原 著

血清金属元素の年齢及び性による差異

大栗美保[1)] 今木雅英[1)] 川端邦弘[1)]
吉田幸恵[1)] 中村武夫[2)] 棚田成紀[2)]

1）大阪府立看護大学医療技術短期大学部
2）近畿大学薬学部公衆衛生学

Difference of serum metals in relation to age and sex in human subjects

Miho Ohguri[1)] Masahide Imaki[1)] Kunihiro Kawabata[1)]
Yukie Yoshida[1)] Takeo Nakamura[2)] Seiki Tanada[2)]

1) Osaka Prefectural College of Health Science
2) Faculty of Pharmaceutical Sciences, Kinki University

要約

我々は、大規模事業所従業員を対象に血清亜鉛、マグネシウム、カルシウム濃度を測定し、性及び年齢要因に関する検討を行った。血清亜鉛、マグネシウム、カルシウムの何れも男女間で統計的に有意な差（$p<0.001$）が認められた。また、年齢による影響はマグネシウムで最も強く認められた。血清マグネシウムの正常範囲の下限とされている1.9mg／dl未満の割合は男性3.9％女性3.4％で、血清カルシウムの正常範囲の下限とされている7.0mg／dl以下の割合は男性1.0％女性4.1％であった。亜鉛については欠乏状態とされている60μg／dl以下の割合が、男性2.4％女性7.5％であった。

以上のように対象集団において、血清亜鉛、マグネシウム、カルシウム濃度が性及び年齢による影響を受けていることを認めた。また、各ミネラルの中では亜鉛において潜在性欠乏の可能性が示唆された。

（臨床環境5：72～78,1996）

Abstract

The relationship between chronic diseases and the metabolism of metals such as zinc, magnesium and calcium, has been examined recently mainly in epidemiological studies and clinical reports. We determined the serum contents of zinc, magnesium and calcium in 1,910 healthy subjects (1,736 men and 174 women) who were 19-69 year-old employees of a large factory, and evaluated the serum levels in reference with the subjects' sex and age.

The mean serum zinc level in the men was 90.3±16.4 μg/dl and in the women was 79.3±13.7 μg/dl. The mean serum magnesium level in the men was 2.22±0.21mg/dl and in the women was 2.17±0.17mg/dl. For calcium, the mean was 8.86±1.07mg/dl in the men and was 8.40±1.00mg/dl in the women. The serum contents of zinc and calcium were significantly higher ($p<0.0001$) in the men than in the women. The serum contents of magnesium in the men was significantly higher ($p<0.001$) than in the women. We examined the effect of age on the serum contents of these metals, and the results indicated that age affected all three metals in serum. Concerning the possibility of latent deficiencies, we observed a high possibility of latent zinc deficiency in the subjects.

(Jpn J Clin Ecol 5：72～78,1996)

《Key words》 serum zinc, serum magnesium, serum calcium, age, sex

別刷請求宛先：大栗美保
〒583 羽曳野市はびきの3－7－30 大阪府立看護大学医療技術短期大学部
Reprint Requests to Miho Ohguri, Osaka Prefectural College of Health Science, Habikino 3-7-30, Habikino, Osaka 583 Japan

Introduction

The relationship between chronic diseases and the metabolism of various metals has recently been examined, mainly in epidemiological studies and clinical reports[1,2], and metals such as zinc, magnesium and calcium have been attracting attention.

As zinc finger transcriptional activator, a regulation factor for DNA expression, zinc has an important role in the regulation of gene expression[3]. Superoxide dismutase (SOD) [EC 1.15.1.1], an enzyme of which zinc is an essential element, eliminates active oxygen and prevents senility and carcinogenesis. It has been reported in a study using rats and rhesus macaques that the SOD activity in blood is correlated with the serum zinc level[4]. It has also been said that there are about 100 enzymes that require zinc for their biological action [3,5]. Zinc is thus involved in many physiological functions, e.g. taste and immune functions[5].

