

ORIGINAL ARTICLE

SERUM LEVELS OF ZN, CU, CR AND NI IN IRANIAN SUBJECTS WITH ATHEROSCLEROSIS

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Abstract

Background-Atherosclerosis is one of the most prevalent diseases in developed countries and is becoming an area of increasing concern in other parts of the world. Trace elements, which play a vital role in health and disease, have been the subject of several investigations concerning their role in the etiology of coronary heart disease in the recent years.

Objective- In order to compare the status of serum zinc, copper, chromium and nickel as well as levels of TG, TC, LDL and HDL-C in male and female patients with atherosclerosis with normal controls, this study was performed.

Methods-Serum levels of the above mentioned elements in sixty patients with angiography proven stenosis of more than 50% in the four major coronary arteries were obtained. The levels were compared with those of 30 normal controls.

Results-Total mean level of serum Zn for the patients was significantly lower than that of controls ($p=0.016$) and a significant difference was observed in male patients as compared to male controls ($p=0.006$). This difference was also observed in the female study group ($p<0.001$). Total mean Cu was significantly higher in patients ($p=0.004$), and this difference was reflected in both males and females ($p<0.01$ and $p<0.001$ respectively). There was no significant difference in the levels of Ni between patients and controls ($p>0.05$), even though the mean level was found to be higher in patients. This result was also found to differ according to sex. Analysis of Cr revealed lower levels in the patient group as compared to controls but again this difference was not significantly different ($p>0.05$). TG, TC and LDL-C were elevated in patients and HDL-C was lower in our patients, but not significantly ($p>0.05$).

Conclusion-Deficiency or suboptimal levels of micronutrients may play a role in the development of atherosclerosis.

Keywords • Zinc • copper • chromium • nickel • atherosclerosis • coronary heart disease

Introduction

In the past years, a number of researchers have shown that classical and extrinsic factors such as smoking, high cholesterol levels and high blood pressure, have a significant role in the pathogenesis of cardiovascular disease. Recently, many other factors have been repeatedly

demonstrated to influence this disease which is one of the most prevalent in the developed world.^{1,2} The search for its etiology has led to some theories that dietary intake of minerals and in particular trace elements may have a role in the progress of atherosclerosis.^{3,4,5} In this regard, deficiency, lack of homeostatic control, or excessive intake of some of these elements may lead to cardiovascular mortality. Some authors have reported low Zn and high Cu levels in patients with atherosclerosis.^{6,7} Little has been reported about the changes, if any,

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Table 1. Serum metals and lipid profile in the control group and patients with CHD.

	Zn ($\mu\text{g/dL}$)	Cu ($\mu\text{g/dL}$)	Cr ($\mu\text{g/L}$)	Ni ($\mu\text{g/L}$)	TG (mg/dL)	TC (mg/dL)	LDL-C (mg/dL)	HDL-C (mg/dL)
Controls (n=30)	137.18 ± 29.92	81.66 ± 20.72	2.37 ± 0.83	0.8 ± 1.03	112.28 ± 47.04	183.85 ± 39.86	106.81 ± 43.99	53.33 ± 12.07
CHD patients (n=60)	71.64 ± 19.68	109.04 ± 36.56	1.47 ± 0.68	1.67 ± 1.57	256.64 ± 144.94	243.65 ± 87.46	160.47 ± 80.55	41.6 ± 15.97
P value	0.016	0.004	$p > 0.05$	$p > 0.05$	0.001	0.001	0.014	$p > 0.05$

in the levels of Cr and Ni of these patients. This research was designed to study the association of zinc, copper, chromium, and nickel in subjects with coronary heart disease.

Materials and Methods

The study consisted of analysis of serum levels of Zn, Cu, Cr and Ni in patients with coronary heart disease (CHD). The experimental group consisted of 60 patients (21 women, 39 men) plus 30 controls (age range: 30-70 years). Patients were selected from cases at Shahid Rajaii Heart Hospital in Tehran and controls were chosen from people with no history of proven CHD. Angiography reports were studied and stenosis percentages of the four major vessels (RCA, LCX, LAD, and LM) were evaluated. The mean percentage of stenosis was then calculated and the patients were divided into groups based on stenosis percent ($> 50\%$ and $< 50\%$). All of our patients had lesions with $> 50\%$ stenosis. Blood samples were collected in metal-free tubes from patients and controls after an overnight fast.⁸ Serum was removed by centrifugation and stored in metal-free tubes at $-86\text{ }^{\circ}\text{C}$. High density lipoprotein cholesterol (HDL-C), triglyceride (TG) and total cholesterol (TC) were determined by biochemical manual kits (Man and Zist Chemie Co.). Cu, Zn, Cr and Ni were determined by atomic absorption spectrophotometry (UNICAM 929) (Flame atomic absorption spectrophotometry for Zn and Cu and graphite electrothermal furnace for Ni and Cr). Samples were diluted with dionized water, with a dilution factor of 4 for Zn and Cu and a dilution factor of 10 for Ni and Cr.

