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A study on the correlation of serum magnesium with intima-media thickness of carotid in hemodialysis patients

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ABSTRACT

Introduction: Atherosclerosis progression in the patients suffering from end-stage renal disease (ESRD) is more than normal population. Magnesium levels are also associated with an increase in atherosclerosis in the common carotid artery. Intima-media carotid calcification is either directly or indirectly related to cardiovascular disease and a higher rate of death among patients with chronic renal failure.**Objectives:** The purpose of the present study was to evaluate the protective role of serum magnesium levels in vascular calcification and the improvement of the carotid intima-media thickness (CIMT).**Patients and Methods:** In this cross-sectional research, the participants were selected from all patients with ESRD in Five Azar Medical Center of Gorgan, Iran. Blood samples collected from research units were tested for serum magnesium level in three times. Patients were referred to a radiologist to measure CIMT. Data collected in all patients were evaluated based on Spearman's correlation test.**Results:** The correlation between serum magnesium level and CIMT was not statistically significant ($P=0.66$ $r=0.04$), however a positive correlation between CIMT and the dialysis adequacy (KT/V) was detected ($r=0.306$, $P=0.006$).**Conclusion:** This study demonstrated no correlation between the serum magnesium level and the CIMT in hemodialysis patients.

Implication for health policy/practice/research/medical education:

Changes in serum magnesium (Mg) may affect some clinical features of patients on maintenance hemodialysis (HD). In HD patients, lower magnesium levels were reported to be associated with increased atherosclerosis of the common carotid artery. So we conducted this study to assess the hypothesis that serum magnesium level of the HD patients can be related to carotid intima media thickness; as the consequences have not been clearly recognized in the Iranian people. It would be useful to provide some clinical recommendations for the prediction of CVD and implement prevention programs for high-risk hemodialysis patients.

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Introduction

About 2 million people worldwide reach the end-stage renal disease each year, increasing by about 5% annually. The most important cardiac complications in hemodialysis patients are structural and functional impairment of left ventricle, atherosclerosis and ischemic heart disease, and congestive heart failure (1-4). Magnesium is the second most abundant cation inside the cell, with the vital function to regulate vascular tone and heart rhythm. Hypomagnesemia has been reported to be a key factor in the pathogenesis of cardiovascular disease (CVD) among

other patients. Although hypomagnesaemia may be a risk factor for vascular calcification, it does not mean that hypermagnesemia has no protective effect. Various studies showed a correlation between magnesium and vascular calcification in patients ESRD. Magnesium is a potent inhibitor in the process of arterial calcification in ESRD patients (5-7). In normal population, total serum magnesium and ionized concentrations are usually between (1.7-2.2 mg/dL) while in ESRD patients, both total concentration and magnesium ionization are often slightly higher than normal which depended upon the

function of the kidneys (8,9). Magnesium has pivotal act in inhibiting the onset or progression of vascular calcification and atherosclerosis, and also preventing stroke and coronary artery disease (10,11). Intima-media carotid calcification is either directly or indirectly related to CVD and is associated with a higher mortality rate in patients with chronic renal failure (12,13). hypermagnesemia may be involved in vascular calcification, and magnesium reduction is associated with the destruction of cardiac contractility and hypotension (14, 15).

The progression of atherosclerosis in dialysis patients is seen to be higher than that of the normal population. Magnesium levels are also associated with increased atherosclerosis in the common carotid artery. Since most studies have investigated the effect of calcium and phosphorus on CIMT. However, information in this field is abundant and proven, while in the case of magnesium, there are still no accurate and registered data (16,17).

Objectives

This study aimed to evaluate the correlation of serum magnesium level with carotid intima-media thickness (CIMT).

Patients and Methods

Study design

This study was conducted on 81 hemodialysis patients with ESRD at the 5th Azar educational center of Gorgan, Iran. There were no criteria for leaving the study. The necessary explanations about the research project and the benefits of Doppler ultrasound were conducted by the presenter. They were assured that their information would be protected until the end of the plan and that the plan had a few possible risks for them and that strategies for confronting them had been considered. They were free to refuse to cooperate with the performers at each stage of the project. Finally, eligible patients were informed consciously after receiving written consent. Before starting, demographic and clinical features all patients such as age, gender, underlying disease, duration of dialysis, dialysis adequacy, albumin, uric acid, triglyceride, cholesterol, hemoglobin, calcium, phosphorus, creatinine and iPTH (intact parathormone), and exclusion criteria including history coronary artery disease or myocardial infarction and patient dissatisfaction were evaluated.

Blood samples were collected from all patients for serum magnesium levels (in order to increase the accuracy of the dietary diversity in ESRD patients). Patients were referred to a radiologist to measure CIMT. Using affinity 50 Phillips, thickness of right and left intima-media of carotid in systolic and diastolic blood pressure were measured.

