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Selenium status in blood, urine, and hair samples of newly diagnosed pediatric cancer patients

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Background/aim: Selenium (Se) is a trace element that has multiple functions. Low Se amounts in serum and hair have been reported in pediatric and adult cancer patients. The aim of our study was to evaluate Se levels in the serum, urine, and hair of pediatric cancer patients with leukemia, lymphoma, and solid tumors when compared with healthy children.

Materials and methods: The concentrations of Se in the serum, hair, and urine of 32 Turkish children as healthy controls and 88 Turkish children diagnosed with acute leukemia (58), lymphoma (16), and solid tumors (14) were measured using inductively coupled plasma mass spectroscopy.

Results: Se levels in the serum and hair of the children with cancer were significantly lower than those of the controls. There were no differences between the leukemia, lymphoma, and solid tumors group. On the other hand, the Se levels of the urine samples were slightly elevated in cancer patients compared with the control group. There was no marked difference in the Se levels of patients with different types of cancer.

Conclusion: Se deficiency might be associated with the development of pediatric cancer. Especially in children, additional studies are needed to define whether low levels of Se may play a role in cancer pathogenesis.

Key words: Childhood, leukemia, lymphoma, solid tumor, selenium

1. Introduction

Cancer is rare in children and adolescents. Furthermore, it is different from adult cancers. Survival rates after childhood cancer have improved dramatically with intensive treatment regimens. There are many major types and countless subtypes of cancer that respond differently to treatment, including leukemia (cancer of the blood cells), lymphoma (cancer of the lymphatic system), and solid tumors (cancer of bone, organ and other tissues such as rhabdomyosarcoma, neuroblastoma, retinoblastoma, osteosarcoma, and renal tumors). Leukemia is the most common type of childhood cancer, accounting for 25% of new diagnoses. Lymphoma is a type of cancer that originates from the lymphatic system. There are 2 main types of lymphoma: Hodgkin's and non-Hodgkin's lymphomas (1).

The role of different trace elements in normal vital activities and the initiation of some disease has long been known (2). Selenium is an important trace element that plays a key role in protecting cells against oxidative damage (3). Oxidative damage can lead to mutations and, therefore, may play an important role in the initiation and progression of carcinogenesis (4). Selenoproteins have an anticancer effect by increasing the production of cytotoxic T-cells and natural killer cells (5). The results of studies about the association between selenium and adult cancer risk have varied. Although some studies suggest that cancer risk is associated with higher Se levels (6,7), some studies have reported no association between Se and high risk (8,9). There have been a few studies about the selenium status of serum and hair in pediatric cancer (10–14), and, to the best of our knowledge, this is the first study about urine selenium status in pediatric cancer patients.

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The aim of this study was to evaluate Se status in serum, hair, and urine samples of newly diagnosed pediatric leukemia, lymphoma, and solid tumor patients and to investigate the probability of a relationship between Se levels and the progression of pediatric cancer.

2. Materials and methods

Between January 2012 and December 2013, 88 pediatric patients with newly diagnosed cancer including acute leukemia (n = 58), Hodgkin's lymphoma (n = 4), non-Hodgkin's lymphoma (n = 12), and solid tumors (5 neuroblastoma, 5 medulloblastoma, 1 Wilms' tumor, 1 hepatoblastoma, 1 rhabdomyosarcoma, and 1 osteosarcoma) were admitted to the Pediatric Hematology–Oncology Division at Şişli Etfal Education and Training Hospital. Furthermore, 32 age- and sex-matched healthy children (brothers or sisters of patients) were enrolled in the study as the control group. All children belonged to middle class families and informed consent was obtained for all children from their parents.

There were 51 male and 37 female (mean age: 6.79 ± 3.88 years) in the study group and 19 male and 13 female (mean age: 6.52 ± 2.52 years) in the healthy control group. There were no statistical differences between the two groups regarding age and socioeconomic status.

This study was approved by the Ethics Committee of the Şişli Etfal Education and Training Hospital. Signed informed content was obtained from all participants' parents at the beginning of the study.

2.1. Biological sample collection and storage

Blood, urine, and hair samples were taken from 32 controls and 88 cancer patients (leukemia or solid tumors) diagnosed in the Pediatric Hematology–Oncology Clinic of Şişli Etfal Education and Training Hospital.

Approximately 2 mL of venous blood was collected from each of the 120 children using sterile syringes and needles. The samples were put into heparinized pretreated clean polypropylene tubes, carefully avoiding external metal contamination and hemolysis.

Hair samples were collected by clipping hair from the back of the head and near the scalp with stainless-steel scissors and putting the clippings into clean plastic bags. Blood and urine measurements were obtained from patients and controls at 0800 hours. Serum was separated with centrifugation at 3500 rpm and stored at –80 °C. Selenium levels were determined using inductively coupled plasma mass spectroscopy (ICP-MS).

