Low Serum Magnesium Levels and Its Association with High Blood Pressure in Children

Fernando Guerrero-Romero, MD, PhD[1,2], Martha Rodríguez-Morán, MD, MSc, PhD[2], Gabriela Hernández-Ronquillo, MD[1], Rita Gómez-Díaz, MSc[3,4], María L. Pizano-Zarate, MD, MSc[3,5], Niels H. Wacher, MD, MSc[6], Rafael Mondragón-González, MD[6], and Luis E. Simental-Mendia, MD, MSc, PhD[1,2], on behalf of the Network of Childhood Obesity of the Mexican Social Security Institute*

Objective To evaluate the association of hypomagnesemia with prehypertension (preHTN) and hypertension in children.

Study design A total of 3954 apparently healthy Mexican children were enrolled in a cross-sectional study. Exclusion criteria were type 2 diabetes; hepatic, renal, or endocrine disease; impaired fasting glucose; chronic diarrhea; and intake of vitamins or magnesium supplements in the previous 6 months. preHTN was defined by systolic and/or diastolic blood pressure ≥90th to <95th percentile and hypertension by systolic and/or diastolic blood pressure ≥95th percentile, according to age, sex, and height percentile. Hypomagnesemia was defined by serum magnesium concentration <1.8 mg/dL (<0.74 mmol/L). To control for potential sources of bias related to age, participants were allocated into 2 groups, aged 6-10 years and 11-15 years.

Results The prevalence of preHTN and hypertension was 12.2% and 6.4%, respectively, in children aged 6-10 years and 13.9% and 10.6% in those aged 11-15 years. Hypomagnesemia was identified in 59 children with preHTN (27.3%) and 52 (45.6%) with hypertension in the 6-10 year age group, and in 115 children with preHTN (36.0%) and 109 (49.6%) with hypertension in the 11-15 year age group. Adjusted multiple logistic regression analysis showed that in children in both age groups, hypomagnesemia was associated with both preHTN (6-10 years: OR, 2.18, $P < .0005$; 11-15 years: OR, 1.38, $P = .018$) and hypertension (6-10 years: OR, 4.87, $P < .0005$; 11-15 years: OR, 1.83, $P = .0002$).

Conclusion Our results indicate that serum magnesium level <1.8 mg/dL is significantly associated with preHTN and hypertension in apparently healthy children. *(J Pediatr 2016;168:93-8)*.

The term "prehypertension" (preHTN) was introduced in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure[1] to characterize those individuals who do not meet the criteria for a diagnosis of hypertension but exhibit high blood pressure (HBP) and increased risk of developing cardiovascular disease. Among children, in 2004 the National High Blood Pressure Education Program Working Group[2] defined preHTN as blood pressure (BP) values ≥90th percentile and <95th percentile according to age, sex, and height percentiles, highlighting that preHTN in children increases the risk of impaired renal and heart function.[3,4]

Magnesium regulates BP by modulating vascular tone through its effects on biochemical reactions that control vascular contraction/dilation.[5] An increasing body of evidence derived from epidemiologic, cross-sectional, and longitudinal studies, as well as from clinical controlled trials, supports an important role of magnesium in the pathogenesis of HBP[6-14]; however, the literature contains no reports on the relationship between low serum magnesium level and HBP early in life. The aim of the present study was to evaluate the association of hypomagnesemia with preHTN and hypertension in children.

Methods

This cross-sectional study was approved by the Mexican Social Security Institute Research Committee and was carried out in accordance with institutional guide-

BMI	Body mass index
BP	Blood pressure
DBP	Diastolic blood pressure
HBP	High blood pressure
HDL-C	High-density lipoprotein cholesterol
preHTN	Prehypertension
SBP	Systolic blood pressure
WC	Waist circumference

From the [1]Biomedical Research Unit of the Mexican Social Security Institute at Durango, Mexico; [2]Research Group on Diabetes and Chronic Illnesses at Durango, Mexico; [3]National Institute of Perinatology from Mexico, Mexico; [4]High Specialty Medical Unit, Specialty Hospital, National Medical Center Century XXI, [5]Family Medicine Unit 4, Mexican Social Security Institute, Mexico; and [6]Research Unit in Clinic Epidemiology, High Specialty Medical Unit, Specialty Hospital, National Medical Center Century XXI, Mexico

*List of members of the Network of Childhood Obesity of the Mexican Social Security Institute is available at www.jpeds.com (**Appendix**).

Supported by the Mexican Social Security Institute Foundation, California. The authors declare no conflicts of interest.

http://dx.doi.org/10.1016/j.jpeds.2015.09.050

lines and the principles of the Declaration of Helsinki. Informed consent was obtained from a parent of each participant and assent was obtained from each participant.

Apparently healthy Mexican children aged 6-15 years from the general population of Mexico City and Durango were consecutively recruited from the participating research units between September 2008 and December 2014. The children were allocated into 2 groups, with HBP and without HBP. The socioeconomic status of the target study population was classified as middle income. To control potential sources of bias related to age, participants were distributed in 2 groups, children aged 6-10 years and those aged 11-15 years.