Like zinc, magnesium performs basic functions in extremely wide areas of the body. More than 300 types of enzymes require magnesium for their activation[6]. There have also been a number of reports on the involvement of magnesium in the development of chronic diseases. Kobayashi was the first to note this relationship in his 1957 epidemiological study[7]. He reported that hypertension was less likely to occur in areas where the local water contained large quantities of magnesium and calcium. Later, it was noted that both magnesium and calcium were related to mortality from heart diseases[1].

Calcium is an important metal in bone formation. It also has a role in signal transmission, utilizing the difference in its contents inside and outside the cells. It is under the control of a more rigid mechanism than are other metals in blood. Hypertension develops[8] or cell death occurs[9] if this mechanism is disturbed. Epidemiological reports describe a calcium deficiency resulting in increases in the incidence of hypertension[2] and colon cancer[10].

The present authors consider it necessary, in the field of preventive medicine, to investigate the factors that affect the in vivo zinc, magnesium and calcium dynamics. However, most of the earlier studies on these metals were limited to animal experiments and clinical observations of patients, and a few reported on normal individuals. We therefore decided to determine the serum content of these three metals in normal subjects, establish age-and sex-specific variations to comprehend the current status of their metabolism, and try to delineate problems such as those related to latent deficiencies of these metals. We determined the serum contents of zinc, magnesium and calcium in healthy employees of a large factory, and evaluated their relationship with age and sex.

Subjects and methods

Subjects were 1,910 healthy Japanese (1,736 men, 174 women) aged 19-69 years old. All subjects were factory workers employed in the same company in Osaka prefecture. They did not exposure to heavy metals at work. Venous blood samples were drawn from each subject. The serum was separated and stored at -80℃ until analysis. The content of zinc, magnesium and calcium in serum were determined by a Zn-Test Wako, a Magnesium B-Test Wako and a Calcium C-Test Wako (Wako Pure Chemical Co.,Ltd.,) according to 5-Br-PAPS method[11], Xylidyl Blue method[12,13] and OCPC method[14], respectively. Statistical analysis was performed using SPSS (Statistical Package for the Social Science) 6.1J procedure. Significance was defined as $p<0.05$.

Results

The mean of serum zinc was $90.3\pm16.4\ \mu$ g/dl in the men and $79.3\pm13.7\ \mu$ g/dl in the women. In both men and women, the histograms of serum zinc indicated a normal distribution (Fig.1). The mean of serum zinc was significantly higher ($p<0.0001$) in the men.

The differences of serum zinc content in age-sex groups are shown in Table 1. In the 19-29 year-old group, 30s and 40s, the serum zinc levels were significantly ($p<0.0001$) higher in the men than in the women. In the 50s and 60s, the serum zinc levels

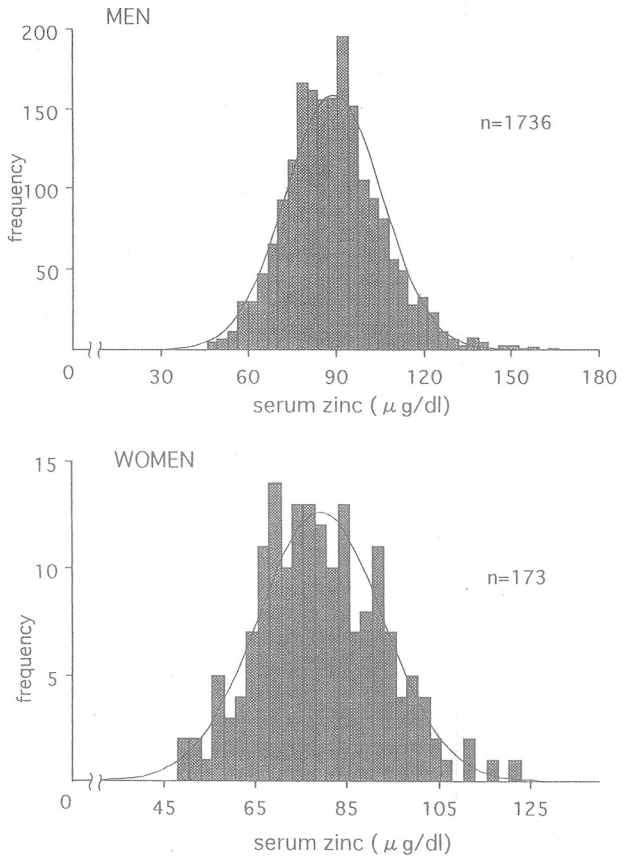

Fig. 1 Distribution of serum zinc

tended to be higher in the men, but the differences were not significant.

