Assessment of Magnesium level Among Hemodialysis Patients and Its Relation to Vascular Stiffness

Thesis

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بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

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Nouran Abdel Fattah

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List of Abbreviations

Abb.	Full term
ACh	Acetylcholine
AGA	Aminoglycoside antibiotics
AI	Augmentation index
Alk Phos	Alkaline Phosphatase
BMP 7	Morphogenetic protein 7
Ca	Calcium;
CAC	Coronary artery calcification
CAPD	Continuous ambulatory peritoneal dialysis
CaR	Calcium sensing receptor
CD	Collecting duct
CI	Confidence interval
CKD	Chronic kidney disease
CNI	Calcineurin inhibitors
CNT	Connecting tubule
COPD	Chronic obstructive pulmonary disorder
CPP	Calciprotein particles
CsA	Cyclosporin A
CSD	Cortical spreading depression
CSF	Cerebrospinal fluid
CT	Connective tissue
CUA	Calciphylaxis
CVD	Cardiovascular disease
CVD	Cerebrovascular disease
DBP	Diastolic blood pressure
DCI	Delayed cerebral ischemia
DM	Diabetes mellitus

List of Abbreviations Cont...

Abb.	Full term
EN	Endothelial cell
ESRD	End-stage renal disease
FEV	Forced expiratory volume
FHHNC type I	Familial hypomagnesemia with hypercalciuria and nephrocalcinosis type I
FVC	Forced vital capacity
GAS6	Growth arrest specific 6 protein
GFR	Glomerular Filtration Rate
HD	Haemodialysis
HDL	High-density lipoprotein
His	Histamine
HPABH4D	Hyperphenyalaninemia and high urinary levels of primapterin
IDH	Intradialytic hypotension
IHD	Ischaemic heart disease
IMT	Intima media thickness
IRH	Isolated autosomal recessive hypomagnesemia
KDIGO	Kidney Disease: Improving Global Outcomes
LDL	Low-density lipoprotein
LVH	Left ventricular hypertrophy
MASH-I	Magnesium and Acetylsalicylic acid in Subarachnoid Hemorrhage
MEP	Maximal expiratory pressure
Mg	Magnesium
MGP	Matrix Gia-protein
MIP	Maximal inspiratory pressure
MRA	Mineralocorticoid receptor antagonists

List of Abbreviations Cont...

Abb.	Full term
NCC	Na-Cl cotransporter
NO	Nitric oxide
OC	Osteocalcin
PCBD1	Pterin-4 α carbinolamine dehydratase 1
PGI2	Prostacyclin
Phos	Phosphorus
PPI	Proton-pump inhibitors
PTH	Parathyrdoid hormone
PVD	Peripheral vascular disease
PWV	Pulse wave velocity
RCTs	Randomized controlled trials
RR	Relative risk
RRT	Renal replacement therapies
RUNX2	Runt-related transcription factor-2
SAH	Subarachnoid hemorrhage
SBP	Systolic blood pressure
SCI	Spinal cord injury
SHPT	Secondary hyperparathyroidism
SLC41A1/A3	Solute carrier family 41 members 1 and 3
SP	Substance P.
TBI	Traumatic brain injury
TM	Tunica media
TNF-α	Tumor Necrosis Factor-alpha
TRPM6	Transient receptor potential melastatin type 6
VC	Valve calcification
VSMC	Vascular smooth muscle cell

ABSTRACT

Background: The pathogenesis of vascular calcification in Chronic kidney disease (CKD) patients is multifactorial and complicated. It has been proposed that Magnesium (Mg) may be implicated in the process of vascular calcification on various levels.

Aim: This study aims to assess the level of magnesium in hemodialysis patients and its relation to the vascular stiffness.

Patients and methods: 100 prevalent hemodialysis patients were included in the study and they were clinically stable with absence of cardiovascular complications, all patients underwent the following laboratory investigation including complete blood picture, median of magnesium level over 3 months, electrolytes, ipth, lipid profile and radiological investigations including transthoracic echocardiography and carotid duplex.

Results: The studied population was divided into two groups, group I included 68 patients with normal mg level and group II included 32 patients with low mg level. There was statistically significant difference between the two groups as regard hemoglobin level (pvalue=0.033), otherwise there was no statistically significant difference as regard other laboratory and radiological investigations. Then they were divided into another two groups according to the presence of mitral valve calcification (MVC), group III involved 85 patients without MVC and group IV involved 15 patients with MVC. There was statistically significant difference between 2 groups as regard aortic wave pulse velocity (aPWV) with (pvalue=0.002), presence of plaques with (pvalue <0.001) and intimal media thickness with (pvalue<0.001). Another group was divided according to presence of aortic valve calcification (AVC) into two groups, first group V included 39 patients without AVC and second group VI included 61 patients with AVC. There was statistically significant difference between two groups as regard age with (pvalue<0.001), ipth with (pvalue=0.033), presence of plaques with (pvalue=0.048) and intimal media thickness with (pvalue<0.001).

Conclusion: There was high prevalence of vascular calcification among hemodialysis patients which may be related to age and hyperparathyroidism but without statistically significant correlation to Mg level.

Keywords: Hemodialysis, Vascular calcification, Magnesium.

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of mortality among patients with end-stage renal disease (ESRD), and cardiovascular mortality in dialysis patients is 10–20 times that seen in the general population ***(USRDS, 2006).***

Although non-atherosclerotic factors such as volume overload and left ventricular hypertrophy are important contributors to the high cardiovascular mortality, accelerated atherosclerosis is one of the primary causes of morbidity and mortality in dialysis patients ***(Soubassi et al., 2006).***

Atherosclerotic changes in the carotid artery mirror pathologic events of generalized atherosclerosis. Carotid intima media thickness (IMT), measured non-invasively by ultrasonography, is a well-established index of atherosclerosis and is directly associated with an increased risk for cardiovascular disease in the general population ***(Faruk et al., 2008).***

Hyperphosphatemia, hypercalcemia, and parathyroid hormone (PTH) play a predominant role in the initiation and progression of vascular calcification in patients with ESRD. At the same time, an inverse relationship between magnesium (Mg) and PTH has been described and there is strong evidence suggesting that hypomagnesemia may play a significant role in the development of cardiovascular diseases in the general population ***(Wei et al., 2006).***

Magnesium (Mg), the fourth most abundant cation in the human body, plays an essential role in numerous biological processes. The importance of this mineral has been particularly recognized due to its anti-atherosclerotic effect. In the general population, a lower serum Mg level and/or lower dietary Mg intake is associated with an increased incidence of hypertension, type 2 diabetes mellitus (DM), metabolic syndrome and CVD including myocardial infarction, stroke, atrial fibrillation and sudden cardiac death ***(Zhang et al., 2012).***

It plays an essential role in a wide range of fundamental cellular reactions and is considered a 'natural calcium antagonist'. Evidence showing that magnesium deficiency promotes inflammation and increases sensitivity to oxidative stress has been accumulating. Atherosclerosis is considered an inflammatory disease and the anti-inflammatory effect of Mg might provide an alternative explanation ***(Mazur et al., 2007).***

Several in vitro studies have shown that Mg deficiency causes vascular constriction, platelet aggregation, inflammation, and oxidative stress, resulting in endothelial cell dysfunction and vascular calcification ***(Maier, 2012).***

The direct protective effects of Mg on vascular calcification have also been demonstrated via multiple pathways, including inhibition of hydroxyapatite formation and suppression of trans-differentiation of vascular smooth muscle cells into osteoblast-like cells ***(Kircelli et al., 2012).***