Archives of Medical Research 45 (2014) 388–393

ORIGINAL ARTICLE

Oral Magnesium Supplementation Improves the Metabolic Profile of Metabolically Obese, Normal-weight Individuals: A Randomized Double-blind Placebo-controlled Trial

Martha Rodríguez-Moran and Fernando Guerrero-Romero

Biomedical Research Unit, Mexican Social Security Institute, Durango, Mexico

Received for publication January 3, 2014; accepted April 30, 2014 (ARCMED-D-14-00008).

Background and Aims. We undertook this study to determine the efficacy of oral magnesium supplementation in the improvement of the metabolic profile and blood pressure in metabolically obese, normal-weight (MONW) individuals.

Methods. A total of 47 MONW individuals with hypomagnesemia were enrolled in clinical a randomized double-blind placebo-controlled trial. Individuals in the intervention group received 30 mL of $MgCl_2$ 5% solution (equivalent to 382 mg of magnesium) and individuals in the control group 30 mL of placebo solution, once daily during 4 months. In the absence of obesity or overweight, the presence of fasting glucose levels ≥100 mg/dL, HOMA-IR index ≥3, triglyceride levels ≥150 mg/dL and/or systolic and diastolic blood pressure ≥140 and 90 mmHg defined the presence of the MONW phenotype. Hypomagnesemia was defined by serum magnesium concentration ≤1.8 mg/dL.

Results. At basal conditions there were no significant differences between groups. At the end of follow-up, changes in the mean of systolic (−2.1 vs. 3.9% mmHg, $p < 0.05$) and diastolic (−3.8 vs. 7.5% mmHg, $p < 0.05$) blood pressures, HOMA-IR index (−46.5 vs. −5.4%, $p < 0.0001$), fasting glucose (−12.3 vs. −1.8% mg/dL, $p < 0.05$) and triglyceride levels (−47.4% vs. 10.1% mg/dL, $p < 0.0001$) were significantly lower in the subjects who received $MgCl_2$ compared with individuals in the control group.

Conclusions. Oral magnesium supplementation improves the metabolic profile and blood pressure of MONW individuals. © 2014 IMSS. Published by Elsevier Inc.

Key Words: Magnesium, Metabolically obese, Normal weight, Glucose, Triglycerides, Hypertension, Insulin resistance.

Introduction

A phenotype has been described of individuals displaying obesity-related characteristics despite not being obese, a phenotype characterized by insulin resistance, hyperglycemia, hypertriglyceridemia, and/or high blood pressure (1–3). In addition to genetics, it has been speculated that this phenotype of metabolically obese, normal weight (MONW) individuals could be related with overeating or the ingestion of high carbohydrate diets that can be the cause of hyperinsulinism in normal-weight individuals (1,4).

Based on a population-based cross-sectional study, we recently found that hypomagnesemia is strongly associated with hyperglycemia, hypertriglyceridemia, and insulin resistance in MONW individuals (5), findings that support our hypothesis that magnesium deficit could be a contributing factor in the development of cardiovascular risk factors in non-obese individuals.

Magnesium, the most abundant intracellular divalent cation (6), is an essential cofactor in the enzymatic process of high-energy phosphate (7), acts as a calcium channel antagonist, and stimulates production of prostacyclins and nitric oxide (8); thus, magnesium is involved in the physiological pathways that regulate glucose and lipid metabolism as well as in the regulation of blood pressure.

A growing body of evidence derived from clinical trials shows that oral magnesium supplementation improves

Addres reprint requests to: Fernando Guerrero-Romero, MD, PhD, Siqueiros 225 esq/Castañeda, 34000, Durango, Dgo., México; Phone: (+52) (618) 812-0997; FAX: (+52) (618) 813-2014; E-mail: guerrero.romero@gmail.com

0188-4409/$ - see front matter.
http://dx.doi.org/10.1016/j.arcmed.2014.05.003

insulin sensitivity, dyslipidemia, and glucose metabolic disorders in diabetic and non-diabetic individuals (9−12) as well as also improving blood pressure in hypertensive individuals (13−15).

