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Reference Ranges of Trace Elements (Selenium, Zinc, Copper) in Tokat Province

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Thesis

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Abstract

Objective: Trace elements copper, zinc and selenium, are found in extremely low amounts in living organisms but have extremely important functions for the organism. These elements take part in enzymatic reactions in the organism, structure of the bones, body growth and in many other vital functions. The aim of this study was to determine serum levels of selenium, zinc and copper in healthy individuals aged 18-65 years and people older than 65 years living in Tokat province.

Method: This is a descriptive cross-sectional study which was conducted as a master's thesis at Selçuk University Medical Biochemistry Laboratory. The sample size in our study was selected considering C28-A3 protocol of the National Committee for Clinical Laboratory Standards (NCCLS), randomly selected 159 healthy individuals aged 18-65 + years were included in the study. Reference interval for serum selenium levels were measured by atomic absorption spectrometer with Zeeman correction, serum zinc and copper reference intervals were measured by flame atomic absorption spectrometer. The analysis of the data was transferred to the computer environment through the Minitab14 statistical program and the related analyzes were performed for each variable.

Results: Of the 159 healthy subjects included in the study, 58 were female and 101 were male. Estimated mean reference values for serum selenium levels (geometric mean, GM) at 95% confidence interval; 73.35 μg / L (70.35-76.35 μg / L); 137.78 μg / L for copper levels (131.13-144.43 μg / L); for zinc levels; 16,47μmol / L (15,88-17,06 μmol / L).

Conclusion: This study esatablishes reference values for serum selenium, zinc and copper levels in healthy adults living in Tokat province. Our results showed a discrepancy with the results' of other countries as reported in the literature. In addition our results suggests that reference values for trace elements are affected by regional differences.

Keywords: Trace Elements; Selenium; Zinc; Copper

Introduction

Trace elements are vital minerals that are required in fair amount of daily consumption to maintain a healthy metabolism. trace elements, can be measured from body fluids and tissues [1]. Trace element sources found in nature varies regionally. Humans receive these elements through air, soil, environmental transport, nutrients and water. Changes in environmental or working conditions, as well as stress, can lead to changes in the absorption of trace elements. Technical food processing, soil fertilization or over-fertilization can cause significant concentration changes of trace elements in the foods [2]. Therefore, differences in the source of elements of each region create different compositions in living organisms [3]. Reference ranges and values are of great importance in helping clinicians to differentiate between sick and healthy individuals. As a result of the analysis performed by each laboratory, it is best to determine its own reference value for each analyte. Se, Zn and Cu are involved in many functions in the body. Trace elements such as zinc (Zn), selenium (Se), and copper (Cu) protect cells against oxidative stress [4].

Se is a potent antioxidant that protects the body from free radicals and plays a role in the structure of glutathione peroxidase enzyme [5]. Adequate consumption of these trace elements helps prevention of diabetes and cardiovascular diseases, delays ageing, strengthens the immune system and decreases the risk of various cancer types by inhibiting tumor growth [6,7].

Zinc; important in more than 300 enzymatic reactions such as DNA and RNA, carbohydrate metabolism and gene expression is involved in the structure of more than 2000 proteins. Zn is not found in free state in the nature, but in connected state. Zn; It is an essential element for lymphocyte transformation and plays a role in visual functions, thyroid hormone homeostasis, wound healing, maternal and infant development during pregnancy, DNA repair, protein synthesis and glucose control. It has an effect on growth hormone, prolactin and thymic hormones. Zn reduces oxidative stress and helps protect the body from cancer by enabling the immune system to develop. Metabolic Zn requirements increases in periods such as puberty, pregnancy and breastfeeding [8,9].

Copper is an essential trace element involved in many tasks as a biocatalyzer in human metabolism. It is a strong peroxidant element. Cu / Zn is a component of superoxide dismutase and acts as a free radical scavenger. It catalyzes the oxidation of oils and ascorbic acid. It is plays role in protein synthesis, tissue regeneration, structure of the bones, ATP synthesis and hemoglobin synthesis. It is a necessary element for the development of the central nervous system [10].

The richest food containing selenium is fish and seafood. Fresh and canned tuna, mackerel and sea bass usually had 1 mg / kg selenium values [11]. Dried fruits like hazelnut and pine nut, soy beans, lentils and green peas have high levels of copper. Bitter chocolate has the highest amount of Cu as an ingredient [11].

High amounts of Zinc can be found also in meat and dairy products, grain and egg, but the highest values are found in pine nut, hazelnut and almond [11].

The aim of this study; The determination of selenium, copper and zinc reference values of Tokat Province , this is of great importance as it is the first study conducted in our country in regional level.

Materıals and Method

Criteria for Inclusion in the Study

- The participants were asked whether they are feeling well today.
- Age range was 18-65 +.
- Partisipants were asked If there is a daily drug or vitamin intake, if it is the name and frequency of the dose was recorded and the if they allowed measurements to be taken.
- The use of drugs for the treatment of estrogen, oral contraceptives and hypothyroidism, previded that registration is permitted.

