

# Serum Mg and Zn levels in postmenopausal women

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**Abstract.** Approximately 30% of a woman's life is spent in the postmenopausal period. This is when steroid hormone deficiency is often accompanied by mineral homeostasis perturbations and deficiencies that could be related to the intensity of any clinical symptoms. The aim of this study was to assess how serum Mg and Zn levels in postmenopausal women correlate with climacteric symptoms, body mass index (BMI), and the time interval since the final menstruation. The study involved 171 healthy, postmenopausal women, who had had their final menstruation at least one year prior to the study and who did not use menopausal hormone therapy. Both hypomagnesaemia and hypozincaemia were detected in the postmenopausal women involved in this study. The analysis revealed statistically significant differences between serum Mg levels, depending on the time interval since the final menstruation ( $p < 0.05$ ). No statistically significant differences were found in serum Mg and Zn levels between women as regards the severity of the climacteric symptoms or BMI ( $p > 0.05$ ). In conclusion, serum Mg and Zn concentrations in postmenopausal women, not using MHT, were low. The average serum Mg levels decreased considerably with the time since the final menstruation. No correlation between BMI and worsening of climacteric symptoms and serum Mg and Zn concentrations in postmenopausal women, not using MHT was found.

**Key words:** Mg, Zn, serum, menopause, climacteric symptoms

## Introduction

Menopause is associated with the cessation of a woman's reproductive functions and the cyclic synthesis of steroid hormones. The average age for menopause in Poland is about 50 years, so about 30% of a woman's life is spent in the

postmenopausal period. This is the time when steroid hormone deficiency is often accompanied by essential mineral deficiencies causing or intensifying serious clinical symptoms [1, 2]. In highly industrialized countries, about 80% of postmenopausal patients show climacteric symptoms, which comprise mainly hot flushes, night

sweats, insomnia, and less commonly melancholia, osteoporosis and atrophic changes within the genitourinary system. Some patients suffer from climacteric symptoms for only one to two years, but in about 40% of women they may last for as long as five to eight years [3]. The occurrence and intensification of climacteric symptoms differ dramatically from one individual to another. In about 30% of postmenopausal women they are very intense and require menopausal hormone therapy (MHT). However, it sometimes happens that attempts to ameliorate these symptoms by means of MHT remain unsuccessful and supplementary treatment is necessary. This can take the form of alternative menopausal therapy (e.g. phytoestrogens), non-hormone therapy or non-pharmacological treatments [4, 5]. Mg and Zn deficiency in postmenopausal women may cause or intensify palpitations, trembling hands and feet, paraesthesia, immune system disorders, dry and rough skin, hair loss, apathy, melancholia, concentration problems, as well as impairments in the areas of vision, hearing, taste and smell [6-8]. Hence our interest in possible correlations between changes typical of the menopausal period and levels of Mg and Zn.

Thus, the aim of this study was to assess how serum Mg and Zn levels in postmenopausal women correlate with climacteric symptoms, body mass index (BMI), and the time interval since the final menstruation.

## Subjects and methods

The study involved 171 randomly chosen, postmenopausal women from West Pomeranian Province (Poland). We used the systematic sampling technique (every third woman was chosen from those who met inclusion criteria). The women were patients of two specialist outpatient clinics invited to take part in the preventive gynaecological screening programme.

The average age ( $\pm$  SD) was  $56 \pm 6$  years; the youngest woman was 42 and the oldest 75 years old. The women were not using menopausal hormone therapy (MHT), and had had their final menstrual period at least one year prior to the study. All women were healthy non-smokers, who undertook moderate physical activity and with a low to zero alcohol intake. They did not use elimination diets (this was one of the exclusion criteria), and did not take any vitamin or mineral

supplements. All of the patients had normal arterial blood pressure. Those with diabetes, thyroid disorders and oncological diseases were excluded. Gynaecological examination and an ultrasound of the reproductive organs were performed in all women. Additionally, climacteric symptoms were measured using the Blatt-Kupperman Index, BMIs were calculated and blood was collected to determine Mg and Zn levels.

Patients included in this study were allocated to group A, B, or C depending on the time interval since menopause: 1-5 years in group A, 5-10 years in group B, and more than 10 years in group C.

