Nutritional status of acute childhood lymphoblast leukemia (ALL) pre &post induction chemotherapy

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Background: The nutritional status of a child on cancer therapy influences both tolerance of and response to treatment especially acute lymphoblastic leukemia.

Aim: 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 .

Patients and methods:Thirty-five cases of newly diagnosed ALL&eighty healthy children as control group underwent somatometric measurement at initial presentation and after completion of induction chemotherapy.

Results: 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.All those children who had lose weight also had skeletal muscle wasting, subcutaneous fat were increased in 27 cases (90%). 5 cases died during induction of remission .

Conclusion: Malnutrition exists in a significant proportion of children with ALL; especially in children with complicated induction phase, while increase in subcutaneous fat occurs in most all children which was probably due to oral steroids.

Key words: All, Children, Anthropometric Measurment .

Introduction

Malnutrition is common among children with cancer, both at presentation and with subsequent anti tumor therapy. Weight loss, deficits in weight for height (wasting) &deficit in height for age (stunting) are observed [1]. Malnutrition in pediatric and adult cancer patients has been associated with intolerance to chemotherapy and increased mortality rates [2], arm anthropometric measurment more sensitive indicators of under nutrition than wt& ht [2].

components of complete nutritional assessment include a medical history ,nutritional history including dietary intake, physical examination, anthropometrics, (weight, length or stature, head circumference, mid arm circumference & triceps skin fold thickness), pubertal staging, skeletal maturity staging and biochemical test for nutritional status[3], wasting occur in any disease state ,because skeletal muscle is the largest reservoir of protein[4].

Aim:

To assess the nutritional status &the changes in body weight & amount of skeletal muscle wasting in children with ALL before & after induction remission of chemotherapy.

Patient &methods:

The study was conducted on 35 children who were diagnosed as ALL in the hematology / oncology unit of the central teaching hospital for pediatric(Baghdad)between July 2005&May 2006.the diagnosis was based on clinical examination ,complete blood picture &bone marrow aspiration, all children were newly diagnosed and not received chemotherapy yet.

Each subject submitted to somatometric measurements using standard technique & instruments Weinera[5].

Body weight was measured with electronic balance, stature (height-vertex) measured by Haltain Stadiometer [6].

Mid arm circumference measurement by using fiberglass tape measure [6].

Triceps skin fold thickness(tsf) following technique given by Tanner and Whitehouse using Harpenden skin fold caliper over triceps Weinera[5].

Muscle mass was evaluated by mid arm circumference using formula[7] :

C2=C1-PS, where C2 means mid arm muscle circumference; C1 mean mid upper circumference;

P=3.145& S = skin fold thickness (mean of biceps and triceps).

Upper arm muscle area(AMA)was calculated using the formula (M=CA-S)2/4Pi

M= upper arm area, Ca= upper arm circumference, Pi=3.145 & S= mean of biceps and triceps skin fold thickness[7].

Body mass index(BMI) calculated by using normogram based on (weight)wt/kg

&(height)ht/square meter , BMI assess adiposity status [8].

Total serum proteins and serum albumin in particular was measured in hospital lab. each of the anthropometric measurement were taken 3 time and the average reading was the final baseline ,repeated measures are taken after completion of the induction of chemotherapy with weekly Vincristin 1.5/M2 for 4 doses. ,pridinsolon 40mg/m2,, L ASPARGINASE 10000U/M2 for 6 doses every other day and anthracyclin 50mg/m2 according to risk protocol and 3 intrathecal triple chemotherapy of methotrxate , hydrocortisone &Ara C. As control group 80 children who were attending outpatient clinic for simple acute upper respiratory infection matched in age and sex were taken with the same anthropometric measurement NCHS (national center for health statisticis percentiles) were used for wt&ht. Tanner standard were taken for triceps skin fold thickness, mid arm muscle cicumfernce and mid arm muscle area categorized with criteria outlined by Jelliffe [7]. Wasting stunting were defined with Waterlow s classification [8]. Statistical analysis was done by using t test, chi – sequare with Yate correction

Result:

