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Determining Serum Zinc Level in Children with Cancer before and 3 Months after Chemotherapy in Kerman Province, Iran

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Abstract

Introduction: Cancer and chemotherapy could decrease serum Zinc level. In this study, serum Zinc level was investigated at the beginning of cancer diagnosis and 3 months after chemotherapy in children with all types of cancer.

Method: In this cross sectional study forty-five 1-15 year old children who were newly diagnosed cancer cases (leukemia, lymphoma and solid tumor) were evaluated. Patients with previous chronic disease were excluded from the study. Serum Zinc level was measured before and 3 months after chemotherapy by an atomic absorption spectrophotometer. The relationship between serum Zn level and malnutrition was also evaluated in both steps.

Results: The mean serum Zn level was 37.26±45.02 µg/dl at the beginning of cancer diagnosis and 11.96±24.59 µg/dl 3 months after chemotherapy (p-value=0.002), which showed a significant statistical reduction. There was no significant statistical difference in Zinc level between groups in regard to age, gender, place of resident and type of cancer.

Conclusion: This study indicated that Zinc level was lower than normal before chemotherapy and further decrease was seen after chemotherapy in all types of cancer among participating patients. Therefore, it is recommended to add Zinc supplement to chemotherapy protocols especially for malnourished patients.

Keywords: Children, cancer, Zinc, chemotherapy, malnutrition.

Introduction

Zinc (Zn) is the second element in human body after Iron in terms of frequency [1]. This element is found in a variety of foods including meat, chicken, seafood, beans, etc. [2,3]. Zn is the only element acting as the co-enzyme for all body enzyme classes and is one of the essential structural components of most proteins, such as signaling enzymes and transcription factors. Moreover, it is vital for RNA transcription and cell activity and division and is involved in activities of more than 300 enzymes [4,5]. Zn is highly important in cell death and survival. In addition, it has a central role in function of immune cells [5]. Zn deficiency can be caused by malabsorption syndromes and other digestive disorders, chronic liver and renal diseases, sickle cell disease, excessive alcohol intake, cystic fibrosis, pancreatic insufficiency, rheumatoid arthritis and other chronic conditions as well as cancer.

One of the most significant reasons of Zn deficiency in body is its low intake through foodstuff [6-16]. Zn deficiency causes many complications including weakening of immune system function, especially cell immunity and increased incidence of infectious and malignant diseases. Zn deficiency leads to weight loss, hypogonadism in men, growth retardation, lack

of appropriate weight gain, anorexia, as well as height and growth disorders. Moreover, Zn deficiency is responsible for retardation of scar healing, prolonged diarrhea, pneumonia, acne formation, white spots on nails, collagen reduction and delayed puberty [16]. The previous experiments show that Zn deficiency could increase cancer risk by affecting DNA failure, genes, decreased defense against oxidative stress and altering the function of immune cells [11].

Malignancies remain the second most common cause of all deaths among people aged between 1 and 14 years [17]. Pediatric malignancies are divided to 3 categories of leukemia, lymphoma and solid tumors [17]. Biological effects of micronutrients (including Zn) on cancer have been understood for many years. Sgarbieri et al. (1999) showed that, in spite of the lack of malnutrition in children suffering from Acute Lymphocytic Lukemia (ALL), their serum Zn level was low [18]. In 2004, Eby et al. utilized Zn in the USA as a part of ALL treatment protocol in a three-year-old girl with reduced serum Zn level and disease recovery was considerably accelerated [19].

It is recommended to add Zn supplement to chemotherapy [19] however, in many centers like our center chemotherapy is still performed without Zn supplementation. The main goals of this study were finding the prevalence of Zn deficient children (before and after chemotherapy) and the effect of chemotherapy on Zinc deficiency.

Materials and methods

This study was performed in a cross sectional manner. The newly diagnosed children with cancer in Afzalipour Hospital (Kerman, Iran) were studied from March 2012 until March 2013. None of these patients had any record of chronic diseases which could result in Zn deficiency. Diagnoses of cancer and its types in all children were confirmed by valid clinical and paraclinical methods.

A questionnaire was filled out by parents and history of hospitalization, which included age, gender, type of cancer, place of residence and history of Zn supplementation was recorded.

Table 1: The serum Zn level at the beginning of diagnosis and 3 months after chemotherapy.

	Beginning of cancer diagnosis	Three months after chemotherapy	p*
Serum Zn level (µg/dl)	37.26±45.02	11.96±24.59	0.002

Data are determined as mean ± standard deviation.
*: Based on Wilcoxon test

Table 2: The relationship between serum Zn level and gender.

Serum Zn level (µg/dl)	Boy (28 patients)	Girl (17 patients)	p *
Beginning of cancer diagnosis	33.25±45.39	43.85±44.97	0.265
Three months after chemotherapy	11.30±16.76	13.06±34.45	0.348

Data are determined as mean ± standard deviation.
* Based on Mann-Whitney test

Clinical examination was performed for determining malnutrition status by measuring weight, height, Mid-Arm Circumference and Triceps Skin Fold. In order to measure serum Zn level, an atomic absorption spectrophotometer was utilized. Normal mean of serum Zn level was considered 50-150 µg/dl.

