Physiol. Res. 43: 107 – 111, 1994

Serum Copper, Zinc and Copper/Zinc Ratio in Males: Influence of Aging

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Received August 2, 1993
Accepted December 7, 1994

Summary

Apparently healthy free-living (non-hospitalized) men aged 8–89 years (n=408) were studied to determine the effect of age on serum copper and zinc concentrations and the copper/zinc ratio. Mean values ± S.D. for age, serum copper and zinc levels and the copper/zinc ratio were as follow: 41.9±22.9 years, 1.15±0.17 μg/ml, 0.93±0.14 μg/ml and 1.25±0.19, respectively. In the elderly subjects above 75 years, a marked increase in serum copper concentrations and the copper/zinc ratio as well as a decrease in serum zinc concentrations were observed. Serum copper concentrations and the copper/zinc ratio correlated positively with age ($p<0.0001$).

Key words

Males – Serum copper – Serum zinc – Copper/zinc ratio – Aging

Introduction

Energy requirements decline with advancing age and this is associated with a reduced intake of micronutrients such as vitamins and essential trace elements (Gibson *et al.* 1985). Dietary intakes of zinc and copper decrease with age and thus both zinc and copper are potentially deficient nutrients in aging (Mertz 1986). The regulation of zinc metabolism changes with age (Wastney *et al.* 1992). It is supposed that copper metabolism may change in humans older than 70 years, however, the data are limited (Johnson *et al.* 1992).

Alterations in zinc and copper metabolism develop during clinical manifestations of cancer, cardiovascular diseases, rheumatoid arthritis and other degenerative diseases. Such alterations involve a decrease in serum zinc concentration with a concominant increase in serum copper concentration (Takikawa 1990, Virtamo and Huttunen 1988, Mussalo-Rauhamaa and Konttinen 1988). A diagnostic, unfortunately not too specific method, exists for estimating serum copper/zinc ratio in certain diseases, particularly in malignant syndromes (Fabris *et al.* 1985, Inutsuka and Araki 1978) and in cardiovascular disorders (Tan *et al.* 1992). These pathophysiological states belong to free radical diseases. The aging process may also be due to free radical reactions (Harman 1988).

The purpose of this study was therefore to investigate if there were any changes in serum zinc and copper concentrations and the copper/zinc ratio during aging. We considered that our results might be of interest because of the high premature mortality rate from cardiovascular diseases and cancer in Czechoslovakia (Food and Health Indicators in Europe, WHO Regional Office for Europe 1990).

Methods

Four hundred and eight apparently healthy males aged 8–89 years participated in this study. According to comprehensive biochemical blood analyses (glucose, total cholesterol, triglycerides, creatinin, transaminase, bilirubin) subjects were considered healthy and they did not suffer from any acute disease. Fasting blood samples were withdrawn by venipuncture into acid washed tubes. Serum was separated after centrifugation at 3000 rpm for 10 min into trace metal-free tubes and stored at −20 °C before analysis. Serum zinc and copper concentrations in the serum were analysed by flame atomic absorption spectrophotometry (PU 9400X, Unicam Analytical

Systems) after simple dilution with bidistilled water (Salmela and Vuori 1984). Accuracy of zinc and copper determination was verified by analysing the standard serum reference material (Seronorm Trace Elements, Nycomed AS, Oslo, Norway). The mean values obtained for serum zinc and copper concentrations for 8 determinations were 1.70±0.03 μg/ml and 1.28±0.02 μg/ml, while the recommended zinc and copper concentrations are 1.70 μg/ml and 1.30 μg/ml, respectively.

The results were calculated using analysis of variance and regression analysis (Statgraphics). The level of significance was set at $p<0.05$.

Table 1
Serum copper, zinc and copper/zinc ratio as based on a study of 408 males aged 8–89 years.

