Nutritional status of children with cancer and its effects on survival

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SUMMARY: Yarış N, Akyüz C, Coşkun T, Kutluk T, Büyükpamukçu M. Nutritional status of children with cancer and its effects on survival. Turk J Pediatr 2002; 44: 35-39.

In the present study we aimed to determine the nutritional status of our patients and to assess its relationship with survival. The nutritional status of 47 patients with cancer was evaluated at diagnosis, three months after initiation of the treatment and at the end of therapy. Weight for height, height for age, and weight for age of children were expressed as percent of standard. Values for each nutritional index were converted into standard deviation (Z) scores. Three-year overall survival (OS) and event-free survival (EFS) rates of patients were determined according to their nutritional status. The overall prevalence of malnutrition at diagnosis was 29.8%. Three months later the malnutrition ratio reached 38.3% and then decreased again to 18.5% at the end of the therapy. Although the prevalence of malnutrition at the third month of treatment was significantly higher from the prevalence at diagnosis (p: 0.001) and at the end of the therapy (p: 0.009), the mean Z scores of the nutritional indexes before and during the treatment were not significantly different. The survival rates of malnourished patients were not different from those of well nourished patients. In conclusion, malnutrition is one of the main problems in children with cancer; hovewer, nutritional status has no effect on survival.

Key words: malnutrition, cancer, children, survival, prognosis.

Malnutrition may be present at diagnosis or develop during the treatment of cancer. Its incidence reaches as high as 40%[1-4]. Malnutrition in cancer patients results from a combination of metabolic abnormalities and decreased food intake. Increased metabolic rates, increased nutritional and caloric requirements, chronic anemia, and protein loss may contribute to development of malnutrition[5-8].

Metabolic factors may include altered protein and carbohydrate metabolism, selective use and redistribution of nutrients by tumor cells, alteration of total lipid mobilization resulting in elevated free fatty acids, and abnormal synthesis of peptides which may distrub normal enzyme activity. The aggressive multimodal therapy (directly or indirectly) and/or the neoplastic process itself are responsible for the metabolic differences observed in cancer patients[5,6,9].

Decreased food intake mainly results from anorexia. Anorexia may be related to both psychological factors and to release of chemicals by the tumor or by the host immune system[10,11]. Patients with cancer have already been consuming less than that recommended and less than their own previous intakes. In addition, decreased taste, mucositis and stomatitis, emesis, intractable diarrhea and malabsorption, dysphagia, pain and psychological factors may interfere with the maintenance of adequate oral intake[5,6,12-15].

Malnutrition is an important health problem in children. It may be suggested that malnutrition causes an increase in morbidity and mortality when it occurs in a patient with cancer. In the present study we aimed to determine the nutritional status of our patients with cancer and to assess its relationship with survival.

Material and Methods

From December 1996 to July 1997, 47 (20 female, 27 male) newly diagnosed patients with cancer were evaluated prospectively. The mean age of patients was 107 ± 49 months (range: 36-190) The diagnosis of patients were lymphoma in 25 (53.2%), brain tumor in five (10.6%), soft tissue

and bone sarcoma in seven (14.9%), and other solid tumor in 10 (21.3%) patients. The stage of disease was early stage (stages I and II) in 14 patients (29.8%) and late stage (stages III and IV) in 33 patients (70.2%). Nutritional status of patients was evaluated at diagnosis and three months after initiation of the treatment in all cases and at the end of therapy in 27 patients. Height was measured to the nearest 0.1 cm, and weight to the nearest 0.1 kg. Measurements were made by one observer according to the standard techniques. The serum albumin, prealbumin and transferrin levels of patients were measured at diagnosis, and during and at the end of the treatment. The normal levels of albumin, prealbumin and transferrin levels were considered as 3.2 g/dl, 0.2-0.34 g/dl and 212-360 mg/dl, respectively.

Assessment of nutritional status was performed using recommended techniques[16,17]. Weight for height (WFH), height for age (HFA), and weight for age (WFA) of children were expressed as percent of standard. Standard was chosen as median value of age and sex-matched reference population[18]. Nutritional status of patients was classified according to Waterlow[19] and Gomez[20] systems. Values for each nutritional index were converted into standard deviation (Z) scores. Standard deviation scores of WFH could not be calculated in 12 patients whose heights were outside the range of the WFH table. The mean values of Z scores were used to compare anthropometric index of patients before and during the treatment. No comparison of Z scores obtained at the end of therapy was done because the treatment periods and consequently time of last evaluation varied widely according to diagnosis and stage of the patients.

