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Nutritional assessment and serum zinc and copper concentration in leukemic children

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ABSTRACT

Context: Malnutrition in childhood cancer is commonly a serious problem. Changes in blood zinc and copper have also been found in malignant diseases.

Objective: To describe the protein-energy nutritional status and serum zinc and copper of children with newly diagnosed leukemia.

Design: Cross-sectional study.

Setting: University referral center.

Participants: 23 children with newly diagnosed acute lymphocytic leukemia (ALL) or acute non-lymphocytic leukemia (ANLL) between the ages of 1 and 10 years. The control subjects were 31 healthy school children of similar age from local schools.

Main measures: Anthropometric measurements of height/age and weight/height, food intake and serum levels of zinc and copper.

Results: Almost the entire group of children were eutrophic. Zinc and copper intake were below the recommended values. Serum zinc levels were significantly lower and serum copper levels were significantly higher in the leukemic group when compared to normal children.

Conclusion: At the time of diagnosis the children suffering from leukemia were not overtly malnourished but blood analysis showed alterations in concentrations of the trace elements zinc and copper.

Key words: Leukemia. Nutritional Assessment. Zinc and Copper.

INTRODUCTION

Malnutrition is one of the major problems in cancer patients. Although not prevalent in all pediatric cancers, malnutrition in childhood cancer is a common, serious problem.¹ Cancer patients usually have inadequate energy and protein intakes, increased metabolic rate and abnormalities in energy, carbohydrate, lipid and protein metabolism.² Cancer therapy with chemotherapy and radiation therapy is also potentially damaging to nutritional status.³

The biological role of trace metals, especially serum zinc (Zn) and serum copper (Cu), in different physiologic and pathologic conditions has been extensively investigated in recent years. Zinc, a constituent of more than 200 enzymes, plays an important role in nucleic acid metabolism, cell replication, tissue repair and growth through its function in nucleic acid polymerases.⁴ Copper is an essential nutrient that is widely distributed in food and water and a component of several metalloenzymes that are required for oxidative metabolism, including cytochrome oxidases, ferroxidases, amino oxidases, super oxidase, ascorbic acid oxidase and tyrosinase.⁵ Changes in blood zinc and copper have been found in lymphoproliferative disorders,^{6,7} as well as in breast, lung and gastrointestinal tumors.^{8,9}

In order to describe the protein-energy nutritional status of our patients with leukemia and in an attempt to help in elucidating the role of the trace elements zinc and copper in malignant diseases, the present study investigated the serum concentrations of zinc and copper, as well as the daily intake of these two elements and the nutritional status in leukemic children.

METHODS

This study comprised 23 children with newly diagnosed acute lymphocytic leukemia (ALL) or acute non-lymphocytic leukemia (ANLL), between the ages of 1 and 10 years admitted to the Pediatric Section of the Hospital das Clínicas of Ribeirão Preto, SP, Brazil. All patients entered the study before receiving the first course of chemotherapy. The group consisted of 17 boys and 6 girls. Socioeconomic indicators for the children's families, such as occupation of the head of the household, education of the parents and family income, demonstrated that these children were mainly from low-income families.¹⁰

The control subjects were 31 healthy school children of similar age from local schools. The control group was used only for comparing serum zinc and copper levels.

Nutritional assessment by anthropometric methods

Standardized anthropometry measurements of body weight and height were performed by trained nurses, within the first 24 hours of admission.

Table 1 - Physical characteristics of the children.

Age	Girls		Boys		Total
	ALL	ANLL	ALL	ANLL	
1 — 3 years	-	-	2	1	3
3 — 6 years	4	-	6	1	11
6 — 10 years	1	1	6	1	9
Total	5	1	14	3	23

ALL - Acute Lymphocytic Leukemia

ANLL - Acute non-Lymphocytic Leukemia

Waterlow's¹¹ classification system of nutritional status, based on the concepts of height-for-age and weight-for-height, was used. Percentage-of-the-median values for each record were calculated from the reference median of the NCHS reference population.¹²

Serum zinc and copper determination

Serum zinc and copper were determined in the pediatric oncology laboratory by atomic spectrophotometry. Normal levels were defined by zinc > 70 ug/dl and copper > 90 ug/dl.¹³

Dietary intake history

Mean daily intakes were assessed through the 24 hour dietary recall method, for one day, performed together with the child's mother. Tallies were translated into estimates of calories, protein, zinc and copper and compared to the RDA nutritional standards.¹⁴

Statistical Methods. Data analysis was performed using the Chi-square and Mann-Whitney tests. Partial correlation was used to study a relationship between two variables. P values ³ 0.05 were considered statistically significant. All results are expressed as mean and standard deviation (SD).

RESULTS

The characteristics of patients are shown in Table 1.

Socioeconomic indicators for the children's families demonstrated that these children were mainly from low income families.

Anthropometric indices used to assess the nutritional status of the children demonstrated a malnutrition prevalence of 30%. Four children presented weight deficits for height (wasting) and three children presented height deficits for age (stunting).