After 3 months, blood samples of the patients were taken again using the aforesaid method and the required measurements of malnutrition were conducted once more. In order to measure the malnutrition, Waterlow criteria (weight/height) and National Center for Health Statistics criteria were utilized [20]. Malnutrition rate was calculated using the criteria of National Center for Health Statistics [21]. Since arm circumference is less affected by total body edema and chemotherapeutic drugs, anthropometric criteria, Triceps Skin Fold, Mid-Arm Circumference of the right arm and Mid Arm Muscle Circumference (using the following formula) were determined.

Mid Arm Muscle Circumference = Mid-Arm Circumference - (Triceps Skin Fold×3.14)

Results

Among 45 children with cancer, there were 28 boys and 17 girls. Six patients were suffering from lymphoma, 21 from leukemia and 18 from solid tumors. In terms of age, 24 patients were below 5 years, 14 between 5 and 10 and 7 over 10 years old. In terms of Zn supplementation, 44 people did not have any history while only one mentioned its consumption.

The mean serum Zn level was 37.26±45.02 µg/dl at the beginning of cancer diagnosis and 11.96±24.59 µg/dl 3 months after chemotherapy (p-value=0.002), which showed a significant statistical reduction (Table1).

There was no significant statistical difference in Zinc level between groups in regard to age, gender, place of resident and type of cancer (Table 2-4).

The results of Zn level before and after chemotherapy in patients with and without malnutrition are showed in table 5 and 6.

Table 3: relationship between serum Zn level and age groups.

Serum Zn level (µg/dl)	Below 5 years old (24 patients	5-10 years old (14patients)	Over 10 years old (7patients)	p *
Beginning of cancer diagnosis	37.08±38.48	34.75±43.63	42.91±41.40	0.823
Three months after chemotherapy	8.2 ±14.23	12.28±19.78	24.02±50.78	0.950

Data are determined as mean ± standard deviation.
* Based on Kruskal-Wallis test

Table 4: The relationship between serum Zn level and various types of cancer.

Serum Zn level (µg/dl)	Lymphoma (6 patients)	Leukemia (21patients)	Solid tumor (18 patients)	p *
Beginning of cancer diagnosis	41.50±50.8	34.84±44.35	38.67±46.42	0.972
Three months after chemotherapy	5.33±9.47	13.76±31.30	12.08±19.16	0.773

Data are determined as mean± standard deviation.
*Based on Kruskal-Wallis test

Discussion

In this study, serum Zn level was 37.26±45.02 µg/dl at the beginning of cancer diagnosis. Considering that normal mean of serum Zn level was considered 50-150 µg/dl, the obtained level of Zinc in this study was less than the normal level of mean serum Zn in children.

In a study by Sagarberi et al. (1999) in Brazil (that is a developing country like Iran), serum Zn level in patients suffering from leukemia was 109± 45 µg/d compared with 122±25 µg/d1 in the healthy group ($p < 0.05$) which indicated a significant difference (18). Although, the Zn level in above study, like our study, was significantly lower in patients compared to controls, but in both healthy and patients groups the Zn level was higher than our study, which may be caused by higher intake in foods.

The mean serum Zn level has been reported to be significantly different between healthy children and those suffering from malnutrition (22). Similarly in our study in patients with malnutrition at the beginning of treatment Zn level was significantly lower than patients without malnutrition, which was statistically significant ($p<0.05$).

Age and gender had no effect on serum Zn level in our study. Although since all patients participating in our study were living in one of Kerman regions and had almost equal geographical and cultural status the place of residence did not show an effect.

The mean serum Zn level, 3 months after chemotherapy was 11.96±24.59 µg/dl, that in comparison with serum Zn level at the beginning of chemotherapy (37.26±45.02 µg/dl) indicated a significant reduction of serum Zn level. In this study, 3 months after chemotherapy, no significant relationship was found between serum Zn level and presence or absence of malnutrition. Therefore, it can be concluded that reduction of serum Zn level in these patients is probably due to different mechanisms from malnutrition.

Lack of significant difference between different groups of children with different cancer types in

Table 5: The relationship between serum Zn level and malnutrition using Waterlow criteria.

WATERLOW(W/L)	No Malnutrition	Malnutrition	p *
Serum Zn level (µg/dl) at the beginning of cancer diagnosis	45.25±45.85 29 patients	32.85±44374 16 patients	0.435
Serum Zn level (µg/dl) 3 months after chemotherapy	14.43±28.38 31 patients	6.51±11.8 14 patients	0.542

Data are determined as mean ± standard deviation.
* Based on Mann-Whitney test

Table 6: The relationship between serum Zn level and malnutrition using Mid-Arm Muscle Circumference method.

MAMC	No Malnutrition	Malnutrition	p.v*
Serum Zn level (µg/dl) at the beginning of cancer diagnosis	49.20±47.83 27 people	29.30±42.06 18 people	0.045
Serum Zn level (µg/dl) 3 months after chemotherapy	13.54±28.18 32 people	8.08±11.95 13 people	0.899

Data are determined as mean ± standard deviation.
* Based on Mann-Whitney test

terms of serum Zn level either before chemotherapy or after chemotherapy indicated that all children with cancer need Zn supplement in their diet during the chemotherapy period.

Finally, low serum Zn level in children with cancer and its more reduction through the course of chemotherapy could indicate high importance of Zn supplementation as a factor for improving cancer treatment. Moreover, in future, it is recommended to conduct more studies to find any relationship of Zn level and initiation and progression of cancer in children.

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