
Trace Element Analyses (Zinc and Selenium) in Pediatric Malignant Lymphomas

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ABSTRACT

Ninety-six untreated patients with Malignant lymphoma's, 81 Hodgkin's disease and 15 Burkitt's lymphoma were studied for zinc (Zn) and selenium (Se) status. Plasma and hair Zn, and Se levels were measured by atomic absorption spectrophotometry. Chronic Zn and Se deficiencies (low plasma and low hair Zn and Se levels together) were found to be associated with Malignant lymphoma's in Turkish children. This was most likely due to poor "nutritional environment" of the patients since majority of the Malignant lymphoma cases were from low socioeconomic class. Supplementation of the patients with physiological doses of Zn and Se, in addition to standard chemo radiotherapy regimen was proposed.

Key Words: Zinc and selenium, Malignant lymphoma.

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INTRODUCTION

There are several reports on serum trace element levels in malignant diseases including leukemia and lymphomas^[1-11]. However, studies on hair zinc (Zn) and selenium (Se) concentrations in pediatric malignant lymphomas are rare^[1,2,9,10,10a]. Although trace element measures in serum or plasma were easier and used more commonly, variations in their blood concentration occur even in some physiological conditions. Furthermore, several pathological states i.e. infections, stress, surgery, trauma and metabolic changes affect serum or plasma trace element levels in a short time, whereas hair trace element concentration provide

good evidence of long term deficiency and/or toxic states^[1,9-12]. Therefore, trace element determinations performed both in blood and hair simultaneously, provide better information according to our experiences^[9-13].

Zinc deficiency on nutritional basis has been shown in children and women in Turkey by our previous studies^[13,14]. In addition, malignant lymphomas are still the second most common malignancies among Turkish children, occurring mostly in low socioeconomic status (SES) group^[10-11]. In our previous studies, chronic Zn deficiency in pediatric Hodgkin's disease (HD) has been demonstrated by low plasma, serum, erythrocyte and hair Zn levels^[1,8-12].

The purpose of present study is to analyze further Zn and Se status in Malignant lymphomas, particularly in Burkitt's lymphoma (BL) and HD in childhood.

MATERIALS and METHODS

Ninety-six untreated patients with Malignant lymphoma's, 81 HD and 15 BL were included in this study. They were admitted to Pediatric Oncology-Hematology Section of the Department of Pediatrics of Ankara University. Their ages ranged from 2.5 to 16 years. Majority of the patients were male and had a low SES background. The diagnosis of malignant lymphomas was established histologically and cytological examinations were also performed in BL whenever necessary^[6,11]. The majority of HD patients were in advanced stages (St III and IV) with the predominance of mixed cellular type histology^[11]. Children with BL were also in advanced stages (C and D groups) according to NIH staging criteria^[6]. Plasma and hair Zn and Se levels were measured by atomic absorption spectrophotometry, as described previously^[10,11,15]. Eighty three and 97 healthy children aged 2.5 to 17 years were included in the study for plasma and hair Zn analyses and in 21 of them Se determinations were performed respectively. Students "t" and paired t-tests were used for statistical analyses.

RESULTS

The results of Zn analyses in plasma and hair of the patients were shown in Table 1 (Figures 1,2). The mean plasma Zn levels in HD ($75.7 \pm 5.5 \mu\text{g/dL}$) and in BL ($70.0 \pm 8.8 \mu\text{g/dL}$) were significantly lower ($p < 0.001$) as compared to that found in 83 control children ($109.8 \pm 12.3 \mu\text{g/dL}$). The mean hair Zn values obtained from control children and HD patients were found to be $184.0 \pm 19.3 \mu\text{g/g}$, and $114.5 \pm 34 \mu\text{g/g}$ respectively. There was a statistically significant difference between these two values ($p < 0.001$).

Fifteen BL patients had even lower mean hair Zn levels of $93.7 \pm 23.2 \mu\text{g/g}$ which was also significantly low as compared to both control and HD hair Zn values ($p < 0.001$). Selenium status in the whole group of malignant lymphomas is shown in Table 2. Plasma Se levels measured in the 2 groups of patients were significantly lower than the controls ($p < 0.001$). Hair Se levels were found to be ranging from $310 \pm 20 \text{ ng/g}$ to $362 \pm 8 \text{ ng/g}$ in 2 to 14 years age group in control children^[15]. The mean hair Se level in 14 patients with

HD and 7 BL were $290 \pm 37 \text{ ng/g}$ and $233 \pm 13 \text{ ng/g}$ respectively. The difference between the mean hair Se in controls ($338 \pm 18 \mu\text{g/g}$) and that of patients was statistically significant ($p < 0.001$).