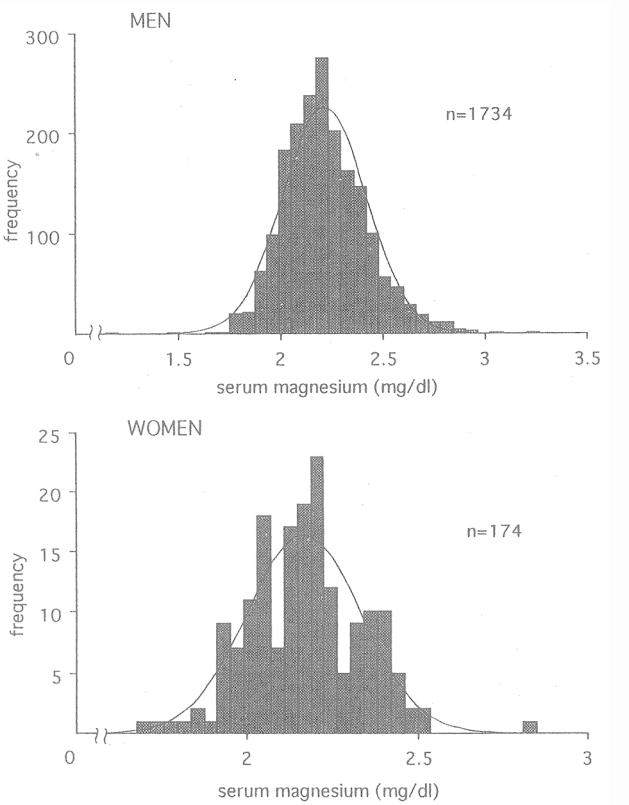

Fig. 2 Distribution of serum magnesium

Table 1 Effect of age and sex on zinc, magnesium and calcium in serum

	Zn(μg/dl)		Mg(mg/dl)		Ca(mg/dl)	
Age	Men	Women	Men	Women	Men	Women
Total	90.3±16.4** (1736)	79.3±13.7 (173)	2.22±0.21* (1734)	2.17±0.17 (174)	8.86±1.07** (1730)	8.40±1.00 (173)
19-29	90.1±16.3** (489)	79.3±12.8 (84)	2.18±0.19 (486)	2.16±0.17 (84)	8.93±1.01** (487)	8.33±0.86 (83)
30-39	89.5±15.6** (328)	75.6±12.8 (32)	2.22±0.21 (327)	2.16±0.19 (32)	8.89±1.11* (325)	8.22±0.90 (32)
40-49	91.2±17.2** (541)	77.9±14.2 (31)	2.26±0.21† (541)	2.17±0.14 (31)	8.83±0.98‡ (539)	8.27±0.95 (31)
50-59	90.8±15.8 (327)	87.2±13.4 (17)	2.23±0.20 (327)	2.22±0.17 (18)	8.76±1.17 (327)	9.03±1.49 (18)
60-69	86.4±15.9 (51)	83.3±18.7 (9)	2.23±0.21 (53)	2.20±0.12 (9)	9.10±1.45 (52)	8.78±1.13 (9)

Values are means ± S.D.
The number of subjects are given in the parenthesis.
**Significant sex difference, P<0.0001.
*Significant sex difference, P<0.001.
‡Significant sex difference, P<0.01.
†Significant sex difference, P<0.05.

As to the effect of age, the serum zinc level in the women was slightly ($p<0.05$) higher in their 50s than in the younger groups, and then decreased in the 60s. The percentage of subjects with a deficient level of serum zinc (≦60 μg/dl) [15] was 2.4% in the men and 7.5% in the women.

