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The relationship between serum magnesium and bioelectrical impedance variables in patients undergoing dialysis

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ABSTRACT

Introduction: The relationship between serum magnesium (Mg) levels with body composition or clinical outcomes of incident dialysis patients remains unclear.
Objectives: The aim of this study was to evaluate the possible correlations between Mg and bioelectrical impedance variables, a method of determining body composition in two groups of hemodialysis (HD) and peritoneal dialysis (PD) patients.
Patients and Methods: This prospective observational study examined the relationships between serum Mg levels and bio-impedance variables including total body fat, body cell mass, extracellular mass, total body water (TBW), intra- and extracellular water (ICW and ECW), ECW/ICW and phase angle (PA) in incident 38 HD and 34 PD patients. The study was conducted in December of 2012 in Mashhad Imam Reza's hospital dialysis center. The correlation between Mg and bio-impedance variables was assessed by applying the student *t* test and Pearson's correlation coefficient.
Results: The average concentration of serum Mg was 1.22 mmol/L in HD patients and 1.20 mmol/L in PD patients which is well above the reference range in normal population. The average amount of body water and also ICW in patients were significantly higher than HD patients. There was no significant relation between serum Mg and bioelectrical impedance variables in HD patients. However, in PD patients, a statistically positive significant correlation was found between serum Mg and ECW ($r = 0.48$, $P = 0.02$) and ECW/ICW ($r = 0.43$, $P = 0.02$) while there was a negative significant correlation between ICW and serum Mg ($r =- 0.48$, $P = 0.02$).
Conclusion: We found a link between serum Mg level and intravascular and extravascular water content in PD patients; however we cannot prove any correlation between serum Mg level and bio-impedance variables in such patients. This could be considered as a sign of Mg role in healthy cell function in PD patients.

Original

Implication for health policy/practice/research/medical education:
In a study on 69 patients who were on hemodialysis (HD) and peritoneal dialysis (PD), we observed no significant relation between magnesium and bioelectrical impedance variables in HD patients. However, in PD patients, a statistically significant correlation was found between serum magnesium levels and extracellular water (ECW), intra-cellular water (ICW), and also ECW/ICW.

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Introduction

Magnesium (Mg) is an important cation in the body that is balanced by its intake and excretion. As Mg has an important effect on cellular physiology, low level of Mg is a significant predictor of mortality in patients undergoing dialysis (1). Intracellular Mg forms an important complex with ATP and it is an important cofactor for numerous enzymatic reactions, transmitters, and synthesis of proteins necessary for normal cell function and energy metabolism (2). It is also involved in multiple processes and as co-enzyme in a variety of processes (3). The kidney has an important role in Mg balance and, although the renal handling of Mg is powerfully adaptable, this ability deteriorates when renal function tends to decrease significantly. The kidneys are fundamental in the maintenance of normal serum Mg concentrations. In chronic kidney disease (CKD) and end-stage renal disease (ESRD), the ability of the kidneys to regulate Mg levels properly declines (4).

Bio-impedance analysis (BIA) is a method that is largely used to determine body composition because of its low cost and ease of working. Studies suggest BIA has good reliability as compared to other applicable methods of body composition analysis (5). Previous evidence emphasized also emphasize that BIA-derived variables (reactance and phase angle) predict clinical outcomes in chronic hemodialysis (HD) patients. Of note, BIA is of a promising objective assessment and monitoring hydration and nutritional status, long-term follow-up, tailor nutrition support, and detect early subtle losses of LBM (lean body mass) in people with CKD receiving dialysis treatment (6). The phase angel (PA) in alternating electric current is the angle between the voltage and current curves. While low PA shows cell death or dysfunction, high values represent healthy cell membranes of all body cells (7). Mg is known to be associated with several factors such as endothelial dysfunction, atherosclerosis, thrombosis and hypertension (8). Few previous studies addressed the association between subclinical inflammation and hypomagnesaemia among dialysis patients (8).There is still very little information, in which the relationship between Mg and body composition was investigated in patients receiving dialysis.

Objectives

To our knowledge, no information is available in the literature about the relationship of serum Mg to body composition in patients receiving dialysis. The aim of this study was to determine the possible correlations between Mg and bio-electrical impedance variables, a method of determining body composition in two groups of HD and peritoneal dialysis (PD) patients.

