Pretransplant Nutritional Habits and Clinical Outcome in Children Undergoing Hematopoietic Stem Cell Transplant

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Abstract

Objectives: **This study sought to investigate the effects of pretransplant nutrient content, nutritional status, and nutritional habits on the clinical outcome of children undergoing hematopoietic stem cell transplant.**

***Materials and Methods*: Forty-one children were enrolled in this study. Dietary assessment was based on a semiquantitative food frequency questionnaire, consisting of 47 food items (including all commonly used prebiotic and probiotic foods in the Turkish cuisine), for the last week before hematopoietic stem cell transplant and a 24-hour dietary recall on admission.**

Results: **Thirteen girls (31.7%) and 28 boys (68.3%) comprised the study group. Of the 41 children, 5 (12.2%) were classified as underweight; 12.2% at risk of being underweight; 53.6% healthy weight; 9.8% overweight; and 12.2% obese. Nutritional status of the children had no effect on the complication rate, duration of febrile neutropenia, and the day of neutrophil and platelet engraftment. Correlation analysis revealed that there was a negative correlation between the day of neutrophil engraftment and the amount of soluble fiber, iron, breast milk, bazlama (a traditional yeast bread), and bulgur consumption. A negative correlation was detected between the number of febrile neutropenia episodes and the amount of yogurt and onion intake. Increased intake of parsley and onion was associated with reduced duration of total parenteral nutrition. The amount of parsley consumption was found to be lower in patients who experienced transplant-related complications.**

Conclusions: **The nutrient contents and nutritional habits of the patients may affect the course of transplant. It might be recommended that "let them eat yogurt, bazlama, bulgur, onion, and parsley."**

Key words: *Prebiotic, Probiotic, Nutritional habits, Children, Hematopoietic stem cell transplant*

Introduction

Hematopoietic stem cell transplant is a complex therapeutic procedure consisting of administration of high-dose chemotherapy, immunosuppressive therapy, and/or radiotherapy, followed by intravenous infusion of hematopoietic stem cells to re-establish marrow function in children with hematologic diseases, solid tumors, and autoimmune disorders.[1-6] Impaired nutritional status before transplant is a negative prognostic factor for outcome after hematopoietic stem cell transplant. Studies have shown that engraftment after hematopoietic stem cell transplant takes place more quickly for better-nourished patients.[7, 8]

Probiotic is defined as a living microbial food ingredient that is beneficial to health. Probiotics may have several beneficial functions, particularly in sick patients, including reduction or elimination of potentially pathogenic microorganisms of various kinds, toxins, mutagens, carcinogens, modulation of the innate and adaptive immune defense mechanisms, promotion of apoptosis after an immune-inflammatory attack, and release of numerous nutrients, antioxidants, growth and coagulation factors, and other factors necessary for recovery.[9, 10] A prebiotic is a nondigestible food ingredient that beneficially affects the host by

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selectively stimulating the growth or activity, or both, of a limited number of bacteria in the colon (*Bifidobacteria* and *Lactobacillus*). Modulation of the microflora of the gastrointestinal tract can occur through diets that contain prebiotics and probiotics. The approach of using diet to induce microbial change offers an important approach toward improved health.[11] Hematopoietic stem cell transplant is associated with substantial mucosal injury and changes in gastrointestinal flora, suppression of the immune system, immune dysfunction, severe hematologic disorders, and toxicity. It is suggested that nutritional factors may play a role in favorable modification of the immune system and the microbial flora in the transplant setting and perhaps, may influence transplant-related events. However, we found several published studies about the association of probiotic and prebiotic content of the diet with transplant-related events.[12, 13]

The aim of this study was to evaluate the effects of pretransplant energy and nutrient contents, nutritional habit (probiotic and prebiotic intake) and nutritional status (eg, underweight, obese) on the clinical outcome (the days of neutrophil and platelet engraftment) and the complications of hematopoietic stem cell transplant (veno-occlusive disease, graft-versus-host disease, and febrile periods).