Study exclusion criteria were type 2 diabetes; hepatic, renal, or endocrine disease; impaired fasting glucose; chronic diarrhea; and intake of vitamins or magnesium supplements in the previous 6 months.

Measurements included BP, weight, height, waist circumference (WC), and biochemical measures, including fasting glucose, total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglyceride, and serum magnesium levels. BP was measured according to the technique recommended in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.[1] In brief, brachial artery BP was measured after at least 5 minutes of rest with the subject seated and the arms bared and supported at heart level, with the use of a baumanometer (Microlife, Heerbrugg, Switzerland) and stethoscope (Littman Classic II; 3M, Neuss, Germany). An appropriate-sized cuff was placed on the left arm, pulse occlusion pressure was determined, and the cuff was inflated to 20 mmHg above that pressure. Systolic BP (SBP) was defined as the first appearance of sound (Korotkoff phase 1); diastolic BP (DBP), by the disappearance of sound (Korotkoff phase 5). Data were collected as the average of 3 readings, each separated by 2 minutes.

Height and weight were measured with the subject in light clothing and without shoes. WC was measured with a flexible steel tape with the subject standing; the anatomic landmark was midway between the lowest portion of the rib cage and the iliac crest. Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in meters squared).

According to age, sex, and percentiles of height and sex, preHTN was defined as SBP and/or DBP ≥90th <95th percentile, and hypertension was defined as SBP and/or DBP ≥95th percentile. Hypomagnesemia was defined as a serum magnesium concentration <1.8 mg/dL (<0.74 mmol/L).[15] Overweight and obesity were defined by BMI ≥85th <95th percentile and by BMI ≥95th percentile, respectively, according to age and sex.[16]

Whole-blood samples were collected from the antecubital vein, after an overnight fast of 8-10 hours. Serum magnesium was measured by a colorimetric method, with an intra-assay variation of 1.4% and an interassay variation of 1.7%. Serum glucose was measured by the glucose-oxidase method, with an intra-assay variation of 1.8% and an interassay variation of 2.1%. Triglycerides were measured enzymatically, and the HDL-C fraction was obtained after precipitation by a phosphotungstic reagent. The respective intra-assay and interassay coefficients of variation were 1.3% and 1.7% for triglycerides and 1.1% and 1.3% for HDL-C. All laboratory measurements were performed using a clinical chemistry autoanalyzer (A15; BioSystems, Barcelona, Spain).

Statistical Analyses

Differences between the groups were established using the 2-tailed unpaired Student t test for comparison of normally distributed quantitative variables (Mann-Whitney U test for skewed data) and the χ^2 test for categorical variables. One-way ANOVA with the Bonferroni post hoc test was used to compare mean differences among more than 2 groups. The relationships between serum magnesium level and SBP and DBP were estimated using the Pearson correlation test. An adjusted multiple linear regression analysis was conducted to evaluate the associations between serum magnesium level (independent variable) and SBP and DBP (dependent variables). A multivariate logistic conditional forward analysis (adjusted according to the significant variables from the bivariate analysis and by the well-known risk factors for HBP) was performed to evaluate the associations between hypomagnesemia (independent variable) and preHTN and hypertension (dependent variables). A P value <.05 defined the level of statistical significance. Data analyses were performed with SPSS 15.0 (SPSS, Chicago, Illinois).

Results

A total of 3954 children, with an average age of 10.9 ± 2.3 years and without significant sex-based differences ($P = .38$), were enrolled. These children included 851 girls and 922 boys in the 6-10 year age group and 1080 girls and 1101 boys in 11-15 year age group. The study group included 1974 children of normal weight (49.9%), 898 children classified as overweight (22.7%), and 1082 children classified as obese (27.4%).

In the children aged 6-10 years, girls had higher triglyceride levels and lower HDL-C levels than boys, whereas in those aged 11-15 years, boys had higher total cholesterol levels than girls, with no other significant differences by sex (**Table I**). In the total study group, the prevalence of HBP (preHTN plus hypertension) was 21.9%, and that of hypomagnesemia was 24.3%.

The overall prevalence of preHTN was 13.1% (12.2% in the 6-10 year group and 13.9% in the 11-15 year group), and that of hypertension was 8.5% (6.4% in the 6-10 year group and 10.6% in the 11-15 year group). The prevalence of hypomagnesemia was 15.3% in the children aged 6-10 years and 31.6% in those aged 11-15 years. In the 6-10 year age group, hypomagnesemia was identified in 59 children with preHTN (27.3%) and in 52 children with hypertension (45.6%). In the 11-15 year age group, hypomagnesemia was identified in 115 children with preHTN (36.0%) and in 109 children with hypertension (49.6%).

The prevalence of preHTN and hypertension showed an increasing trend in parallel to changes in body weight from normal weight to obesity. In children of normal weight, the prevalence of preHTN was 12.5% in children aged 6-10 years