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Paul Fein, Venkata Suda, Cezary Borawsky, Hitesh Kapupara, Anastasya Butikis, Betty Matza, Jyotiprakas Chattopadhyay, Morrell M. Avram

Relationship of Serum Magnesium to Body Composition and Inflammation in Peritoneal Dialysis Patients

Magnesium is one of the most abundant cations in the body and is involved in many cell functions. Serum magnesium concentration is maintained within a narrow range by the kidney and digestive tract. It has been reported that a lower serum magnesium level is a significant predictor for mortality in hemodialysis patients. Body composition and inflammation are important predictors of mortality in peritoneal dialysis (PD) patients. The objective of the present study was to examine the relationship of serum magnesium with body composition and inflammation in PD patients. Our study enrolled 62 PD patients treated at the Long Island College Hospital between November 2000 and July 2008. Demographic, clinical, and biochemical data were recorded. Body composition parameters were determined by bioelectrical impedance analysis (BIA). High sensitivity C-reactive protein (hs-CRP), a marker of inflammation was measured by the immunoturbidimetric method.

In these patients (mean age: 55 years; 63% African American; 55% women; 25% with diabetes), the mean (± standard deviation) serum magnesium and hs-CRP were 1.597 ± 0.28 mEq/L and 13.70 ± 21 mg/L respectively. Serum magnesium was directly correlated with serum markers of nutrition: albumin ($r = 0.42, p = 0.001$), creatinine ($r = 0.43, p = 0.0001$), and total protein ($r = 0.44, p < 0.0001$). Serum magnesium was also directly correlated with phase angle, a BIA parameter and marker of cellular health (correlation coefficient: $r = 0.35; p = 0.006$), and inversely correlated with the extracellular mass/body cell mass ratio ($r = -0.34, p = 0.008$), a highly sensitive marker of malnutrition. We observed an inverse correlation between serum magnesium and hs-CRP ($r = -0.37, p = 0.02$) in PD patients.

In conclusion, lower serum magnesium is associated with poorer nutrition status, deteriorating cellular health, and increased inflammation, which may contribute to the increased risk of mortality in PD patients.

Key words
Magnesium, bioelectrical impedance analysis, BIA, inflammation, nutrition

Introduction
Despite improvements in dialysis technology and survival rates since 2000, the current mortality rate of peritoneal dialysis (PD) patients remains high. Identification of various risk factors and aggressive risk factor modification are important strategies to improve outcomes in these patients. Malnutrition and inflammation are important contributors to morbidity and mortality in PD patients (1,2).

In dialysis patients, body composition is closely related to nutrition indicators and chronic illnesses (3). Bioelectrical impedance analysis (BIA) has been recognized as a simple, noninvasive technique for the determination of body composition and fluid status in dialysis patients (4). We and others have investigated the relationship of BIA-derived body composition parameters with markers of nutrition and with morbidity and mortality in PD patients (5,6).

Magnesium is the fourth most abundant cation in the body, a cofactor for enzymatic reactions involved in many cell functions central to cellular homeostasis. Serum magnesium is maintained within a narrow range by the kidney and digestive tract. Studies, including those in animal models, have shown that hypomagnesemia is associated with increased levels
of high-sensitivity C-reactive protein (hs-CRP), circulating endothelin, and cytokines, which are indicative of a generalized inflammatory state (7,8). The relationship of serum magnesium with body composition and inflammation has not been studied in PD patients.

**Patients and methods**

Our study enrolled 62 PD patients treated at Atlantic Peritoneal Dialysis unit at the Long Island College Hospital between November 2000 and July 2008. Upon approval of the study protocol by the institutional review board, informed consent was obtained from each study patient. On enrollment, demographic, clinical, and biochemical data were recorded. The concentration of magnesium in the dialysate was 0.5 mEq/L. Patients were followed to February 2010.

**Laboratory analyses**

The BIA measurements were obtained using an impedance plethysmograph (800 mA, 50 kHz). The electrical impedance values, resistance, and reactance for the patients were used in a computerized calculation [Cyprus version 1.0 (BIA-101: RJL/Akern Systems, Clinton Township, MI, U.S.A.]) of body composition parameters, including extracellular mass (ECM) and body cell mass (BCM). In a subgroup of 41 patients, hs-CRP, a marker of inflammation, was measured by the immunoturbidimetric method.

**Statistical analyses**

Continuous variables are expressed as mean ± standard deviation. For selected comparisons between group means, a parametric ($t$-test) or nonparametric (Mann–Whitney test) test was used. Correlations are reported as either a Pearson correlation coefficient or a Spearman rank correlation coefficient. Calculations were performed using SPSS for Windows (version 12.0.1: SPSS, Chicago, IL, U.S.A.).

**Results**

**Demographics and patient characteristics**

The mean age of the patients was 55 ± 16 years. Most (63%) were African American, 55% were women, and 25% had diabetes. Mean time on dialysis at enrollment was 46 ± 44 months.