Materials and Methods

Patients

Forty-one patients who were seen in the outpatient clinic of the Pediatric Bone Marrow Transplant Unit at our institution between June 2006 and June 2008 were voluntarily enrolled in this study. Written informed consent was obtained from all of the parents or subjects. All protocols were approved by the local ethics committee of the institution before the study began, and they conformed to the ethical guidelines of the 1975 Helsinki Declaration. The age and sex distribution, indications for hematopoietic stem cell transplant, and stem cell sources are shown in Tables 1 and 2.

Dietary assessment and management

Throughout the transplant period until neutrophil engraftment, a low-bacteria diet (neutropenic diet) was offered to all subjects. Education concerning appropriate food choices within the diet was provided to each participant throughout their hospitalization; no other dietary limitations were applied. From admission until hospital discharge,

Table 1. Demographic and clinical characteristics of children undergoing HSCT (n=41).

Characteristic	Mean ± SD	Range
Age (y)	9.7 ± 4.3	1-17
Sex (female/male)	13/28	—
Weight (kg)	33.4 ± 18.7	9.2-91
Height (cm)	131.0 ± 27.4	75-178
Body mass index (kg/m^2)	17.9 ± 3.7	13.6-28.7
Median nucleated marrow cells (× 10^8/kg)	6.0	2.1-15.0
Median mononuclear cells (× 10^8/kg)	5.9	2.6-15.1
Median CD34+ marrow cells (× 10^6/kg)	3.5	1.2-15.0
Median day of neutrophil engraftment	15	9-25
Median day of platelet engraftment	22	10-41
Median number of erythrocyte transfusions	5	1-12
Median number of thrombocyte transfusions	7	1-20

Abbreviations: HSCT, hematopoietic stem cell transplant

Table 2. Additional clinical characteristics of children in study (n=41).

Characteristic		n	%*
Nutritional status	Underweight or risk of underweight	10	24.4
	Healthy weight	22	53.6
	Overweight or obese	9	22.0
Diagnosis	Adrenoleukodystrophy	3	7.3
	Acute myeloid leukemia	5	12.2
	Acute lymphoblastic leukemia	1	2.4
	Chronic myeloid leukemia	8	19.5
	Myelodysplastic syndrome	1	2.4
	Aplastic anemia	5	12.2
	MHC Class II deficiency	1	2.4
	Fanconi aplastic anemia	3	7.3
	Hemophagocytic syndrome	1	2.4
	Wiskott-Aldrich syndrome	1	2.4
	Osteopetrosis	1	2.4
	Thalassemia major	11	26.8
Stem cell source	Bone marrow	25	61
	Peripheral stem cell	11	26.8
	Cord blood	3	7.3
	Bone marrow + cord blood	2	4.9
Donor	Sibling	33	80.5
	Mother	6	14.6
	Father	1	2.4
	Twin	1	2.4
Donor HLA antigen	HLA 5/6 compatible	3	7.3
	HLA 6/6 compatible	38	92.7
Conditioning regimen	Busulfan-cyclophosphamide	17	41.5
	Busulfan-cyclophosphamide-ATG	8	19.5
	Cyclophosphamide-ATG	4	9.8
	Busulfan-cyclophosphamide-melphalan	4	9.8
	Fludarabine-cyclophosphamide-ATG	3	7.3
	Fludarabine-busulfan-ATG	2	4.9
	Fludarabine-cyclophosphamide-TBI	1	2.4
	Busulfan-cyclophosphamide-thiotepa	1	2.4
	Cyclophosphamide-etoposide-TBI	1	2.4
GVHD prophylaxis	Cyclosporine-Mtx	37	90.2
	Cyclosporine	3	7.3
	Cyclosporine-mycophenolate mofetil	1	2.4
BMT complications	Veno-occlusive disease	0	0
	Acute GVHD	6	14.6
	Chronic GVHD	2	4.9
	Grade 3-4 mucositis	6	14.6
	Hemorrhagic cystitis	1	2.4
Outcome	Died	3	7.3
	Alive without disease	38	92.7

