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Original Article

Influence of magnesium status and magnesium intake on the blood glucose control in patients with type 2 diabetes☆

Cristiane Hermes Sales [a], Lucia Fátima Campos Pedrosa [b], Josivan Gomes Lima [c], Telma Maria Araújo Moura Lemos [d], Célia Colli [a,*]

[a] Department of Food and Experimental Nutrition, Faculty of Pharmaceutical Sciences, University of São Paulo, Av. Prof. Lineu Prestes, 580, Bl. 14. Butantã, São Paulo, SP CEP 05508-000, Brazil
[b] Department of Nutrition, Federal University of Rio Grande do Norte, Av. General Cordeiro de Farias, s/n, Petrópolis, Natal, RN 59010-180, Brazil
[c] Department of Clinical Medicine, Federal University of Rio Grande do Norte, Av. General Cordeiro de Farias, s/n, Petrópolis, Natal, RN 59010-180, Brazil
[d] Department of Clinical and Toxicological Analyses, Federal University of Rio Grande do Norte, Av. General Cordeiro de Farias, s/n, Petrópolis, Natal, RN 59010-180, Brazil

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SUMMARY

Background & aims: This study was undertaken to assess magnesium intake and magnesium status in patients with type 2 diabetes, and to identify the parameters that best predict alterations in fasting glucose and plasma magnesium.
Methods: A cross-sectional study was carried out in patients with type 2 diabetes ($n = 51$; 53.6 ± 10.5 y) selected within the inclusion factors, at the University Hospital Onofre Lopes. Magnesium intake was assessed by three 24-h recalls. Urine, plasma and erythrocytes magnesium, fasting and 2-h postprandial glucose, HbA1, microalbuminuria, proteinuria, and serum and urine creatinine were measured.
Results: Mean magnesium intake (9.37 ± 1.76 mmol/d), urine magnesium (2.80 ± 1.51 mmol/d), plasma magnesium (0.71 ± 0.08 mmol/L) and erythrocyte magnesium (1.92 ± 0.23 mmol/L) levels were low. Seventy-seven percent of participants presented one or more magnesium status parameters below the cut-off points of 3.00 mmol/L for urine, 0.75 mmol/L for plasma and 1.65 mmol/L for erythrocytes. Subjects presented poor blood glucose control with fasting glucose of 8.1 ± 3.7 mmol/L, 2-h postprandial glucose of 11.1 ± 5.1 mmol/L, and HbA1 of 11.4 ± 3.0%. The parameters that influenced fasting glucose were urine, plasma and dietary magnesium, while plasma magnesium was influenced by creatinine clearance.
Conclusions: Magnesium status was influenced by kidney depuration and was altered in patients with type 2 diabetes, and magnesium showed to play an important role in blood glucose control.

1. Introduction

Magnesium is an essential mineral for the human body, principally because of its role in the regulation of cellular processes and its function as a cofactor in a wide range of metabolic reactions. Many enzymes that catalyze phosphorylation and dephosphorylation reactions, including those involved in glycolysis, are activated by the formation of $MgATP^{+2}$ complexes, which are the real substrates for these enzymes.[1,2]

Alterations in the distribution of magnesium within the body have been associated with several diseases and especially diabetes, a disorder representing a global public health problem of increasingly serious concern.[3,4] Although some epidemiological studies have suggested that adequate magnesium intake reduces the risk of development of type 2 diabetes, there are still contradictions with respect to the role of low magnesium intake as a predictor factor for

Abbreviations: HUOL, University Hospital Onofre Lopes; BMI, body mass index; WC, waist circumference; CCr, creatinine clearance; HbA1, glycated hemoglobin; BDS, Brazilian Diabetes Society; D, difference between the observed average intake by each subject; SD_D, standard deviation of D; EAR, estimated average requirement.

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* Corresponding author. Tel.: +55 11 3091 3651; fax: +55 11 3815 4410.
E-mail addresses: cristianehermes@yahoo.com.br (C.H. Sales), lpedrosa@ufrnet.br (L.F.C. Pedrosa), josivanlima@gmail.com (J.G. Lima), telmaml@yahoo.com.br (T.M.A.M. Lemos), cecolli@usp.br (C. Colli).

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this disease.[5–10] The importance of magnesium for individuals with diabetes can be explained on the basis of maintenance of glucose homeostasis along with activation of the factors involved in sensitivity of tissues to insulin, the receptors of which are phosphorylated only in the presence of $MgATP^{+2}$.[2,11]

Some studies have shown that the magnesium intake by patients with diabetes is often below recommended levels.[12,13] Additionally, there is evidence that the magnesium status of patients with diabetes tends to alter, and that low body concentrations of this mineral may influence the evolution of the disease and generate further complications.[14–17]

Despite reports describing the occurrence of hypomagnesemia among patients with diabetes,[18,19] few investigations have considered dietary intake of magnesium in the Brazilian population, and none has examined the levels of magnesium in patients with type 2 diabetes. Hence, the aim of the present study was to evaluate the intake of magnesium and the levels of the mineral in urine, plasma and erythrocytes in subjects with type 2 diabetes. Additionally, attempts were made to identify those parameters that best predict alterations in fasting glucose and plasma magnesium.

