Original Article

Magnesium, Zinc, Copper, Manganese, and Selenium Levels in Postmenopausal Women with Osteoporosis. Can Magnesium Play a Key Role in Osteoporosis?

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Abstract

Introduction: There has been a resurgence of interest in studies concerning the role of elements in the development and maintenance of the skeleton. The aim of the study was to assess the plasma and red blood concentrations of some elements in postmenopausal women with osteoporosis. Materials and Methods: Seventy-seven postmenopausal women with osteoporosis aged 61 years (median interquartile range, 7.5; range, 46 to 74) and 61 age- and BMI-matched healthy postmenopausal women aged 60 years (median interquartile range, 8.0; range, 44 to 76) were included in the study. Element concentrations in plasma and red blood cells including magnesium (Mg), zinc, copper, manganese, and selenium were measured by atomic absorption spectrophotometry in both postmenopausal women with osteoporosis and healthy postmenopausal women. Results: Only statistically significant difference between the osteoporotic (51.51 [15.40] µg/mL) and healthy subjects (54.54 [15.42] µg/mL) was observed in red blood cell (RBC) magnesium concentration ($Z = -2.07$, $P = 0.039$). However, no significant difference was found between patient and control groups, both in plasma and in red blood concentrations, for zinc, copper, manganese, and selenium. Conclusion: Mg levels in red blood cells are significantly lower in postmenopausal women with osteoporosis. It is concluded that Mg transport mechanism(s) into the cell could be affected in patients with osteoporosis.

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Key words: Copper, Magnesium, Manganese, Osteoporosis, Selenium, Zinc

Introduction

Osteoporosis is a condition in which an increased risk of fracture takes place due to a reduction of bone mineral content. It occurs as a result of an imbalance between bone formation and bone resorption. It is defined as a disease characterised by low bone mass and microarchitectural deterioration of bone tissue leading to increased bone fragility and therefore to an increase in fracture risk.[1] Although scientific attention has focused on the subject, there is still a lack of clear understanding of the pathophysiology of the various forms of osteoporosis. Many risk factors have been identified for osteoporosis including; genetic factors, race, sex, age, menopausal state, smoking, alcohol intake, exercise, and nutrition.[2,3]

The risk of nutritional disturbances, in particular element and vitamin deficiencies, is high during menopause. The contribution of elements in normal development and maintenance of the skeleton is related to their catalytic functions in organic bone matrix synthesis.[4]

In recent years, there has been a resurgence of interest in studies concerning the role of elements in the development and maintenance of the skeleton.[5-7] Magnesium (Mg) appears to be important in bone cell activity. It is shown to be mitogenic for osteoblasts and its depletion causes cellular growth inhibition, in vitro.[7] Copper (Cu), a cofactor for lysyl oxidase, is required in the cross-linking of collagen and elastine. Cu deficiency causes inhibition of bone growth and osteoporosis as observed in Menkin's disease, an inhered inability to absorb Cu.[8] Prolonged manganese (Mn) deficiency has been reported to produce skeletal abnormalities, such as osteoporosis, and congenital disorders of skeleton, such as chondrodystrophy.[9] The other element Zinc (Zn) is an essential mineral that is a component of more than 200 enzymes and is known as to be necessary for

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normal collagen synthesis and mineralization of bone.[10] Selenium (Se) is another essential trace element of fundamental importance to human health.[11] Several studies have shown that bone tissue in man could be have been affected by Se deficiency.[12]

To understand the status of elements on postmenopausal women with osteoporosis, we have investigated the Mg, Zn, Cu, Mn, and Se levels in postmenopausal women with osteoporosis and without osteoporosis.

Material and Methods

Patients

Seventy-seven postmenopausal women with osteoporosis aged 61 years (median interquartile range, 7.5; range, 46 to 74); body mass index (BMI) 27.3 kg/m² (5.2; range 20 to 42.9) and 61 age- and BMI-matched healthy postmenopausal women aged 60 (median interquartile range, 8.0; range, 44 to 76); BMI 29.8 kg/m² (5.2; range, 24.3 to 40.6) were included in the study. Women were eligible for our study if they (i) had similar dietary behaviour and (ii) good general health as determined by medical history and routine clinical blood analysis (complete blood counts and differential count). Dietary behaviour was assessed by using the only national dietary assessment study[13] since no national food frequency questionnaire has been available.

