prevalence in Pediatric Patients Undergoing Hematopoietic Stem Cell Transplantation (HSCT)

Pediatric patients in the current study reported various GI symptoms before HSCT and during acute HSCT recovery. As expected, GI symptoms were most frequent two months after HSCT; however, most of the GI symptoms were present to some degree before HSCT and four months after HSCT. Symptom severity and the distress caused from symptoms were ranked in the lower range, possibly because many pediatric patients with cancer have experienced multiple symptoms on a daily basis throughout treatment and have come to accept many symptoms as a normal part of treatment (Woodgate & Degner, 2003). Symptom persistence during the four-month period demonstrates the need for thorough assessments in pediatric patients throughout HSCT recovery.

Because the research was conducted with a small sample size from a single institution, the generalizability of the study findings to settings beyond the study population cannot be determined. Additionally, the six patients who reported forgetting as the reason they failed to complete the questionnaire may have been experiencing symptoms that they did not want to discuss, therefore revealing a bias in the study's results. Future studies should be conducted with a larger sample size.

Implications for Nursing

As more pediatric patients receive HSCT for treatment of various malignant and nonmalignant diseases, nurses should be aware of the issues involved in patient care. Pediatric patients experience multiple GI symptoms after discharge following HSCT, and the symptoms continue throughout the recovery phase. Evaluation of the symptom experience, including presence, frequency, and severity of GI symptoms, along with anthropometric changes, should be included in every nursing assessment. A thorough examination of the pediatric patient's well-being will effectively guide nursing interventions to produce better outcomes. An overall lack of accepted and congruent practice in regard to GI symptom assessment in pediatric patients during the lengthy recovery phase after HSCT is apparent, possibly because little research has focused on the persistence of GI symptoms in pediatric patients during the extended HSCT recovery. Nurses should be aware of the importance of evaluating the growth and symptom experience of all pediatric patients during HSCT recovery; with the increased awareness and understanding of the persistence of GI symptoms, more thorough nutritional and physical assessment measures will become a routine part of pediatric patient care. A complete assessment can assist with defining an individual treatment plan to optimize well-being. With better nutritional health, pediatric patients undergoing HSCT can experience optimal growth, development, and quality of life.

Because a patient's history is such an important component of any evaluation process, more research is needed to explore the meaning of the symptoms that pediatric patients experience during HSCT recovery and their significance. A phenomenological qualitative study would allow for a more in-depth understanding of what influence various GI symptoms have on appetite during HSCT recovery. Additionally, further qualitative studies should be performed to evaluate the meaning of nutritional issues and how they influence pediatric patients several years after HSCT. Quantitative research studies are needed to further evaluate anthropometric measurements and GI symptoms on a long-term basis to determine issue longevity. Studies with large sample sizes must be used to assess growth patterns and the GI symptom experience so that accurate generalizations can be made. Further studies should be conducted to analyze various nursing interventions and patient or parent nutritional educational information for their effectiveness. With this research knowledge, standards of care and effective management strategies can be developed, leading to more positive nutritional outcomes among pediatric patients recovering from an HSCT.

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