In this group, mean serum magnesium was 1.597 ± 0.28 mEq/L (range: 0.8 – 2.10 mEq/L). A lower than normal serum magnesium level (<1.3 mEq/L) was seen in 6 patients (9.7%). At enrollment, mean serum albumin, creatinine, total protein, and hs-CRP were $3.71 ± 0.59$ g/dL, $11.38 ± 4.2$ mg/dL, $7.30 ± 0.75$ g/dL, and $13.70 ± 21$ mg/L respectively. Mean phase angle was $6.06 ± 1.6$ degrees, and mean ECM/BCM ratio was $1.21 ± 0.2$.

Serum magnesium was directly correlated with serum markers of nutrition: albumin ($r = 0.42, p = 0.001$), creatinine ($r = 0.43, p = 0.0001$), and total protein ($r = 0.44, p < 0.0001$). Serum magnesium was also directly correlated with phase angle ($r = 0.35, p = 0.006$), a BIA parameter and marker of cellular health, and inversely correlated with ECM/BCM ratio ($r = –0.34, p = 0.008$), a highly sensitive marker of nutrition. We also observed an inverse correlation between serum magnesium and hs-CRP ($r = –0.37, p = 0.02$; Table I).

**Discussion**

In this study, we showed that a lower level of serum magnesium in PD patients is associated with poorer nutrition status and cellular health and increased inflammation. To our knowledge, no information is available in the literature about the relationship of serum magnesium to body composition and inflammation in PD patients.

Malnutrition is highly prevalent in PD patients. It is well established that serum levels of markers of nutrition such as albumin, creatinine, and prealbumin are lower in malnourished patients, and that lower levels of these markers are associated with increased mortality in those patients (1,9–11). Serum albumin is widely used as a marker of nutrition in dialysis patients. Serum creatinine is a marker of somatic protein stores. Direct correlations between serum magnesium and markers of nutrition such albumin, creatinine, and total protein indicate an association between magnesium and nutrition status in PD patients. It has been reported that 25% of total serum magnesium is bound to albumin and 8% to globulins (12). Some of the observed correlations of magnesium with albumin and total protein may be a result of magnesium binding to proteins.

We used BIA analysis to study the relationship of serum magnesium to body composition. The ECM/BCM ratio, the relationship between intracellular and extracellular space, has been reported to be one of the most sensitive indexes of malnutrition (13). The higher the ECM/BCM ratio, the poorer the nutrition status. A lower level of serum magnesium is associated with a
higher ECM/BCM ratio— that is, a poorer nutrition status. The direct relationship between serum magnesium and phase angle, an indicator of cellular health and integrity, may reflect the importance of maintaining a physiologically normal level of serum magnesium in PD patients.

One of the interesting findings in the present study is the association of lower levels of serum magnesium with increased inflammation as determined by hs-CRP. It has been reported that, in hemodialysis (HD) patients, hypomagnesemia is a risk factor for subclinical inflammation, as demonstrated by elevated levels of hs-CRP (7). In non-dialysis patients, magnesium depletion is independently associated with elevated hs-CRP, suggesting that hypomagnesemia and low-grade inflammation are interactive risk factors (14). In heart-failure patients, oral magnesium supplementation significantly attenuates blood levels of CRP (15). In postmenopausal women, high magnesium intake is associated with lower concentrations of certain markers of systemic inflammation and endothelial dysfunction (16).

Deficiency of serum magnesium has been reported in HD and PD patients alike (17). In PD patients, the PD solution affects serum levels of magnesium. Commercially available PD solutions contain either 0.5 mEq/L or 1.5 mEq/L magnesium. Our PD patients have been dialyzed with a PD solution containing magnesium 0.5 mEq/L. Hypomagnesemia itself is an important contributor to morbidity and mortality by its various metabolic activities. It has been reported that a lower serum magnesium level is a significant predictor for mortality in HD patients (18). Chronic deficiency is associated with multifocal cellular necrosis, accumulation of intracellular calcium, increased platelet aggregation, coronary vasoconstriction, atherogenesis, and cardiac arrhythmia (19). Magnesium protects against the deleterious effects of reactive oxygen species and inhibits the calcium overload that occurs after reperfusion. There may be a benefit in increasing the magnesium level in the dialysis solution or in giving supplemental magnesium to patients. Routine measurement of serum magnesium concentration is recommended.

Conclusions
Lower serum magnesium is associated with poorer nutrition status and cellular health and with increased inflammation, which may contribute to the increased risk of mortality seen in PD patients. Serum magnesium concentration should be routinely monitored. Factors affecting serum magnesium concentration, including dietary magnesium intake and supplementation, should be investigated in terms of better survival for PD patients.

References


Corresponding author:
Paul A. Fein, MD, Avram Division of Nephrology, Long Island College Hospital, 339 Hicks Street, Brooklyn, NY 11201 U.S.A.
E-mail: pafmd@juno.com