Patients who had surgical menopause, secondary osteoporosis or other medical conditions that may affect the bone metabolism or elements status such as kidney diseases, diabetes mellitus, drug used (e.g. diuretics) were excluded from the study. Patients who were treated with bisphosphonates, calcitonin, anabolic steroids, hormone replacement therapy, calcium, and vitamin D previously at any point of time since the beginning of menopause were also excluded. Patients with vertebral fractures were excluded from the study as well in order to achieve homogeneity. Table 1 summarises the demographic and clinical characteristics of the patient and control groups.

Bone Mineral Density

The diagnosis of osteoporosis was based on spine bone mineral density (BMD) measurements. Patients with spine BMD 2.5 standard deviations below a reference range (T score less than -2.5) were accepted as having osteoporosis. The reference range was established using our own data obtained from a Turkish population of normal healthy women using dual energy X-ray absorptiometry. BMD (gr/cm²) was determined at level of the first to fourth lumbar vertebrae by dual energy X-ray absorptiometry (Hologic QDR-4500, USA). The body-mass index (BMI) was calculated by dividing subjects' weight (in kg) by the square of their height (in meters).

Table 1. Demographic and Clinical Characteristics of Patients (n = 77) and Controls (n = 61)

	Patients Median (IR)	Controls Median (IR)	z	*P*
Age (y)	61.0 (7.5)	60.0 (8.0)	-1.44	0.151
Age of menopause (y)	46.0 (6.5)	47.0 (8.0)	-0.02	0.980
BMI (kg/m²)	27.3 (5.2)	29.8 (5.2)	-0.06	0.548
BMD (g/cm²)	0.71 (0.08)	0.96 (0.09)	-10.,07	0.001

Serum Parameters

In order to determine element levels, venous blood samples were drawn from both groups into tubes with Na_2–EDTA. Samples were transferred to the laboratory on ice and centrifuged for 5 minutes at 5000 rpm at 4°C. Plasma and erythrocytes were then separated. The erythrocytes were washed with 0.9% NaCl 3 times and haemolysed with cold distilled water. Plasma and erythrocyte lysate were stored at –70°C until the analysis. Plasma and erythrocyte Se, Cu, Zn, Mg, and Mn levels were measured by atomic absorption spectrophotometry. The graphite furnace atomisation procedure was used for the Se and Mn determination, while the flame atomisation procedure was used for the Cu, Zn, and Mg determination.

Statistical Analysis

All statistical analyses were performed using a statistical software package, SPSS for Windows v 13.0 (SPSS Inc., USA). On the first hand, the distribution of the data was analysed using Kolmogorov-Smirnov Test. Non-parametric statistical methods were chosen as it was found that the data distribution does not comply with the normal distribution. Respectively, all data given in the text are expressed as median (interquartile range). Data from independent groups were compared using Mann-Whitney U test. Alpha was set to 0.05 in all calculations.

Results

Measured element concentrations, both in plasma and in red blood cells, are shown in the Tables 2 and 3. The only statistically significant difference between the osteoporotic and healthy subjects was observed in red blood cell (RBC) Mg levels ($Z = -2.07$, $P = 0.039$). No significant difference was observed between patient and control groups both in plasma and in red blood concentrations for Zn, Cu, Se, and Mn.

Discussion

The main finding of this study is that there are significant differences between patient and control groups in terms of red blood Mg concentrations. However, no significant difference was found between patient and control groups

Table 2. Element Concentrations in Plasma

Element	Patients Median (IR)	Controls Median (IR)	z	*P*
Magnesium (μg/mL)	19.48 (2.22)	19.64 (2.50)	-0.10	0.920
Zinc (μg/mL)	3.71 (1.60)	4.09 (3.03)	-1.54	0.120
Copper (μg/mL)	0.98 (0.60)	0.98 (0.78)	-0.31	0.751
Manganese (ng/mL)	5.34 (1.85)	5.09 (1.34)	-0.66	0.500
Selenium (ng/mL)	76.98 (32.44)	78.98 (24.14)	-0.20	0.831

Table 3. Element Concentrations in Red Blood Cells

Element	Patients Median (IR)	Controls Median (IR)	z	*p*
Magnesium (μg/mL)	51.51 (15.40)	54.54 (15.42)	-2.07	0.039*
Zinc (μg/mL)	7.62 (1.83)	7.35 (2.23)	-0.52	0.600
Copper (μg/mL)	0.45 (0.18)	0.41 (0.20)	-1.52	0.120
Manganese (ng/mL)	14.76 (4.29)	15.54 (3.94)	-0.60	0.540
Selenium (ng/mL)	400.45 (68.91)	432.45 (65.40)	-1.86	0.060

* Significantly different from control group (P <0.05)

both in plasma and in red blood concentrations for Zn, Cu, Se, and Mn.