On the basis of BMI measurements, the patients were divided into three groups: women with normal BMI (BMI: 18.5-24.0), overweight women (BMI: 25-29), and those who were obese (BMI >30). No underweight women (BMI <18.5) were found in the group examined. Body mass and height measurements were taken in accordance with commonly accepted rules i.e. in the morning, on an empty stomach, after urinating, with light clothes on, and without shoes.

The patients were informed about the aim of the study and gave their written consent to take part. The study was conducted with the consent of the Bioethical Commission of the Pomeranian Medical University in Szczecin (permission number KB-0080/187/09 14 December 2009).

## Assessment of Mg and Zn levels in blood serum

Serum Mg concentrations between 1.87 and 2.4 mg/dL, and Zn levels between 75 and 130  $\mu$ g/dL were accepted as laboratory reference norms [9]. In order to measure Mg and Zn concentrations, 5 mL of cubital vein blood were collected into Vacutainer tubes without anticoagulant. The blood was drawn in the treatment room and delivered to the laboratory in accordance with binding rules and procedures. The blood was spun down at 4,000 rpm for 10 min and the serum harvested. Serum Mg and Zn concentrations were determined by flame atomic absorption spectrometry (PU 9100X, Philips, Cambridge, UK). Diluted serum samples were introduced directly into the flame. The samples were 1:80-diluted with lanthanum solution in hydrochloric acid. The analytical wavelengths were 285.2 nm for Mg and 213.9 nm for Zn. Concentration values were read from the calibration curve. Internal quality

control within the laboratory was performed on two levels *i.e.* using two types of serum, namely serum with normal Mg and Zn concentrations and serum with Mg and Zn concentrations below normal. A simple 2-2SD Westgard rule was used for result acceptance. This rule states that if one control measure exceeds the mean  $\pm$  2SD, it is necessary to repeat the control measurement. If its result is within the expected values, then we assume that the previous deviation was a random incident, and the run should be accepted as "in control". However, if the control measure exceeds the mean  $\pm$  2SD again, a systematic error is likely, and the results cannot be accepted as reliable (the run should be rejected). In such circumstances, troubleshooting was performed and testing was repeated. The control results were plotted on Levey-Jennings charts.

The laboratory tests were performed in the Department of Biochemistry and Chemistry at the Pomeranian Medical University in Szczecin (Poland) in accordance with the PN-EN ISO 15189 guidelines.

### Assessment of climacteric symptoms

The patients used the Blatt-Kupperman Index to assess the incidence and severity of 11 menopausal symptoms such as hot flushes, sweats, insomnia, nervousness, melancholia, vertigo, weakness, arthralgia, headache, palpitations and paraesthesia [10]. The symptoms were weighted as follows: hot flushes ( $\times$  4), paresthesias ( $\times$  2), insomnia ( $\times$  2), nervousness ( $\times$  2), and all other symptoms ( $\times$  1). Each symptom on the Blatt-Kupperman index was rated from 0 to 3 for no, slight, moderate, and severe complaints. To calculate the Blatt-Kupperman index, the values assigned to particular symptoms were multiplied by the values reflecting their severity. The highest potential score was 51.

The accepted norms were as follows: a score of 0-16: no climacteric symptoms, 17-25: slight climacteric symptoms, 26-30: moderate climacteric symptoms and higher than 30: severe climacteric symptoms.

### Statistical analysis

Statistical analyses were performed using Statistica for Windows. Quantitative variables were

characterized by min. and max. values, arithmetic mean, median and standard deviation. The Kruskal-Wallis test for multiple independent samples was used in the analyses. The correlation was assessed with Pearson's linear correlation coefficient. The accepted significance level was  $p \leq 0.05$ .

## Results

### Mg and Zn concentrations in blood serum

Serum Mg levels in the whole population of women involved in this study ranged from 0.87 to 2.36 mg/dL, with an average of 1.53 mg/dL  $\pm$  0.28 mg/dL, while Zn concentrations ranged from 43 to 118  $\mu$ g/dL, with an average of 72  $\mu$ g/dL  $\pm$  14  $\mu$ g/dL. Only 12.3% of women had Mg levels within the normal range, 5.8% had hypermagnesaemia and 81.9% - hypomagnesaemia. Zn concentrations above 70 mg/dL were found in 42.7%, and below 70 mg/dL in 57.3% of women. Pearson's linear correlation coefficient was used to analyse the correlation between serum Mg and Zn levels in the women participating in this study (-0.0388), however, a significant correlation between these variables was not found ( $p > 0.05$ ).

