

Protein Energy Malnutrition and Skeletal Muscle Wasting at Diagnosis and After Induction of Remission Chemotherapy in Childhood ALL

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Abstract

Malnutrition is a common problem among children in developing countries. The nutritional status of a child on cancer therapy influences both tolerance of and response to treatment especially acute lymphoblastic leukemia. The aim of study to assess the nutritional status in children with acute lymphoblastic leukemia (ALL) initially at presentation and to determine the change in body weight and amount of skeletal muscle wasting after induction of remission chemotherapy. A prospective observation study in Central Teaching Hospital of Children in Baghdad, Iraq for the period (July 2005 – May 2006). Thirty-five cases of newly diagnosed ALL underwent somatometric measurement and subcutaneous fat at initial presentation and after completion of induction chemotherapy. Malnutrition (weight for age <80%) was documented in 20 cases (57%) but cumulative incidence of malnutrition (weight for age <80%, height for age <95%, weight for height <90%, triceps skin fold thickness < 5th centile, mid arm circumference < 5th centile) was found in 28 cases (77.1%). Eight cases (26%) lose weight during induction range (0.5-3 kg), most of them had complicated course (infection and bleeding) during induction chemotherapy. Seventeen cases (48%) had muscle wasting during induction. Malnutrition exists in a significant proportion of children with ALL; especially in children with complicated induction phase lose significant weight and have significant muscle wasting, while increase in subcutaneous fat occurs in almost all children which probably due to oral steroids.

Introduction

Nutritional state affects every pediatric patient response to illness. Good nutrition is important for achieving normal growth and development. Nutritional assessment therefore should be an integral part of the care for every pediatric patient. Routine measures for abnormalities of growth should be performed on all pediatric patients. (1)

Those patient with chronic illness and those at risk for malnutrition have detailed nutritional assessment done (2). Components of a complete nutritional assessment include a medical history, nutritional history including dietary intake, physical examination, anthropometrics (weight, length or stature, head circumference, midarm circumference, and triceps skin fold thickness). (3)

The use of age, gender, and disease specific growth charts is essential in assessing nutritional status and monitoring nutrition intervention. (4)

Malnutrition can defined as biologic manifestation of the combined effects of the

inadequate dietary intake and disease both, which are related to social and economic development (5). The aim of study to assess the nutritional status in children with acute lymphoblastic leukemia (ALL) initially at presentation and to determine the change in body weight and amount of skeletal muscle wasting after remission of induction chemotherapy, and to see the effect of nutritional status on the course of the disease.

Patients and Methods

The prospective study was carried out on children diagnosed to have acute lymphoblastic leukemia (ALL) who were admitted in the hematology – oncology unit of Central Teaching Hospital of Pediatric in Baghdad Iraq between July 2005 and May 2006. The study group composed of 35 children (23 males and 12 females) aged between 2 – 12 years. The diagnosis of ALL was established by the basis of standard investigations including complete blood counts and bone marrow aspiration patients

who had received chemotherapy prior to referral were excluded from the study.

Each subject was assessed for the following somatometric measurements using standard techniques and instruments ;1-Body weight was measured with minimum using an electronic balance.2- Stature (height – vertex) was measured by Holtain stadiometer .3-Mid arm and upper arm circumference was measured by using tape measure. 4- Triceps skin fold thickness was measured following the techniques given by Tanner and Whitehouse using Harpenden skin fold caliper over triceps. 5- Assessment of muscle mass was made by calculating mid upper arm circumference using a formula devised by Jelliffe and Jelliffe: $C_2 = C_1 - PS$

Where C_2 means mid upper arm muscle circumference; C_1 mean mid upper arm circumference; $P = 3.145$ and $S =$ Skin fold thickness (mean of biceps and triceps). 6-Upper arm muscle area (AMA) was calculated by using a formula devised by Jelliffe and Jelliffe: $M = (C_a - S)^2 / 4\pi$

Where in $M =$ upper arm muscle area; $C_a =$ upper arm circumference; $P_i = 3.145$; and $S =$ mean of biceps and triceps skin fold thickness (22). 7-Body mass index was calculated to assess the adiposity status as the following:

Body mass index (BMI) = Body weight (kg)/[Height (meter)]² (24).

