ASSOCIATION BETWEEN LOW SERUM MAGNESIUM LEVELS AND THE EXTENT OF ATHEROSCLEROTIC PROCESS IN HAEMODIALYSIS PATIENTS

Massimetti C., °Achilli P, °Madonna M.P., Muratore MT ^, *Fabbri G.D., *Brescia F., Feriozzi S.
Nefrologia e Dialisi, °Cardiologia, ^Laboratorio,*Radiologia, Ospedale Belcolle, Viterbo, Italy

INTRODUCTION

Cardiovascular diseases (CVD) account for nearly 40% of all deaths in patients (pts) with end-stage renal disease (ESRD). That is the result of a mix between traditional and a growing number of non-traditional risk factors. In particular, mineral disorder in ESRD is considered as a prominent contributor to the development of atherosclerosis and vascular calcification. Experimental studies have shown that magnesium (Mg) deficiency causes vascular constriction, platelet aggregation, inflammation, and oxidative stress, resulting in endothelial cell dysfunction and vascular calcification. Clinical studies in ESRD have reported that hypomagnesemia was significantly associated with peripheral arterial calcification, and an increased carotid intima-media thickness (CIMT). Oral Mg supplementation in pts on hemodialysis improves CIMT.

The aim of this study was to determine the hypothetical association between sMg and carotid artery alterations in a haemodialysis population.

SUBJECTS AND METHODS

- Retrospectively from january 2006 to december 2012 one hundred and eighty patients on hemodialysis were investigated for:
-sCa, sPO4, sMg, PTH, HDL- and LDL cholesterol, haematocrit, homocysteine, C-reactive protein (CRP), and albumin;
- Ultrasonographic assessments of carotid artery intima-media thickness (CIMT); In 131 patients was also performed echocardiographic examination;
- Systolic (SBP) and diastolic blood pressure (DBP);
- Mean intake of calcium salts and vitamin D;
- In all patients were recoded previous cardiovascular events (CVE).

RESULTS

In table 1 are reported main baseline characteristics of hemodialysis patients. They have a long dialysis vintage, sMg meanly in normal range, and high values of CIMT. Figure shows the main correlationes come out from the study. Serum Mg was also negatively correlated with CVE, CRP, LDL-C (r=-.194, P<.01; r=-.214, P<.01; r=.276,P < .001; respectively). Carotid IMT, besides PO4 and LVMi, was correlated with age, dialysis vintage, PTH levels, CRP, homocysteine, and DBP (r = .415, P < .000; r = .215, P < .01; r = .244, P < .001; r = .258, P < .001; r = .198, P < .05; r = -.212, P < .01; respectively). Table 2 shows stepwise multiple regression analysis with the final model contained five predictor variables for CIMT. In table 3 are reported clinical characteristics according to quartiles for sMg, and shows as the higher sMg levels the lesser CIMT values and frequence of CVE. Tables 4 and 5 show main differences between patients without (A) or with (B) previous CVE, group B showed the higher CIMT values, and sMg levels slightly lesser than group A.

Table 1. Baseline characteristics

Age, y/o	56 ± 15	Triglycerides, mg/dl	170 ± 85
Dialysis vintage,	59 ± 49	C-reactive protein, mg/L	4.0 ± 4.7
months	89/91	Homocysteine, µMol/L	31.3 ± 27.2
Gender (M/F)	13	Albumin, gr/dl	4.0 ± 0.3
Diabetes, %	17	Systolic BP, mmHg	137 ± 22
CVE, %	8.9 ± 0.8	Diastolic BP, mmHg	78 ± 12
Ca, mg/dl	5.4 ± 1.2	CIMT, mm	1.41 ± 0.75
P, mg/dl	2.2 ± 0.4	LVMi, g/m^2	151 ± 48
Mg, mg/dl	48 ± 12	$CaCO_3$, g/day	1.7 ± 0.8
Ca x P product,	400 ± 340	(n° pts)	(85)
mg^2/dl^2	35 ± 5	Vitamin D, µg/week	3.2 ± 2.5
PTH, pg/ml	155 ± 39	(n° pts)	(90)
Haematocrit, %	43 ± 14	rHhEPO, IU/kg/b.w./w	143 ± 105
Cholesterol, mg/dl	80 ± 35	(n° pts)	164
HDL-cholesterol, mg/dl			
LDL-cholesterol, mg/dl			

Table 2. Multiple regression analysis for assessing the predictors of CIMT values (stepwise method)

Ajusted R2 = .426; F6,174=19.99, P<.001

Parameter	β	P
Age	.451	0.000
SBP	.358	0.000
DBP	-.313	0.001
PTH	.152	0.011
Mg	-.147	0.012
PO4	.126	0.037

