

## ARTICLE

# Plasma Zinc and Copper Levels In Children of Families with History of Cardio-vascular Disease

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## Abstract

Zinc and copper are beneficial to health, growth and development, and also for the prevention of cardiovascular-disease (CVD) with regard to improved dietary habits as a preliminary step in CVD prevention. This study was conducted among 2-18-year old children with significant family risk for premature CVD in comparison to controls.

**Materials and Methods:** One hundred randomly selected children of parents who had premature myocardial infarctions were included in the study. The controls were 100 individuals randomly selected from the case group's neighbors and matched for age, sex and socioeconomic status. A four-day food record questionnaire was used to assess zinc and copper intakes,

**Results:** The daily average intake of zinc was significantly lower in the case than in the control group ( $6.89 \pm 2.97$  vs.  $8.30 \pm 2.45$  mg,  $P=0.047$ ). The mean serum zinc level was not significantly different between both groups ( $82.12 \pm 14.1$  vs.  $92.26 \pm 23.7$   $\mu\text{g/dL}$ ,  $P>0.05$ ). The daily intake and serum level of copper were not significantly different between the

case and the control groups. No case of copper deficiency was found. The mean systolic blood pressure was not significantly different between the zinc-deficient and zinc-sufficient subjects.

Although the mean diastolic blood pressure of the former was higher than the latter, there was no statistically significant difference. About 23.7% of all studied sample had mild to moderate degrees of failure to thrive, with significantly lower daily intake and serum zinc level than other subjects ( $5.41 \pm 1.06$  mg,  $82.09 \pm 12.74$   $\mu\text{g/dL}$  vs.  $6.89 \pm 2.14$  mg,  $99.25 \pm 27.15$   $\mu\text{g/dL}$ , respectively,  $P<0.05$ ).

**Conclusion:** We propose that children, especially those with significant family risk of premature CVD, place increased emphasis on the consumption of foods rich in zinc.

**Key words:** Zinc, copper, premature cardiovascular disease, blood pressure

## Introduction

During the last few years the importance of trace elements

in health and disease has significantly increased. Zinc and copper are known to be essential trace elements in the human body (1-4). Zinc deficiency in human beings was first reported in 1960 in Iran, Egypt, and Turkey (5-6), and has always been a nutritional problem in the Middle East. This may be due to the prevalence of diets typically low in zinc and high in fiber and phytates impairing zinc absorption (6-7). More than 100 enzymes require zinc as a co-factor for different metabolic pathways. It is especially important for growth and development, but there is also considerable evidence showing a possible involvement of zinc and copper in the pathogenesis of cardiovascular disease. Different hypotheses have been proposed for this effect. Briefly, it can be said that low zinc blood levels is believed to cause atherosclerosis in cases where minimal trauma inside the vessels have insufficient zinc for their repair.

Copper is known to be essential for enzymatic activity, which forms the cross-linkages of normal elastin in vessels. A deficient copper intake may lead to abnormal vessel wall formation and thus to pathological changes, which may lead to CVD (8-12). Also, it has been shown that the copper/zinc ratio has an inverse correlation with blood pressure (13)

In the 1950s Holman et al, focused their attention on juvenile atherosclerosis (14). Although early prevention of atherosclerosis is recommended for all children, it is vital for children from high risk families for premature CVD (such as myocardial infarction, stroke, sudden death, peripheral vascular disease occurring in women < 65 and in men < 55 years of age). This study was carried out in light of the increased incidence of major CVD risk factors in children and adolescents in the community in recent years (15), especially with regard to the history of zinc deficiency in the country.

The main objective of the study was to compare serum levels and daily intakes of zinc and copper in the children of parents with a family history of coronary vascular diseases.

## Materials and Methods

Using simple random sampling, 100 children and adolescents of parents with premature myocardial infarction (MI) who were hospitalized in the Coronary Care Units of advanced hospitals were selected (CI=95%) and invited (by written invitation) to the Pediatric Clinics. The control group included 100 children (ages 2-15 years; mean age:  $9.0 \pm 5.5$  years for males and  $8.5 \pm 5.0$  years for females) of neighbors of the case group subjects matched for age, sex, and socioeconomic status. Body weight (with minimum clothing), height (barefoot, standing against the wall), and blood pressure (under WHO standards using a mercury manometer with suitable cuff) were measured and recorded. Also, fasting venous blood samples were taken (8:30-10:00 AM) and transferred to acid-washed test tubes, the sera separated, kept at  $-18^{\circ}\text{C}$ , and sent to the laboratory. The serum zinc and copper levels were measured using Flame Atomic Absorption Spectro-photometry. To determine food and nutrient intakes, a four-day food intake questionnaire was designed. Using this questionnaire, and available Food Composition Tables, the daily zinc and copper intakes (mean of the 4 days) were calculated. The software contained pictures of different local foods and the usual amounts consumed, so that the interviewee (the mother in the household) could easily state how much of each food had been consumed. The project was approved by the Institute Ethics Review Committee. Informed consent was taken from all participants. SPSS® (Windows Version 6, Chicago, Illinois) was used to analyze the data. Student's t tests and Mantel-Hanzel tests were used for comparison.  $P < 0.05$  was considered a statistically significant difference.