Patients and Methods

Study population

We performed this cross-sectional study on HD and PD patients in Mashhad Imam Reza hospital dialysis center in 2012. All our cases were on regular three times a week dialysis schedule for at least three months and had stable condition over the two last months. In our sample population there were also a number of patients who were on intravenous iron, erythropoietin, folic acid and vitamin B-complex therapy due to medical indications.

For more accuracy, patients who were hospitalized over the two last months, and who had congestive heart failure, malignancy or pace maker, febrile patients, patients who had diarrhea or active infectious disease or had used diuretics were excluded.

In all patients, Mg and other biochemical variables including albumin, hematocrit were measured by accurate routine laboratory methods. Blood samples were taken via patients' brachial vain before starting the dialysis session. We obtained the total body fat, body cell mass, extracellular mass, total body water (TBW), intra- and extracellular water (ICW and ECW), ECW/ICW and phase angle, by means of bio-impedance analyzer model 619 made by Maltron company. All bio-impedance variables were evaluated in the morning before and two hours right after the mid-week HD session. In PD patients it was done after efflux of dialysate.

Ethical issues

The study followed the tenets of the Declaration of Helsinki. The institutional ethical committee at Mashhad University of Medical Sciences approved all study protocols. Accordingly informed consent was taken from all patients before any intervention. This study was supported by a research project, as an internal medicine residency dissertation by Zahra Ataee in Mashhad University of Medical Sciences (Thesis# 2662).

Statistical analysis

We calculated the average and standard deviation for each bio-impedance variable in both HD and PD groups. The relation between patients' serum Mg and bio-impedance variables performed by applying the student test and Pearson's correlation coefficient. We used SPSS program for statistical analysis. *P* value was considered less than 0.05.

Results

The study population consisted of 69 patients who were on HD or PD in Mashhad Imam Reza hospital. Out of 69 patients, 38 patients (55.1%) were on HD and 31 patients (%44.9) were on PD. In terms of gender distribution, 15(39.5%) and 9 (29%) of our patients were in HD and PD groups, respectively, while it was 23(60.5%) and 22 (70.9%) for females, respectively. The male to female ratio in patients on HD and PD were almost equal (P=0.365). In addition, there was no significant difference in terms of hematocrit, albumin and Mg levels between the two groups (Table 1).

Table 1. Average distribution of dialysis vintage, hematocrit, albumin, Mg and bio-electrical impedance variables in both patient groups

Variable	Patient group			*P* value
	HD patients	PD patients	Total	
	Mean ± SD	Mean ± SD	Mean ± SD	
Dialysis vintage	46.34 ± 48.33	26.16 ± 24.46	37.28 ± 40.46	0.02
Hematocrit (%)	34.85 ± 5.60	35.97 ± 5.00	35.35 ± 5.34	0.40
Albumin (g/dL)	4.36 ± 1.05	4.16 ± 0.63	4.27 ± 0.88	0.37
Mg (mmol/l)	1.22 ± 0.41	1.20 ± 0.28	1.21 ± 0.35	0.85
Lean body mass (kg)	69.93 ± 8.33	66.50 ± 15.73	68.39 ± 12.24	0.25
Body fat (kg)	30.06 ± 8.33	30.27 ± 11.25	30.15 ± 9.68	0.93
Whole body water (L)	51.66 ± 5.63	53.04 ± 9.89	52.28 ± 7.80	0.47
ECW (L)	45.40 ± 7.35	38.21 ± 7.61	42.17 ± 8.24	≤0.001
ICW (L)	54.58 ± 7.35	61.77 ± 7.61	57.81 ± 8.24	≤0.001
Body cell mass (kg)	38.26 ± 4.40	39.05 ± 4.53	38.62 ± 4.44	0.47
Extracellular mass (kg)	32.55 ± 5.99	30.09 ± 6.29	31.45 ± 6.20	0.10

Our data also showed that the average amount of ECW, body cellular mass and extracellular body mass were similar in both groups while the average of whole body water and ICW in PD patients were significantly more than that of HD patients (Table 1).