### The relationship between BMI, the time interval since the final menstruation and the escalation of climacteric symptoms, and serum Mg and Zn levels in postmenopausal women

The analysis of Mg and Zn levels in blood serum depending on BMI, the time since the final menstruation and the escalation of climacteric symptoms is shown in *table 1*.

Considering the BMI variable, the highest Mg and Zn levels were noted in overweight women (median Mg 1.48 mg/dL and median Zn 65  $\mu$ g/dL). The lowest levels were noted in obese women (Mg 1.44 mg/dL and Zn 63  $\mu$ g/dL). The differences were not statistically significant ( $p > 0.05$ ).

The analysis revealed statistically significant differences between serum Mg concentrations depending on the time interval since the final menstruation ( $p < 0.05$ ). The lowest, average serum Mg concentration (1.42 mg/dL) was recorded in group C (over 10 years since the final menstruation), and the highest (1.52 mg/dL) in

**Table 1.** Mg and Zn levels relationship with BMI, the time from the last menstruation and the Blatt-Kupperman Index score

| Variable                            | n                             | Me | Min-Max | Q <sub>1</sub> -Q <sub>3</sub> | H<br>(2, N= 171) | p         |       |
|-------------------------------------|-------------------------------|----|---------|--------------------------------|------------------|-----------|-------|
| BMI                                 |                               |    |         |                                |                  |           |       |
| Mg (mg/dL)                          | Within the norm               | 68 | 1.46    | 1.02-2.28                      | 1.33-1.61        | 1.060498  | >0.05 |
|                                     | Overweight                    | 67 | 1.50    | 0.87-2.36                      | 1.37-1.69        |           |       |
|                                     | Obesity                       | 36 | 1.44    | 0.87-2.16                      | 1.29-1.63        |           |       |
| Zn (µg/dL)                          | Within the norm               | 68 | 64      | 46-118                         | 57-77            | 0.6781803 | >0.05 |
|                                     | Overweight                    | 67 | 67      | 43-114                         | 58-77            |           |       |
|                                     | Obesity                       | 36 | 63      | 45-113                         | 55-73            |           |       |
| The time from the last menstruation |                               |    |         |                                |                  |           |       |
| Mg (mg/dL)                          | A: 1 to 5 years               | 89 | 1.49    | 0.87-2.25                      | 1.38-1.66        | 7.516921  | <0.05 |
|                                     | B: 5-10 years                 | 53 | 1.52    | 0.87-2.36                      | 1.31-1.74        |           |       |
|                                     | C - more than 10 years        | 29 | 1.42    | 0.95-1.78                      | 1.25-1.52        |           |       |
| Zn (µg/dL)                          | A: 1 to 5 years               | 89 | 65      | 43-118                         | 56-75            | 0.4535712 | >0.05 |
|                                     | B: 5-10 years                 | 53 | 64      | 44-114                         | 59-72            |           |       |
|                                     | C: more than 10 years         | 29 | 68      | 50-100                         | 57-79            |           |       |
| The Blatt-Kupperman Index           |                               |    |         |                                | H<br>(3, N= 171) | p         |       |
| Mg (mg/dL)                          | No climacteric symptoms       | 99 | 1.50    | 0.87-2.36                      | 1.34-1.69        | 3.453156  | >0.05 |
|                                     | Slight climacteric symptoms   | 30 | 1.40    | 1.06-2.10                      | 1.29-1.64        |           |       |
|                                     | Moderate climacteric symptoms | 19 | 1.45    | 1.10-1.89                      | 1.38-1.59        |           |       |
|                                     | Severe climacteric symptoms   | 23 | 1.44    | 0.87-2.02                      | 1.34-1.57        |           |       |
| Zn (µg/dL)                          | No climacteric symptoms       | 99 | 65      | 44-114                         | 57-74            | 1.001627  | >0.05 |
|                                     | Slight climacteric symptoms   | 30 | 67      | 43-113                         | 63-78            |           |       |
|                                     | Moderate climacteric symptoms | 19 | 64      | 47-118                         | 57-80            |           |       |
|                                     | Severe climacteric symptoms   | 23 | 64      | 50 - 108                       | 56 - 78          |           |       |