Age groups (years)	n	Cu (μg/ml)	Zn (μg/ml)]	Cu/Zn
8–20	56	0.98 ± 0.14^{a} (0.73; 1.22)	0.83 ± 0.12^{a} (0.64; 1.05)	1.19 ± 0.11^{a} (0.97; 1.36)
20–34	128	1.12 ± 0.15^{b} (0.87; 1.43)	0.94 ± 0.14^{cd}(0.71; 1.20)	1.20 ± 0.16^{a} (0.92; 1.48)
35–49	70	1.11 ± 0.13^{b} (0.91; 1.45)	0.92 ± 0.13^{bc}(0.72; 1.20)	1.22 ± 0.18^{a} (0.90; 1.62)
50–74	110	1.24 ± 0.16^{c} (0.95; 1.51)	0.98 ± 0.13^{d} (0.72; 1.25)	1.28 ± 0.16^{b} (1.00; 1.69)
75–89	44	1.31 ± 0.13^{d} (1.05; 1.51)	0.87 ± 0.13^{ab}(0.67; 1.15)	1.53 ± 0.21^{c} (1.19; 1.93)
Total	408	1.15±0.17 (0.83; 1.49)	0.93±0.14 (0.67; 1.20)	1.25±0.19 (0.94; 1.71)

The results are expressed as means ± S.D. In parentheses are 2.5 and 97.5 percentiles. ^{a,b,c,d} *- different superscripts indicate significantly different means ($p<0.05$) in the same column*

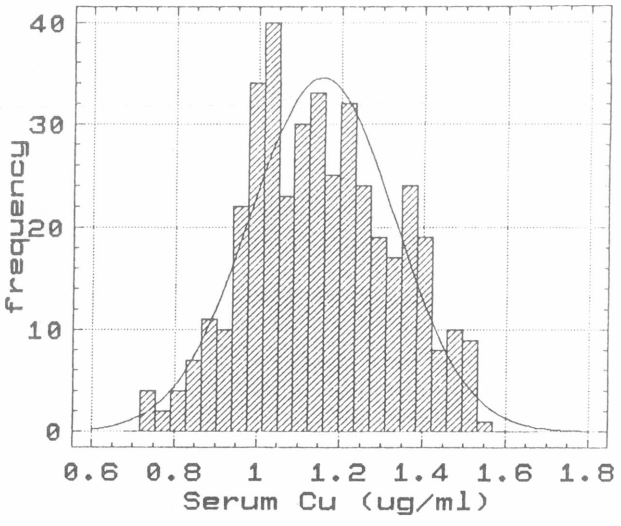

Fig. 1
Frequency distribution of serum copper concentration in 408 healthy males.

Results

The age of the subjects studied ranged from 8 to 89 years, with a mean of 41.9±22.9 years (x±S.D.).

Table 1 lists the serum copper and zinc concentrations and the copper/zinc ratio in males divided into five age groups (at 15-year interval). The serum copper concentration increased with age in all the investigated groups with the exception of the 35 to 49-year group where the serum copper level is the same as in the group 20–34 years old. Serum zinc levels increased up to the age of 74 years and markedly decreased after 75 years. The serum copper/zinc ratio increased gradually in all age groups. The serum copper and zinc values were close to the normal distribution (Figs 1 and 2).

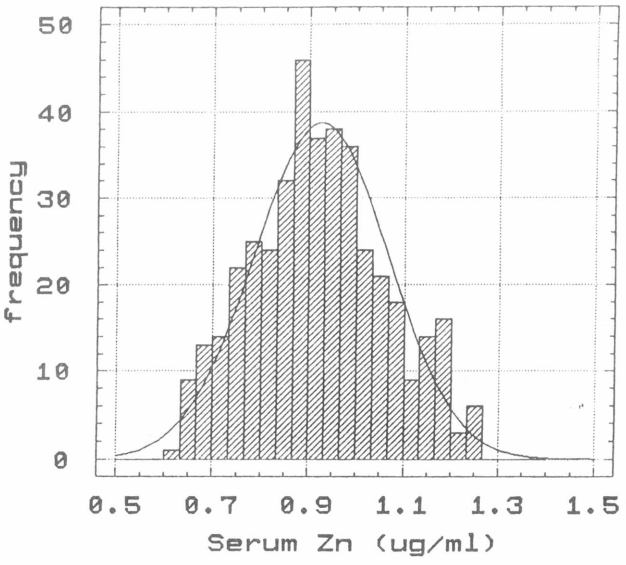

Fig. 2
Frequency distribution of serum zinc concentration in 408 healthy males.

