Section: Medicine

Original Research Article

THE ROLE OF SERUM MAGNESIUM IN PREVENTING CAROTID ATHEROSCLEROSIS IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Abstract

Background: Cardiovascular disease is the most common consequence of chronic renal disease, as well as the leading cause of death. Hemodialysis patients had a more dynamic progression of atherosclerosis than the normal population. The current study was conducted to assess the relationship between carotid atherosclerosis and calcification and blood Magnesium levels in CKD patients, as accelerated atherosclerosis is thought to be one of the leading causes of cardiovascular mortality in CKD patients. **Materials and Methods:** This cross-sectional study was conducted for a year at the Department of General Medicine, Tertiary Care Teaching Institute of India. The study comprised a total of 80 patients. The cases were subjected to following investigations: Hb, TLC, DLC, Serum Urea, Serum creatinine, Serum magnesium, LFT, Serum Na+/K+/Ca++, Serum alkaline phosphate, Serum phosphorus, Para thyroid hormone, Serum lipid profile, Hba1C, Carotid Doppler ultrasonography to measure intima-media thickness of common carotid artery, Urine routine and microscopy, Ultrasound whole abdomen. **Result:** Males make up 62.5% of the patients in this study, while females make up 37.5%. There was no significant link between age and CIMT, nor did management differ with age, and efforts to identify risk factors for CKD advancement have largely focused on patient characteristics other than age. Serum magnesium levels were shown to be adversely linked with CIMT of bilateral carotid arteries (p0.05) in our study. **Conclusion:** In patients with chronic kidney disease, a low serum Mg level is strongly related with an increased risk of atherosclerosis.

INTRODUCTION

Cardiovascular disease (CVD) is regarded as one of the leading causes of death and morbidity worldwide. Improvements in risk factors have resulted in lower incidence rates and, as a result, a decrease in mortality. Traditional cardiovascular risk factors, such as ageing, obesity, hypertension, diabetes, dyslipidemia, infammation, and so on, cannot explain a significant proportion of cases, and thus new risk factors are being sought.[1] Cardiovascular diseases are the leading causes of morbidity and mortality in CKD patients, owing to accelerated atherosclerosis. As compared to the general population, other factors such as genetic factors, inflammation, hyperparathyroidism, and malnutrition affect the pathogenesis of atherosclerosis in CKD.[1] In this regard, factors related to mineral metabolism, such as magnesium (Mg) concentration, may play a role in the development of cardiovascular disease (CVD).[2-5]

A link between low serum Mg2+ levels and CVD in CKD and the general population has recently been proposed.6 Vascular calcification in CKD is associated with the distribution of various mineral disturbances such as high calcium and phosphorus concentrations, loss of mineralization inhibitors such as carboxylated matrix gla protein (carboxylated MGP) and fetuin A, apoptosis of vascular smooth muscles, and an active process of osmosis Calcium and phosphorus nanocrystals are released intracellularly after being taken up by VSMCs via endocytosis. This leads to expression of osteogenic transcription factors including Runx2 and BMP2, mineralization of Extracellular matrix,

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decreased expression of calcification inhibitory proteins including MGP.[6,7] The intracellular burst of calcium causes apoptosis and release of apoptotic bodies containing Calcium and phosphate particles, which along with decreased amounts of calcification inhibitors (including Fetuin A and MGP) provide a nidus for mineral nucleation and maturation. Third, magnesium inhibits Wnt/beta-catenin signaling, which is a mediator of osteogenic transformation.[8-11] Magnesium acts on the calcium sensing receptors (CaSR), and stimulation of the CaSR by calcimimetics inhibits VSMC calcification. Fourth, magnesium inhibits Wnt/beta-catenin signalling, which is an osteogenic transformation mediator.

As a result, the current study was planned to assess the relationship of carotid atherosclerosis and calcification with blood Magnesium levels in CKD patients, as accelerated atherosclerosis is thought to be one of the leading causes of cardiovascular mortality in CKD patients.

MATERIALS AND METHODS

The current cross-sectional study was carried out for a year at the Department of General Medicine, Tertiary Care Teaching Institute of India. The institutional ethical committee provided ethical approval, and all participants provided signed informed consent. The study comprised a total of 80 patients.

Patients with chronic renal disease in stages IV and V (patients with either kidney damage or a glomerular filtration rate (GFR) of less than 30 ml/min/1.73 m2 for at least 3 months; according to the CKDEPI Classification) were eligible for the current study.

