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# Relations between serum magnesium and calcium levels and body composition and metabolic parameters in women with fibromyalgia

Aline Andretta<sup>1\*</sup> , Maria Eliana Madalozzo Schieferdecker<sup>2</sup>, Ricardo Rasmussen Petterle<sup>3</sup>, Eduardo dos Santos Paiva<sup>4</sup> and César Luiz Boguszewski<sup>5</sup>

## Abstract

**Objective:** Correlate serum magnesium (Mg) and Calcium (Ca) levels with body composition and metabolic parameters in women with fibromyalgia (FM).

**Patients and methods:** Cross-sectional study compared with a control group paired by age and body mass index (BMI) of adult women diagnosed with fibromyalgia. All participants went through assessment of their body composition through dual-energy X-ray absorptiometry (DXA) and had blood samples collected for dosing of Mg, Ca, C-reactive Protein (CRP), lipidogram and glycemia. Results: 53 women with FM (average age  $48.1 \pm 8.2$  years, average BMI  $26.6 \pm 4.5$  kg/m<sup>2</sup>) and 50 control women (average age  $47.1 \pm 9.9$  years, average BMI  $25.6 \pm 3.6$  kg/m<sup>2</sup>) participated in the study. Serum levels turned out to have inverse correlation with CRP in the FM group ( $r = -0.29$ ,  $p = 0.03$ ) and with BMI and glycemia in the control group ( $r = 0.31$ ;  $p = 0.02$  and  $r = 0.48$ ;  $p = 0.0004$  respectively). Serum levels of calcium correlated with triglycerides ( $r = 0.29$ ;  $p = 0.03$ ) in the FM group and with glycemia in the control group ( $r = 0.64$ ;  $p = 0.0001$ ).

**Conclusions:** In patients with FM, magnesemia turned out to have inverse correlation with CRP and calcemia had positive association with triglycerides.

**Keywords:** Fibromyalgia, Magnesium, Calcium, Glycemia, Lipidogram

## Introduction

Fibromyalgia (FM) is a rheumatological condition characterized by diffuse, chronic musculoskeletal pain associated to various other symptoms, such as fatigue, sleep disorders, depressive episodes and cognitive and intestinal dysfunction [1, 2].

Generalized chronic pain has been recently associated to an increase in mortality risk and especially to death by cancer and cardiovascular conditions [3].

In addition to chronic pain, patients with FM usually have higher body mass indexes (BMI) and are physically inactive, two risk factors that contribute to the development of metabolic syndrome. A study by Loevinger et al. (2007) found that women with fibromyalgia are 5.56 times more likely to have metabolic syndrome than healthy control subjects, given that they have higher levels of arterial blood pressure, larger waist circumference, higher glycated hemoglobin, as well as higher serum levels of triglycerides and cholesterol [4].

The longitudinal study Nord-Trøndelag Health (HUNT) identified BMI as an independent risk factor for the development of FM and concluded that being overweight has an increased FM risk [4].

Recently, the importance of dietary nutrients has been recognized in the treatment of FM and detection of

\* Correspondence: [alineandretta@hotmail.com](mailto:alineandretta@hotmail.com)

A cross-sectional study that evaluated the correlation between serum magnesium (Mg) and calcium (Ca) levels with the body composition and metabolic parameters in women with fibromyalgia and women without it.

<sup>1</sup>Department of Internal Medicine, Federal University of Parana (UFPR), Curitiba, PR, Brazil. Rua General Carneiro, 181, Curitiba, PR 80060-900, Brazil  
Full list of author information is available at the end of the article



unbalanced levels of vitamins and minerals in body fluids and tissues [5].

Several studies have shown that patients with chronic pain do not follow the recommended dietary intake levels of most vitamins and minerals [6–9].

Additionally, numerous studies have investigated the impact of magnesium (Mg) in the quality of life of patients with pain [10]. The deficiency in Mg has been associated to cephalgia, migraine, fibromyalgia, increase in c-reactive protein levels (CRP), osteoporosis, cardiovascular disease, changes in the metabolism of glucose and other conditions [11]. Low serum magnesium levels seem to be predictive of Metabolic Syndrome and Type-2 Diabetes [12].

Magnesium frequently acts as natural antagonist of Calcium. The two cations compete in the modulation of muscular contraction, as well as in the regulation of several enzymatic reactions involved in energy metabolism, signal transduction and brain activity [13, 14].