All biological samples were dissolved with a microwave device for metal analyses and the metal analyses of the biological samples were performed with ICP-MS. The amount of selenium metal in all samples was determined.

2.2. Standard solutions

Metal stock solutions of 1000 mg/L were used as standards and prepared by dilution with deionized distilled water. Calibration of the ICP-MS instrument was done with this solution produced by Merck. Solutions were prepared for ICP-MS at suitable concentrations for analysis.

Prior to use, all plastic and glass equipment was washed with detergent and distilled water and then washed with a 10% HNO_3 solution. Finally, deionized water was used. Only chemicals used in analytical purity assays and ultrapure water were used in the preparation of the solutions.

2.3. Instruments

A PerkinElmer Sciex Elan DRC-e model inductively coupled plasma mass spectrometer was used for metal analysis and a Milestone Ethos 900 brand of microwave dissolution device was used for sample preparation.

2.4. Sample preparation with microwave oven

Biological samples were dissolved in the Milestone Ethos 900 microwave device in 100-mL Teflon containers. Next, 1 g of each sample was placed into a sample cup in the device. Then 6 mL of 65% HNO_3 and 3 mL of 30% H_2O_2 were added to each biological sample.

Sealed containers were placed into the microwave device and the dissolution procedure was performed, with the process being 4 min at 250 W, 5 min at 400 W, 4 min at 250 W, 5 min at 400 W, 6 min at 550 W, and 8 min of ventilation. After the dissolution time, the containers were kept at room temperature for cooling. Then the cups were removed, the contents of cups were added to 50-mL flasks, and the volume of each flask was filled to 50 mL with bidistilled water.

2.5. Spectroscopic analyses

ICP-MS is an analytical technique that breaks molecular bonds and ionizes atoms of samples by using a high temperature plasma, usually argon. Ions are sent into the samples and the second stage of the vacuum through a cone interface. Here, a coupled lens system focuses the ions to quadruple the mass spectrometer. Then, the ions are sorted by mass and analyzed by a scanning electron multiplier. Samples are generally sent into the device as a solution through a nebulizer. ICP-MS can measure different masses very quickly, which is why it was used as the multi-element analysis technique in this study.

2.6. Statistical analysis

Data were expressed as mean ± standard deviation for each group. A nonparametric analysis was carried out on the Se level data with a Mann–Whitney U test to examine the differences between the control and all patient groups. P values less than 0.05 ($P < 0.05$) were accepted as significant. All statistical analyses were performed using SPSS 15.0 (15).

3. Results

Characteristics of the study and control groups are given in Table 1. The study included 88 Turkish patients with different malignancies (51 male and 37 female, mean age: 6.79 ± 3.88 years) and 32 Turkish healthy children (19 male and 13 female, mean age: 6.52 ± 2.52 years). The age range of the subjects varied from 0.5 to 16 years. There were no significant differences regarding environmental exposure during pregnancy in terms of maternal exposure to vaccination, smoke, passive smoke, tattoos, and pesticides. The patients did not differ significantly from the healthy children in terms of age, sex, body mass index, sleep problems, and nutrition (types of food, milk, and meat).

The Se concentration results of both the control and patient groups and a comparison of serum Se levels are presented in Table 2. The mean Se levels were 162.62 ± 26.38 μg/L, 154.00 ± 30.64 μg/L, 147.75 ± 16.34 μg/L, and 202.37 ± 21.45 μg/L for the leukemia, lymphoma, solid tumor, and control groups, respectively. The serum Se levels of the 3 cancer patients groups were significantly lower in comparison to those of the healthy children ($P < 0.001$, $P < 0.011$, and $P < 0.001$ for the leukemia, lymphoma, and solid tumor groups, respectively). However, there were no statistically significant differences among the three cancer subtypes (data not shown).

Since selenium is excreted mainly via the urine, a urine analysis is important for assessing Se status in children (16). Table 3 summarizes the Se concentration in the urine of both the control and patient groups and gives a comparison of urine Se levels. The mean levels of urine Se were slightly elevated for cancer patients compared to the control, at 72.65 ± 14.95 μg/L, 73.53 ± 11.04 μg/L, 75.61 ± 12.25 μg/L, and 59.84 ± 13.40 μg/L for the leukemia, lymphoma, solid tumor, and control groups, respectively. Differences between the control and patients groups were statistically significant at $P < 0.017$, $P < 0.029$, and $P < 0.010$ for the leukemia, lymphoma, and solid tumor groups, respectively. However, there were no statistically significant differences among the cancer subtypes (data not shown).

Hair Se levels for the whole group of hematologic malignancies and the control group are shown in Table 4. The mean values for hair Se concentration of patients were reduced compared to the control group, at 0.47 ± 0.16 ng/g for leukemia patients ($P < 0.048$), 0.49 ± 0.17 ng/g for lymphoma patients ($P < 0.095$), 0.45 ± 0.12 ng/g for solid tumor patients ($P < 0.027$), and 0.63 ± 0.2 for the control group. Although the hair Se level was lower for lymphoma patients than the control group, this difference was not statistically significant ($P < 0.095$). In contrast, the Se levels for both the leukemia ($P < 0.048$) and solid tumor ($P < 0.027$) groups were significantly lower than those for the control group, but there was no statistically significant difference among the malignancies subtypes according to hair Se level (data not shown).