Abbreviations: ATG, antithymocyte globulin; BMT, bone marrow transplant; GVHD, graft-versus-host disease; HLA, human leukocyte antigen; MHC, major histocompatibility complex; Mtx, Methotrexate; TBI, total body irradiation

*Totals may not add up to 100% because of rounding.

body weight was measured daily on an electronic digital scale that was accurate to 0.1 kg. Height was measured at admission by a stadiometer that was accurate to the nearest 0.1 cm. Body mass index (BMI) was calculated with the following formula: weight (kg)/height (m^2). The BMI was assessed with World Health Organization 2007 Child Growth Standards charts.[14] The patients were grouped into 5 categories: underweight, at risk of being underweight, healthy weight, overweight, and obese. These weight categories were in accordance with the cutoff points of below the fifth percentile, fifth to below the 15th percentile, 15th to below the 85th percentiles, 85th to below the 95th percentile, and above the 95th percentile.[14, 15]

Dietary assessment was based on a semiquantitative food frequency questionnaire, consisting of 47 food items (including all of the commonly used prebiotic and probiotic foods in the Turkish cuisine), for the last week before transplant and a 24-hour dietary recall on admission. Also, any change in dietary habits after hematopoietic stem cell transplant were asked about when the subjects were seen for follow-up. The Nutrition Information System (BeBis) Software program (EBISpro for Windows, Stuttgart, Germany; Turkish version BeBiS; using data from the Bundeslebensmittelschlüssell 11.3 database and other sources) was used to assess the energy and nutrient intake of the subjects. Energy and nutrient intakes of individuals were compared with the dietary reference intake values.[16] Intakes lower and upper than 33% of the dietary reference intake were considered as inadequate and over.[16]

Assessment of toxicity

Severity of oral mucositis was graded daily according to adapted common toxicity criteria for stomatitis in patients undergoing bone marrow transplant.[17] Total parenteral nutrition therapy was started for any of the following reasons: treatment of mucositis of at least grade 3, insufficient oral intake (including refusal to eat owing to nausea, pain, or loss of appetite), and supplementation of oral intake to reach energy goals. The assessment of oral mucosa, according to common toxicity criteria, indicated grade 0 if no pain was present with a normal-appearing mucosa; grade 1 if painless ulcers, erythema, or mild soreness with no lesions was present; grade 2 if mucositis with painful erythema, edema, or ulcers were present, but the patient was able to swallow secretions; grade 3 for mucositis preventing swallowing of secretions; and grade 4 for mucositis requiring tracheal intubation.

The presence and severity of acute graft-versus-host disease were assessed daily by the transplant attending physician and nurses and was graded according to Glucksberg criteria.[18] Infections were defined by the presence of positive cultures or abnormal results of specific molecular, histologic, or other diagnostic tests or if there were pathognomonic radiologic findings (eg, pneumonia). The presence of fever and neutropenia was sufficient to define febrile neutropenia. Neutrophil engraftment day was defined as the first of 3 sequential days in which the absolute neutrophil count was 500/mm^3 or higher. Assessment of regimen-related toxicities (hepatic, pulmonary, and renal) was made daily during hospitalization by the transplant attending physician and nurses according to the National Cancer Institute common toxicity criteria.

Statistical Analyses

Statistical analyses were performed with SPSS software (SPSS: An IBM Company, version 11.0, IBM Corporation, Armonk, New York, USA). The normality of data distribution was checked using the Kolmogrov-Smirnov test. The correlation analysis was performed between the transplant course (the day of neutrophil and thrombocyte engraftments, the number of episodes of febrile neutropenia, the duration of febrile neutropenia, the use of total parenteral nutrition, and the duration of total parenteral nutrition), and the consumed amounts of proteins, carbohydrates, lipids, trace elements, minerals, soluble and nonsoluble fibers, vitamins, and prebiotic and probiotic foods. The independent-samples *t* test or Mann-Whitney *U* test for skewed data was used to compare the differences between groups, and a 1-way analysis of variance (Kruskal-Wallis test for skewed data) was used to compare the differences among more than 2 groups. A chi-square test was done to compare proportions, and Fisher exact test was used when applicable. Statistical significance was established at $P \leq .05$.