The median follow-up time was 39 months (range: 2-44). The follow-up time was short in some patients because of death. The patients diagnosed as malnourished were treated with administration of a high calorie and protein diet, and vitamin and mineral supplements. Total parenteral nutrition was not routinely given in those children. To analyze the effect of nutritional status on prognosis, three-year overall survival (OS) and event-free survival (EFS) rates of patients were determined according to their nutritional status. The patients with lymphoma were also analyzed separately, since they were the largest and unique group.

Student's t test was used for comparison of mean values. Frequency of malnutrition before, during and at the end of the therapy was compared using the chi-square and Fisher's exact probability tests. Frequency of malnutrition according to the patient's characteristics was also compared using the chi-square and Fisher's exact probability tests. Kaplan-Meier method was used for survival analysis, and curves were compared with long-rank test[21].

Results

The overall prevalence of malnutrition at diagnosis was 29.8% (14 patients). While 16 (34%) patients lost 2% to 17.2% (mean: 7.4 ± 5.2%) of their initial weight throughout three months, conversely 10 patients (20.0%) gained weight. Three months after initiation of the treatment the nutritional status of 14 patients malnourished at diagnosis was as follows: malnutrition completey resolved in three patients, the degree was decreased in three patients, malnutrition was still present to the same degree in five patients and the degree was increased in three patients. Seven patients who were well nourished at diagnosis became malnourished by the third month of the treatment. Malnutrition ratio reached 38.3% after three months of treatment, and decreased again to 18.5% at the end of the therapy. The degree and type of malnutrition at diagnosis, three months later and at the end of the therapy are shown in Table IA-IB. Although the prevalence of malnutrition at the third month of the treatment was significantly higher than that at diagnosis (p: 0.001) and that at the end of the therapy (p: 0.009), the mean Z scores of the HFA, WFA, WFH before and during the treatment were not significantly different (Table II). We could not find any relationship between the nutritional status and sex or age of patients, or type of cancer at any time of the evaluation. Ten of 14, 15 of 18 and four of five malnourished patients had advanced stage disease at diagnosis, at the third month, and at the end of therapy respectively. However, the difference between the patients with early and advanced stage disease in malnutrition ratio was not statistically significant. There was no relationship between the serum albumin levels and nutritional status. The prealbumin and transferrin levels of patients were significantly related with presence of malnutrition on admission and during the treatment (p: 0.05 for prealbumin, p: 0.001 for transferrin at diagnosis;.

p: 0.006 for prealbumin, p: 0.02 for transferrin at third month of the treatment). There was no relationship between the serum prealbumin and transferrin levels and nutritional status of patients at the end of the treatment.

found in OS and EFS rates between patients with malnutrition at diagnosis which improved partially (degree of malnutrition improved) or completely at the third months, patients with malnutrition at diagnosis who remained

Table I A-B. Nutritional Status of Patients

Table I A

Type of malnutrition	At diagnosis	At third month	At the end of therapy***
A* Wasted	9 (19.2%)	13 (27.7%)	3 (11.1%)
C* Wasted + stunded	4 (8.5%)	4 (8.5%)	1 (3.7%)
Stunted	1 (2.1%)	1 (2.1%)	1 (3.7%)
Total malnutrition	14 (29.8%)	18 (38.3%)***	5 (18.5%)
Normal	33 (70.2%)	29 (61.7%)	22 (81.5%)

Table I B

Degree of malnutrition	At diagnosis	At third month	At the end of therapy***
0°, Normal	33 (70.2%)	29 (61.7%)	22 (81.5%)
1°, Mild	6 (12.8%)	9 (19.23%)	5 (18.5%)
2°, Moderate	6 (12.8%)	7 (14.9%)	0
3°, Severe	2 (4.2%)	2 (4.2%)	0

* A: Acute, C: Chronic.

** The prevalence of malnutrition at the third month was significantly higher than that at diagnosis (p: 0.001) and at the end of therapy (p: 0.009).

*** 27 patients were evaluated atthe end of therapy.

Table II. Z Scores of Anthropometric Indexes of Patients

Z scores	At diagnosis	At third month
Z score for WFA	-0.63 ± 0.99 (-3.47; + 0.78)	-0.72 ± 0.93 (-3.30; + 1.26)
Z score for HFA	-0,55 ± 1.10 (-2.90; + 1.60)	-0.52 ± 1.14 (-3.07; + 1.50)
Z score for WFH	-0.23 ± 1.34 (-2.60; + 3.4)	-0.22 ± 1.22 (-2.97; + 1.9)

* mean ± SD (minimum; maximum).