Results

The mean level of serum Zn was significantly

lower in patients than controls ($p=0.016$). A significant difference of Zn levels in males and females between patients and controls was also seen ($p=0.006$ and $p=0.000$ respectively). Total mean Cu levels were higher in the patients with $p=0.004$, and there was a significant difference between the levels detected in male and female patients and controls ($p=0.004$ and $p=0.001$ respectively). Mean level of Cr in the serum of patients was lower than that of controls but this difference was not significant ($p > 0.05$). The level of Ni in the patients was higher but not significantly different ($p > 0.05$) from controls. These results also differed according to gender. Other biochemical parameters such as TG, TC and LDL-C showed higher levels in patients with the exception of HDL-C which was lower, but not significantly ($p > 0.05$). Table 1 presents the mean levels of all parameters under study for the patient and control groups. These values have been calculated in different sexes and a higher level of Cu in female patients and a lower level of Zn in male patients was evident ($p < 0.01$). The levels of Cr and Ni in both sexes were not significantly different between patient and control group (Table 2).

Discussion

Possible etiological role in the imbalance of homeostasis of certain minerals in the development of coronary artery diseases has been the subject of much discussion. Various experimental models, clinically and statistically, have shown that the nutritional status of elements such as Zn and Cu may have some effect on the pathogenesis of coronary heart disease.⁹⁻¹¹ In particular, the status of Zn has been shown to have an important

correlation in the metabolism of cholesterol and HDL, two important molecules involved in the

Table 2. Serum trace element levels in the control group and patients with CHD (males and females).

	Zn ($\mu\text{g/dL}$)	Cu ($\mu\text{g/dL}$)	Cr ($\mu\text{g/L}$)	Ni ($\mu\text{g/L}$)
Female				
controls (n=15)	129.88 \pm 20.98	91.63 \pm 14.07	2.20 \pm 0.79	0.62 \pm 0.67
patients (n=21)	63.4 \pm 18.70	123.29 \pm 36.04	1.57 \pm 0.69	1.09 \pm 1.15
P value	P=.006	P=.004	p>0.05	p>0.05
Male				
controls (n=15)	144.48 \pm 36.07	71.69 \pm 21.88	2.55 \pm 0.86	0.99 \pm 1.29
patients (n=39)	76.08 \pm 18.96	101.36 \pm 34.92	1.38 \pm 0.67	1.2 \pm 1.73
P value	P=.000	P=.001	p>0.05	p>0.05

disease. The results of this investigation demonstrate that hypozincemia and hypercupremia were consistent with other studies. Animal experimental evidence suggests that the dietary Zn/Cu ratio may be a significant factor in coronary heart disease.⁷ The exact mechanism of alteration of these trace elements is not known. Some factors such as dietary deficiency, anorexia and possible use of drugs may be major components. Besides these factors, low serum Zn levels have been related to excess release of steroids due to the release of leucocyte endogenous mediators which redistributes the body Zn from serum and may cause a drop in serum Zn and also due to elevated levels of α -macroglobulin which is a transport protein containing large amounts of Zn.¹² A decrease in the levels of Zn and HDL-C strongly suggests the role of Zn in cholesterol and lipid metabolism as observed by Wen Yong.⁶

Increased levels of Cu may be due to a rise in the copper-binding capacity of ceruloplasmin. In our study, serum Cu was positively related to TC, TG and LDL-C, which suggests that high serum Cu levels may induce the development of CHD. The increase in Cu may also be due to injury and subsequent necrosis of myocardial cells.^{13,14}

Cr deficiency has been shown to increase aortic lesions. Data in relation to this are scarce and even though our findings indicate lower Cr levels in patients, further investigation is needed to clarify this point.¹⁵

The role of Ni in CHD has been implicated. Low concentration of exogenous nickel chloride has been shown to induce coronary vasoconstriction in rat hearts.¹⁶ This acts as an endogenous vasoactive substance. Hypernickemia has been reported in patients with acute myocardial infarction and unstable angina pectoris. Even though our patients' Ni levels were not significantly higher, this is only the preliminary result and further investigation of lipid peroxidation in heart cells, specifically in workers exposed to high levels of Ni in the working environment and its relation to CHD, is needed.

Deficiency or suboptimal intake of micronutrients may play a role in the etiology of CHD. Although there have been some reports that trace elements do not play a role in atherosclerotic changes of arteries, this conflict may be due to differences in the analytical or methodological techniques. We feel that more investigation will clarify the extent of changes in these essential elements, which can become a reliable diagnostic aid in CHD, and the extent of change having prognostic implications.

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