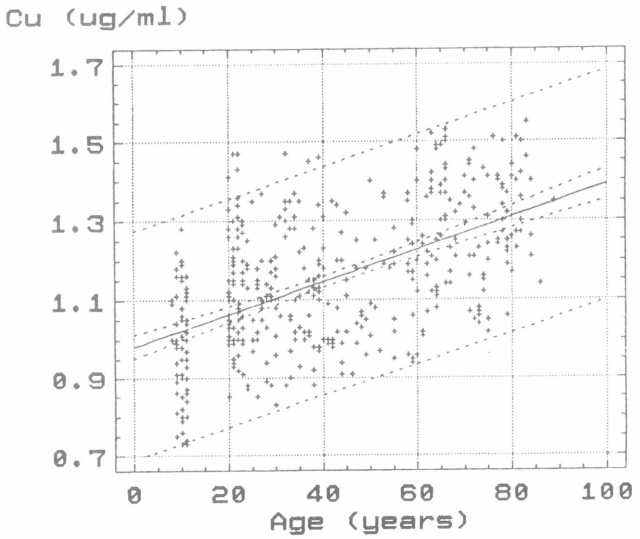

Fig. 3
Correlation between serum copper concentration and age in healthy males.

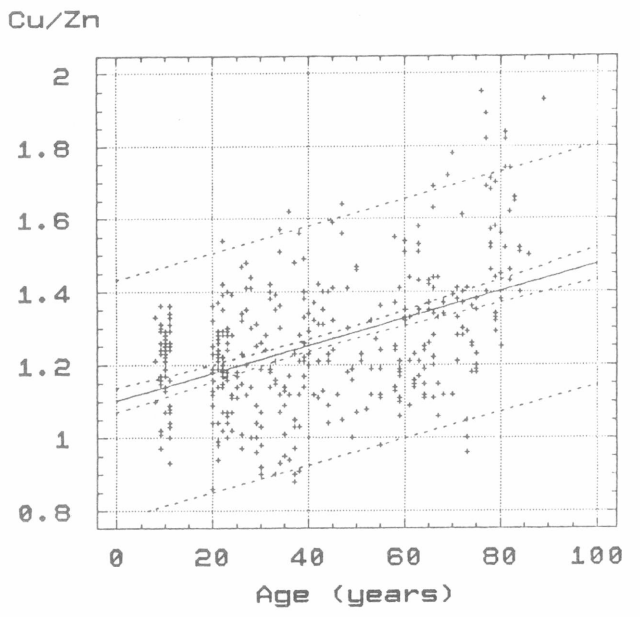

Fig. 4
Correlation between serum copper/zinc ratio and age in healthy males.

There was a highly significant positive linear correlation of serum copper concentrations and the copper/zinc ratio with age ($r=0.536$, $p<0.0001$ and $r=0.456$, $p<0.0001$, respectively) (Figs 3 and 4).

A slight upward trend existed between serum zinc concentrations and age ($r=0.201$, $p<0.0001$), see multiplicative model in Fig. 5.

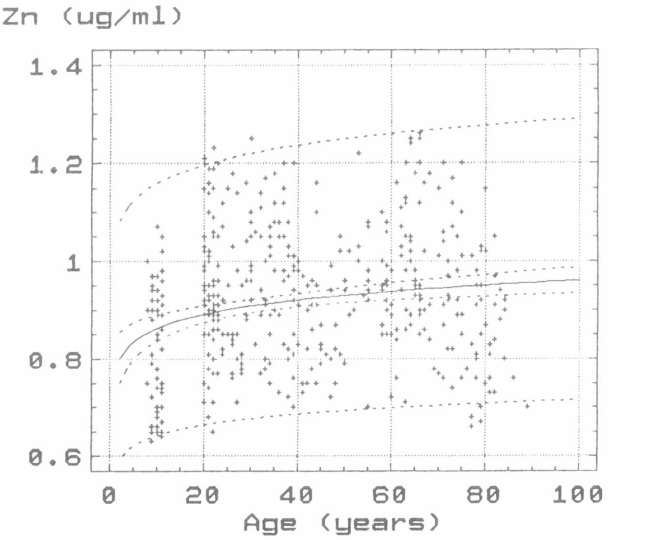

Fig. 5
Correlation between serum zinc concentration and age in healthy males.

