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Magnesium, Zinc and Copper Status in Osteoporotic, Osteopenic and Normal Post-menopausal Women

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Serum concentrations of magnesium, zinc and copper were measured in post-menopausal women with osteoporosis (*n* = 40), osteopenia (*n* = 40) or normal bone mineral density (*n* = 40) as classified on the basis of the T-score of the femur neck and dual energy X-ray absorptiometry results. Mean concentrations of magnesium and zinc were significantly lower in osteoporotic women than in both osteopenic women and normal women. In addition, magnesium and zinc concentrations in osteopenic women were significantly lower than in normal women. There were no statistically significant differences observed between the osteopenic, osteoporotic and control groups with respect to copper levels. The clinical significance of these changes needs further elucidation, but trace element supplementation, especially with magnesium and zinc and perhaps copper, may have beneficial effects on bone density.

KEY WORDS: Magnesium; Zinc; Copper; Osteoporosis; Osteopenia; Menopause

Introduction

Osteopenia, defined as a bone mineral density that is lower than normal but not low enough to be classified as osteoporosis, generally increases in severity with age and is most prevalent in women who are post-menopausal. Among post-menopausal women, osteopenia generally occurs at an earlier age than osteoporosis; therefore, additional benefits or risks associated with a particular treatment need to be taken into consideration. Osteopenia is often called 'pre-osteoporosis' as it sometimes leads to osteoporosis. The gradual nature of bone loss, as patients progress from osteopenia to osteoporosis, is characteristic of the chronic nature of the condition.[1 – 6]

Osteoporosis is a common condition in the elderly. It affects women more than men because they have a smaller bone mass and, once women are post-menopausal, they produce less oestrogen, which reduces the body's ability to retain calcium in the bones. Osteoporosis leads to degeneration of the spine, producing a humpback, and fragile bones that are easily fractured. The prevalence of this condition is creating an elderly population that is vulnerable and weak.[3,4,7]

One factor contributing to bone density loss in the elderly may be subclinical magnesium (Mg), zinc (Zn) and/or copper (Cu) deficiencies due to a reduced dietary

intake and reduced absorption of these micronutrients. Mg, Zn and Cu are essential cofactors for enzymes involved in the synthesis of various bone matrix constituents. Paradoxically, calcium supplementation may accentuate the problem of reduced Mg, Zn and Cu levels by impairing the absorption of simultaneously ingested Zn and the retention of Mg and Cu.[8 – 10]

The role of Mg, Zn and Cu in bone metabolism has been investigated in animals on Mg- and Zn-deficient diets.[11] Few all in one studies, however, involving osteoporotic, osteopenic and normal post-menopausal women, have described the changes in these elements, hence the present study was designed to investigate these changes in these groups of women.

Patients and methods

PATIENT SELECTION

Post-menopausal women attending the Orthopaedics Department of the Erciyes University Medical Faculty for a regular check-up were selected randomly and assessed for inclusion in the study. Women were defined as post-menopausal if they were > 55 years of age and there had been no menstruation for ≥ 6 months prior to entry into the study. Women 50 – 55 years of age were classified as postmenopausal if their plasma follicle stimulating hormone (FSH) level was > 50 IU/l and their plasma estradiol concentration was < 100 pmol/l. Using the World Health Organization's classification criteria[12] based on bone mineral density, the post-menopausal women were classified as having osteoporosis, osteopenia or normal bone mineral density on the basis of the femur neck T-score and dual energy X-ray absorptiometry (DEXA) results.

In order to eliminate the effect of intestinal parasites on element status, stool samples from potential subjects were examined for intestinal parasites using wet mount preparations in 0.9% NaCl, diluted Lugol's iodine and a flotation technique in saturated saline solution; only parasite-negative subjects were selected for the study.[13] Patients who were smokers, who had known pathologies or who were taking steroids or medications such as iron for anaemia, were excluded from the study.

The study was approved by the ethics committee of the Medical Faculty, Erciyes University and all patients provided written informed consent for their participation.

MEASUREMENT OF SERUM MAGNESIUM, ZINC AND COPPER

Venous blood samples for serum preparation were obtained between 08.00 and 09.00 after 12 h of fasting from all the participating patients and collected in polystyrene tubes. The tubes were centrifuged at 500 ***g*** for 15 min, the serum removed and then immediately stored at –20 °C until analysis.