Of the 35 cases 23(65%) were male &12(35%)female, median age was 5.8 years as seen in(table1(1) ,complete blood picture showed only 4 cases had WBC higher than 50000/cc & 19 cases had hepatosplenomegaly >5 cm , and subtype of leukemia were L2 mainly . (Table 2) show 27(77.1%) had one or more abnormal somatometric parameter denoting malnutrition at initial therapy, while 8 cases(22.9%) were normal parameters, 16 cases (45.7%)had isolated fat malnutrition (triceps skin fold thickness<5th centile), 17 cases 48.5%had wasting according to WT for HT, 10 cases (58.5%)had mild wasting(80-90%of WT for HT), 5 cases (29.5%)had moderate wasting (70-80% of WT for HT) &the remaing two cases (11%) had severe wasting (<70% of WT for HT).

Malnutrition cases (WT for age <80%) at the beginning of induction is 20 cases(57%), 10 cases(50%)had mild malnutrition (75-90% of WT for age) 7 cases (35%) had moderate malnutrition(60-74% of WT for age) 3 cases(15%) had sever malnutrition(<60% of WT for age).

Table 1 patient characteristics at presentation

Age	**(1-4)years=13**	**(5-8)years=13**	**(912)years=9**	**Total 35**
Male: female	8:6	12:4	3:2	23:12
	7	11	4	22
W.B.C>50000	1	3	0	4
Hepatosplenomegaly >5 cm	8	9	2	19
Type of ALL	L1=8	L2=26	L3=1	35

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Table (2) indices of malnutrition at presentation and after induction.

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

Changes in body composition (triceps skin fold thickness) after remission induction are shown in table (2,3) most of the patient gained wt 23 cases(65.7%), but 8 cases(22.8%) demonstrated loss of wt range 0.5-3kg ,& 4 cases (11.4%)had the same wt, those with wt loss had complicated coarse.

Fat increased (triceps skin fold thickness)in 27 cases (90%) of the 30 lived children while decreased in 3 cases(10%) $p<0.001$.

The mid arm muscle circumference increased in 9 cases (27%) while it decreased in 18(54%) & still constant in 3 cases(10%).

The body mass index at presentation revealed 19 cases (54.25%) below 5th centil, while after induction; there was increase in body mass index in 4 cases.

Six cases (17.1%) showed low total serum albumin(below 3.5g/dl)at presentation with mean (3.9g/dl),that was increased in 7 (20%)after induction chemotherapy in comparisoin to the control (4.1g/dl).

Sustained 1st remission was documented in 14 cases(93%) of cases of 15 cases of malnutrition &15(100%)of 15 cases of well nourished children, 5 (25%) of the malnutrition children died because of infection ,central nervous system bleeding,2 died in the 2nd week of induction ,one in the 3rd week the other two died at the end of 4th week(table 4). Infection &bleeding were the most important complication during weeks of induction chemotherapy , 7(20%) had infection(pneumonia & gastroeneritis) ,8 cases (22.8%)had bleeding, 5 of them had died during induction chemotherapy (bleeding &infection)(p value <0.01) (table4).

Table(3) changes in body composition before& after induction with the control

parameter	Pre-chemotherapy Mean ± SD	Post-chemotherapy Mean ± SD	control
Weight (Kg)	19.51 ± 6.78	19.62 ± 6.85	20.1± 6.6
Triceps skin fold thickness (mm)	6.58 ± 2.10'	7.81 ± 2.63	7.9± 2.7 *
Mid arm muscle circumference (cm)	13.12 ± 2.16	12.95 ± 2.31	13.2± 2.4
Mid arm muscle area (cm2)	15.13 ± 4.62	14.76 ± 4.75	15.2 ± 4.85
Body mass index (kg/m2)	15.86 ± 2.76	15.96 ± 2.91	16.1± 2.96
Serum albumin (g/dl)	3.9 ± 0.7	3.8 ± 0.9	4.1 ± 0.8

*significant p value <0.01

Table (4) Outcome of follow up of ALL children

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

Discussion

The nutritional status of a child on cancer therapy influence both tolerance of & response to treatment[9],children with cancer represent a high risk group for protein energy malnutrition duo to side effect associated with treatment, mild to moderate

malnutrition is common in leukemia patient at diagnosis &relapse [10].