Results

A total of 41 children; 13 girls (31.7%) and 28 boys (68.3%) comprised the study group. Demographic and clinical characteristics of the children are

shown in Table 1. The mean (± standard deviation [SD]) age of the children was 9.7 ± 4.3 years (range, 1 to 17 y). The mean weight of the study group was 33.4 ± 18.7 kg (range, 9.2 to 91 kg); the mean height, 131.0 ± 27.4 cm (range, 75 to 178 cm); and the mean BMI, 17.9 ± 3.7 kg/m^2 (range, 13.6 to 28.7 kg/m^2). According to the World Health Organization growth standards, a total of 12.2% of children were classified as underweight; 12.2%, at risk of underweight; 53.6%, healthy weight; 9.8%, overweight; and 12.2%, obese.

The mean energy intake of the children was 1901 ± 771 kcal/d (70.4 ± 5.95 kcal/kg). The mean protein intake of the children was 73.90 ± 29.78 g/d (2.7 ± 0.22 g/kg); fat intake, 74.0 ± 34.8 g/d (2.7 ± 0.25 g/kg); and carbohydrate intake 228.2 ± 110.9 g/d (8.5 ± 0.80 g/kg). Of the total daily energy intake for all children in the study group, a mean of 16.8% ± 5.2% was supplied from protein; 34.6% ± 7.1% supplied from fat, and 48.8% ± 7.9% supplied from carbohydrates. The nutritional status of the children according to the dietary reference intake and the percentage of children who received nutrients below and over the reference ranges are summarized in Table 2. The mean energy and nutrient intakes of children according to the dietary reference intake are shown in Table 3.

Table 4 shows the amounts of foods the children ate, including probiotic and/or prebiotic (breast milk, buttermilk, cow's milk, ice cream, yogurt, fruit juice, cheese, kefir, haricot bean, kidney bean, chickpeas, sparrowgrass, leek, spinach, cabbage, lettuce, purslane, parsley, bulgur, rye, macaroni, tomato, garlic, onion, banana, strawberry, black mulberry, biscuit, cake, chocolate, bread, bazlama [traditional bread with yeast, made at home]) taken by children are shown in Table 4. Some patients consumed soybean (n=1), chard (n=2), raspberry (n=1), blackberry (n=6), Jerusalem artichoke (n=3), broccoli (n=2), and artichoke (n=3).

Table 3. Mean energy and nutrient intakes of children before HSCT according to dietary reference intake (DRI) (%).

Daily energy and nutrients	Mean ± SD (range)	DRI recommendation	Below DRI (%)	Over DRI (%)
Energy (kcal)	1900.6 ± 770.6		32.5	10
Protein (g)	73.9 ± 29.8	13-52	5	85
Fat (g)	73.97 ± 34.78	—		
Carbohydrate (g)	228.2 ± 110.9	130		
Energy from protein (%)	16.8 ± 5.2	10-35	—	5
Energy from fat (%)	34.6 ± 7.1	25-35	5.3	44.7
Energy from carbohydrate (%)	48.8 ± 7.9	45-55	27.5	2.5
Dietary fiber (g)	17.8 ± 8.5	19-38	60	2.5
Soluble fiber (g)	7.0 ± 3.9	—		
Insoluble fiber (g)	10.00 ± 5.86	—		
Vitamin A (μg)	1030.4 ± 1248.7	300-900	20	50
Vitamin E (mg)	9.82 ± 8.74	6-15	55	30
Vitamin B6 (mg)	1.26 ± 0.59	0.5-1.3	12.5	50
Thiamine (mg)	0.77 ± 0.31	0.5-1.2	22.5	15
Riboflavin (mg)	1.40 ± 0.58	0.5-1.3	12.5	70
Folate (μg)	240.4 ± 100.5	150-400	25	15
Vitamin B12 (mg)	3.97 ± 2.84	0.9-2.4	20	67.5
Vitamin C (mg)	90.3 ± 79.6	15-75	25	57.5
Calcium (mg)	730.2 ± 339.6	500-1300	47.5	5
Magnesium (mg)	225.0 ± 88.2	80-410	25	30
Iron (mg)	10.3 ± 4.0	7-11	20	30
Zinc (mg)	10.2 ± 4.0	3-11	7.5	55