In HD patients group, there was no significant statistical correlation between serum Mg level and bio-electrical impedance variables including; phase angle, LBM, body fat, whole body water, ICW, ECW, ECW /ICW, body cellular mass and extracellular mass according to the Pearson's correlation coefficient (Table 2).

In PD group, no significant statistical correlation was found between serum Mg level and phase angle, LBM, body fat, whole body water, ICW, ECW, body cellular mass and extracellular mass; However, Pearson's correlation coefficient showed a significant statistical correlation between serum Mg level and ECW and ECW/ICW (Table 2).

Figure 1 shows scattered curve of relation between Mg and extracellular fluid in both HD and PD patients. The graph illustrates the significant relation between Mg and extracellular water in the PD group.

Figure 2 indicates the scattered curve of relation between Mg and intracellular fluid in HD and PD patients. The significant correlation between Mg and the variable is shown in the PD group.

Discussion

Our results showed that the average concentration of serum Mg was slightly higher than normal range and the average amount of body water and also intracellular water in PD patients was significantly higher than HD patients. Our study data also showed a considerable relation between serum Mg and intra- and extracellular fluid only in PD patients in comparison to HD patients. In our study, the average concentration of serum Mg was 1.22 mmol/L in HD patients and 1.20 mmol/L in PD patients which is well above the reference range in normal population (typically 0.70–1.00 mmol/L). In patients undergoing HD and PD, the concentration of both ionized and total Mg were often slightly evaluated higher than normal range and have been shown to be dependent on residual renal function, dietary or pharmacological intake and elimination by dialysis (9). We observed that the average amount of body water and also intracellular water in PD patients were significantly higher than HD patients. In patients undergoing PD, the fluid change in each body segment is different in response to PD fluid exchange (10). Moreover, in PD patients, fat-free and body cell mass was better preserved and is correlated with factors

Table 2. Average distribution of bio-electrical impedance variables in both patient groups

Variable	Patient group					
	HD patients		PD patients		Total	
	R	*P* value	R	*P* value	R	*P* value
Phase angle	0.05	0.79	0.20	0.28	0.11	0.40
Lean body mass	0.01	0.95	0.02	0.91	0.002	0.99
Fat	0.01	0.95	0.12	0.52	0.05	0.65
Whole body water	0.09	0.58	0.12	0.51	0.09	0.44
ECW	0.024	0.88	0.48	0.02	0.15	0.20
ICW	0.02	0.885	-0.48	0.02	0.16	0.20
ECW/ICW	0.08	0.65	0.43	0.02	0.19	0.12
Body cellular mass	0.06	0.72	0.01	0.94	0.04	0.72
Extracellular mass	0.14	0.41	0.19	0.31	0.22	0.22

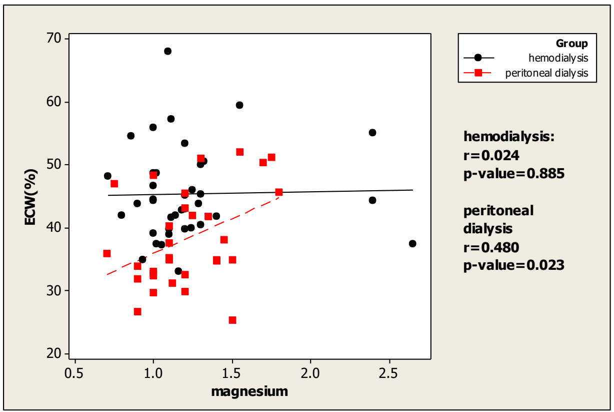

Figure 1. Relationship between Mg (mmol/L) and extracellular fluid in both study groups.

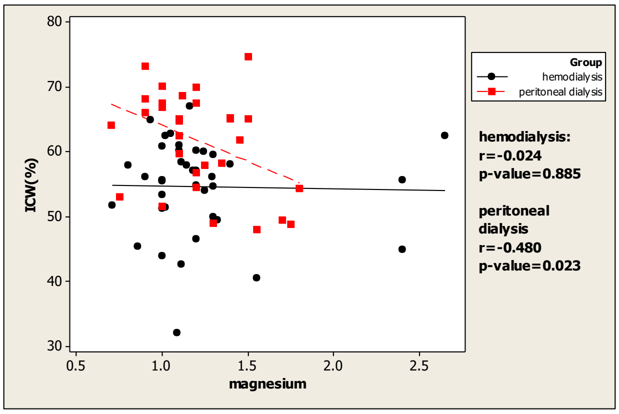

Figure 2. Relationship between Mg (mmol/L) and intracellular fluid in both study groups.