The mean of serum magnesium was 2.22±0.21mg/dl in the men and 2.17±0.17mg/dl in the women. In both men and women, the histograms indicated a normal distribution (Fig.2). The mean of serum magnesium in the men was significantly higher ($p<0.001$) than in the women (Table 1). The serum magnesiun levels in the men tended to be higher than in the women in each age group, but the

differences were not significant except for 40s ($p<0.05$).

The percentage of subjects with a under normal level of serum magnesium (<1.9mg/dl) [16] was 3.9% in the men and 3.4% in the women.

The mean of serum calcium was 8.86±1.07mg/dl in

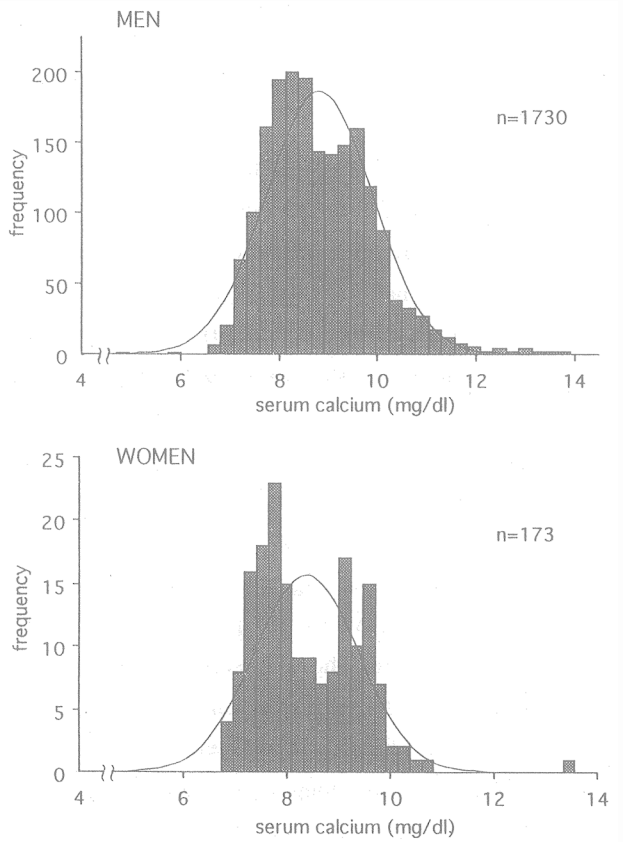

Fig. 3 Distribution of serum calcium

the men and 8.40±1.00mg/dl in the women ; significantly higher ($p<0.0001$) in the men (Fig.3). The differences between men and women in each age group are shown in Table 1. In 19-29 year-old group, 30s and 40s groups, the serum calcium levels were significantly higher ($p<0.0001$, $p<0.001$, $p<0.01$) in the men. In the 50s groups, the serum calcium level in the women was higher than in the men. The percentage of subjects with a deficient level of serum calcium (≦ 7.0mg/dl) [17] was 1.0% in the men and 4.1% in the women.

The correlation coefficients between age and serum

Table 2 Correlation coefficients relating age to the serum metals

	Men	Women
	r=	r=
Serum zinc	0.010	0.121
Serum magnesium	0.125**	0.081
Serum calcium	-0.041 †	0.173*

**p<0.001 *p<0.05 †p=0.085

zinc, magnesium and calcium are shown in Table 2. In the men, serum magnesium was significantly ($r=0.125$, $p<0.001$) correlated with age. Serum calcium was significantly correlated with age in women. Serum zinc was not significantly correlated with age in either men or women.

Discussion

Many papers have reported that various disease conditions are related to metals such as zinc, magnesium and calcium in the body. We believe that clarifying the dynamics of zinc, magnesium and calcium in the body and discovering those lifestyle and environmental factors that cause fluctuations in the amounts of these metals will eventually lead to the key of health promotion. Most of the extant studies on zinc, magnesium and calcium are on patients encountered in clinical medicine; there are only a few epidemiological studies on normal subjects. We therefore considered it important to conduct a survey on healthy subjects to: (1) clarify the effects of age and sex factors, and (2) discover individuals who may appear outwardly normal but suffer from a mild, latent deficiency of any of these metals. We determined the serum content of zinc, magnesium and calcium in healthy subjects on a large scale. The mean levels of the three serum metals in the present study were similar to others reported in the literature[15,16].

