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Comparison of Trace Elements Levels in Atrial Fibrillation Patients and Healthy Group

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: The aim of this study is to measure the concentration of Zinc (Zn), copper (Cu) and selenium (Se) in the blood serum of Atrial Fibrillation (AF) patients as compared to healthy subjects in both genders.
Methods: This study, conducted on patients with AF (n = 50) and controls (n = 24) were evaluated by available method. Blood samples were taken from the patients and analysis of trace elements was performed by atomic absorption spectrophotometer. Statistical analyses were done using IBM-SPSS 22.0.
Results: Zn and Se concentrations were evaluated in AF patients and healthy group. Zn and Se concentration in AF patients is much lower than in healthy group ($p<0.008$, $p<0.000$). AF patients showed a significantly higher Cu concentration than the healthy group ($p<0.000$). The data of the present study revealed that the concentrations of all trace elements had a significant difference in the serum of AF patients with respect to the healthy group ($p<0.05$).
Conclusion: We found that concentrations of Zn & Se levels were significantly decrease in the in the serum samples of AF patients compared with the controls group.

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Keywords: Atrial Fibrillation; trace elements; zinc; copper; selenium.

ABBREVIATIONS

Zn : Zinc
Cu : Copper
Se : Selenium
AF : Atrial Fibrillation
LDL : Low-Density Lipoprotein
SOD : Superoxide Dismutase
HF : heart failure

1. BACKGROUND

Trace elements such as Zn, Cu, and Se are micronutrients which are obtained by some foods and are available as a dietary supplement. Zinc (Zn) is an enzymatic cofactor that helps to keep bio-membranes contrary to per oxidative injury [1,2]. Zn has an essential role in several biological events like nucleic acid, protein synthesis, lipid, and carbohydrate metabolism. In addition, zinc is one of the antioxidants and protective agents of the membranes against lipo-peroxidation and denaturation of proteins. It hinders the cytokines activities. Zn with deactivation of the superoxide radicals converts them to safe forms. Furthermore, Zn causes the reduction of the damage of the myocardium through reduced construction of hydroxyl radicals [1-3]. Additionally, lack of Zn creates some problems for cell membrane phospholipids to free radical destruction and oxidative variations [4]. Zn is necessary for stabilizing the plasma membrane structure and metabolic processes. The primary function of zinc is to decrease the production of free radicals such as hydroxyl radicals in the cardiac cells because they are very harmful. Hence, Zn deficiency probably raises the vulnerability of the cell membrane phospholipids to oxidative alterations and free radicals' injuries [4].

Copper (Cu), an essential mineral is a cofactor for several enzymes [5,6]. Its concentration in the liver is very high since the liver is involved in detoxification mechanisms. Copper contributes to such processes like absorption, consumption, and manufacturing hemoglobin. This mineral prevents fatty acids from oxidation by ceruloplasmin. Ceruloplasmin results in destruction of DNA and cell membrane. Furthermore, it contributes to enzymatic reactions, the bone and connective tissues construction [7,8]. Recent findings have shown that in healthy individuals with normal copper levels, diastolic blood pressure and low-density lipoprotein (LDL) cholesterol levels are lower than in those with higher copper levels [9]. Copper deficiency caused many health problems such as reduction in the ratio of Zn/Cu in liver and superoxide dismutase (SOD), cardiac Cytochrome C oxidase activities, and anemia. Accordingly, the levels of Zn and Cu are co-regulated, so variants in the level of Zn and the proportion of Zn/Cu are related to these micronutrients' properties [7,8].

Selenium (Se) is another important compound that has been shown to play a role in the body's biological activities and functions. Despite the small size of this compound in the body, but its important role in organs such as the heart and liver has made selenium an important element in the body [10-12]. In other words, a very small amount of selenium is generally required as nutrients supporting the immune systems and body health [13] . Studies showed that selenium-deficient in the soil of Finland country created health problems and diseases such as cancer and heart diseases for the people living there. Furthermore, vitamin E enhances the function of selenium. One study showed that the consumption of selenium together with vitamin E synergist's mental position reduced anxiety, depression, anorexia, and fatigue in the elderly [7,8]. Also, selenium is necessary for the proper functioning of the thyroid gland [13-15].

Atrial fibrillation, as one of the greatest risk factors in cardiovascular diseases may be controlled by nourishment. Common cardiac arrhythmias are recognized by the absence of P waves and the existence of adjustable frequencies. Also, the interval between beats is irregular. In atrial fibrillation, the pumping function is the less effective, so the cardiac output amount is less than normal [16] It is expected the relation between trace elements and AF disease, however there are controversially results have been reported in the previous studies that zinc levels serum in patients significantly lower than in the healthy people [17,18]. Whereas, a pervious study on the north of Iran reported no signify-cance difference between heart failure (HF) and normal people in Se level [16]. Plasma Se level in HF and normal people depend on the Se concentration in the Soil/water of geographical zone [19].