Although animal and epidemiologic studies have demonstrated a positive correlation between Mg intake and bone density, few studies that assessed Mg status in patients with osteoporosis have been performed. It has been shown that perimenopausal and postmenopausal women with severe osteoporosis had significantly lower serum ionised Mg levels.[14] Reginster et al[15] reported decreased Mg levels in red blood cell but not the serum levels in patients with osteoporosis and vertebral fractures. In another study, Gur et al[16] reported Mg levels in serum were lower among patients with postmenopausal osteoporosis than the controls. The effect of Mg deficiency on bone metobolism has been shown in various studies. Mg appears to be important in bone cell activity. It is mitogenic for osteoblasts in culture[17] and its depletion causes cellular growth inhibition in vitro.[18] Decreased collagen formation, sulfation of glyco-saminoglycans,[19] and decreased tetracycline labelling[20] have also been observed. These above-cited studies suggest that the variation in Mg concentration may directly affect bone metabolism. Nevertheless, Mg status has been assessed in quite few osteoporotic patients. These results, however, are not consistent from one study to another and are often difficult to compare. The potential mechanism(s), which may cause Mg level decrease in red blood cells but not in the serum levels, is unclear at present for patients with osteoporosis. It may, at least theoretically, arise from the deterioration of the transportation mechanism(s) of Mg into the cell.

The current study concludes that there is no significant difference between the postmenopausal women with osteoporosis and postmenopausal women without osteoporosis in terms of Cu, Zn, Se, and Mn levels in plasma and in red blood cells.

Similarly, Reginster et al[21] reported that there is no significant difference in postmenopausal women with osteoporosis in terms of Cu and Zn levels in plasma as compare to the non-osteoporotic controls. However, Steidl et al[22] found that serum Zn levels were lower among patients with postmenopausal osteoporosis than in controls. Gur et al[16] reported similar results; Zn, Cu, levels in serum were lower among patients with postmenopausal osteoporosis than the controls. It has been known that Zn and Cu are essential cofactors for enzymes involved in synthesis of various bone matrix constituents, and play a particularly important role in the regulation of bone deposition and resorption. However, there are still some unanswered questions, particularly regarding mineral status in the elderly and in those with osteoporosis.[6]

Although the importance of Se and Mn for bone metabolism is unknown, Se and Mn are essential trace elements with fundamental importance to human health. Only a few studies that assessed Se and Mn status in patients with osteoporosis have been performed. Bureau et al[23] reported that there is no significant difference between postmenopausal women under hormone replacement therapy and those not having such treatment in terms of Se levels in serum. Reginster et al[21] reported that Mn level in serum is less in postmenopausal women with osteoporosis compared to the non-osteoporotic controls.

In addition, Mg, Cu, Zn, Mn, and Se levels in patients with osteoporosis are not well defined in the literature. Some researchers have reported reduced levels while others have reported the reverse. Plasma or serum concentrations are commonly used as indicators of status, but are notoriously unreliable since they can be affected by several factors unrelated to the body levels, such as medication, including hormone-replacement therapy, diuretics and laxatives. This unreliability is reflected by the inconsistencies in the literature regarding plasma levels of these minerals in the elderly.[6]

As a conclusion, our study data indicate that Mg levels in red blood cells are significantly lower in postmenopausal women with osteoporosis in contrast to healthy postmenopausal women, whereas no significant difference was found regarding Cu, Zn, Mn, and Se levels, both in red blood cells and in plasma. Mg transport mechanism(s) into the cell could be affected in patients with osteoporosis. Although it is known from the studies that a lack of elements in the diet may affect the bone structure, further studies are needed to reach a clear assumption about element status.

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