Currently, little is known about the relation between chronic pain conditions, metabolic disorders and the roles of Mg and Ca in women with FM. However, studies have found associations between serum Mg and Ca levels and metabolism of lipids and cardiovascular disease risk [15–18].

This study aims at correlating serum magnesium and calcium levels with body composition and metabolic parameters in women with fibromyalgia.

## Materials and methods

Observational analytical cross-sectional study approved by the Research Ethics Committee of the Hospital de Clínicas of the Federal University of Paraná (HC/UFPR) according to its approval no. 8786 dated 27 March 2012. The study analyzed women in ages between 18 to 60 years, selected at the Rheumatology Outpatient Clinic at the HC/UFPR, who had been diagnosed with FM according to criteria set forth by the American College of Rheumatology (ACR) in 1990 [1]. The reason for including only women in the study was the low prevalence of fibromyalgia among men. The control group consisted of women with the same age span who did not have FM and other associated clinical conditions.

Patients with fibromyalgia and depression or anxiety were only included if their treatment had remained unchanged for 3 months. The exclusion criteria were: use of calcium and magnesium supplements, medication change over the previous 4 weeks, use of corticosteroids or anticytokine agents, pregnancy, lactation, and a diagnosis of diabetes, decompensated endocrine diseases, infectious diseases (over the previous 4 weeks), demyelinating neurological diseases, peripheral neuropathies, inflammatory articular diseases, systemic autoimmune diseases, severe cardiovascular diseases,

malignancy (over the previous year), and severe psychiatric diseases (substance abuse, schizophrenia, psychosis). Nonsteroidal anti-inflammatory agents were suspended 48 h before collection of blood samples, and all other medications were required to remain unchanged for at least 30 days.

After having executed an Informed Consent Agreement, all women underwent anthropometric assessment, analysis of body composition and collection of blood samples.

The anthropometric assessment was performed by means of body mass index (BMI), consisting of the relation between body weight in kilograms and body height squared in meters:  $BMI = \text{weight}/\text{height}(\text{m})^2$ . The ranges are as follows: underweight  $< 18.5 \text{ kg}/\text{m}^2$ , eutrophic between 18.5 and  $24.9 \text{ kg}/\text{m}^2$ , overweight between 25 and  $29.9 \text{ kg}/\text{m}^2$ , and obese  $> 30 \text{ kg}/\text{m}^2$  [19].

The assessment of body composition was performed by means of dual-energy X-ray absorptiometry (DXA) using the Lunar Prodigy Advance DPX device at the Endocrinology and Metabolism Service of UFPR (SEMPR) with a specialized technique. Results were issued using Encore Version 12.10 software stating fat body mass (FBM) and lean body mass (LBM) in grams then converted to kilogram (kg), and FBM in percentage.

Blood samples for measuring serum magnesium (Mg) and calcium (Ca), ultra-sensitive C-reactive protein (US-CRP), total cholesterol (TC), low-density lipoproteins (LDL), high-density lipoproteins (HDL), triglycerides (TG) and glycemia were drawn in the morning after a 10–12-h fast. They were then placed in ice and centrifuged at 4 °C. The serum was stored at –80 °C for later analysis at the UFPR Clinical Analysis Laboratory.

## Statistical analysis

Analyses have been performed by R software version 3.0.2 (R Development Core Team, 2013). The Shapiro-Wilk test was performed to assess data normality. To test statistical differences between the two groups, the parametric Student's t-test was performed when data conformed to normality and the non-parametric Wilcoxon-Mann-Whitney test was performed for non-normal data. To establish correlation between the results, the Pearson correlation coefficient was used for data that conformed to normality and Spearman's correlation coefficient was adopted for non-normal data. Significance level was assumed to be 95% ( $p < 0.05$ ).

## Results

Fifty-three women with FM and 50 women without it participated in this study. The average age, BMI, and fat body mass and lean body mass percentage were equivalent in the groups (Table 1).