Table 1. Demographic characteristics of the patient and control groups.

	Patients	Control
Number	88	32
Age, years (mean ± standard deviation, min–max)	6.79 ± 3.88 (0.5–16)	6.52 ± 2.52 (3–15)
Gender (female/male)		
Female	37 → 42.05%	13 → 40.6%
Male	51 → 57.95%	19 → 59.4%
Any other disease	No	No
Vitamin-mineral supplementation (yes/no)	No	No
Malnutrition	No	No
Normal body mass indices (BMI) (yes/no)	Yes	Yes
Hematologic malignancies subtype		
Leukemia	58/88	-
Lymphoma	16/88	-
Solid tumor	14/88	-

Table 2. Serum selenium levels of the patient and control groups.

	Patient	Control	P value*
Serum Se level (μg/L)			
Leukemia (n = 25)	162.62 ± 26.38		0.001
Lymphoma (n = 13)	154.00 ± 30.64	202.37 ± 21.45	0.011
Solid tumor (n = 2)	147.75 ± 16.34		0.001

Se = selenium; data are expressed as mean ± SD; * = Mann–Whitney U test.

Table 3. Urine selenium levels of the patient and control groups.

	Patient	Control	P value*
Urine Se level (μg/L)			
Leukemia (n = 25)	73.53 ± 11.04		0.017
Lymphoma (n = 13)	72.65 ± 14.95	59.84 ± 13.40	0.029
Solid tumor (n = 2)	75.61 ± 12.25		0.010

Se = selenium; data are expressed as mean ± SD; * = Mann–Whitney U test.

Table 4. Hair selenium levels of the patient and control groups.

	Patient	Control	P value*
Hair Se level (ng/g)			
Leukemia (n = 16)	0.47 ± 0.16		0.048
Lymphoma (n = 16)	0.49 ± 0.17	0.63 ± 0.20	0.095
Solid tumor (n = 16)	0.45 ± 0.12		0.027

Se = selenium; data are expressed as mean ± SD; * = Mann–Whitney U test.

4. Discussion

Pediatric cancer affects all ethnic and socioeconomic groups. Increased cancer rates in children have been associated with inherited predisposition, radiation, electromagnetic fields, chemicals, and viral infections. Selenium is a trace element that protects cells against oxidative stress. In general, the pediatric population is considered more likely to be at risk for selenium deficiency due to the diversity of food quality and intake after birth, including sex, geological, and geochemical factors (i.e. drinking water and locally produced food). Selenium levels are expected to be much more heterogeneous in childhood than in an adult population. Leukemia is a malignant disease that is susceptible to antioxidant enzyme and essential elements alterations. Low Se levels have been reported in pediatric cancer patients (10–14,17).

In mineral/trace element deficiency, biological samples such as blood, urine, and hair (18) are most often used for biological monitoring. Whole blood, serum, and urine levels may show variability throughout a day; however, unlike blood serum and urine, hair provides historical information about intracellular accumulations and concentrations of trace elements in the body as well as nutritional condition over a long time (19–21).

In our study, we investigated the Se levels of the serum, urine, and hair of children with leukemia, lymphoma, and solid tumors. Selenium is a trace element that plays an important role in the protection against oxidative stress in cells. Oxidative stress produces free radicals, which are involved in the pathogenesis of many diseases including hematologic malignancy (5).

The relationship between the trace element Se and the etiology of cancer remains contentious and interesting, despite the large number of published epidemiologic studies (10). Although selenium levels in plasma, serum, or whole blood samples reflect a short-term index of selenium status, hair selenium concentrations give information about long-term selenium status due to its slower turnover rate.

There have been several reports regarding decreased blood Se levels of adult cancer patients (5,13,22); however, there have been a limited number of studies that investigated Se status in childhood malignancies (10–14,17,23). Different hypotheses are suggested for explaining the relation between reduced Se levels and hematologic malignancies (10). The first hypothesis states that enhanced uptake of selenium by the neoplastic tissue might be responsible for depleting the trace element content in the blood and other tissues. Thereby, serum selenium concentrations are reduced (24). Secondly, the reduced Se concentration with disease progression might be due to dietary changes (10,24).

In conclusion, the present study gives support to the hypothesis of the relationship between Se concentrations in serum, urine, and hair samples of newly diagnosed pediatric cancer patients. We found a significant Se deficiency related to leukemia, lymphoma, and solid tumor cancer subtypes. Our overall results suggest the importance of low Se status and the presence of an oxidant/antioxidant imbalance in childhood hematologic malignancies. The relationship between Se deficiency and childhood hematologic malignancies needs to be confirmed in further studies.

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