Exclusion from Study Criteria

- Diabetes treated with insulin or oral medication.
- Chronic liver or renal failure.
- The presence of blood results indicating an other serious disease.
- Hospitalization or illness in last 4 weeks.
- Blood donation with in last 3 months.
- HBV, HCV and HIV carriers.
- Pregnancy or having children under 1 year of age.
- Use of alcohol and tobacco products.
- The study was started in the last 12 weeks considering the participation of a research product or study.

The NCCLS C28-A3 protocol recommends a sample size of at least 120 (male and female 60 * 2) in the study area. In this study we conducted in Tokat province, NCCLS's C28-A3 protocol was taken into consideration and the sample size of our study consisted of 159 people, 101 males and 58 females between the ages of 18-85. Random venous blood samples were obtained from 159 healthy adults over the age of 18 (Table 1) living in and around Tokat between from June 2012 to June 2013. The samples were examined according to the allowance of the Selcuk University Research Ethics committee and the guidelines of NCCLS. Samples obtained were centrifuged at 5000 rpm for 10 minutes, stored in the freezer at temerature -80 ° C until the study day. On the day of analysis, the samples were kept in room conditions to adapt and were tested in Varian AA240 Zeeman corrected atomic absorption spectrometer for Se analysis and in flame atomic absorption spectrometer for Zn and Cu analysis. We also examined from samples routine hemogram,routine biochemistry and TSH analysis were also performed.

Gender	Male	Female	Total
N	101	58	159
%	63.52	36.48	100

Table 1: Distribution of individuals in terms of their gender.

Selenium Analysis

200 µl serum samples taken from the study tubes were placed in the Teflon tubes in order to deproteinize in the microwave oven. 800 uL 0.1% HNO_3 was added to tubes, then 120 ºC heat was applied at 220 bar pressure for 15 minutes.

They were allowed to cool to room temperature. 100 µl of resultant sample was added to 200 µl of 0.1% HNO_3 for dilution and the samples were placed in tube spots. Measurements were obtained from Varian AA240 Zeeman corrected atomic absorption spectrometer at 196 nm.

Zinc and Copper Analysis

500 µl of serum samples were taken and the solution was diluted by adding 2 ml of 1% HNO_3. Resultant samples were used for copper and zinc measurements with heated atomic absorption spectrometer operated with acetylene gas. Copper measurement was performed at 324.7 nm wavelength and for zinc measurement at 213.9 nm wavelength.

Statistical Analysis

Datas acquired from specimens then transferred to a digital format via Minitab14 statistics program, further analysis were operated on this platform.

To perform further analysis in parametric method, the probability distribution of the reference group data was assumed to fit a normal distribution. Before the statistical analysis was performed, the data was tested for conformity with the Anderson-Darling test. Normally distributed variables were compared with the following models.

Variables Showing Normal Distribution were Compared with the Following Models

$$Y_j = \mu + e_j$$ H_0:

Hypothesis (There are no difference)

By the way

Y_j: Y variable *j*. observation μ: overall average

e_j:Leftovers

$$Y_{ij} = \mu + F_i + e_{ij}$$ H_1

:Hypothesis (There are difference)

By the way

Y_{ij}: Y_{ij} variable i: The group j: Observation F_i: *F factor i: level of action* e_{ij}: Leftovers

Logarithmic transformation was applied to variables that do not show normal distribution. Nonparametric tests were performed in cases where the variables did not show normal distribution as a result of transformation. Reference range limits were calculated based on the 95% center of normal distribution (2.5% and 97.7% percentages). Parametric tests were used for the data showing normal distribution.

Results

The distribution of the participants according to age, gender, smoking and exercise startus were given in Table 2.

	Selenium (µg/L) (Average±SD)	Zinc (µmol/L) (Average±SD)	Copper (µg/L) (Average±SD)
Female	73,37±14,73	15.47±3,90	130.5±51,52
Male	73,44±23,12	17.06±3,85	126.0±35,63
Smoker	72,68±19,96	16,14±3,56	128.5±99,42
Non smoker	73,80±20,98	17,13±4,51	127.0±119,77
Exercise	80,05±20,13	16,15±4,05	127.0±68,95
Non-exercising	72,65±28,6	16,55±3,22	128.0±112,27
18-29	76,47±18,17	16,45±3,8	123,0±38
30-39	74,43±19,36	16,16±3,8	126,5±36
40-49	73,96±17,48	17,44±3,8	128,0±51
50-64	69,06±17,03	16,12±3,8	153,0±53
65+	62,23±16,51	16,14±3,8	161,0±36

Table 2. Table of distribution of Se, Zn and Cu by sex, smoking status, exercise status and age.

According to Table 2, Following Results were Obtained for Zn Levels

- There was a statistically significant difference was found male individuals and female individuals (p:0.01).
- Statistically individuals significant difference was not found in terms of age distribution between male and values of female individuals (p:0.053).
- Non-smokers were found to have higher amount of Zn, which was statistically significant.
- There is a significant difference between exercise and non-exercise.

