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SHORT COMMUNICATION

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ASSESSMENT OF TRACE ELEMENTS IN SERUM OF ACUTE LYMPHOBLASTIC AND MYELOID LEUKEMIA PATIENTS

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***Aim*: Trace elements play a key role in human metabolism. The aim of the present study was to measure essential trace elements in the serum of patients with acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). *Materials and Methods*: 32 patients with ALL and 16 patients with AML were studied. The control group consisted of 36 subjects. Serum levels of the trace elements selenium, copper and zinc were measured by spectrophotometry. *Results*: The mean of copper concentrations in the groups of patients with AML and ALL was significantly higher than in the control group ($p < 0.0001$), whereas serum levels of selenium and zinc were significantly lower in AML patients ($p < 0.0001$). Also in ALL patients the levels of selenium and zinc were significantly decreased compared with the control group ($p < 0.0001$; $p = 0.0003$). *Conclusion*: Our results indicate that the levels of zinc and selenium are significantly decreased and copper levels are significantly increased in the serum of patients with acute leukemia (AML, ALL).**

***Key Words*: acute lymphoblastic leukemia, acute myeloid leukemia, zinc, copper, selenium, spectrophotometry.**

Leukemia is one of the most common cancers worldwide and is classified into main two types (acute and chronic leukemia). Acute lymphoblastic leukemia (ALL) is the most common type of leukemia among children, and almost 80% of children with leukemia are allocated to this type. These abnormal cells in the differentiation of normal cells have stopped and may inhibit natural erythropoesis [1]. Acute non-lymphocytic leukemia, also known as acute myeloid leukemia (AML), is the most frequent type of leukemia in adults; the bone marrow produces abnormal myeloblasts. In AML, heterogenous disorder in blood stem cells, diagnosis is often difficult because early symptoms may be similar to the other common diseases [2, 3]. For its diagnosis are used the blood and bone marrow smears for identification of leukemic myeloblasts. ALL can be distinguished from AML by the methods of immunocytology [4]. A combination factors involved in the onset and progression of cancer, can be noted [5].

Trace elements normally appear in low levels in the human body and play an essential role in the enzyme systems in many metabolic processes [6]. Trace elements including zinc (Zn), copper (Cu), selenium (Se) and some others are part of enzymes that play regulatory role in a large number of biological reactions. These elements affect immune responses and the production of free radicals [7]. Levels of trace elements in the body are implicated in some diseases including cancer, diabetes, hypertension and heart disease [8]. Their changes reflect the importance of evaluating these elements in the diagnosis and prediction of disease [9]. These elements are present in the hair, nails, serum, plasma, urine and saliva and may be altered in cancer patients [10]. The impact of various factors including trace elements and heavy metals in cancer etiology has been studied [11].

Copper is an essential trace element in the living organism being the most common catalytic cofactor in many biological processes [12]. In mammals, copper is an important component of some metalloproteins, including ceruloplasmin and cytochrome oxidase [13], cytochrome C, superoxide dismutase. Increased copper levels in cancer have been reported in many tumor types including cervical, breast, ovarian, gastric, prostate cancer and leukemia [14]. Reduction of copper levels results in the dysfunction of superoxide dismutase and cell apoptosis [15].

Zinc is one of several trace elements that plays a major role in metabolic processes in the body and is present in the structure of more than 300 enzymes [14, 15]. Zinc is required for DNA synthesis, transcription of RNA, cell division, and cell proliferation. In cancer cell, zinc can modulate telomerase activity [14].

Selenium is an important component in two enzymes: glutathione peroxidase and thioredoxin reductase [16]. This essential trace element have anticancer properties [17]. Studies using animals have shown that selenium treatment reduces tumor recurrence, inhibits cell growth and angiogenesis, stimulates apoptosis, protects against oxidative damage and increases the immune function [17]. In carcinogenesis selenium plays a protective role by reduction of DNA damage [18].