DISCUSSION

It is of interest that chronic Zn deficiency associated with malignant lymphomas (HD and BL) persist over the years^[1,8-12]. Hair trace element analyses, in addition to their low plasma levels provide good evidence of long term trace element deficiency. Therefore, decreased plasma and hair Zn-Se concentrations found in the patients with malignant lymphomas in this study, may be taken as an indication of chronic trace element deficiency, possibly associated with poor nutrition and/or low SES of the patients, since majority of malignant lymphoma cases were from low SES^[1,8-12]. It is of interest to note that both plasma and hair Zn and Se levels were even lower in BL than that of HD patients. Rapid growth and destruction of tumor cells may be responsible for lower trace element levels in BL, as compared to that of HD, in which tumor progresses slowly. It is a well known fact that Zn deficiency may cause the impairment of cell-mediated immunity in several parameters^[7-11]. Effects of Zn deficiency on immune system in pediatric HD has already been shown by our group^[8-11]. Immune status evaluated previously in 10 BL cases at initial presentation, revealed significantly low levels of CD₄ and CD₈ cells and diminished DHR to 2 antigens to be associated with Zn deficiency^[6]. Interestingly, elevations of some cytokines such as TNF- α and IL-2R levels also were shown by our group to be associated with Zn deficiency in pediatric HD recently (Table 3)^[17]. This is an important finding and requires further study in HD. In fact, recent studies by Prasad revealed that Zn deficiency in humans mainly affected the cytokine production of Th₁ cells. IL-2 and IFN- γ are considered to be the products of Th₁ cells and their production decreased during Zn deficiency which was corrected by Zn repletion^[18]. In addition, production of TNF- α and IL-1- β have been shown to be increased in Zn deficient cells suggesting that Zn deficiency may cause activation of monocytes-macrophages and these toxic cytokines play a role in free radical generation. Therefore, Zn may function as an effective antioxidant^[18].

Furthermore, the importance of Se for optimal function of the immune system has now been well es-

Table 1. Zinc status in pediatric malignant lymphoma's (Hodgkin's disease and Burkitt's lymphoma)

	Control	Hodgkin mean ± SD	Burkitt
Plasma Zn (µg/dL)	109.8 ± 12.3 (83)*	75.7 ± 12.3 (81)	70.0 ± 8 (10)
	p < 0.001		p = 0.15
	p < 0.001		
Hair Zn (µg/g)	184.0 ± 19 (97)	114.5 ± 18.4 (68)	93.7 ± 23.2 (15)
	p < 0.001		
	p < 0.001		

* No in parenthesis indicate no of studied cases.

Table 2. Selenium status in malignant lymphomas (Hodgkin's and Burkitt's lymphoma)

	Hodgkin	Control	Burkitt
n	(14)	(26)	(7)
Plasma Se (ng/mL)	42 ± 7*	50 ± 5	36 ± 4
	p < 0.001		p < 0.001
HAIR Se (ng/g)	290 ± 37	338 ± 18	233 ± 13
	p < 0.01		p < 0.001
	p < 0.001		

* All the values are expressed as mean ± SD.

tablished^[19]. Selenoenzymes are also effective antioxidants that protect immune cells from oxidative damage. The decrease of trace elements, namely Zn and Se deficiencies may have various metabolic and clinical implications. The decrease in Zn may potentiate the toxicity of other metals such as iron, and copper. Selenium deficiency may interfere with free radical mediated damage and may be associated with progression of cancer^[20]. The efficacy of Se supplementation for cancer prevention and treatment also shown in some recent reports^[21,22]. Further study on Se in a larger group of malignant lymphomas in Turkish children is required. Moreover, European study in childhood malignancy including lymphoma, did not reveal significant changes in serum Se levels^[3]. "Nutritional environment" of Turkish patients may have a role in this difference^[9-11,16].