Owing to subject importance and influence of various area of geography on the trace elements concentration in term of soil and water [20,21] we investigated relation of a few trace elements

concentrations in blood sampling of AF patients and control groups in Fasa city from Fars province. In this study, we indicated the comparison of plasma levels of copper, selenium and zinc in the atrial fibrillation patients and healthy people of both genders.

2. PATIENTS AND METHODS

2.1 Study Design

This case control study was conducted within Vali-e-Asr Hospital in Fasa, Iran during 2019-2020. This study conducted on patients with Atrial Fibrillation (n = 50) and controls (n = 24) were evaluated by available method, all persons were fasting and none of them had signs of infection. The sampling method was convenience sampling. Furthermore, data were collected through a checklist and para clinical results.

2.2 Inclusion and Exclusion criteria

Inclusion criteria included persons with age 35-70 years, natural hemoglobin, lack of chronic hypertension.

Exclusion criteria, patients with a history of chronic hypertension, smoking or drug abuse, overt or gestational diabetes, hemoglubino-pathies, megaloblastic anemia, kidney disease, seizure, prior significant illness, personal or thyroid hormone disorders.

2.3 Selection

Both groups participated randomly in the study after we obtained the informed consents. The charactiristics of the control group were the same as the case group. The only difference was that after clinical trials and angiograpy, it was determined that these individuals did not have AF.

The experimental group consisted of 50 patients who presented for Atrial Fibrillation and were referred to the Hospital. All 50 patients diagnosis of AF was done by a special cardiologist base of patients, electrocardiogram (ECG). The control group included 24 healthy subjects. Selection of controls was done from a normal population (the patient's visitor / neighborhood) with matching for age, gender and livelihood status. The patients were selected regardless of the size of the atria. The etiology of the atrial fibrillation or echo index was not critical, so we could include them. In addition, the ejection fraction of patients was normal. The sera from the two groups were taken for trace element analysis.

2.4 Biologic Samples and Data Collection

Blood samples for the trace elements determination were preserved in tubes containing the standard values for heparin at 4°C in decontaminated containers. Then, the samples were centrifuged for 5 minutes at 3,000 RPM. The elements were analyzed by an atomic absorption spectrometer (model 240, Warian Company) that was equipped with a Zn standard Art No: Hc 62775, and the wavelength of the system for Zn was 213nm, Cu standard Art No: Hc 114735 and that for Cu were 324nm, and Se standard Art No: Hc946651. Also, the wavelength of the system for SE was 196 nm. All standard reagents were obtained from Merck, Germany. Both experimental and control groups were asked to fill out a checklist containing the demographic characteristics such as age, age gender and body mass index.

2.5 Statistical Analysis

Data were analyzed using descriptive statistics. The unpaired (two sample) student t-test was used to estimate the significant changes in the blood level of trace elements in AF patients and Controls subjects. SPSS V.25 (SPSS Inc., Chicago, Ill., USA) was used to apply for statistical analysis. Statistical significance was assessed at the 5% level.

3. RESULTS

The mean age was 39.36±3.61 and 36.12 ±5.06 years in the AF patients and controls groups. Respectively, there is no significant difference between two groups. Patient demographic data were shown in (P = 0.09). The gender was evaluated in both groups. In patient group 59% were male and 41% female and in control group, 54% male and 46% female, respectively. No statistically significant difference was found between two groups Gender (p=0.19). The mean weight in AF patients and Controls groups were 81.14 ± 7.63 kg and 72.20 ± 11.92 kg, respectively. There was a statistically significant difference between AF patients and Controls groups (P=0.03).

The mean of Zn concentration of the serum in AF patients was=792.60 ± 87.92 and in the normal group was=615.79± 171.55 PPM.

Table 1. Demographic data in AF patients and controls groups

Parameters		AF patients group (n=50)	Controls (n=24)	P-value
Age (year)		26.93 ±5.61	28.86 ±6.42	0.09
Gender	Male	59%	54%	p=0.19
	Female	41%	46%	
Weight(kg)		72.20 ± 11.92	70.03 ±17.25	P=0.03

Table 2. Comparison of serum Zn and Se, Cu concentrations according to cognitive status

Variables	AF patients group (Mean ± SD)	Controls group (Mean ± SD)	P value
Zn (PPM)	792.60 ± 87.92	915.79± 171.55	0.008
Se (PPM)	80.43 ± 21.52	99.27± 17.28	<0.001
Cu (PPM)	1382.32± 184.92	1150.58± 204.92	<0.001