In our study when weight for age was taken a criteria for assessing malnutrition showed that only 20 cases (57%) table 2&3 had malnutrition, Ursula Roha, Sao Paulo [11] showed 30% of affected children with ALL were malnourished on admission.

If arm anthropometric measurements was included additionally the cumulative prevalence of malnutrition raise to (77.1%). A survey in India show there is 52% prevalence of malnutrition according to weight for age in-patient with ALL if arm anthropometry was included, the cumulative prevalence of malnutrition rose to 88%, our study is similar or slightly less than Rajesh et al. study [12]. The wt for Ht method of assessing malnutrition can be erroneous in the presence of large intra abdominal malignant disease [12]. Reilly j j et al(13) suggest that wt for ht does have an influence on out come in ALL but the mechanism is unclear , lower weight for height was also associated with shorter remission[2] .

According to weight for age, 10 cases (50%) had mild malnourished, 7 cases (35%) had moderate, and 3 cases (15%) had severe malnutrition. Researches [2] had observed shorter period of remission in malnourished children as defined by ht for age, wt for age.

Tamminga et al[14]observed that at the time of diagnosis, wt ,ht, wt for ht & mid arm cir were normal in all patient with ALL in his study.

while survey from Mexico had however shown that there was a high prevalence of malnutrition in ALL, in which 21.2%of the patient evaluated had evidence of malnutrition (15) relatively less than Rajesh et al. which is explained by Delbecque-Boussard et al.[15] as there is low intake of energy, carbohydrate and protein in case 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, other studies[15&16] show no significant change in body wt during initial intensive chemotherapy in cases of ALL.

There is a great effect of prednisolone during the weeks of induction by increase food intake, which is related to relieve of symptoms and euphoria, over caring for children during illness period. A complicated cases (infection, bleeding, febrile neutropinea stomatitis) can decrease oral intake and lead to weight loss.

In our study there was a significant increase in triceps skin fold thickness 27 cases (90 %) $p< 0, 01$; Rajesh et al[12] show increase in triceps skin fold thickness, but another study by Koskelo et al. documented increase of 33% of adipose tissue[14], while Delbecque et al documented no change in body composition [15]. Children with ALL who were undernourished as defined by low body mass index had lower 5 year survival, increase relapse rate &more frequent reduction in chemotherapy doses (Lobato et al) [17].

Corticosteroid therapy causes alteration in fat metabolism, which had a net effect of increase body fat and redistribution of body fat causing trunkal obesity. In our study, there is significant increase in skin fold thickness. This increment perhaps due to the effect of steroid & over eating & over introduction of best food by the parents.

In our study there was only 0.7% decrease in mid arm muscle circumference, 0.2% decrease in mid arm muscle area, it s in agreement with Rajesh et al. [12] study where is only 0.2% decrease in mid arm muscle circumference, and 0.01% decrease in muscle area, another study showed there is no change in mid arm muscle circumference[15], we also found no significant changes in mid arm circumference , this may due to a large high quality amount of protein in diet (Rajesh Kumar 12). Plasma protein seems the most sensitive indicator of visceral protein status.[10] ,serum albumin reduced at diagnosis & improved during remission[10] ,in comparable to those healthy control children it is of no significance ($p <0.001$)(table 3) .

Patient with malnutrition had a tendency for infection related complication during initial therapy in comparison to normal nutritional status six vs one(table4). Anthropometric &biochemical parameter are prone to error &often reflect past rather than current nutritional status [9] so the nutrition status of child with cancer is ongoing from the the time of diagnosis to many years of treatment[2], but still arm anthropometrics may be more sensitive indicator of under nutrition than wt &ht [2]. Pedrosa F et al found no relationship between nutritional status& survival in those patients treated with cancer[18]. In conclusion Malnutrition exists in a significant proportion of children with ALL. If induction chemotherapy is complicated, children lose significant weight with muscle wasting &increase in subcutaneous fat occurs in almost all patients due to therapy with steroid, larger scale prospective studies are essential for planning nutrition interventions.

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