Exclusion criteria included chronic liver illness, heart failure or unstable coronary artery disease, a recent history of chronic diarrhoea, cancer, and chronic infections, and recent use of Mg-lowering medicines such as thiazide diuretics, PPI, and aminoglycoside antibiotics.

The following tests were performed on the patients: Hb, TLC, DLC, Serum Urea, Serum Creatinine, Serum Magnesium (Technology: Photometry; Method: Modified Xylidyl Blue Reaction Method), LFT (including serum albumin), Serum Na+/K+/Ca++, Serum alkaline phosphate, Serum phosphorus, Para thyroid hormone, Serum lipid profile, Hba1C, Caroti

Statistical Analysis

The collected data was assembled and input into a spreadsheet programme (Microsoft Excel 2007) before being exported to the data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). The confidence level and level of significance for all tests were set at 95% and 5%, respectively.

RESULTS

Males make up 62.5% of the 80 cases, while females make up 37.5% [Table 1]. Our findings reveal that CKD is more frequent in men than in women. In our study, the average age of ESRD patients was 50.4 years old.

According to the findings, 82% of the patients had hypertension, and 30% of the 80 patients had diabetes mellitus. There was no significant link between age and CIMT, nor did management differ with age, and efforts to identify risk factors for CKD advancement have largely focused on patient characteristics other than age.

The value of CIMT was found to be unrelated to the patient's gender or any comorbidity, such as diabetes mellitus or hypertension. The mean urea and creatinine levels were 120.80 mg/dl and 7.58 mg/dl, respectively.

Calcium levels were discovered to be low, whereas phosphorus and parathyroid hormone levels were found to be increased. Magnesium levels were found to be low in 22 CKD patients, with levels less than 1.9 mg/dl.

The kidneys were determined to be bilaterally undersized, with the right kidney measuring 6.1-7.8 cm and the left kidney measuring 5.2-7.9 cm. The link of several factors such as serum calcium, phosphorus, and parathyroid hormone with CIMT values and hence cardiovascular risk in CKD patients was not shown to be statistically significant. In 24 CKD patients with low magnesium levels, CIMT was shown to be high (>1 cm) [Table 2].

Serum magnesium level was found to be negatively correlated to CIMT of bilateral carotid arteries (p0.05) in our study, indicating that accelerated atherosclerosis associated with vascular calcification of intima and media layers and arterial stiffening is a common finding in CKD patients with hypomagnesemia.

Table 1: Distribution of cases according to Gender of the patient (n=80)

Gender	Number	Percentage (%)
Male	50	62.5
Female	30	37.5
Total	80	100

Table 2: Association of risk of CVD according to magnesium level (n=80)

Location	Serum Magnesium level	CVD risk absent	CVD risk present	P value
Right CIMT	Low (<1.9)	4	22	0.002*
	Normal (1.9-3.1)	48	2	
	High (>3.1)	4	0	

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Left CIMT	Low (<1.9)	4	22	0.05*
	Normal (1.9-3.1)	48	2	
	High (>3.1)	4	0	

* indicates statistically significance at p≤0.05

DISCUSSION

Increasing data indicates that established risk factors fail to explain all of the risk for CVD, prompting the search for novel or emerging risk factors. The current investigation was undertaken at the outset of a randomised trial recruiting patients with CHD to determine an independent connection between serum Mg and IMT-CC, a marker of carotid atherosclerotic vascular disease, in a high-risk population. The findings revealed that higher levels of IMT-CC were related with lower levels of serum Mg concentration. This inverse relationship was independent of traditional CVD risk factors such as abnormalities in lipid and glucose metabolism; though it was attenuated after adjusting for anthropometric factors such as gender, age, waist circumference, and SBP, as well as medication (insulin and diuretic use), it remained highly significant.

The findings of our study, which showed that CKD is more common in males than females, were consistent with the findings of Yorifuj et al, who documented in their study that 69% of the patients were males and 31% were females.[12] The findings of patients with hypertension and Diabetes Mellitus were consistent with the findings of Parati et al, who demonstrated that hypertension is highly prevalent in CKD, particularly in patients with ESRD receiving hemodialysis.[13]

There was a significant increase in serum urea in the studied group, which was consistent with the findings of Ali et al, who reported that the mean of serum was 139.69+27.59 mg/dl in the studied group and 22.59+6.30 mg/dl in the control group, with statistical significance as p0.001.[14] There was a significant increase in serum creatinine in the studied group, which was consistent with the findings of Sliem H. et al,[15] (2011) showed that the mean serum creatinine in hemodialysis patients was (8.6 2.2 mg/dl) and (0.7 0.2 mg/dl) in the control group, with statistical significance (p<0.05).