In our study, there were enrolled 32 AML and 16 ALL patients. The age of the patients and control group varied from 20 to 71 years. Serum samples were collected from March 2011 to May 2012. Diagnosis of leukemia was confirmed in all cases. The control group consisted of 36 nominated individuals that matched by age and gender. The study was approved by Pasteur Ethical Research Committee. The consent forms were completed and signed by the patients. This study was designed and approved by Ethics Committee of Pasteure institute of Iran and performed in accordance with its guideline's.

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Abbreviations used: ALL – acute lymphoblastic leukemia; AML – acute myeloid leukemia.

Table. Serum trace element concentrations (μg/ml) in leukemia patients (ALL, AML) and control group

Elements	Control group (n = 36)	Patients		*p* value (compared to the control group)
		AML (n = 32)	ALL (n = 16)	
Copper	7.40 ± 1.53	15.90 ± 2.20	13.10 ± 2.90	0.0001
Zinc	7.10 ± 1.30	3.90 ± 0.95	5.23 ± 1.06	0.0161 (AML) 0.0003 (ALL)
Selenium	3.70 ± 1.73	1.90 ± 0.92	0.57 ± 0.20	0.0161

The blood samples were taken before using any treatment. To provide the red blood cell and serum samples, blood specimen was collected from each patient. The blood samples were centrifuged at 3000 rpm for 15 min and the red blood cell fraction and plasma were separated and transferred to fresh tubes and used for further investigations. Then sera were stored at –70 °C until analysis.

Samples of serum were diluted with deionized water (Millipore) at a ratio of 1:5. The amounts of copper and zinc measured using a flame atomic absorption spectrophotometer (Thermo Jarrel Ash, Germany) at the wave lengths of 324.7 nm and 213.9 nm, respectively. Selenium was measured using a graphite furnace spectrophotometer (GBC, Sense AA model) at the wave length of 196 nm. The results obtained were analyzed using SPSS software (16.0) and represented as means ± standard deviations (SD). Values $p < 0.05$ were considered statistically significant.

The results of the trace element analysis in healthy subjects and in cancer patients are summarized in the Table. Copper concentrations were significantly higher in the cancer patients (AML, ALL) than in healthy subjects ($p < 0.0001$). Serum levels of selenium were lower in cancer patients compared with the control group ($p < 0.0001$). Levels of zinc in blood serum of ALL and AML patients were significantly lower ($p = 0.0003$, $p < 0.0001$) than in healthy subjects. The concentrations of copper and selenium were significantly higher in AML patients compared with in ALL cases ($p < 0.0001$, $p = 0.0161$), whereas zinc amounts were lower in AML patients than ALL patients ($p < 0.0161$).

The relationship between trace elements and cancer as inhibitory or causative factors has been shown in many studies [8–19]. Copper serum concentration are increased in leukemia, lymphomas, sarcomas, bronchogenic carcinomas, melanomas and gynecological cancers, and Hodgkin's disease [20]. Also, it was reported that copper levels were increased in ALL patients compared with the control group, whereas zinc values were significantly lower in these patients [21]. In our study, we showed that the amount of copper was significantly higher in the patients with ALL and AML than healthy subjects, and that the levels of copper were significantly higher in AML than in ALL patients.

Many articles have introduced zinc/copper ratio as a diagnostic marker for various cancer types [22]. In children with ALL, plasma zinc concentrations are lower and copper concentrations are higher than in healthy children [23]. The present study, serum levels of zinc are shown to be significantly lower in blood serum of leukemia patients compared with the control group. Moreover, it was observed that zinc values were insignificantly higher in ALL patients than in AML patients.

Various studies represent the role of selenium in the diet as an antioxidant that decreases cancer mortality risk for such diseases as breast cancer, colon cancer, leukemia, lung cancer, ovarian cancer and prostate cancer [24]. A study of selenium levels in adult patients with different types of leukemia showed low selenium levels in these patients [25]. Our findings indicated that serum levels of selenium were significantly lower in the AML and ALL patients than in the healthy subjects, and were significantly higher in AML patients compared with ALL patients.

This study concluded that in patients with acute leukemia (ALL, AML), copper levels were increased whereas the selenium and zinc values were decreased compared to healthy subjects.

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