N: the number of women in the sub-group; Me: median; Min-Max: minimum value - maximum value; Q<sub>1</sub>- Q<sub>3</sub>: the first quartile - the third quartile; H: Kruskal-Wallis test; p: significance level

group B (5 to 10 years since the final menstruation). Women, whose final menstruation was up to five years prior to examination, had an average Mg level of 1.49 mg/dL. Statistically significant differences were found between women from group C and women from other groups ( $p < 0.05$ ). The average serum Zn level was similar in all groups of women. Statistically significant differences were not demonstrated ( $p > 0.05$ ).

No statistically significant differences were found in serum Mg and Zn levels between the women as regards the severity of climacteric symptoms ( $p > 0.05$ ). The highest average Mg concentrations were recorded in women with the least intense climacteric symptoms (group 0): 1.50 mg/dL. The highest zinc concentrations were noted in women with slight climacteric symptoms: 67 µg/dL (table 1).

## Discussion

According to the study results, Mg concentrations in postmenopausal women, not using MHT, were low and decreasing with the time since the final menstruation, while Zn concentrations remained at the same low levels and did not depend on the time interval variable.

Our results for average serum Mg levels in postmenopausal Polish women, not using MHT, were lower than those found in the studies conducted by Bednarek-Tupikowska [11]. This may be due to the fact that the women analysed by that author and those involved in our study had different menopausal statuses (different age and menstrual period statuses) at the time of the biochemical analyses. Bednarek-Tupikowska examined younger women, and in her study the time interval since the final menstruation was only 20.3 months, while in our study it was, on average, 6.6 years [11].

The analysis of available data does not provide any clear explanation for hypomagnesaemia and hypozincaemia in postmenopausal women. Excessively low levels of Mg and Zn in blood serum may result from their greater excretion by kidneys. As was reported by McNair *et al.*, renal Mg excretion increases in postmenopausal women and is only reduced by the administration of MHT, which restores the levels of this mineral to premenopause levels [12]. Other authors reported that women using MHT had higher serum Zn concentrations and lower losses of urinary Zn and Mg, than women who had not used the therapy [13]. However, the results obtained by Zofkova *et al.* did not reveal any changes in serum Mg levels in postmenopausal women while taking MHT or after this therapy [14]. Also Bednarek-Tupikowska claimed that women both using and those not using MHT had similar Mg levels in serum and in blood [11]. According to Ikeda neither menopause nor MHT influence the concentrations of these minerals, so Ca, Mg and Zn levels in urine do not significantly change over a life span. The patients involved in our study did not use MHT because they had no classical indications for such a therapy, which might have affected our results [15].

No statistically significant correlation between average serum Mg and Zn levels and worsening of climacteric symptoms in postmenopausal women, who did not use menopausal hormone therapy,

was shown in our study, even though the lowest Mg and Zn levels were found in those women who demonstrated the most severe climacteric symptoms. This partially diverges from the results found in the literature, since numerous reports show that certain menopausal symptoms may be related not only to the lower levels of steroid hormones, especially estrogens, but also, though much less frequently, to the altered Ca to Mg ratio in blood serum [16-18]. Similar conclusions were drawn by Park *et al.*, who applied a four-week supplementation with Mg, and thus reduced incidences and severity of hot flushes in more than a half of the women examined [19].

In our study, no effect of BMI on average serum Mg and Zn levels in postmenopausal women, not using MHT, was demonstrated. On the other hand, there are findings concerning serum Zn levels and BMI, which show that there is a negative correlation between BMI and Zn levels in postmenopausal women and a positive correlation between BMI and total Zn levels in women of reproductive age [20]. Although our study does not provide evidence of an clear effect of BMI on serum Zn levels, average Zn levels in overweight women were higher than in women with a normal BMI.

In conclusion, Mg and Zn concentrations in postmenopausal women, not using MHT, remain at low levels. The average serum Mg level decreases considerably with the time since the final menstruation. No correlation was found between BMI or worsening of climacteric symptoms and serum Mg and Zn concentrations in postmenopausal women, not using MHT.

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