**Table 1** General characteristics of the participants with fibromyalgia and controls

Variables	Fibromyalgia <i>n</i> = 53		Controls <i>n</i> = 50		<i>p</i> -Value
	Mean ± SD	median (min-max)	Mean ± SD	median (min-max)	
Age (years)	48.1 ± 8.2	49 (26–60)	47.1 ± 9.9	50 (23–60)	0.8018
BMI (Kg/m <sup>2</sup> )	26.6 ± 4.5	26.8 (15.2–38.6)	25.5 ± 3.6	24.9 (19.2–32.9)	0.2123
Lean mass (%)	60.4 ± 7.5	59.8 (43.8–82.1)	60.2 ± 6.9	58.9 (48.4–77.9)	0.89
Fat mass (%)	39.6 ± 7.5	40.1 (18–56.2)	39.8 ± 6.9	41.1 (22.1–51.6)	0.877
<b>Laboratory tests</b>					
Magnesium serum (mg/dL)	2.2 ± 0.1	2.2 (1.8–2.6)	2.2 ± 0.2	2.2 (1.8–2.6)	0.577
Calcium serum (mg/dL)	9.7 ± 0.5	9.6 (8.8–11.2)	9.6 ± 0.4	9.7 (8.8–10.3)	0.3163
US-CRP (mg/dL)	0.3 ± 0.4	0.2 (< 0.09–1.9)	0.3 ± 0.4	0.1 (< 0.09–2.6)	0.454
TC (mg/dL)	210.4 ± 35.4	207 (140–287)	203.3 ± 30.4	201.5 (133–266)	0.279
LDL (mg/dL)	138.5 ± 30.8	135 (81–209)	130.9 ± 27.7	129 (62–196)	0.196
HDL (mg/dL)	47.1 ± 11.1	46 (30–84)	50.3 ± 12.2	49 (28–78)	0.133
TG (mg/dL)	123.6 ± 67.6	100 (35–311)	110.6 ± 67.6	96 (44–427)	0.283
Glycemia (mg/dL)	82.9 ± 8.9	82 (59–101)	83.9 ± 9.2	83 (60–103)	0.593

BMI body mass index, US-CRP C- ultra-sensitive C-reactive protein, TC total cholesterol, LDL low-density lipoproteins, HDL high-density lipoproteins, TG triglycerides. Student's t test for the parametric data and the Wilcoxon Mann-Whitney test were used for the non-parametric. *p* < 0.05 is statistically significant

No significant differences in quantities of serum Mg, Ca, CRP-US, TC, LDL, HDL, TG e glycemia were found in the groups (Table 1).

BMI had positive correlation with the levels of serum Mg in the control group ( $r = 0.31$ ;  $p = 0.02$ ). Percentages of fat body mass and lean body mass did not correlate with levels of serum Mg and Ca (Table 2).

In relation to the metabolic parameters, the level of serum Mg correlated negatively with CRP-US ( $r = -0.29$ ;  $p = 0.03$ ), and TG had positive correlation with the level of serum Ca ( $r = 0.29$ ;  $p = 0.03$ ) for women with FM. In the control group, levels of serum Mg and Ca had positive correlation with glycemia ( $r = 0.48$ ;  $p = 0.0004$  and  $r = 0.64$ ;  $p = 0.001$ , respectively) (Table 2).

Due to the solid correlation found between levels of serum Mg and Ca and glycemia, the FM group and the control group were divided in BMI < 25 Kg/m<sup>2</sup> and BMI ≥ 25 Kg/m<sup>2</sup>. With such division, it was possible to detect that the correlation between glycemia and calcemia was maintained in the groups with BMI < 25 Kg/m<sup>2</sup> ( $r = 0.64$ ;  $p = 0.0005$ ) and with BMI ≥ 25 Kg/m<sup>2</sup> ( $r = 0.63$ ;  $p = 0.001$ ). Magnesemia correlated with glycemia only in the control group with BMI ≥ 25 Kg/m<sup>2</sup> ( $r = 0.59$ ;  $p = 0.003$ ). Women with FM did not have such correlations (Table 3).

## Discussion

The reduction of levels of serum micronutrients in patients with FM is a rather controversial subject. Although some studies have shown lower intracellular and serum contents of Mg and higher Ca levels in patients with FM [20–23], our study did not find such difference in levels of serum Mg and Ca in the FM group or in the

control group. Nevertheless, it is fundamental to analyze such fact more deeply, given that studies have employed different methodologies for measuring minerals and produced varying serum, erythrocyte, leucocyte, urinary, muscular and hair levels.

Numerous studies have reported that patients with fibromyalgia have high body mass indexes and are more likely to develop metabolic syndrome [3, 24, 25]. However, in this research, the study group was equivalent to the control group in terms of BMI, therefore, it was not possible to notice differences in connection with body composition and metabolic parameter between the groups.