The estimated average daily intake of calories, proteins, zinc and copper are summarized in Table 2. Average daily intake of calories of this population was 1681 kcal (SD 357), daily intakes ranged from 949 to 2212

Kcal. For protein, the estimated average daily intake was 66g (SD 16), daily intakes ranged from 29.3 to 87.9 g. For zinc, the estimated average daily intake was 8.2mg (SD 2.9), daily intakes ranged from 4.0 to 13.7 mg and for copper was 0.47mg (SD 0.26), daily intakes ranged from 0.15 to 1.14 mg. No statistically significant difference in the mean intakes of these nutrients between sex and age groups was found.

Serum zinc concentration was significantly decreased in the leukemic group, compared to the control group [109 (SD 45) ug/dl vs. 122 (SD 25) ug/dl] ($p < 0.05$), and serum copper concentration was significantly increased in the leukemic group, compared to the control group [195 (SD 90) ug/dl vs. 120 (SD 42) ug/dl] ($p < 0.05$), as demonstrated in Figures 1 and 2.

DISCUSSION

Anthropometric and Biochemical Nutritional Assessment

In our study 30% of the children were malnourished on admission. This rate of malnutrition was similar to that observed in other studies.^{15,16}

Four of our children presented weight deficit for height on admission. It has been suggested that the cause of this weight loss could be due to both decreased caloric intake and increased energy requirement.² Three of our children presented height deficit for age. A similar

incidence was demonstrated by Victora et al.¹⁷ in his study of the nutritional status of children of urban and rural areas of southern Brazil.

The majority of data presented on malnutrition in children with cancer is derived from children who have been under therapy for considerable lengths of time; among these children, malnutrition is frequent and it is often severe. However, a child with newly diagnosed disease seems to have the same average nutritional status as is seen in the population from which the child comes.¹⁸

Although the majority of the children in our study were well-nourished on admission, the start of chemotherapy or radiotherapy can alter the balance from adequate nourishment to malnourishment. Assessment of nutritional status at the time of diagnosis and during treatment is therefore essential for planning nutritional intervention.

Mean Daily Intakes

Calories. The estimated average daily intake of calories in this population was close to the recommended dietary allowance (RDA) (1800 to 2400 Kcal). Reduced energy intake was seen only in patients from the upper age range (6 to 10 years) (Table 2). This low caloric intake may be attributable to the loss of appetite presented by these children prior to diagnosis.

Protein. The average daily intake of protein for these children exceeded the RDA (16 to 23g)

Table 2 - Dietary calories, protein, zinc and copper intake by age and sex (Mean and Standard Deviation).

Years (Age)	Calories (Kcal)	Protein (g)	Zinc (mg)	Copper (mg)
Girls				
0 — 3 years	—	—	—	—
3 — 6 years	1720 (477)	55.7 (15)	7.3 (2.9)	0.49 (0.12)
6 — 10 years	1463 (323)	50.8 (14)	6.8 (3.0)	0.43 (0.11)
Boys				
0 — 3 years	1621 (443)	69.8 (18)	9.5 (2.2)	0.43 (0.25)
3 — 6 years	1651 (439)	66.7 (20)	8.1 (3.3)	0.51 (0.32)
6 — 10 years	1783 (218)	74.8 (11)	9.1 (3.0)	0.54 (0.32)

in all age groups. Dietary sources of protein for these children were mainly milk, meat, eggs, pasta and cereals.

Zinc. The present study documented a mean daily intake of zinc which was lower than the mean RDA of 10 mg/day for these age groups. In general, the best sources of dietary zinc are the most expensive food items, especially meats. As the majority of the children in this study subsisted on low-income diets, they are at particular risk for marginal or inadequate zinc nutrition. Dietary zinc deficiency is now known to occur in children and adolescents from widely diverse areas all over the world.¹⁹

Copper. This study also demonstrated that the mean daily copper intake of these children was less than the recommended dietary allowance

Figure 1 - Serum Zinc Concentration (ug/dl) in Normal and Leukemic Children

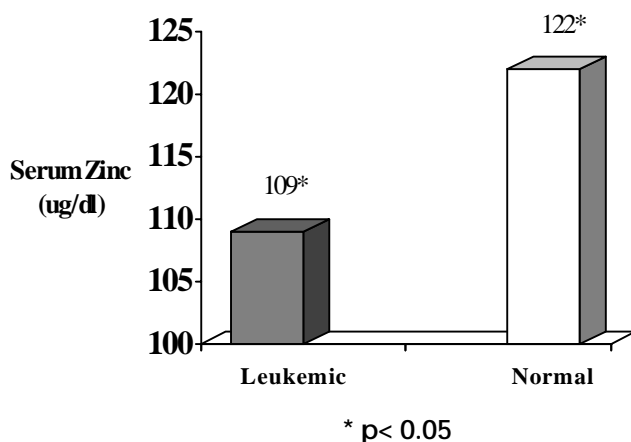
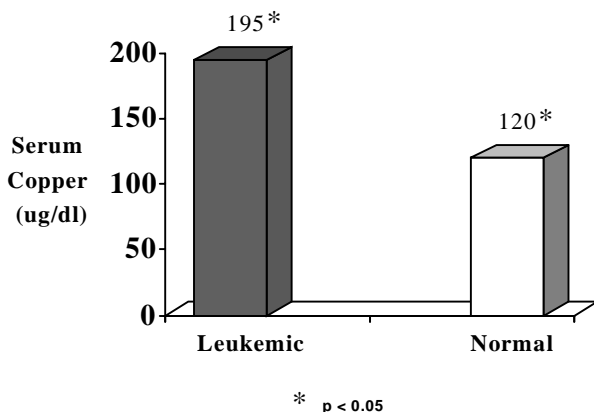