Because magnesium intake is inadequate in the customary western diet (16) and that prevalence of MONW individuals varies from 12.7−23.5% (17−19), these findings highlight the magnitude of this health problem, determine the role of magnesium in the development of metabolic disturbances of individuals with normal weight, and may be an issue of interest for clinicians as well as for executives involved in public health policy decisions. In this regard, to the best of our knowledge there are no previous reports in regard to the efficacy of magnesium supplementation in the improvement of metabolic disturbances in normal-weight individuals with cardiovascular risk factors; thus, the objective of this study was to determine the efficacy of oral magnesium supplementation in the improvement of the metabolic profile and blood pressure in MONW individuals.

Materials and Methods

With the protocol approval by the Mexican Social Security Institute Research Committee and after obtaining written informed consent, a randomized double-blind placebo-controlled trial was carried out.

The sampling strategy was based on inviting the participation of non-obese healthy individuals cared for in the Biomedical Research Unit of the Mexican Social Security Institute in Durango, a city in northern Mexico.

MONW individuals, men and non-pregnant women, aged 20−60 years were eligible to participate if they had hypomagnesemia. A standardized interview, clinical examination, and laboratory tests were performed to determine the presence of body mass index (BMI) ≥25 kg/m^2, smoking, alcohol intake, acute or chronic diseases, new diagnosis of diabetes as well as intake of oral supplements and/or vitamins, which were exclusion criteria.

Participants were randomly allocated to receive either magnesium supplementation or placebo, once a day for 4 months. Given that the Recommended Dietary Allowance for magnesium intake is 400 mg in men and 320 mg in women (16), under fasting conditions subjects in the intervention group received 30 mL of $MgCl_2$ 5% solution (equivalent to 382 mg of magnesium) and individuals in the control group received 30 mL of placebo solution. In addition, subjects in both groups were advised to consume a diet with 40% carbohydrates, 40% lipids, and 20% proteins as well as to perform physical activity at least 30 min three times per week.

Screening was performed in 427 subjects, 274 (64.4%) women and 153 (35.8%) men; 378 (88.5%) individuals were not included in the study because they did not fulfill the inclusion criteria or due to the presence of exclusion criteria; thus, a total of 49 MONW individuals with hypomagnesemia were enrolled and randomly allocated into groups in study. Two subjects dropped out of the study: one from the intervention group due to adverse effects (mild diarrhea) and the other from the control group as a result of being lost to follow-up, events that occur within the first 15 days of follow-up. Therefore, 16 (66.7%) women and eight (33.3%) men in the intervention group and 15 women (65.2%) and eight (34.8%) men in the control group who successfully completed the follow-up period were included in the intent to treat analysis (Figure 1).

Definitions

In normal-weight individuals (BMI ≥20, <25 kg/m^2) the MONW phenotype was defined by the presence of fasting hyperglycemia (fasting glucose levels ≥100 mg/dL), insulin resistance (HOMA-IR index ≥3), hypertriglyceridemia (triglyceride levels ≥150 mg/dL), and/or hypertension (SBP and DBP ≥140 and 90 mmHg) (5). Hypomagnesemia was defined by serum magnesium concentration ≤1.8 mg/dL (20).

Measurements

Under fasting conditions and standing position, anthropometric measurements were performed with the subjects wearing light clothing and without shoes. Weight and height were measured using a fixed scale with a stadiometer (Tanita TBF-215, Tokyo, Japan). BMI was calculated as weight (kilograms) divided by height (meters) squared. Waist circumference (WC) was measured to the nearest centimeter with a flexible steel tape; the anatomic landmarks used were midway between the lowest portion of the rib cage and the superior border of the iliac crest. HOMA-IR index was calculated using the formula: fasting insulin (U/mL) *x* fasting glucose (mmol/L)/22.5 (21).

The technique for measurement of BP was recommended by the 2013 Task Force for the Management of Arterial Hypertension of the European Society of Hypertension and of the European Society of Cardiology (22).

Assays

Whole blood sample was collected from an antecubital vein 8−10 h after overnight fasting and after a 2-h postload glucose. Serum magnesium concentration was measured by colorimetric method; inter-assay coefficient of variation (CV) was 2.1%. Plasma glucose was measured using the glucose-oxidase method; inter-assay CV was 1.2%. Triglycerides were measured enzymatically and HDL-cholesterol fraction was obtained after precipitation by phosphotungstic reagent. Inter-assay CVs were 3.9 and 3.0% for triglycerides and HDL-cholesterol, respectively. Insulin levels were measured by microparticle enzyme immunoassay (Abbott Axsym System, Abbott Laboratories, Abbott Park, IL) with inter-assay CV of 5.1%.