Serum calcium levels were substantially lower than normal in our investigation. This was consistent with the findings of Ali et al, who reported in their study that serum phosphate, alkaline phosphatase, and iPTH levels were significantly higher in the study patients than in the healthy controls.[14]

In our study, 80% of the patients had higher iPTH levels, 20% had normal iPTH levels, and the mean iPTH level was. This was consistent with Chutia and Abraham's findings that 95.2% of patients had hyperparathyroidism and 4.8% had normal iPTH levels.[16] In our study, the mean magnesium level was 2.20 mg/dl, with 22 patients having hypomagnesemia, 56 having normal Mg2+ levels, and 4 having hypermagnesemia, which was consistent with Zaher et al who discovered a significant decrease in serum magnesium levels in children with CKD on regular HD than in controls. When a 0.5 mEq/l dialysate Mg2+ is utilised, Wal-Visscher et al found that hypomagnesaemia is much more prevalent (5-33%). This was agreed upon by Zaher M. et al,[17] (2016) discovered a significant decrease in serum Mg levels in children with CKD receiving regular HD compared to controls. D. Spiegel,[9] (2011) demonstrated that serum Mg in HD patients reduces considerably following hemodialysis sessions. M. Alhosaini. According to et al. (2014),[18] both CKD and ESRD patients on dialysis have normal serum Mg levels and, in some cases, low serum Mg concentrations (hypomagnesaemia). E. Van de Wal-Visscher. et al,[19] (2018) found that when a 0.5 mEq/L dialysate Mg is employed, hypomagnesaemia is significantly more prevalent (5-33%). Reduced gastrointestinal uptake due to acidosis, poor nutrition, and absorption can all explain hypomagnesaemia. Patients with CKD typically have much lower intestinal Mg absorption than healthy persons, most likely due to a lack of active vitamin D. In addition, the usage of Low-Mg dialysate (0.25 mmol/L or 0.5 mEq/L) is a risk factor for hypomagnesaemia in both hemodialysis and peritoneal dialysis patients.

It may also be a side effect of a variety of medications, including thiazide diuretics, proton pump inhibitors, aminoglycoside antibiotics, and calcineurin inhibitors.[19] Proton pump inhibitors are known to impair the adaptive increase in active intestinal Mg absorption in the face of Mg depletion and may thus predispose to hypomagnesaemia in both CKD and ESRD patients.[20,21]

Reduced gastrointestinal uptake due to acidosis, poor nutrition, and absorption can all explain hypomagnesaemia. Patients with CKD typically have much lower intestinal Mg2+ absorption than healthy persons, most likely due to a lack of active vitamin D. Also, the use of Low-Mg2+ dialysate is a risk factor for hypomagnesaemia in patients on both hemodialysis and peritoneal dialysis.[18] Furthermore, our study found no significant correlation between serum Mg and laboratory data (and this was in agreement with Yorifog et al who found no significant differences in the PTH and vitamin D levels between two categories of Mg2+ levels, lower and normal). In another study, CIMT was reduced following Mg supplementation Mortazavi M. Turgut, F., et al,[22] (2008) found a significant inverse relationship between the absolute change in serum Mg concentrations and right CIMT after 2 months of Mg treatment, leading them to conclude that Mg supplementation may be useful in slowing the progression of atherosclerosis in chronic dialysis patients. Mg's role in atherosclerosis is unknown, but it has been suggested that Mg has an anti-atherosclerotic effect, possibly due to its anti-

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inflammatory and antioxidant properties; conversely, Mg deficiency promotes endothelial dysfunction and also promotes hydroxyapatite formation and calcification of vascular smooth muscle cells by inhibiting endothelial proliferation, upregulating plasminogen activator inhibitor1 and vascular cell adhesion molecule-1

The current study has limitations in that the sample size is modest, and bigger similar investigations are needed in the future to corroborate the conclusion.

CONCLUSION

In patients with chronic kidney disease, a low serum Mg level is strongly related with an increased risk of atherosclerosis. Though more prospective studies on a larger population will be needed to determine whether long-term administration of oral Magnesium supplements to CKD patients on intermittent haemodialysis therapy can delay arterial calcification, lowering the risk of cardiovascular mortality in such patients. As a result, Mg2+ might be thought of as a modifiable risk factor for cardiovascular morbidity in CKD patients.

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