## Results

With regard to the serum zinc level of the case and control groups combined, the mean value was not significantly different from the reference value ( $86.5 \pm 19.0$  vs.  $102.0 \pm 20.0$  ug/dL,  $P > 0.05$ ). The difference between the

Table 1. Distribution of subjects according to sex and Zinc status

Serum Zinc Level(ug/dL)	Boys case	Control	Total	P*value	Girls case	control	total	P value
<80	26	10	40	0.04	24	20	44	0.35
80-120	22	34	56	0.07	25	28	56	0.26
>120	2	4	6	0.06	1	4	5	0.32

Table 2. Comparison of mean serum zinc and copper levels for both groups

Elements ( $\mu\text{g/dL}$ )	Case(n-100) Mean +SD	Median	Control(n-100) Mean+SD	Median	P(t test)
<b>Zinc</b>	84.15+14.50	75	92.50+24.0	86	0.09
<b>Copper</b>	124 $\pm$ 30	120	124 $\pm$ 18	124	0.85

mean daily zinc intake was not different between girls and boys ( $7.40\pm 3.05$  vs.  $8.50\pm 5.15$  mg,  $P=0.74$ ). As shown in Table 1, the values for zinc were lower for cases compared to the control group, but the difference was not significant between case and control girls ( $P=0.35$ ). No case of copper deficiency was found. The mean serum copper level in both groups combined was highest in the 6-9 year old group ( $130.60\pm 26.80$   $\mu\text{g/dL}$ ) and lowest in the 14-18 year old group ( $110\pm 16.05$   $\mu\text{g/dL}$ ). With regards to zinc, the highest value

diastolic blood pressure of the former was higher than the latter, there was no statistically significant difference ( $72.22\pm 14.87$  vs.  $66.87\pm 8.3$  mm Hg,  $P>0.05$ ).

### Discussion

Hyperlipidemia, hypertension, obesity and diabetes are known risk factors for CVD. However, in some cases, other factors would increase the susceptibility to CVD in families with this history. It has been suggested that in

Table.3. Comparison of daily intake of zinc and copper for both groups

Elements ( $\text{mg/dL}$ )	Case(n-100) Mean+SD	Median	Control(n-100) Mean +SD	Median	P(t test)
<b>Zinc</b>	6.90+3.00	6.15	8.30+2.50	7.15	0.045
<b>Copper</b>	1.90+3.50	1.15	1.35+1.20	0.95	0.340

was in the 6-9 year old group ( $88.60\pm 24.05$   $\mu\text{g/dL}$ ) and the lowest was found in the 10-13 year old group ( $82.50\pm 22.85$   $\mu\text{g/dL}$ ). There was no fixed trend in serum zinc and copper values with increasing age. As shown in Table 2, there was no significant difference between the mean serum levels of zinc and copper in the case and control groups.

The daily intake of zinc (Table 3) was significantly lower in the case than in the control group ( $P=0.045$ ). The intake of the two groups combined was  $7.30\pm 1.50$  mg, the difference between the boys and girls being non-significant ( $8.5\pm 5.0$  vs.  $7.5\pm 3.0$  mg,  $P=0.96$ ).

With regard to daily copper intake, there was no significant difference between case and control groups (Table 3). Also, there was no significant difference between boys and girls ( $1.7\pm 2.9$  vs.  $1.3\pm 1.2$  mg,  $P>0.05$ ) The mean systolic blood pressure was not significantly different between case children and the control subjects ( $103.06\pm 17.98$  vs.  $103.59\pm 15.04$  mm Hg,  $P>0.05$ ). Although the mean

susceptible families, children need to be screened for risk factors that may predispose them to later CVD including their dietary habits. It is important even for a healthy person to have a balanced diet with a proper ratio of macro as well as micronutrients including trace elements. The trace elements zinc and copper play a vital role in human metabolism as these are reportedly the main cofactors of key enzymes of endothelial and vascular epithelial functions. Therefore, other factors involved in the initiation and progression of atherosclerosis should be prevented from childhood, especially in children with a strong family history of CVD (1-4,8-12)

Based on these implications, the status of trace elements in growing children was assessed in a community basis similar to that carried out in Finnish and Japanese children (14,15) In the present study, the serum level of zinc was  $86.8\pm 19.6$   $\mu\text{g/dL}$ , which was lower, although not significantly different from the reference value ( $100.0\pm 20.0$   $\mu\text{g/dL}$ ).

Also, while the serum zinc and copper levels in girls were lower than boys in the Finnish study, no sex difference was seen in our study. On the other hand, the serum copper level was higher in our study ( $122.2 \pm 23.6$  ug/dL) than both the reference value and that of the Finnish children ( $115.6 \pm 35.9$  ug/dL) (14). Another finding of the Finnish study was that the serum levels of zinc and copper increased with age (16). In our study, there was no fixed trend, but in all age groups, the copper level was higher than the reference value. A study in Japan showed an inverse relationship between the serum copper level, age of the children and a normal level of copper (15).

The differences in serum zinc and copper levels and their daily intakes between our cases and Western populations can be explained by variations in dietary habits and types of foods consumed. For example, our foods contain large amounts of fiber and phytates that interfere with zinc absorption. In addition to adequate copper intake from foods, many families still use copper containers. The findings of our study show that zinc intake of children with a family history of CVD was significantly lower than that of other children and adolescents matched for age, sex and socio-economic status.

Physicians, particularly pediatricians, should make recommendations to families to consume more zinc-rich foods, with special emphasis on families at risk of CVD. This is an important step in promoting growth as well as preventing the initiation and progression of atherosclerosis.

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