Serum Magnesium Concentration Is a Significant Predictor of Mortality in Peritoneal Dialysis Patients

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We previously reported that lower serum magnesium is associated with poorer nutrition status, impaired cellular health, and increased inflammation in peritoneal dialysis (PD) patients. The present study was designed to investigate the prognostic value of serum magnesium for mortality in PD patients.

From November 2000 to July 2008, the study enrolled 62 patients, recording their demographic, clinical, and biochemical data. Patients were followed to September 2011. Mean age of the patients was 55 ± 16 years, and in this cohort, 55% were women, 63% were African American, and 25% had diabetes. Mean serum magnesium was 1.597 ± 0.28 mEq/L. Maximum follow-up was 10.8 years. During the follow-up period, 27 patients died (43.5%). Serum magnesium was significantly higher in the patients who survived than in those who did not (1.757 mEq/L vs. 1.515 mEq/L, p = *0.04).*

*Patients were then stratified by enrollment magnesium. After 10.8 years of observation, cumulative survival was significantly better in patients with an enrollment serum magnesium greater than 1.6 mEq/L than in patients with an enrollment serum magnesium of 1.6 mEq/L or less (*p = *0.04). Multivariate Cox regression analysis revealed that serum magnesium is a significant predictor of mortality (relative risk: 0.984;* p = *0.048) after adjusting for age, race, sex, diabetes, and months on dialysis at enrollment.*

In conclusion, lower serum magnesium is a significant predictor of higher mortality in PD patients. Factors affecting the serum magnesium concentration in PD patients should be investigated in more detail.

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Key words
Magnesium, mortality, nutrition

Introduction

Magnesium is the 4th most common cation in the body, a cofactor for enzymatic reactions involved in many functions central to cellular homeostasis. Studies have indicated that magnesium deficiency is associated with various clinical disorders including diabetes, hypertension, coronary artery disease, and osteoporosis (1,2). Magnesium deficiency has been implicated in various cardiovascular disturbances (3,4). Magnesium depletion is independently associated with elevated serum high-sensitivity C-reactive protein, suggesting that hypomagnesemia and low-grade inflammation are interactive risk factors (5).

In healthy populations, serum magnesium is maintained in the normal concentration range by the kidneys, the gastrointestinal tract, and bone. Hypomagnesemia has been reported both in hemodialysis (HD) and peritoneal dialysis (PD) patients (6,7), but the literature contains few reports about the relationship between serum magnesium and comorbidities in dialysis patients (8–10). In HD patients, hypomagnesemia has been reported to be associated with increased serum levels of high-sensitivity C-reactive protein (11). We recently reported that lower serum magnesium in PD patients is associated with poorer nutrition status, impaired cellular health, and increased inflammation (12). Lower serum magnesium has been reported to be a significant predictor of mortality in HD patients (13). The relationship between serum magnesium and mortality has never been studied in PD patients.

Methods

The present study enrolled 62 PD patients treated at 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 the study patients. Patients were followed until September 2011. On enrollment, demographics and clinical and biochemical data for the patients were recorded. The concentration of magnesium in the dialysates used by this population was 0.5 mEq/L. All serum magnesium values were corrected for serum albumin using this formula (14):

$$\text{Albumin-corrected magnesium} = \text{magnesium} + 0.005\,(40 - \text{albumin}),$$

where magnesium is expressed in millimoles per liter, and albumin is expressed in grams per liter. The resulting magnesium values were converted to milliequivalents per liter.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation. For selected comparisons between group means, parametric (t-test) or nonparametric tests (Mann–Whitney test) were used. Observed survival was plotted using the Kaplan–Meier method (15). The log-rank test was used to assess differences between the survival curves. Independent predictors of survival were determined by Cox regression analysis. Calculations were performed using the SPSS software application (version 12.0.1 for Windows: SPSS, Chicago, IL, U.S.A.).

Results

Mean age of the patients was 55 ± 16 years. In this cohort, 55% were women, 63% were African American, and 25% had diabetes. Mean dialysis vintage at enrollment was 46 ± 44 months. At enrollment, mean serum magnesium and albumin-corrected magnesium were 1.597 ± 0.28 mEq/L and 1.626 ± 0.26 mEq/L respectively.