Concentrations of Mg, Zn and Cu in serum were determined using Zeeman atomic absorption spectrometry (Hitachi Z-8000 spectrometer, Hitachi, Tokyo, Japan). Standard solutions were freshly prepared from individual stock solutions containing 1 g/l of each of Mg, Zn and Cu. Serum samples were prepared by dilution with deionized distilled water (1:5, serum:water). The viscosity of the standard solutions was matched to the viscosity of the diluted serum by adding an appropriate amount of glycerol. The total levels of Mg, Zn and Cu in the samples were determined by regression analysis of the sample absorption data on the standard curve.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS® software package version 11.0 for Windows (SPSS Inc., Chicago, IL, USA). Results were expressed as means ± SD. To

compare two groups of continuous variables, an independent samples *t*-test was used. A *P*-value < 0.05 was considered to be statistically significant.

Results

A total of 120 post-menopausal women aged between 43 and 80 years were included in the study. Of these, 40 had osteoporosis, 40 had osteopenia and 40 had normal bone mineral density. The mean (± SD) ages of the osteoporotic, osteopenic and control groups were 58 ± 8, 57 ± 9 and 59 ± 6 years, respectively.

The serum Mg, Zn and Cu levels are given in Table 1. The mean concentrations of Mg and Zn were significantly lower ($P = 0.001$) in osteoporotic women than in either osteopenic or normal women. In addition, Mg and Zn concentrations in osteopenic women were significantly lower than in normal women ($P = 0.048$ and $P = 0.001$, respectively). No statistically significant differences were observed between the osteopenic, osteoporotic and normal groups with respect to Cu levels.

Discussion

Osteopenia is a progressive condition that places patients at risk for increased morbidity and mortality if untreated. Patients with bone loss of at least 1.0 SD from normal are considered osteopenic, whereas those with bone loss of at least 2.5 SD are considered to be osteoporotic.[1–5]

The minerals Mg, Zn and Cu are all essential for health. They help promote strong bones and are involved in the interaction of more than 300 enzyme reactions. They are also necessary for the transmission of nerve impulses, temperature regulation, detoxification, energy production, and the formation of healthy bones and teeth.[11,14,15]

The causes of osteopenia and osteoporosis are multifactorial, involving genetics, endocrine function, exercise and nutritional considerations.[16,17] Several trace elements, and particularly Mg, Zn and Cu, are essential in bone metabolism as cofactors for specific enzymes and it has been known for at least three decades that Mg and Zn are essential for organic bone matrix synthesis. Although the roles of Mg and Zn are reasonably well understood, the physiological role of Cu in bone metabolism and homeostasis is unclear. Only a limited number of longitudinal studies have reported the effects of Mg, Zn and Cu on post- and pre-menopausal osteoporosis.[1,5,10]

The present study demonstrated lower levels of Mg and Zn in serum samples from post-menopausal women with osteoporosis and osteopenia than in normal women. This may be related to uncoupling of bone formation as a result of loss of bone mass. Element deficiency may occur for several reasons; deficiencies are primarily due to

TABLE 1:
Serum magnesium, zinc and copper levels in post-menopausal women with osteopenia, osteoporosis or normal bone mineral density

	Normal ($n = 40$)	Osteopenia ($n = 40$)	Osteoporosis ($n = 40$)
Magnesium (mg/l)	27 ± 4	22 ± 2[b]	17 ± 2[a,c]
Zinc (mg/l)	0.82 ± 0.13[a]	0.63 ± 0.09[a]	0.47 ± 0.1[a,c]
Copper (mg/l)	1.60 ± 0.08	1.59 ± 0.09	1.54 ± 0.12

[a]$P = 0.001$ and [b]$P = 0.048$ vs normal bone mineral density group.
[c]$P = 0.001$ vs osteopenic group.

renal wasting and are exacerbated by dietary element deprivation, gastrointestinal losses with diarrhoea or vomiting, as well as concomitant use of drugs such as diuretics and aminoglycosides. Element deficiency may contribute to increased bone loss due to its effects on mineral homeostasis. In Mg and Zn depletion, there is often hypocalcaemia due to impaired parathyroid hormone secretion, as well as renal and skeletal resistance to parathyroid hormone action.

Low Mg and Zn levels and a potentially unchanged level of Cu could be a characteristic feature of the serum profile of post-menopausal women with osteoporosis, but the clinical significance of this needs further elucidation. On the basis of these results, trace element supplementation up to the recommended daily allowance, especially with Mg and Zn and perhaps with Cu, may have beneficial effects on bone density.

The present study indicates that the association between osteoporosis/osteopenia and Mg, Zn and Cu status deserves further inquiry. On the basis of these results, augmenting diets low in Zn and Mg with high Zn and Mg foods may be beneficial in post-menopausal women.

Conflicts of interest

No conflicts of interest were declared in relation to this article.

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