Each of the anthropometric measurement were recorded thrice and average was regarded as the final baseline data value. These measurements were taken in children with ALL at the time of diagnosis, before initiating chemotherapy. Repeated measurements were carried out in these subjects after completion chemotherapy which is depending on the classification of ALL; as standard risk protocol which consist of : 4 doses of intravenous vincristine 1.5mg /m² weekly ,oral prednisolone 40 mg /m² daily , intra muscular L –Asparaginase 10000 U/m² as alternate day for 6 doses and weekly intrathecal injection of methotrexate, hydrocortisone and cytarabine for three doses; so the duration was 4 weeks .

For high-risk protocol treatment like above with weekly intravenous

administration of doxorubicin (Adriamycin) 25mg/m² for three weeks. Total serum albumin was measured by the hospital lab at the time of presentation and after induction, and compared by the normal values.

Eighty normal healthy children were taken from different areas to assess the nutritional status by various parameters mentioned above; 52 of them (65%) were males while 28 (35%) are females; 28 (35%) at age (1-4), 28(35%) at age (5-8) the remaining 24(30%) at age (9-12).

National charts standards were used for weight and height Tanner standards were taken for triceps skin fold thickness, mid arm muscle circumference and mid arm muscle area were categorized in accordance with international standards given by Jelliffe. Wasting and stunting were defined in accordance with criteria outlined Waterlows classification

Statistical analysis was done by using T test for each of the absolute generated body dimensions .(26)Chi square with Yates correction was applied to quantify the magnitude of the difference recorded in terms of percent occurrence rates of malnutrition in relation to age groups , sex ,disease status and complications during induction chemotherapy .(2)

Results

Of the 35 cases of ALL;23 cases (65%) were males while 12 cases (35%) were females, 13 cases (37 %) were in the age of (1-4) years , 13 cases (37%) between (4-8) years and the remaining 9 cases (26%) between (8-12) years ,median age was (5.8) . 4 cases (11.4%) had white blood cells count above 50000, 22 cases (62%) had hemoglobin less than 100g/l and 19 cases (55%) had hepatosplenomegaly of more than 5 cm below costal margin.

Eight cases (22.8%) were ALL L₁, 26 cases (74.2%) ALL L₂, 1 case (3%) ALL L₃. 23 cases (65%) on standard risk protocol and 12 cases (35%) on high risk protocol of the hospital.

Most children went into remission after induction therapy; sustained first complete remission was documented in 14 cases (93%) of 15 cases of malnourished children and 15 cases (100%) of 15 cases of well nourished

children, 5 (25%) of malnourished children died because of infection and central nervous system bleeding due to thrombocytopenia; 2 cases died after the 2nd week; 1 case died after the 3rd week; the other 2 cases died after the 4th week of induction chemotherapy.

Infection and bleeding were the most important complication during the weeks of induction chemotherapy; 7 cases (20%) had infection (pneumonia, and gastroenteritis), 8 cases (22.8%) had bleeding from nose, gastrointestinal tract, and central nervous system, 5 of them had been dead during induction (significant p value < 0.01), table (4).

Twenty-seven cases (77.1%) of the 35 children had one or more abnormal somatometric parameter denoting malnutrition at initial therapy, while 8 cases (22.9%) were normal parameters, table (2). 16 cases (45.7%) had isolated fat malnutrition (triceps skin fold thickness), 17 cases (48.5%) had wasting (according to weight for height), 10 cases (58.5%) had mild wasting (80-90% of weight for height), 5 cases (29.5%) had moderate wasting (70-80% of weight for height) and the remaining 2 cases (11%) had severe wasting (<70% of weight for height).

Malnourished cases (weight for age <80%) at the beginning of induction is 20 cases (57%), 10 cases (50%) had mild malnutrition (75-90% of weight for age), 7 cases (35%) had moderate malnutrition (60-

74% of weight for age), 3 cases (15%) had severe malnutrition (<60% of weight for age) table (3). Changes in body composition (triceps skin fold thickness) after remission induction are shown in tables (2,3), most of the patients gained weight (23) cases (65.7%) but 8 cases (22.8%) demonstrated loss of weight range 0.5-3Kg, and 4 cases (11.4%) had the same weight. The cases lose weight had a complicated course during induction chemotherapy (bleeding and infection).

Fat assessed anthropometrically, increase all most all cases of (triceps skin fold thickness) in 27 cases (90%) of 30 lived children, while decreased in 3 cases (10%). The mid arm muscle circumference increase in 9 cases was (27%), whilst a decrease was documented in 18 cases (54%) who had manifested weight loss, and still constant in 3 cases (10%). Body mass index at presentation revealed 19 cases (54.25%) below 5th centile while after induction, there was increase in body mass index in 4 cases. This means that 15 cases (42.8%) still below 5th centile.