Transplant course

The clinical course of hematopoietic stem cell transplant, the day of neutrophil and platelet engraftment, stem cell source, complications, and survival of patients are shown in Tables 1 and 2.

Table 4. Amount of probiotic and prebiotic foods taken by children before HCST.

Nutrients (g/d)	n	Median (g/d)	Mean ± SD (g/d)
Cow milk	30	200	287.4 ± 194.0
Breast milk	2	114	114.3 ± 121.2
Buttermilk	32	143	147.0 ± 120.3
Ice cream	32	51	65.8 ± 43.8
Yogurt	37	200	150.0 ± 107.0
Fruit juice	31	114	181.4 ± 187.6
Cheese product made with fruit	18	37	38.4 ± 35.3
Soybean	1	4	4.0
Haricot bean	36	9	14.7 ± 13.0
Kidney bean	17	9	11.0 ± 16.4
Chickpeas	27	9	11.5 ± 11.8
Red lentil	35	9	13.9 ± 18.9
Green lentil	13	9	8.9 ± 5.1
Chard	2	66	65.7 ± 62.7
Linseed	1	0	0.3
Artichoke	3	21	16.9 ± 14.4
Leek	22	12	17.0 ± 10.6
Spinach	33	21	23.4 ± 14.2
Cabbage	12	13	15.2 ± 8.4
Lettuce	32	30	57.4 ± 71.3
Purslane	10	21	19.8 ± 15.4
Jerusalem artichoke	3	11	28.5 ± 37.4
Broccoli	2	6	6.2 ± 0.7
Parsley	32	11	16.5 ± 16.6
Wheat flour	21	17	27.8 ± 24.7
Rye flour	1	115	115.0
Whole cereals	3	30	50.0 ± 52.9
Bulgur	37	17	20.6 ± 18.0
Macaroni	38	17	24.9 ± 19.0
Tomato	37	140	179.4 ± 125.4
Garlic	22	1	2.4 ± 2.9
Onion	33	90	92.5 ± 74.2
Banana	38	68	106.3 ± 100.8
Strawberry	25	36	78.8 ± 105.9
Blackberry	6	8	40.0 ± 78.8
Black mulberry	10	32	46.0 ± 43.7
Raspberry	1	72	71.5
Biscuit	37	39	53.3 ± 53.3
Cake	37	29	38.5 ± 31.1
Chocolate	36	38	32.5 ± 21.2
Bread (fermented)	41	125	157.2 ± 117.5
Bread (unfermented)	2	27	26.7 ± 33.0
Bazlama (fermented bread)	21	46	70.4 ± 50.8

Among the 41 children who underwent hematopoietic stem cell transplant, 27 (65.9%) children had 1 episode of febrile neutropenia, 5 had two episodes (12.2%), and 1 had three episodes (2.4%) during the 100 days after the procedure. Eight children (19.5%) did not experience fever during this period. Thirteen children (31.7%) received total parenteral nutrition for grade 3 or 4 mucositis or impaired oral nutrition. Duration of total parenteral nutrition was longer than 10 days in most of these 13 children (n=11).

Fifteen children had complications related to hematopoietic stem cell transplant within 100 days after the procedure. Of these 15 children, 6 had acute graft-versus-host disease, 2 had chronic graft-versus-host disease, 6 had grade-3 or grade-4 mucositis, and 1 had hemorrhagic cystitis. None of them had veno-occlusive disease. Additionally, 3 children had *Cytomegalovirus* reactivation, 1 had pleural effusion, 1 had idiopathic pneumonia, and 1 had failure of thrombocyte engraftment. Three children died during follow-up. One death was because of blastic transformation of chronic myeloid leukemia. The second child experienced leukemic relapse and died, and the third died of acute graft-versus-host disease.