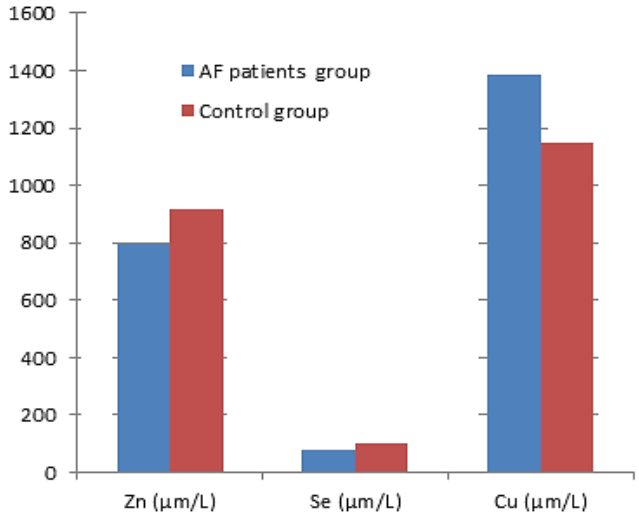

Fig. 1. Comparison of serum Zn and Se, Cu concentrations in AF patients and controls groups

AF patients showed a significant lower Zn concentration than the control subjects (P =0.008) (Fig. 1).

The mean value of Se concentration in the plasma was 80.43 ± 21.52 in the AF patients and 99.27± 17.28 PPM in the control subjects. The AF patients had a significantly lower serum Se concentration than the control subjects (P value <0.001) (Fig. 1).

The mean of serum Cu concentration was 1382.32 ± 184.92 in the AF patients and 1150.58 ± 204.92 PPM in the control subjects. The patients suffering from AF exhibited a significantly higher serum Cu concentration than that of the control group (p value <0.001) (Table 2).

Therefore, the ratio of Cu concentration in the AF group to Zn concentration in the AF group was 1382.320/792.60. Also, Cu/Zn ratios for AF patients were higher than in the control group. The proportion of copper to zinc in the serum was clinically more critical than the absolute level of each one of these trace elements.

4. DISCUSSION

The data of the current research demonstrated changes in the serum level of trace elements in AF patients compared to the control group. Copper levels in the patient group were significantly higher than the control group, but zinc and selenium levels in the patient group were lower than the control group. In this regard, various studies have shown the important role of trace elements on the body [22-24]. As in the results shown, zinc deficiency leads to increase copper concentration and also increased Cu/Zn ratio over 1.5 as well, which our results confirms the shortage of Zn. Zn deficiency is indicative of

increased level of copper in the plasma [24]. The results of this study in relation to zinc element were similar with those obtained by another researcher [22,25,26] .

In the normal condition, the metal-binding antioxidants prevent the production of the free radical induced during injury. Any changes in the status of trace elements would cause an alternation in the enzyme activities and, consequently, it would change the susceptibility of the injured tissues to oxidative stress [2,8].

In previous experiments, scientists have shown that Zn decreases the synthesis of hydroxyl radicals since these substances are very injurious for the cardiac muscle cells [3]. Furthermore, lack of Zn may raise the vulnerability of the phospholipids in the plasma lemma to the injury induced by free radical and oxidative variations [4]. Besides, both elements of Zn and Cu have a key role in the activity of enzymes act as an antioxidant, like Cu/Zn-SOD [7].

The ratio of Cu to Zn in this study is similar to the results obtained by Ghaemian and his colleagues [16]. Clinically, the Cu to Zn ratio is more important than the level of each one of such trace elements alone [8].

Heart failure (HF) is considered as one of the reasons for AF. The trace elements such as Cu and Zn have been shown to change in heart failure, such as ischemic cardiomyopathy [27]. Alcohol consumption is also correlated with heart failure and an increased serum copper but no Se has been reported after single dose of alcohol taken by healthy person [28].

In the present study, selenium was lower in patients. The reason for this can be attributed to the positive role of Se on the enzyme glutathione peroxidase. Glutathione affects cell health by reducing cellular stress.

This enzyme is involved in the removal of peroxide group from cardiac muscle cells; therefore, it probably leads to reduction of arrhythmias. Furthermore, the activity of this enzyme is strongly related to the existence of selenium. Se as a micronutrient increases the glutathione peroxidase activities in the mitochondrial and cytoplasm area of the cardiac cells [8,13-15].

5. LIMITATIONS

The first limitation was the population of healthy individuals who in many cases refused to undergo medical examinations and their replacement was removed.

The second limitation was the cross-sectional nature of the present study, which could help to find more accurate results in a clinical trial study.

6. CONCLUSION

Our data suggested that changing the levels of these elements can affect patients. In cardiac patients, Cu should be considered and in these patients.More research on these micronutrients could help understand their best levels in people with fibrillation.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

This study protocol was approved by the local Ethics Committee of Fasa University of Medical Sciences (Code: 88070).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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