Discussion

The ranges of serum zinc and copper concentrations reported in the present study are in agreement with earlier published values (McMaster *et al.* 1992, Grandjean *et al.* 1992, Dluhopolček *et al.* 1990).

Serum zinc levels rose slightly but significantly with age. However, serum zinc concentrations of elderly subjects were significantly lower than those of middle-aged adults. The data dealing with the influence of age on serum zinc levels are inconsistent. Grandjean *et al.* (1992), Payette and Gray-Donald (1991) and McClain and Stuart (1990) found that serum zinc decreased with age in men, while others observed either no significant differences between any of the age groups (Takikawa 1990) or even slightly upwards trends (McMaster *et al.* 1992). The decline in zinc serum concentration observed in our study is in accordance with the study of Bro *et al.* (1986). It is related to the higher zinc requirements due to rapid growth in this period. In the present study there was a significant age-related increase in serum copper concentration and this has been confirmed by others (Kant *et al.* 1989, McMaster *et al.* 1992, Grandjean *et al.* 1992). The age-associated rise in serum copper levels is explained by the free radical theory of aging (Harman 1988). The decrease of serum levels of readily oxidized substances such as ascorbic acid and mercaptans with advancing age may, at least in part, be responsible for the increase of serum copper in aging process. The growing number of free radical diseases includes the two major cases of death, cancer and cardiovascular diseases. The progressive increase

in serum copper levels with age may be accompanied by increased rate of atherogenesis (Harman 1988). Elevated levels of copper have consistently been found in humans with cardiovascular diseases (Virtamo and Huttunen 1988). Males with a history of myocardial infarction have a significantly higher serum copper and lower zinc levels than those with a negative history (Tan *et al.* 1992). The association has been reported between high levels of serum copper and the occurrence of cancer (Coates *et al.* 1989). In the present study, the copper/zinc ratio significantly increased with aging but did not reach such high values that were found in free radical diseases particularly in cancer (Fabris *et al.* 1985) and myocardial infarction (Tan *et al.* 1992).

Zinc and copper are antioxidant trace elements, but, copper also acts as a prooxidant agent (Halliwell and Gutteridge 1985). Both copper and zinc are cofactors for the enzymatic activity of superoxide dismutase (Saggu *et al.* 1989), which protects cells against damage from free radicals. It could be hypothesized that a decline in this enzyme function might be associated with increased risk from age-related diseases. Zinc plays a biochemical role analogous to that of vitamin E by stabilizing membrane structures and thus reducing peroxidative damage to the cell (Bettger and O'Dell 1981).

There has been much speculation that zinc deficiency is more common in the elderly population. Zinc intake in the elderly parallels that of the caloric consumption and decreases with age (McGandy *et al.* 1986). A lower than recommended intake of copper has been described in the elderly (Bogden *et al.* 1990). Elderly people may benefit from zinc supplementation. Attention, however, has to be paid to the doses of zinc supplements. Regular high-doses of oral zinc cause copper deficiency and an inadequate dietary copper intake has been suggested to be a factor in the etiology of cardiovascular diseases (Medeiros 1985).

In the aging process as in free radical diseases there is a dominant increase in the serum copper concentration. A marked increase of serum copper and a decrease of serum zinc concentrations were observed in men above 75 years of age. Based on our results, we suggest that zinc deficiency may exist in elderly people in Slovakia and that zinc supplementation would be suitable. It is of great importance to assess the zinc intake in our population according to the hypothesis that zinc deficiency is an important public health problem (Sandstead 1991). It is quite possible that elderly persons could be suffering from some age-induced condition which might influence the increase of copper and the decrease of zinc levels in the serum.

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