Effect of nutrient content, dietary intake, and nutritional status on clinical course

Before and after the procedure, the nutritional habits of the children did not change. Nutritional status of the children had no effect on the frequency of complications (60% for risk of underweight or already underweight, 41% for healthy weight, and 67% for overweight or obese; $P > .05$), the duration of febrile neutropenia (mean ± SD, 4.9 ± 4.6 days for risk of underweight and underweight, 3.2 ± 2.8 days for healthy weight, and 3.3 ± 3.1 days for overweight or obese; $P > .05$), the day of neutrophil engraftment (mean ± SD, 15.4 ± 4.1 days for risk of underweight and underweight, 15.9 ± 3.2 days for healthy weight, and 14.9 ± 2.5 days for overweight or obese; $P > .05$) or the day of platelet engraftment (mean ± SD, 22.6 ± 8.7 days for risk of underweight and underweight, 23.2 ± 7.2 day for healthy weight, and 21.6 ± 6.4 days for overweight or obese; $P > .05$).

The mean soluble fiber intake was 7.0 ± 3.9 g/d, and the mean iron intake was 10.3 ± 4.0 mg/d (Table 2). The correlation analysis revealed that there was a negative correlation between the day of neutrophil engraftment and the consumed amount of soluble fiber and iron (Table 5). Neutrophil engraftment was faster in patients who consumed higher amounts of dietary soluble fiber ($r = -0.393$, $P = .012$) and iron ($r = -0.365$, $P = .02$). Additionally, the specific nutrients of breast milk ($r = -0.388$, $P = .03$), bazlama ($r = -0.506$, $P = .02$), and bulgur ($r = -0.477$, $P = .003$) also were found to be associated with shorter time to neutrophil engraftment (Table 5).

Table 5. Mean energy and nutrient intakes of children before HSCT according to dietary reference intake (DRI) (%).

	r	*P*
Correlation between some nutritional factors and neutrophil engraftment day		
Amount of consumed soluble fiber	−0.393	.01
Amount of consumed iron	−0.365	.02
Duration of breastfeeding	−0.388	.03
Amount of consumed fermented bread	−0.506	.02
Amount of consumed bulgur	−0.477	.003
Correlation between some nutritional factors and duration of febrile neutropenia		
Amount of consumed yogurt	−0.422	.009
Amount of consumed onion intake	−0.457	.008
Amount of consumed fruited cream cheese, ready-made	0.491	.04
Amount of consumed haricot bean	0.338	.04
Correlation between some nutritional factors and duration of TPN intake		
Amount of consumed onion intake	−0.659	.04
Amount of consumed parsley	−0.733	.03

The mean amount of yogurt intake was 150.0 ± 107.0 g/d. There was a negative correlation between the duration of febrile neutropenia and the amount of yogurt ($r = -0.422$, $P = .009$) and onion intake ($r = -0.457$, $P = .008$; Table 5). However, consumption of ready-made fruited cream cheese ($r = 0.491$, $P = .04$) and haricot bean ($r = 0.338$, $P = .04$) was associated with longer duration of febrile neutropenia (Table 5).

The consumption of vitamin C was inadequate in 10 children (24.4%). The mean duration of febrile neutropenia was 6.1 ± 4.7 days for children who consumed insufficient amount of vitamin C, and the duration of febrile neutropenia was 2.8 ± 2.4 days for children who consumed sufficient amount of vitamin C ($P = .03$).

There was a negative correlation between the duration of total parenteral nutrition and the amount of parsley ($r = -0.733$, $P = .03$) and onion intake ($r = -0.659$, $P = .04$; Table 5). Children who received total parenteral nutrition (n=10) had consumed significantly less fruit juice than did children (n=21) who did not receive this therapy (mean ± SD, 61.6 ± 59.3 g/d vs 238.4 ± 201.6 g/d; $P = .001$). The amount of garlic consumed by children who received total parenteral nutrition (n=6) was 0.68 ± 0.28 g/d, and that consumed by

children who did not receive total parenteral nutrition (n=16) was 3.00 ± 3.14 g/d.