including dialysis modality and also malnutrition which can affect serum albumin concentrations (10). Volume overload is a common problem in HD or PD patients. In volume overloaded patients, the extra water represents a part of lean mass instead of demonstrating this as a third body component (10). In HD patients, body weight loss due to water reduction exclusively occurs in fat-free and body cell mass compartments, while no changes in fat mass are observed (10). In contrast, excess water in HD patients is proportionally distributed among three studied compartments (10). In the current study, it could result that the differences observed in two groups of dialysis patients are mostly due to the higher degree of volume overload in PD comparing to HD patients.

Our study data also showed a considerable relation between serum Mg and intra- and extracellular fluid in PD patients; however, we could not find any relation between the level of this ion and bio-electrical impedance variables in HD patients. Extracellular mass (ECM) is metabolically inactive, whereas body cell mass (BCM) is metabolically active tissues of the body (11). Based on Rymarrz et al study, a correlation was detected between serum Mg concentration and total intracellular erythrocyte Mg concentration while the level of Mg concentration in mononuclear white cells was not related to serum Mg level, therefore should not be considered as an index of Mg overload (11). The distribution of fluid between ECF and ICF is a primary determinant of body resistance. Therefore, BIA equations developed in normal-weight individuals, have raised doubts about the ability of these methods to assess body water compartments in obese individuals or during the severe reduction in body mass that occurs due to their abnormal fluid distribution (12), that vary in their ability to accurately quantify the body compartments in obese individuals.

Recent reports have indicated that volume overload, low lean tissue index, and low fat tissue index measured via body composition monitors, were related to high mortality rates in dialysis patients (13). While there was a relationship between serum Mg level and body composition parameters in PD patients, no similar relationship has been recognized in HD patients (13).

A sufficient amount of serum Mg seems to be necessary for cell functions such as membrane excitability, contractility as well as metabolism; hence this key element is necessary for maintaining healthy muscle function and physical performances (1). In addition, phase angle (PhA) has a prognostic value that can indicate either cell death or malnutrition, which are determined by changes in cellular membrane integrity (7). A great number of studies have shown a strong tie between PhA which is determined by bioelectrical impedance measurement methods and nutritional condition as well as its impact on dialysis patient survival (6,7,14). According to our results, there was no statistically significant relationship between PhA and Mg levels, as a nutritional status index in both PD and HD patients. Despite the utility of phase angle as a tool for the assessment of the nutritional status of patients, all studies do not support the phase angle as an appropriate indicator of disease-related malnutrition (14,15). In the study by Fein et al, a direct relationship was found between serum Mg and phase angle. This reflects that normal level of Mg plays an important role in these patients (16). Additionally, there was a correlation between serum Mg and phase angle, but its correlation with the extracellular mass/body cell mass ratio, a highly sensitive marker of malnutrition, was inverted (17). In another study on non-dialysis athletes there was a positive association between changes in serum and RBC Mg level and PhA (18). Among non-dialysis women with increased total fat mass, total Mg serum concentration was significantly lower compared to women with normal body composition (19). Previous studies mostly evaluated correlations between serum Mg and BIA variables in hypomagnesemic dialysis patients. However, in our research we did not divide patients into subgroups including hypomagnesemia and this can explain discrepancy between our study and previous ones.

Conclusion

In conclusion, within the scope of body composition assessment, our results highlight a link between serum Mg level and intravascular and extravascular water content in PD patients. However, we could not prove any correlation between serum Mg level and bio-impedance variables in HD patients.

Limitations of the study

The results of our bio-impedance analysis may be affected by study design including the relatively small number of patients, all possible confounding factors and the length of the study.

Authors' contribution

AZ, FS and ZA were the principal investigators of the study. MH was included in preparing the concept and design. MS, KS and TZ revisited the manuscript and critically evaluated the intellectual contents. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

Conflicts of interest

The authors declare no conflict of financial interest.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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