2. Materials and methods

The study was approved by the Ethics Committees on Research of the University Hospital Onofre Lopes (HUOL, Natal, RN, Brazil) and of the Faculty of Pharmaceutical Sciences, University of São Paulo (protocol CAAE # 0005.0.294.018-06). Written informed consent was obtained from all participants prior to the commencement of the study.

2.1. Subjects

A cross-sectional study was carried out in patients with type 2 diabetes selected from those attending the Endocrinology Clinic at HUOL as outpatients between February and June 2008. The size of the study population was defined by the requirement to detect a difference of 0.075 mmol/L in plasma magnesium with a power of 0.9070% and a 5% α-level, and was calculated using the Student *t*-test for independent samples assuming a normal distribution of plasma magnesium.

Fifty-one patients were selected, consecutively, on the basis of medical records considering the following inclusion criteria: (a) medical diagnosis of type 2 diabetes; (b) age range 25–65 years; (c) non-pregnant/non-lactating women; (d) absence of kidney failure as defined by the levels of serum creatinine (<124 μmol/L for women; <133 μmol/L for men); (e) absence of digestive, thyroid, congenital and infectious diseases; (f) no recent history of alcohol abuse, use of vitamin and mineral supplements or medication that could interfere in the analysis of magnesium (except for antidiabetic and antihypertensive drugs).

2.2. Study design

The selected participants were requested to visit the hospital three times during the period of a month and were submitted on each occasion to a 24-h food recall. Patients were formally invited to participate in the study during their first hospital visit, following which their arterial blood pressure was measured by a doctor and anthropometric measurements were assessed by a responsible researcher. Subjects were also submitted to an interview, which was based on a previously structured questionnaire, applied by a researcher. At the second visit, patients delivered urine samples that they had collected (in mineral-free flasks) over the previous 24-h, and blood samples were collected by vein puncture from the 12–14 h fasting subjects. In order to determine postprandial serum glucose, a further blood sample was collected 2-h after the breakfast. During the third visit, patients received personal nutritional orientation together with the results of the biochemical analyses that would serve as references for subsequent medical follow-up.

2.3. Blood pressure and anthropometric measurements

All measurements were made in duplicate. Blood pressure was determined using a mercury sphygmomanometer and readings were taken from the upper left arm with the patient sitting down. Body weight was assessed using Plenna (Sao Paulo, SP, Brazil) calibrated digital scales (0.1 kg precision) with patients wearing light clothes and no shoes. Height was evaluated (0.1 mm precision) using a Cardiomed (Curitiba, PR, Brazil) stadiometer. Body mass index (BMI) was expressed as the quotient between weight (kg) and height squared (m^2). Waist circumference (WC) was estimated at the end of a normal expiration using a Cardiomed non-extendible tape held in a horizontal plane around the abdomen at the level of the iliac crest. Patients were classified according to BMI and WC following the recommendations of the World Health Organization as adopted by the American Diabetes Association.[3]

2.4. Biochemical analyses

All biochemical analyses were carried out in triplicate with a 10% variation limit set as the criterion for repetition of the assay. Kidney function was determined through the analysis of urine albumin, urine protein, and urine and serum creatinine. Microalbuminuria was measured turbidimetrically using a Biosystems (Barcelona, Spain) kit, while proteinuria was assessed from the end point of the pyrogallol red-molybdenum(VI) complex reaction. The levels of creatinine in urine (24-h collection) and serum were estimated using the alkaline picrate method without precipitation (Jaffe's reaction) with the aid of Labtest Diagnostica (Lagoa Santa, MG, Brazil) kits. Creatinine clearance (CCr; mL/s/1.73 m^2) was calculated from the expression:

$$\mathrm{CCr} = \left(\frac{1.73 \times 24-\text{h urine creatine(mg/dL)} \times 24-\text{h urine volume(mL/s)}}{\text{serum creatine(mg/dL)}}\right) \Big/ \text{body surface area}\left(\mathrm{m}^2\right) \quad (1)$$

Serum fasting glucose and 2-h postprandial glucose were measured using the glucose oxidase enzyme method, while glycated hemoglobin (HbA1) was determined by ion-exchange chromatography, both analyses being performed with the aid of Labtest Diagnostica kits. Glycemic control was assessed on the basis of the glycemia standards proposed by the Brazilian Diabetes Society (BDS)[20] for the treatment of patients with type 2 diabetes, namely: fasting glucose <6.11 mmol/L, 2-h postprandial glucose <7.77 mmol/L, and HbA1 < 9.0%.

Magnesium status was evaluated directly by measuring the levels of the mineral in urine, plasma and erythrocytes by flame atomic absorption spectrometry (AAnalyst 100; Perkin Elmer, Norwalk, CT, USA) according to previously standardized and validated protocols.[21] Flasks and glassware were demineralized prior to analyses, and the precision and accuracy of the methods were verified using certified standards (Trace Elements Serum L-I and Urine Blank; Seronorm, Billingstad, Norway) with urine, plasma and erythrocyte pools being