As for the effect of sex, men exhibited significantly

higher serum contents of zinc, magnesium and calcium than women. Some researchers have reported that there is no sex-related difference in the serum magnesium content[18,19], but Thijs et al recognized a difference between the sexes in the serum magnesium level in their epidemiological survey of 959 men and 1,018 women[20]. We also noted a male-female difference in the serum magnesium level. Our present study was based on a large-scale group of subjects who lived in a single area and engaged in the same type of occupation, and we believe that the results are fairly reliable.

We examined the effect of age on the serum contents of zinc, magnesium and calcium. The results indicated that these metals are also affected by aging. Arakawa et al[19] determined the serum content of these metals in 626 healthy subjects, ranging in age from newborn to 76 years, and they observed changes related to age. Our results of serum zinc are similar to those of Arakawa et al.[19] An interesting finding was that the serum zinc content was lower in women in their 30s, with the sex-related difference being the greatest of the age groups. During their 30s, both men and women begin to experience a decline in physical strength, but at this age they also gain independence and assume added responsibility at home or at their place of work. We suspect that they suffer from stress caused by changes in daily life associated with their social positions. Furthermore, physiological changes in women associated with childbirth and lactation are other factors that may affect the serum zinc level. According to the present data, women in their 50s exhibited a serum zinc content that was higher than the groups under 50. We suspect that there is some correlation between the serum zinc content and menopause. Because serum zinc level in women using contraceptive pill are lower compared with women not using birth control pills and this may be explained by the induction of hepatic metallothionein synthesis by the female sex steroids, particularly estrogens[20,21].

Our finding that the serum magnesium contents increased with age is similar to that of Arakawa et al[19] except the significant difference between men and women in this study.

Concerning serum calcium, our finding that in men it decreased with age was similar to that of Arakawa et al.[19] Our finding that in their 50s the serum calcium was higher than in the other age groups conflicts with the data from Arakawa et al,[19] but is in accord with the finding of Thijs et al.[20] We speculate that the reason of high calcium content in women in their 50s is the effect of menopause.

Our second objective, examining the possibility of latent deficiencies of zinc, magnesium and calcium was informative. Severe zinc deficiency is extremely rare. This occurrences have been reported in some patients who were under total parenteral nutrition[22]. However, there are reports on the possibility of a mild or intermediate zinc deficiency among older people, infants, and those in developing countries where the food supply is scarce[23,24]. Even in Japan, a survey based on gustatory function showed the possible existence of mild zinc deficiency among otherwise healthy young women[25]. According to our present results, the percentage of workers who were seemingly healthy but were judged to be deficient in serum zinc was 2.4% of the men and 7.5% of the women. Ishida et al[25] conducted a study on young women and reported that 20% exhibited serum zinc levels that were below what Solomons et al called a normal level (70～125 μ g/dl)[26]. When we examined our results according to the standards set by Solomons, 8.8% of the men and 26.0% of the women had zinc levels below normal. When the normal zinc level proposed by Wada et al was adopted (84～159 μ g/dl)[15], 36.0% of the men and 64.2% of the women failed to meet the normal level. Even if we consider the deviations in test results due to differences in the analytical methods, the incidence of zinc deficiency was higher than we originally expected. We expect that the status of latent zinc deficiency is more prevalent than we have expected.

Compared with the serum zinc level, the serum magnesium and calcium contents are far more rigidly

controlled by homeostasis in the body. It has been said, therefore, that it is difficult to determine their deficiency states accurately using serum. In the present study, however, 3.9% of the men and 3.4% of the women showed a serum magnesium level below normal, and 1.0% of the men and 4.1% of the women exhibited a serum calcium level below normal, suggesting that these subjects are suffering from magnesium and calcium deficiencies.

The results of the present study indicate that serum zinc, magnesium and calcium may be affected by aging, and the levels of these metals in the men were significantly higher than in the women. We also found latent zinc deficiencies in some subjects. We believe that future studies on this subject should be directed to the relationship of these serum metals with lifestyle factors.

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