Hypomagnesemia and mortality in patients with type 2 diabetes

José A. Curiel-García¹, Martha Rodríguez-Morán², Fernando Guerrero-Romero²

¹ General Hospital of the Mexican Social Security Institute at Durango; Av. Normal y Predio Canoas S/N; 34067, Durango, Dgo. Mexico; ² Biomedical Research Unit of the Mexican Social Security Institute, Durango, Mexico, and Research Group on Diabetes and Chronic Illnesses, Durango, Mexico; Canoas 100, 34067 Durango, Dgo., Mexico

Correspondence: F. Guerrero-Romero, MD, PhD, FACP, Siqueiros 225 esq./Castañeda, 34000 Durango, Dgo., Mexico <guerrero_romero@hotmail.com>

Abstract. To evaluate if hypomagnesemia, at the time of admission in the Intensive care Unit (ICU), is associated with a higher mortality in critically ill patients with type 2 diabetes. Fourteen consecutive critically ill patients with type 2 diabetes admitted in the ICU of a teaching General Hospital serving an inner city population were enrolled in a follow-up study. Parenteral or enteral nutritional support, surgical procedures, malignancy, traumatism or physical injury, pulmonary and/or cardiovascular diseases, chronic renal failure, hepatic cirrhosis, cerebrovascular disease, and disorders of the thyroid gland, were exclusion criteria. Hypomagnesemia was defined by serum magnesium levels < 0.66 mmol/L (1.6 mg/dL). At the time of admission in the ICU, 10 (71.4%) individuals had hypomagnesemia. Mortality rates in the hypomagnesemic and normomagnesemic individuals were 80 and 25%, respectively. Serum magnesium levels were significantly lower in the subjects who died (0.51 [0.41, 0.62] mmol/L) compared with those who survived (0.85 [0.65, 1.11], mmol/L), p = 0.01. The logistic regression model adjusted by APACHE II score and hsCRP levels showed that hypomagnesemia is independently associated with mortality (OR 1.9, CI 95% 1.2-14.7). Hypomagnesemia at the time of admission in the ICU seems to be associated with high mortality in critically ill patients with type 2 diabetes.

Key words: hypomagnesemia, diabetes, critical care, mortality

Magnesium, the fourth most common plasma cation and the second intracellular cation [1-3] is normally kept in a narrow range from (0.7 to 1.1 mmol/L) [3]. Magnesium regulates ion channels [4], has a co-enzymatic activity in the reactions concerning ATP [5], exerts a vasodilator effect [6], and plays an important role in neuromuscular transmission [2].

Diabetes has been reported among the most frequent causes for hypomagnesemia [5, 7]. Furthermore, hypomagnesemia is frequently found on admission of critically ill medical patients in the Intensive Care Units (ICU), in whom the incidence of hypomagnesemia varies from 20 to 66% [4, 8-13]. Although hypomagnesemia at the time of admission to ICU has been associated with an increased mortality rate [11, 14, 15], the results are controversial, with some reports showing the absence of association with higher fatality [10, 13]. Magnesium deficiency is a significant predictor for mortality in cardiovascular and hemodialysis patients [16, 17]; however, there are no previous reports about hypomagnesemia and mortality in critically ill patients with type 2 diabetes. Thus, we evaluated the hypothesis that hypomagnesemia, at the time of admission in the ICU, is associated with a higher mortality in critically ill patients with type 2 diabetes.

Materials and methods

Patients

Previously approved by the Mexican Social Security Institute (MSSI) Research Committee and after obtaining informed consent from the family of participants, an observational follow-up study was carried out. Consecutive critically ill patients with
type 2 diabetes who were admitted in the ICU of the teaching General Hospital of the Mexican Social Security Institute at Durango, Mexico, serving an inner city population, were enrolled.

Parenteral or enteral nutritional support, surgical procedures, malignancy, trauma or physical injury, pulmonary and/or cardiovascular diseases, chronic renal failure, hepatic cirrhosis, cerebrovascular disease, and disorders of the thyroid gland, were exclusion criteria. In addition, because using incident outcomes is a well-recognized methodological-design strategy to reduce source of bias, subjects with a history of hypomagnesemia were not included. For this purpose, a detailed and exhaustive clinical and physical examination was performed.

Definitions

Hypomagnesemia was defined as serum magnesium levels < 0.66 mmol/L (1.6 mg/dL) [15].

The Acute Physiology and Chronic Health Evaluation (APACHE) II score was used for estimation of the severity of the medical condition [18]. Specialists assigned to ICU established pharmacological treatment and medical support criteria. The critically ill condition of the patient with type 2 diabetes was defined by the presence of an acute severe complication that impeded maintenance of homeostasis by the patient himself and which was life threatening. The cut-off point of the APACHE II score for defining the critically ill condition was equal to or greater than 20 points. Subjects who, before admission in the ICU, were taking hypoglycemic drugs or receiving insulin therapy were considered as subjects with type 2 diabetes. Trained personnel of the ICU performed the diagnosis of diabetes and classified the critically ill condition.