WFA: Weight for age.
HFA : Height for age.
WFH: Weight for height.

Three-year OS and EFS rates were 70% and 65%, respectively, for the whole group. There was no significant difference between the survival rates of malnourished and well nourished patients neither at diagnosis nor during or at the end of the therapy (Table III). When the patients were separated into two groups according to the stage of their disease (early or late stage), the OS and EFS rates of malnourished and well nourished patients were also not significantly different at any time of the evaluation. No significant difference was

malnourished to the same or a higher degree at the third month, and patients who were well nourished at diagnosis but became malnourished by the third month. When patients with lymphoma were evaluated separately, no difference was found in OS and EFS rates of patients according to their nutritional status at diagnosis, nor during or at the end of the treatment.

Table III. Three Year Overall (OS) and Event-Free Survival (EFS) Rates of Patients According to Nutritional Status

	Patients with malnutrition			Patients without malnutrition		
	No. of Pts.	OS (%)	EFS (%)	No. of Pts.	OS (%)	EFS (%)
At diagnosis	14	69	83	33	71	97
At third month	18	70	83	29	70	96

Discussion

Malnutrition is one of the main problems in children with cancer. Malnutrition is reported to be relatively uncommon at diagnosis[1,2,5,22]. We found a significantly higher incidence during the treatment, although we found its incident as high as 29.8% at diagnosis. This result

suggests that the metabolic changes resulting from the therapy and the decreased oral intake due to chemotherapy complications such as mucositis and vomiting were the major reasons for malnutrition. It is reported that malnutrition is more frequent with advanced stage disease and recurrent tumor. Children with advanced stage Wilms' tumor and Ewing's sarcoma have a particular risk for malnutrition[1,2,22-24]. We could not find any relationship between the stage of disease and nutritional status of patients, nor between the type of cancer and nutritional status of patient, perhaps because of the small number of patients in each cancer group.

Malnutrition increaes morbidity and mortality in pediatric cancer cases. Organ systems such as hematological system, gastrointestinal system and immune system are affected by malnutrition[24,25]. Malnutrition immunocompromises the host and increases his/her susceptibility to infections[24-26]. Malnutrition is significantly associated with increased physiological instability and quantity of care[27]. Chemotherapeutic toxicity is correlated with poor nutritional status of the patients. Nutritional support improves treatment tolerance and prevents treatment delay and dose reduction[23,25,28-30]. Besides these, the pharmacokinetics of several anticancer drugs have been shown to vary with changes in body fat, consequently nutritional status may change the effects of drugs on tumor tissue[31,32].

Although there are some reports showing that nutritional status has a prognostic effect on children with cancer, we could not find any relationship between the nutritional status and survival. It was reported that risk of death was high in undernourished patients with ALL in remission-induction phase[33]. Similarly a significant influence of weight-for-height standard deviation scores on relapse time of newly diagnosed ALL patients was observed[32]. It was reported that well nourished patients with stage IV neuroblastoma had better one-year event-free and overall survival rates than malnourished patients[23]. However, van Eys[34] observed only slightly improved survival in well nourished patients with stage IV neuroblastoma, and showed that nutritional support had no effect on survival. In another study children with neuroblastoma and Wilms' tumor were compared. In the Wilms' tumor group the anthropometric measurements correlated with subsequent development of complications, although the neuroblastoma group had significantly lower anthropometric measurements[35]. Donaldson et al.[22] showed that malnourished patients with localized disease had a poorer survival rate; however, survival of patients with advanced tumors did not differ significantly according to nutritional status. In our study most of the patients with malnutrition had advanced stage disease, although it was not statistically significant. There are a lot of factors affecting prognosis and survival. Characteristics of the host and tumor which affec survival may also affect the nutritional status of patients. We could suggest that the type of cancer, stage of disease, and specific molecular and genetic factors might be more important than nutrition in determing survival of our patients.

In conclusion, malnutrition is an important problem in children with cancer. The highest ratio is obtained during the treatment. It can be suggested that cancer treatment and its complications are the major factors causing malnutrition. Although it is known that malnutrition causes some secondary problems and increases morbidity, we could not determine an effect on survival.

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