Six cases (17.1%) showed low total serum albumin (below 3.5 g/ dl) at the time of presentation with mean (3.9 g/dl) that was increased to 7 cases (20%) after induction chemotherapy; while the normal mean of serum albumin in the control cases is 4.1 g/dl with 8 cases (10%) of 80 cases below 3.5 g/dl.

Table (1) indices of malnutrition at presentation and after induction.

Indices of malnutrition	At presentation		After induction.	
	Number	Percent	Number	percent
Wt for age <80%	20	55	18	54.1
Wt for ht. <90%	17	48.5	15	42.8
Ht. for age <95%	20	55	20	55
Triceps skin fold thickness <5th centile	16	45.7	11	31.4
Midarm muscle circumference <5th centile (5)	15	42	20	57.1
S. albumin <3.5 g/dl (visceral protein)	6	17.1	7	20
Body mass index < 5 th centile (5)	19	54.25	15	42.8
Cumulative	27	77.1	29	82.8

Table (2) changes in body composition after induction .

Outcome	Malnourished group n=20	Well nourished group n=15
Infection	6	1
Bleeding	7	1
Remission	14	15
Death	5	0

Significant p value <0.01

Table () Outcome of follow up of ALL children

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Discussion

Malignancy contributes significantly to morbidity and mortality in pediatric population. Malnutrition is a significant health problem in developing countries, this study designed to find out the prevalence of malnutrition in children with acute lymphoblastic leukemia and the effect of induction chemotherapy on the nutritional status.

The height and weight may have erroneous in detecting malnutrition in the presence of large intra-abdominal and mediastinal masses or organomegaly.

Arm anthropometry had been advocated for detecting malnutrition in childhood cancer. In our study when weight for age was taken a criteria for assessing malnutrition only 20 cases (57%) had malnutrition, if arm anthropometry was

included additionally the cumulative prevalence of malnutrition raise to (77.1%).

According to weight for age, 10 cases (50%) had mild malnourished, 7 cases (35%) had moderate, and 3 cases (15%) had severe malnutrition.

The prevalence of malnutrition in Iraqi children according to control study of certain group of healthy children in different area s revealed 42% of them were malnourished according to weight for age. A survey in India show there is 52% prevalence of malnutrition according to weight for age. In-patient with ALL.

A survey from Mexico had shown that there was a high prevalence of malnutrition in ALL, where in 21.2% of the patient evaluated had evidence of malnutrition, Tamminga et al. observed that at the time of diagnosis, weight, height, weight for height, and mid arm circumference were normal in

all patient with ALL.⁽²⁷⁾ Delbecque-Boussard et al. Showed that there is low intake of energy, carbohydrate and protein incase of ALL at time of diagnosis

There was overall increase in weight (mean increase 0.5Kg) but this increment is not significant ($p > 0.05$) 8 cases (27%) showed loss of weight from (0.5-3 Kg), 6 of them (75%) had complicated induction chemotherapy.

There is a great effect of prednisolone (40 mg/m^2) during the weeks of induction by increase food intake, which is related to relieve of symptoms and euphoria. A complicated cases (infection, bleeding) can decrease oral intake and weight loss.

There was a significant increase in triceps skin fold thickness 27 cases (90 %) $p < 0, 01$; Rajesh et al. show there was increase in triceps skin fold thickness,

Koskelo et al. made other study that showed increase 33% of adipose tissue but another study documented no change in body composition after induction

Corticosteroid therapy causes alteration in fat metabolism, which had a net effect of increase body fat and redistribution of body fat causing truncal obesity. In our study, there is significant increase in skin fold thickness. This increment perhaps due to the effect of steroid.

There was only 0.7% of decrease in mid arm muscle circumference, 0.2% decrease in mid arm muscle area, Rajesh et al. study show there is only 0.2% decrease in mid arm muscle circumference, and 0.01% decrease in muscle area, another study was show there is no change in mid arm muscle circumference, we also found no significant changes in midarm circumference, this may due to a large amount of protein in diet although we did not inquire of type of diet or follow up diet.

The finding of our study that malnutrition had a significant proportion of children of ALL, patient with malnutrition had a tendency for infection related complication during initial therapy in comparison to normal nutritional status. Further changes in muscle mass and body fat occur because of chemotherapy.

As a conclusion, Malnutrition exists in a significant proportion of children With ALL, If induction chemotherapy is

complicated, children lose significant weight and have significant muscle wasting, increase in subcutaneous fat occurs in almost all children, which is probably a consequence of therapy with oral steroid.

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