During the study period, 27 patients died (43.5%). Serum magnesium (1.515 mEq/L vs. 1.757 mEq/L, $p = 0.04$) and albumin-corrected serum magnesium (1.579 mEq/L vs. 1.754 mEq/L, $p = 0.035$) were significantly lower in the patients who died than in those who survived.

Patients were followed for up to a maximum of 10.8 years. After the patients were stratified by mean enrollment serum magnesium, cumulative survival (Kaplan–Meier) was observed to be significantly better in patients with an enrollment serum magnesium greater than 1.6 mEq/L than in patients with an enrollment serum magnesium of 1.6 mEq/L or less ($p = 0.04$, Figure 1).

By univariate Cox regression analysis, serum magnesium was a significant predictor of mortality [relative risk (RR): 0.142; $p = 0.009$]. Independent predictors of mortality were identified using multivariate Cox regression analysis. Adjusting for age, sex, race, diabetes, and enrollment dialysis vintage, serum magnesium was an independent predictor of mortality (RR: 0.984; $p = 0.048$). Other significant predictors of mortality were age (RR: 1.045; $p = 0.012$) and dialysis vintage at enrollment (RR: 1.015; $p = 0.002$; Table I).

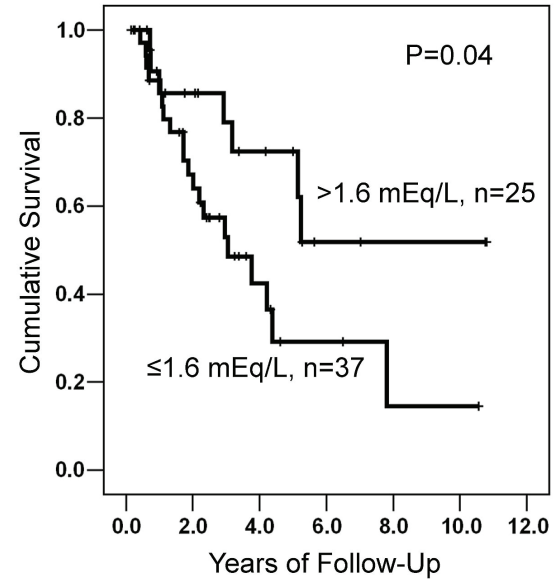

FIGURE 1 Observed survival (Kaplan–Meier) in peritoneal dialysis patients by serum magnesium at enrollment.

TABLE I Independent predictors of mortality in peritoneal dialysis, by multivariate Cox regression analysis

Variable	*Relative risk*	p *Value*
Age (years)	1.045	0.012
Sex (men vs. women)	1.98	0.12
Race (other vs. African American)	1.58	0.31
Diabetes (yes vs. no)	1.89	0.21
Dialysis vintage at enrollment (months)	1.015	0.002
Serum magnesium (mEq/L)	0.984	0.048

Discussion

The present study shows that serum magnesium is an independent predictor of all-cause mortality in PD patients, independent of demographic and clinical parameters. To our knowledge, the literature contains no information about the relationship between serum magnesium and mortality in PD patients. It is interesting to note that, in our study, even the single measurement of enrollment serum magnesium was an independent predictor of mortality in PD patients. Ishimura *et al.* (13) reported that lower serum magnesium concentration is a significant predictor of mortality in HD patients.

Several mechanisms might be involved in the increased mortality risk associated with a lower level of serum magnesium. We previously reported that lower serum magnesium is associated with poorer nutrition status, deteriorating cellular health, and increased inflammation, which might contribute to an increased risk of mortality in PD patients (12). Malnutrition and inflammation are highly prevalent and important contributory factors to the higher mortality risk in PD patients (16,17). Lower levels of serum magnesium have been reported to be associated with an increased risk of cardiovascular and non-cardiovascular mortality in HD patients (18). In such patients, hypomagnesemia has been reported to be associated with increased inflammation (11). It was recently reported that serum magnesium might affect clinical outcomes by directly modifying the bioactivity of the adipose tissue–derived protein adiponectin (19).

Conclusions

Enrollment serum magnesium is a strong independent predictor of mortality in PD patients. Serum magnesium concentration should routinely be monitored. Factors that contribute to lower a serum magnesium concentration (such as dietary intake and dialysate concentration) should be thoroughly studied. The current dialysate magnesium concentration is 0.5 mEq/L. To prevent magnesium depletion, a higher concentration should be considered.

Disclosures

All authors declare that no financial conflict of interest exists.

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