Figure 2 - Serum Copper Concentrations (ug/dl) in Normal and Leukemic Children



(RDA) of 0.7 to 2.0 mg/day. The richest sources of dietary copper include shellfish, meats, nuts, seeds and legumes. Although the diets of our children contained reasonable amounts of fish, meats and legumes, it seems that the quantity ingested was insufficient.

Because information on the copper content of foods is incomplete and values are often missing from databases, copper intake is often underestimated.²⁰

Trace Elements

Serum Zinc. The decreased serum zinc concentration in the leukemic group is in agreement with previous data.²¹

Mean serum zinc level in our children was slightly lower than found in our control group and lower than found by Fisberg et al²² in healthy children.

The determination of circulating levels of zinc either in plasma or serum has been the most widely used approach for the assessment of zinc nutrition. Metabolic states other than a change in Zn nutritional status alter the labile Zn pool. Stress, infection, food intake, short-term fasting and hormonal state all appear to influence the amount in the plasma.²⁴ In this study no significant correlation was found between serum zinc concentration and nutritional status, infection or food intake.

Serum Copper. The increased copper concentration observed is similar to that observed by other workers.²¹

Mean serum copper level in our children was significantly higher than found in our control group and higher than demonstrated by Braga²³ in healthy children.

Since many conditions can alter blood copper concentration, different variables such as inflammatory conditions, infectious diseases and copper intake were studied to determine their relative contributions. No positive correlation was found between these variables and serum copper levels.

Trace Elements vs. Cancer

This study demonstrated altered serum

zinc and copper levels in patients with newly diagnosed leukemia.

The blood serum levels of zinc and copper in malignant diseases have been the subject of a multitude of investigations, and their possible involvement has been well-recognized in many cancerous conditions. Altered zinc and copper concentrations in the plasma or serum have been previously reported in cancer patients.^{21,24,25}

The general trend towards slightly decreased zinc concentrations in malignant diseases supports the experimental results obtained by Brown et al.²⁶ suggesting that zinc deficiency is associated with the etiology of cancer.

Several studies^{27,28} show that serum Cu levels in malignant disease increase in relation to disease activity. Remission is usually associated with the return of Cu levels to normal ranges. Serum Cu is suggested as a useful index for the extent of leukemia and malignant lymphoma, and may predict response to chemotherapy.

Recent studies suggest that the use of blood zinc and copper concentration and the copper/zinc ratio (Cu/Zn) may be useful parameters for estimating the presence and prognosis of malignant tumors.^{6,9,29}

A far more comprehensive study of the basic mechanism for alteration of serum copper and zinc and its significance in all malignancies is needed.

CONCLUSIONS

This study showed that neither body composition nor energy intake changed significantly at the time of diagnosis. Long-term follow-up is needed, however, to prevent severe weight loss.

Energy and protein intakes were adequate in almost all children. Fifty-six percent of the subjects consumed less than the recommended allowance for zinc and ninety-two percent consumed less than the recommended allowance for copper.

Serum zinc levels were decreased and

serum copper levels increased in ALL or ANLL children when compared to healthy controls. Further studies are necessary, however, to better interpret these findings.

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RESUMO

Introdução: Crianças portadoras de doenças malignas tendem a ter seu estado nutricional comprometido, podendo apresentar também alterações nas concentrações sanguíneas de zinco e cobre.

Objetivo: Investigar os parâmetros antropométricos e os oligoelementos zinco e cobre em uma amostra de crianças portadoras de leucemia.

Local: Centro de Referência Universitário

Participantes: 23 crianças com diagnóstico recente de leucemia linfóide aguda (LLA) ou leucemia não linfóide aguda (LNLA), com idade entre um e 10 anos. O Grupo Controle foi formado por 31 crianças saudáveis da mesma faixa etária.

Variáveis estudadas: Foi feito um estudo transversal, onde foram avaliados os dados antropométricos de peso e estatura, a ingestão de calorias, proteínas, zinco e cobre e os níveis séricos de zinco e cobre assim como a ingestão destes minerais.

Tipo de Estudo: Estudo Transversal

Resultados: A maioria das crianças não apresentou comprometimento do estado nutricional e a análise da ingestão alimentar demonstrou que a ingestão de zinco e cobre estava abaixo das recomendações do RDA. Os níveis séricos de zinco foram significativamente menores e os níveis séricos de cobre significativamente maiores nas crianças com leucemia quando comparadas às crianças controle.

Conclusão: O estudo demonstrou que a maioria das crianças eram eutróficas ao diagnóstico, porém apresentavam níveis séricos alterados de zinco e cobre.