Assays

Venous whole blood samples, for measurement of serum magnesium and hsCRP, were collected on admission and discharge from the ICU. During their stay in the ICU all patients received insulin treatment for glucose control. Other kinds of hypoglycemic drugs were discontinued. Serum magnesium levels were measured using the colorimetric method; the intra and inter-assay coefficients of variation were 1.0 and 1.5%. Serum glucose levels were determined by the glucose-oxidase method using a Data Pro Plus random access clinical analyzer, Arlington TX, USA.

Statistical analysis

Nominal data are presented as percentages and numerical data by median (25, 75 percentile). Differences between the groups were assessed using the Mann-Whitney U test or the Chi-square test. Multiple logistic regression analysis adjusted by the APACHE II score was used to compute the odds ratio (OR) between hypomagnesemia and mortality. A 95% Confidence interval, and a P value < 0.05 defined the level of statistical significance. Data were analyzed using the statistical package SPSS for Windows 10.0.

Results

Fourteen diabetic patients of 55.5 (35.5, 69) years of age, with systolic and diastolic blood pressures of 90 (90, 111.5) mmHg and 55 (40, 65) mmHg were enrolled. Abdominal sepsis (n = 9), Fournier’s syndrome (n = 3), and Edwin angina (n = 2) were diagnoses of admission in the ICU. Necrotizing cholecystitis or empyema and perforation of the gallbladder were the main sources of abdominal sepsis. The duration of hospitalization in the ICU was 4 (0.4, 14) days, (14 [10, 14] versus 0.5 [0.12, 6], p = 0.003, for the subjects who survived and died, respectively). At discharge, the serum magnesium was measured within the last 12 hours of stay in the ICU in the subjects who survived, and within 12 hours before death in the subjects who died.

At the time of admission in the ICU, the APACHE II score, fasting glucose, hsCRP, and serum magnesium levels, were 26 (25, 29), 7.7 (5.4, 13.0) mmol/L, 24.9 (14.6, 27.7) mg/dL, and 0.55 (0.42, 0.66) mmol/L, respectively; a total of 10 (71.4%) individuals had hypomagnesemia.

The general mortality rate was 64.3%. The mortality rates in the hypomagnesemic and normomagnesemic individuals were 80 and 25%, respectively. At the time of admission in the ICU, the subjects who died and survived had comparable APACHE II scores (27 [26-29] versus 26 [25-29], p= 0.09) and hsCRP levels (25.8 [17.2, 28] versus 20.4 [10.8, 30.5] mg/dL, p = 0.61). However, serum magnesium levels were significantly lower in the subjects who died (0.51 [0.41, 0.62] mmol/L) compared with those who survived (0.85 [0.65, 1.11], mmol/L), p = 0.01.

Throughout their stay in the ICU, individuals who survived significantly improved their serum magnesium (p = 0.03) and hsCRP (p = 0.04) levels (figure 1).

The logistic regression model adjusted by the APACHE II score and hsCRP levels showed that
Hypomagnesemia (OR 1.9, CI95% 1.2-14.7) is independently associated with mortality.

Discussion

No previous studies exist to evaluate the association between low serum magnesium levels, on admission in the ICU, and mortality among critically ill patients with type 2 diabetes. Our finding shows a high percentage of subjects with hypomagnesemia at the time of admission in the ICU. This percentage, higher than previously reported in medical critically ill patients [4, 8-13], might be explained by taking into account that hypomagnesemia is a common finding in both critically ill patients and subjects with type 2 diabetes [7, 13]. Thus, routine determination of serum magnesium concentrations appears recommendable because of its significance for the prognosis and treatment of diabetic individuals admitted in the ICU. Furthermore, our results showed that the death rate was three times as high for the group with hypomagnesemia on admission as for the normomagnesemic group with equivalent APACHE II scores; a finding similar to previous reports in non-diabetic critically ill patients [11, 14, 15]. In addition, our results showed that subjects who died did not improve their serum magnesium levels during their stay in the ICU, a finding that supports the hypothesis that hypomagnesemia is associated with a worse prognosis.

Furthermore, it has been reported that patients with high hsCRP levels at ICU admission had more severe organ dysfunction and higher mortality rates [19], highlighting that a decrease in CRP level after 48 h is associated with a lower mortality rate, compared with subjects who do not improve their hsCRP concentration [19]. In agreement with previous reports; in this study, although the subjects showed elevated hsCRP levels at baseline, the survivors significantly decreased their hsCRP concentration. Recently, we reported a strong positive association between low serum magnesium levels and chronic inflammatory responses, a finding that suggests that hypomagnesemia and low-grade inflammation are interactive risk factors [20, 21].

The limitations of our study that should be mentioned are: First, measurement of magnesium was limited to the serum compartment. Because magnesium deficiency can exist even when magnesemia is normal [1, 22], misclassification of subjects with hypomagnesemia could be a source of bias. However, in this study, hypomagnesemic subjects had severe hypomagnesemia, a condition that is most often associated with a true depletion of magnesium in the organism [1]. Furthermore, it has been reported that insulin treatment, which was used in all the patients in this study, is associated with worsening of the intracellular magnesium status [22]. Second, the small sample size could be a limitation for the analysis of data; however, it had enough power to show a significant association between hypomagnesemia and mortality.

Conclusions

Hypomagnesemia detected at the time of admission in the ICU is associated with an increased mortality in critically ill patients with type 2 diabetes.
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