The amount of garlic consumption also was insufficient in children who received total parenteral nutrition (P = .03).

The amount of parsley consumption was lower in patients who experienced any transplant-related complication (acute graft-versus-host disease, chronic graft-versus-host disease, grade 3 or grade 4 mucositis, and hemorrhagic cystitis) than that of patients who had no such complications (9.1 ± 7.5 g/d vs 20.4 ± 18.8 g/d, P = .02).

Other foods and nutrients had no effect on the clinical course of hematopoietic stem cell transplant.

Discussion

This study investigated whether the amounts of micronutrients, macronutrients, and foods including probiotics and/or prebiotics that children consumed before bone marrow transplant had any influence on transplant-related events and the clinical course of transplant. Interestingly, a negative correlation was detected between the day of neutrophil engraftment and the amount of soluble fiber and iron consumption. Additionally, the specific nutrients of breast milk, bazlama, and bulgur were found to be associated with faster time to neutrophil engraftment. A negative correlation between the number of febrile neutropenia episodes and the amount of yogurt and onion intake also was determined in this study. However, consumption of ready-made fruited cream cheese and haricot bean was associated with longer duration of febrile neutropenia. The duration of febrile neutropenia also was found to be significantly longer in patients who consumed an insufficient amount of vitamin C. Additionally, increased intake of parsley and onion was associated with reduced duration of total parenteral nutrition.

The amount of parsley consumption was found to be lower in patients who experienced complications after hematopoietic stem cell transplant (acute graft-versus-host disease, chronic graft-versus-host disease, grade 3 or grade 4 mucositis, and hemorrhagic cystitis) than that of patients who had no transplant-related complications. Similarly, Gerbitz and associates[13] showed that oral administration of *Lactobacillus rhamnosus* GG before and after transplant results in improved survival and reduced graft-versus-host disease in a murine transplant model. They recommend "let them eat yogurt" for patients undergoing bone marrow transplant.

In the present study, it was determined that children who received total parenteral nutrition consumed less garlic than that of children who did not receive total parenteral nutrition. Lu[12] reported that garlic consumption is effective against *Cytomegalovirus* infection, and that it is used in the author's Chinese bone marrow transplant clinic, with encouraging results. To obtain a better prognosis in patients undergoing hematopoietic stem cell transplant, one should consider dietary intake of foods containing a sufficient amount of vitamin C, iron, and soluble fiber.

This study showed nutritional status (malnutrition or obesity) alone had no effect on neutrophil engraftment, complications of HSCT, and duration of febrile neutropenia. On the contrary, Yokoyama and associates[8] showed significant correlation between the marrow recovery time and the initial nutritional state in patients who underwent hematopoietic stem cell transplant. Additionally, Papadopoulou and associates[2] reported that poor nutritional status was associated with a greater frequency of febrile and vomiting episodes and a longer hospital stay. These contrary findings might be because of differences in the patients enrolled in the studies and the severity of malnutrition. Most of our patients were classified as healthy weight (53.6%), overweight (9.8%), or obese (12.2%) according to the World Health Organization growth standards.

There are some limitations of this study. One is that the patients were evaluated only by self-report checklists. Another limitation is that separated analyses of the groups in regard to the underlying disease of the patient, the conditioning regimen, the kind of stem cell sources, and HLA antigen compatibility of donors could not be performed because of a limited number of cases. More studies are required to better establish the efficacy and role of nutrition in children who undergo hematopoietic stem cell transplant. To our knowledge, this is the first study of the effect of nutritional habits in children undergoing hematopoietic stem cell transplant.

In conclusion, the nutrient contents and nutritional habits of the patients may affect the

course of transplant. Therefore, our recommendation might be: "Let them eat yogurt, fermented bread, bulgur, onion, and parsley."

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