A relevant fact found in our study, though, was the inverse correlation between levels of serum Mg and CRP-US in the FM group. Several current evidences support the role of magnesium in pain reduction by blocking central sensitization through its effect on N-methyl-d-aspartate receptors [26]. Other findings have shown the important role that Mg plays in the physiopathology of inflammation. Lower blood concentrations of Mg influence inflammatory response due to an increase in pro-inflammatory cytokines. A meta-analysis published by Simental-Mendia et al. (2017) concluded that the supplementation of Mg lowers CRP levels and, consequently, has a major adjuvant role in the treatment of low-degree chronic systemic inflammation. Such mechanisms still require further understanding but may be related to the action of Mg as a natural antagonist of Ca given that higher levels of intracellular Ca and the activation of processes that contribute to inflammation take place while Mg is deficient [27–30].

Another relevant fact found in the FM group is the correlation in triglycerides levels with levels of serum

**Table 2** Relationship between serum magnesium and calcium levels with the variables: body composition and metabolic parameters

Variables	Magnesium serum		Calcium serum	
	FM	CT	FM	CT
BMI				
r	-0.001	<b>0.31</b>	0.27	0.18
p	0.99	<b>0.02*</b>	0.05	0.2
Lean mass				
r	-0.05	-0.26	-0.18	-0.22
p	0.71	0.06	0.18	0.12
Fat mass				
r	0.05	0.26	0.18	0.22
p	0.72	0.06	0.18	0.12
US-CRP				
r	<b>-0.29</b>	-0.006	0.21	0.2
p	<b>0.03*</b>	0.96	0.11	0.17
TC				
r	0.182	0.08	0.24	0.18
p	0.19	0.56	0.08	0.21
LDL				
r	0.2	0.01	0.17	0.57
p	0.15	0.92	0.21	0.69
HDL				
r	0.03	-0.12	-0.03	0.03
p	0.83	0.39	0.79	0.79
TG				
r	0.08	0.26	<b>0.29</b>	0.25
p	0.53	0.07	<b>0.03*</b>	0.08
Glycemia				
r	-0.01	<b>0.48</b>	0.24	<b>0.64</b>
p	0.93	<b>0.0004*</b>	0.08	<b>0.001*</b>

FM fibromyalgia group, CT control group, BMI body mass index, US-CRP C-ultra-sensitive C-reactive protein, TC total cholesterol, LDL low-density lipoproteins, HDL high-density lipoproteins, TG triglycerides. r: correlation coefficient. \* P < 0.05 is statistically significant

Calcium. The relation between metabolic parameters with levels of serum Mg and Ca in persons with FM has not been described by research to date. Nevertheless, numerous studies with adult subjects have correlated an increase in calcemia with increased total cholesterol [18] and a progressive increase in Metabolic Syndrome [16, 17].

Despite the fact that Mg levels did not produce a relation with the lipid profile in this research study, lower Mg concentrations appear to be associated to a reduction in HDL and increase in LDL and TG levels [15].

In both groups in our study (FM and control), glycemia has remained fairly normal. However, it is important to notice that levels of serum Mg and Ca correlated strongly with glycemia in the control group, and such correlation did not exist in the FM group. After separating the groups in lower than- and higher than 25 kg/m<sup>2</sup>, the correlation between calcemia and glycemia continued to exist in both subgroups of the control group, and the correlation between glycemia and Mg levels only continued to exist in the control subgroup with BMI ≥ 25 kg/m<sup>2</sup>.

Apparently, there is something in the physiopathology of fibromyalgia that makes patients have different responses from the control group. A study by Malatji et al. (2017) detected that patients with FM have an abnormal metabolic state [31].

Although in this study magnesemia has correlated positively with glycemia, other studies have already shown that lower levels of serum Mg serum and higher levels of serum Ca must be considered as risk factors for cardiovascular diseases, given they correlate with hypertension, diabetes and atherosclerosis [12, 32].

Several research studies have found direct association between calcemia and diabetes risk [16, 33, 34]. Their findings have shown the association of calcemia to glycemia, fasting insulin, resistance to insulin, and inverse correlation with the function of β-cells, thus suggesting that alterations in homeostasis of serum calcium are substantially correlated to abnormalities in the metabolism of glucose [35]. Therefore, higher levels of serum calcium may be interpreted as an independent risk factor for the development of diabetes [36].