Biochemical analysis

Prior to a session of dialysis process, venous blood samples were collected to assess, total calcium, total cholesterol, phosphorus, triglycerides, hemoglobin, blood

urea nitrogen, creatinine, uric acid, iPTH, serum albumin and Kt/V. Xylene blue method was used to determine the serum level of magnesium, which ranges from 1.7 to 2.2 mg/dL in healthy individuals.

Ethical issues

The research followed the ethical principles of the Declaration of Helsinki. This study that was approved by the Ethics Committee of Gorgan University of Medical Sciences, Iran (IR.Goums.REC.1397.231). In addition, all participants signed informed written consent to participate in the intervention. This article has been adapted from the residency thesis written by Zahra Aghaalitafreshi in the internal medicine department of the university.

Statistically analysis of data

The data obtained from the measurements were analyzed by SPSS version 16 software after encoding and logging. Descriptive statistics such as mean, standard deviation, frequency and percentage, and charts were used to describe the data. To investigate the correlation between quantitative variables with regard to non-normality of data, Spearman's correlation coefficient and Kruskal-Wallis test were used to compare quantitative variables in different types of etiology, Kolmogorov-Smirnov test were performed to determine the normal distribution of data and the significance level was 0.05.

Results

Baseline information

In this study, 81 subjects aged 20- 87 years consisted of 35 males and 46 females. The clinical and demographic information of participants are listed in Table 1. In this study, the ESRD etiology were hypertension, diabetes mellitus, urinary tract infection, trauma, and Lupus. The mean duration of dialysis in this study was 4.82 ± 4.62 years. The least duration of dialysis was one year and the maximum duration of dialysis was 23 years.

Vascular and biochemical measurements

Table 2 shows the vascular and biochemical measurements. The mean serum level of magnesium in the patients (2.40 ± 0.24 mg/dL, range 1.45–3.29 mg/dL) was greater than the

Table 1. Baseline characteristics

Variables	n = 81
Age, years (range)	53 (20-87)
Sex, M/F	35/46
Etiology of chronic kidney disease, number of patients	
Hypertension	42
Diabetes mellitus	32
Urinary tract infection	5
Trauma	1
Lupus	1

Table 2. Biochemical and vascular assessment

Variables	Mean± standard deviation
Laboratory finding	
Magnesium (mg/dL)	2.4 ± 0.24
Hemoglobin (g/dL)	11.4 ± 1.8
Blood urea nitrogen (mg/dL)	53.9 ± 15.2
Creatinine (mg/dL)	10 ± 2.4
Albumin (g/dL)	4.1 ± 0.38
Total cholesterol (mg/dL)	145 ± 41
Triglycerides (mg/dL)	144 ± 92
Total calcium (mg/dL)	8.9 ± 0.73
Phosphorus (mg/dL)	4.9 ± 1.05
Uric acid (mg/dL)	7.25 ± 1.37
Intact parathyroid hormone (pg/dL)	564 ± 314
Kt/V	1 ± 0.38
Vascular assessment	
CIMT (mm)	0.66 ± 0.15

Abbreviation: CIMT, carotid intima-media thickness

normal range (1.7–2.2 mg/dL). The statistical correlation of CIMT with serum magnesium level was insignificant ($r=0.04$, $P=0.66$).

In this study, the correlation of serum magnesium levels with the IMT of left and right carotid was also investigated separately for systolic and diastolic pressure. The correlation of serum magnesium level with right

IMT in systolic pressure and the correlation of serum magnesium level with intima-media thickness of right carotid in diastolic pressure were not significant ($P>0.05$). Additionally, the correlation between the levels of serum magnesium, and the thickness of intima media of the left carotid in the systolic pressure and diastolic pressure were also not significant ($P>0.05$).

In all patients, the correlation of CIMT with laboratory variables and duration of dialysis based on Spearman's correlation test was shown in Table 3.

There is a statistically significant negative correlation between the CIMT and the parameters of phosphorus ($r=-0.258$, $P=0.021$), plasma hemoglobin levels ($r=-0.252$, $P=0.022$) while a positive correlation between CIMT and the dialysis adequacy (KT/V) was detected ($r=0.306$, $P=0.006$; Table 4).

Discussion

The progression of atherosclerosis in ESRD patients is more than the normal population. The results of our study showed no significant correlation between CIMT and serum magnesium level in ESRD patients.