In view of the recent information on antioxidant

and immunostimulatory effects of Zn and Se and chronic deficiency of these trace elements shown in pediatric malignant lymphomas in this study, supplementation of the patients with physiological doses of Zn and Se, in addition to standard chemoradiotherapy regi-

Table 3. Serum TNF- α and IL-2R levels in pediatric Hodgkin's disease

Group	No	TNF- α (pg/mL)	sIL-2R (U/mL)
Hodgkin (active stage)	23	946 ± 433	3552 ± 1551
Normal Control	10	35 ± 16.7	557 ± 125
p		< 0.001	< 0.001

(from ref. 17 with some modification)

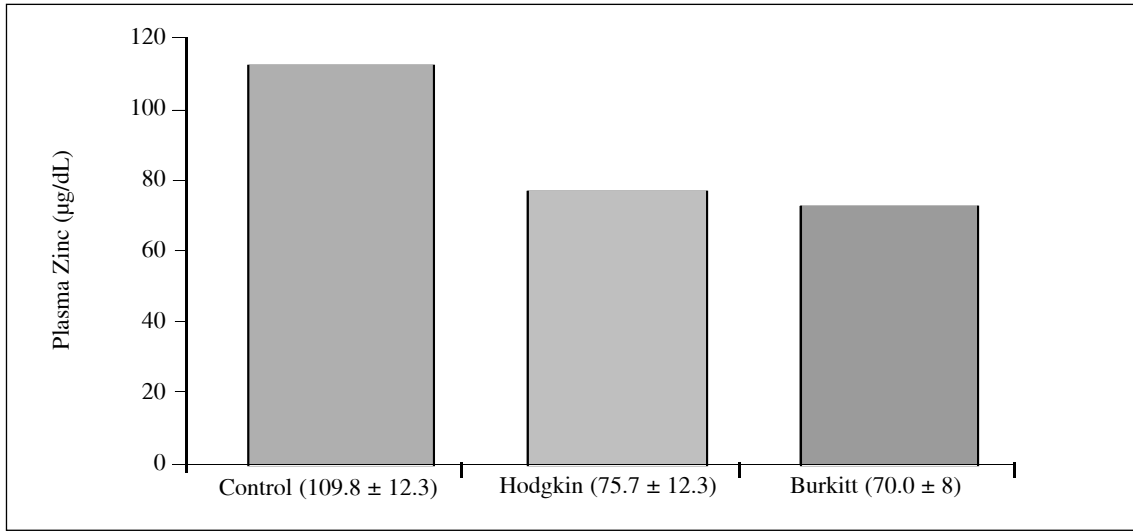


Figure 1. Zinc status in pediatric malignant lymphomas (plasma zinc).

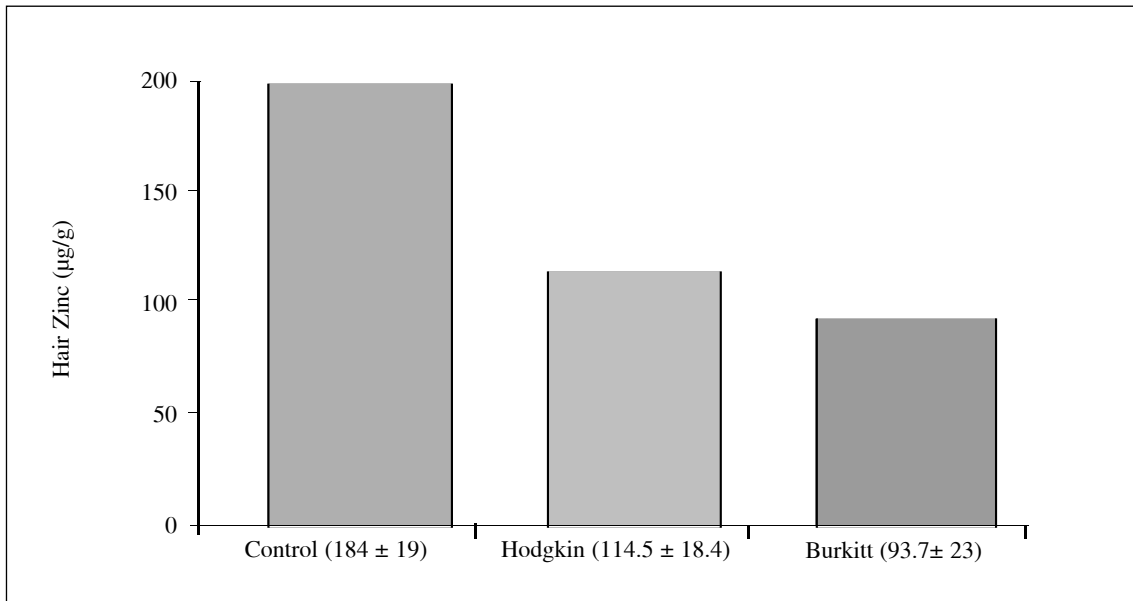


Figure 2. Hair zinc levels in malignant lymphomas.

mens, may be tried^[9,21,22].

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