**Table 3** Correlation between glycemia and serum magnesium and calcium levels in the groups divided by body mass index (BMI)

	Grupo FM				Grupo Controle			
	Magnesium serum		Calcium serum		Magnesium serum		Calcium serum	
Glycemia	BMI < 25 (n = 24)	BMI ≥ 25 (n = 29)	BMI < 25 (n = 24)	BMI ≥ 25 (n = 29)	BMI < 25 (n = 25)	BMI ≥ 25 (n = 25)	BMI < 25 (n = 25)	BMI ≥ 25 (n = 25)
r	0.16	-0.31	0.34	-0.13	0.12	0.59	0.64	0.63
p	0.44	0.09	0.1	0.47	0.55	<b>0.003*</b>	<b>0.0005*</b>	<b>0.001*</b>

\* P < 0.05 is statistically significant

In another study, an increase in calcemia related to all components of the Metabolic Syndrome (MS), except HDL cholesterol. The high serum calcium levels found in these persons may result from greater intestinal absorption, increased bone reabsorption, renal absorption, or a combination of said factors [17].

In spite serum levels correlating to the risk of developing diabetes, magnesium levels are associated to improved glucose metabolism. Studies have shown a relation between supplementation of magnesium and improvement in diabetes [37]. Others have shown favorable results with supplementation of magnesium to improve sensitivity to insulin [38, 39] and to improve the capacities of  $\beta$ -cells, thus compensating the variations in sensitivity to insulin [40]. Another study has shown that supplementation of Mg reduced cardiovascular risk globally by reducing levels of total cholesterol, LDL and TG and increasing HDL levels [41].

The present study has limitations related to serum mineral dosage, which does not seem to be a good predictor of intracellular reserves. In addition, serum Ca values were not corrected by albumin, and it was not possible to measure complementary tests such as ionic Ca, Vitamin D, PTH (parathyroid hormone), and the menopausal status of the subjects, which would help to better analyze the metabolism of these minerals.

Finally, it is noteworthy that this was a cross-sectional study, which has a number of limitations inherent to its methodology. Further studies are proposed that explain in detail the mechanisms that influence these results, and whether there is anything in the pathophysiology of fibromyalgia that causes patients to have different responses from the control group.

## Conclusion

Women with FM have shown inverse relation between levels of serum magnesium and CRP, and positive relation between calcemia and triglyceride levels. These findings suggest that magnesium and calcium may have a relevant role in metabolic disorders and inflammations in women with fibromyalgia. New research studies must be developed in order to better unveil the mechanisms of said minerals in the physiopathology of fibromyalgia and their relation with metabolic disorders.

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## Authors' contributions

All authors participated sufficiently in the work. They were present during research, evaluation and data collection, as well as in the elaboration of statistical analyzes and in the intellectual contribution related to research

and references. All authors assume public responsibility for the content of the article. If requested, authors will provide the data required for review by publishers. All authors read and approved the final manuscript.

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## Availability of data and materials

If requested, authors will provide the data required for review by publishers.

## Ethics approval and consent to participate

The Human Research Ethics Committee of Hospital de Clínicas, Federal University of Parana (CEP-HC/UFPR), manifests itself by the approval of Research Project number 8786 on 27.03.2012, CAAE: 00979612.9.0000.0096. All patients who agreed to participate received and signed an informed consent.

## Consent for publication

The authors, declare that this manuscript is original, has not been published before and is not submitted for any other publication.

The authors confirm that the article was read and approved by all authors and that all authors participated sufficiently in the work, also assuming public responsibility for the content of the article.

## Competing interests

The authors declare that they have no competing interests.

## Author details

<sup>1</sup>Department of Internal Medicine, Federal University of Parana (UFPR), Curitiba, PR, Brazil. Rua General Carneiro, 181, Curitiba, PR 80060-900, Brazil.

<sup>2</sup>Department of Nutrition, Federal University of Parana (UFPR), Curitiba, PR, Brazil. <sup>3</sup>Statistical Federal University of Parana (UFPR), Curitiba, PR, Brazil.

<sup>4</sup>Department of Internal Medicine, Federal University of Parana (UFPR), Curitiba, PR, Brazil. <sup>5</sup>Endocrine Division (SEMPR), Department of Internal Medicine, Federal University of Parana (UFPR), Curitiba, PR, Brazil.

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