Magnesium levels are also associated with an increase in atherosclerosis in the common carotid artery. This inverse correlation with arterial calcification showed the protective effect of serum magnesium in vascular calcification and improving the thickness of intima media

Table 3. Evaluation of dialysis duration and adequacy of dialysis and laboratory parameters with intima media of right and left carotid t in systolic and diastolic blood pressure

Variables	CIMT systole Right	CIMT diastole Right	CIMT systole Left	CIMT diastole Left
Ca correlation	-0.043	0.029	-0.057	-0.022
Coefficient P value	0.70	0.79	0.61	0.84
P correlation	-0.217	-0.173	-0.255	-0.071
Coefficient P value	0.05	0.12	0.02	0.53
Albumin correlation	0.111	-0.041	0.133	0.029
Coefficient P value	0.32	0.71	0.23	0.79
Hemoglobin correlation	0.163	0.130	0.147	0.254
Coefficient P value	0.14	0.24	0.19	0.02
TG correlation	0.112	0.004	0.049	0.008
Coefficient P value	0.32	0.96	0.66	0.94
Cholesterol correlation	0.108	0.074	0.105	0.100
Coefficient P value	0.33	0.51	0.35	0.37
PTH correlation	0.217	0.068	0.102	-0.004
Coefficient P value	0.05	0.54	0.36	0.97
Uric acid correlation	0.043	-0.137	0.000	-0.092
Coefficient P value	0.70	0.22	1	0.41
Kt/V correlation	0.304	0.096	0.266	0.152
Coefficient P value	0.006	0.396	0.016	0.175
Dialysis time correlation	0.031	0.016	0.053	0.087
Coefficient P value	0.78	0.88	0.64	0.43
BUN correlation	0.057	0.173	0.042	0.186
Coefficient P value	0.61	0.12	0.71	0.096
Creatinine correlation	-0.018	0.029	0.075	0.120
Coefficient P value	0.87	0.79	0.50	0.28

Abbreviations: CIMT, carotid intima-media thickness; Ca, calcium; P, phosphorus; BUN, blood urea nitrogen; PTH, Parathyroid hormone; TG, triglyceride

Table 4. Evaluation of laboratory variables of phosphorus and hemoglobin and Adequacy of dialysis with thickness of intima media of carotid

Variables	CIMT
P	
Correlation Coefficient	-0.258
P value	0.021
Kt/V	
Correlation Coefficient	0.306
P value	0.006
Hemoglobin	
Correlation Coefficient	0.252
P value	0.022

Abbreviations: CIMT, carotid intima-media thickness; P, phosphorous.

of carotid(16, 17). Calcification of intima media, either directly or indirectly, is associated with CVDs or will lead to more cardiac morbidity in patients with chronic renal failure (12). There are numerous studies evaluating the role of calcium and phosphorus in the intima media of carotid, and the information in this area is abundant and proven; However in the case of magnesium, there is still no accurate and well-documented information. Therefore, we conducted this study. According to this hypothesis, the question was answered by asking whether the increase in serum levels of magnesium would improve the cardiovascular outcome of dialysis patients.

In this study, the blood samples collected from research units were tested for serum magnesium level in three times. The average serum magnesium concentration in the patients was greater than the normal range. The mean total CIMT was less than 1 mm among 81 subjects (0.66 ± 0.15 mm).

According to our findings, the correlation oh serum magnesium levels with left and right CIMT were investigated separately for systolic and diastolic pressure, which all were not significant.

We found a statistically significant negative correlation between CIMT and parameters of serum phosphorus, plasma hemoglobin while there was a positive correlation between CIMT with Kt/V.

In a similar study conducted by Li et al, low-serum magnesium concentration was a major contributor to cardiovascular mortality in dialysis patients. They concluded that, the use of higher concentrations of magnesium in the dialysis fluid and the diet of patients may lead to better survival for patients (18).

Lee and colleagues also estimated the mean serum level of magnesium in 27 patients during the last three months, including the month of the test, was measured. Analysis of uniformity indicated a significant positive correlation of serum magnesium level with flow mediated dilation ($r=0.561$, $P=0.003$). The results showed that as serum magnesium levels decreased, CIMT subsequently increased ($P=0.221$) (18).

Moreover, the relationship between the serum

magnesium levels and the CIMT (right and left common carotid arteries) were separately examined in this study, for systolic and diastolic pressures, which were not significant.

Besides, a significant negative relationship was observed between the CIMT and the parameters of serum phosphorus and plasma hemoglobin, while there was a positive relationship between the CIMT and the dialysis therapy adequacy (Kt/V).

One other investigation by Ortega et al found that the serum magnesium could not be an independent predictor of future mortality and cardiovascular events in ESRD patients (19), which had confirmed the results of the present study.

Conclusion

The results of the given study had correspondingly revealed that the serum magnesium levels had not affected the CIMT, and no statistically significant relationship had been established in this respect.

Limitations of the study

This research has limitations that include low sample size and failure to investigate other causes of increased magnesium levels and mentioning them as exclusion criteria.

Authors' contribution

TE: concept, design, manuscript preparation and final revision. AZ, MHG: performing experiments, data collection and writing proposal and also statistical analysis. MM and TS; providing the first draft and manuscript editing. All authors read and signed the final paper.

Conflicts of interest

The authors declare that they have no conflict of interest.

Ethical considerations

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

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