According to Table 2, Following Results were Obtained for Cu Levels

- No difference was found between groups in terms of sex (p:0.204), but there was a significant difference between age groups (p:0.001). With the advancing age, higher levels of Cu was observed.

According to Table 2, Following Results were Obtained for Se Levels

- No difference was found in terms of sex (p:0.192).
- A significant difference was found between the age groups. (p:0.0274).
- There was a significant difference in smoking status. (p:0.025).
- There was a difference between the groups in terms of exercise habits. (p:0.035).

As a Result of Our Study

Zn Concentration: 16,47 µmol/L. Compared to mean Zn levels in reference textbooks 7-15 µmol/L, our mean results is coherent with the literature.

Cu Concentration: 137,78 µg/L. Compared to mean Zn levels in reference textbooks 75-155 µg/L, our mean results is coherent with the literature.

Se Concentration: 73,35 µg/L. Compared to mean Zn levels in reference textbooks 35-135 µg/L, our mean results is coherent with the literature.

Discussion

Trace elements are fundamental for composition of the organisms but toxic effects of their excessive levels may alter various biological functions. Different opinions have been published in the literature for determining the normal levels of these elements. A reason for these wide range of results is the difficulty of obtaining proper measurements and the interactions of the trace elements between each other. Another reason is the variability of the reference ranges available for these elements.

Determination of the concentration of trace elements in the blood in our study depends to a large extent on the use of reference ranges. Therefore, precise determination of reference ranges becomes important. Previously published studies are summarized in Table 3.

Study	Number of samples	Selenium(Se) (μg/L)	Zinc (Zn) (μmol/L)	Copper (Cu) (μg/L)
Farzın, et al. [12]	115	99,10±21,78	8,90±1,60	95,00±20,00
Kazi, et al. [13]	120	77,00±13,50	10,20±2,20	-
Rukgauer, et al. [2]	68	80,00±36,00	16,60±1,00	165,00±86,00
Bocca, et al. [14]	215	140,00	98,16	1036
Bunch, et al. [15]	50	173,74 - 276,40	-	-
Hussain, et al. [16]	450	-	24,07	-
Tratnik, et al. [17]	1084	105	101,04	951
Choi, et al. [18]	227	(120.0–171.8)	8,721	(86.3–120.0)
Estecha, et al. [19]	327	79,5	-	-
Michalska-Mosiej, et al. [20]	67	77,969 ± 12,73	-	-
Liu, et al. [21]	1400	39.9–111.6	11,32	107.0–362.4
Ayoglu, et al. [22]	57	100-114	10,7-23,7	100-110
Sepehri, et al. [23]	180	76,74	14,535	92,55
Skalnaya, et al. [24]	128	105–164	10,7-22,95	80-155
Lee, et al. [25]	167	58-234	10,09-16,83	75-145
Sahebari, et al. [26]	100	90.92 ± 22.77	13,464±2,4	1124.21 ± 315.78
Our Study	159	73,35±20,40	16,47±3,82	73,44±23,12

Tablo 3. Comparison of the limit of determination of Se, Zn and Cu with previously published studies.

With the comparison of our sudy with the other studies given in Table 3. The results below were found.

- Our results are closer to previously reported Se ranges.
- Zinc values are found to be in the optimal range as previously reported
- Our results for copper levels seems to be the lowest in the literature.

In our study, selenium and copper values were lower compared to the other studies. This is due to the fact that nutrient sources rich in selenium and copper are mostly found in seafood. Values obtained in the studies performed in sea bordering areas are higher compared to our study. This result is influenced by the differance of direct fish and sea food (tuna, shrimp, oyster) consumption. Although, compared to other studies our zinc results were in the spesified optimal range, they were found to be lower from some other regions. The reason for this is the low level of zinc in soil and plant analyzes conducted in our country. Zinc levels are known to be decreasing in societies like ours where bread is consumed frequently. Therefore, zinc values were low in laboratory analysis.

Soil quality, content and mineral richness affect the health status of individuals. With the consumption of nutrients grown in the soil, the minerals settle directly in the human body and take part in various metabolic events. A peculiar structure of the soil can lead to differences in human blood in terms of certain values (such as trace elements). The best way to eliminate this difference is to take supplementary nutrients and foodstuffs. Thus, the lack of this elements in humans can be eliminated. It is necessary to raise awareness among people about the consumption of food rich in selenium, zinc and copper elements, which play an important role in the human body. In order to increase the average values of trace elements (selenium, zinc and copper) taken into consideration, it would be beneficial to carry out different studies on enriching food quality.

Conclusion

In this study, serum selenium zinc and copper values were determined for Tokat province.

Serum selenium and copper levels were within normal reference ranges, while zinc levels were found in high limit ranges. Determining the levels of trace elements necessary for human health is important to decide whether food supplements are needed or not. Determination of the reference values of selenium, copper and zinc trace elements in Tokat province will make a great contribution to the evaluation of these elements. This study will be important in raising awareness about consumption of foods rich in trace elements in individuals with trace element deficiencies.

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