Main correlationes

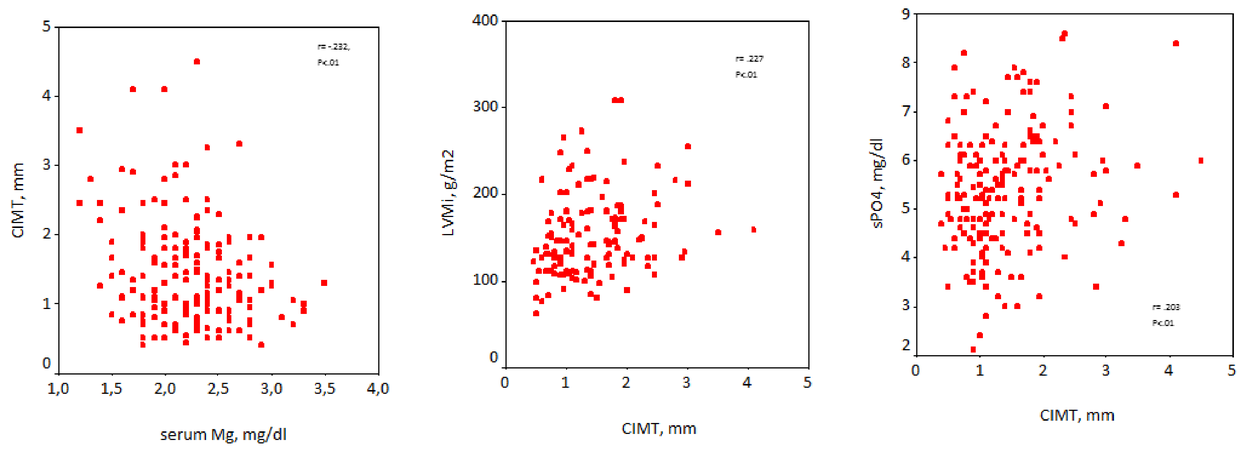

Table 3. Baseline characteristics of 180 HD patients according to sM level quartiles

Quartiles of sMg level (sMg level range (mg/dl))

Characteristics n° pts	1 (<1.8) (n=25)	2 (>1.8, <2.2) (n=83)	3 (≥2.2, <2.5) (n=44)	4 (≥2.5) (n=37)
Age, y/o	59±13	56±15	51±14	55±15
Dialysis vintage, months	51±34	67±51	55±54	49±44
Gender, M/F	20/5	36/47	20/24	20/17
CV events, % of pts	36	20	7	13
Ca, mg/dl	8.8±0.9	9.0±0.7	9.0±0.8	8.9±0.7
P, mg/dl	5.2±0.9	5.4±1. °	5.3±1.4°	5.4±1.3
PTH, pg/ml	353±236	368±283	456±416	383±400
HDL-cholesterol, mg/dl	36±16	41±13	45±16	46±14
LDL-cholesterol, mg/dl	77±23	76±35°	85±34	83±40°
C-reactive protein, mg/L	5.71±7.28	4.24±4.86	3.69±3.48	2.64±2.63°
Homocysteine, µMol/L	36±37	31±32	27±13	30±15°
Systolic BP, mmHg	141±24	149±47	137±20	137±21
Diastolic BP, mmHg	78±12	78±13	78±10	77±14
CIMT, mm	1.78±0.95	1.37±0.79	1.38±0.61*	1.20±0.54§
LMi, g/m^2	146±29	141±24	141±24	173±63*
$CaCO_3$, g/die (%)	1.4±0.7 (36)	1.7±0.8 (54)	1.8±0.9 (52)	1.7±0.8 (27)
Vitamin D (p.o/e.v), µg/w	3.6±3.1 (52)	2.5±1.8 (51) °	3.9±2.7 (50)	4.6±3.2 (40)

P vs quartile 1:§ <0.001; *<0.01; ° <0.05

Table 4. Clinical characteristics in patients without (A) and with cardiovascular events (B)

CVE n° patients	A (n=149)	B (n=31)
Age, years	53 ± 14	66 ± 11
Dialysis vintage, months	58 ± 50	65 ± 44
Sex, males/females	69/80	21/10
Diabetes, %	11	28
CaT, mg/dl	9.0 ± 0.8	8.8 ± 0.7
PO4, mg/dl	5.4 ± 1.2	5.2 ± 1.4
CaT x PO4 product, mg/dl	49 ± 11	46 ± 13
Mg, mg/dl	2.2 ± 0.4	2.0 ± 0.4
PTH, pg/ml	415 ± 353	323 ± 257
Hct, %	35 ± 5	35 ± 4
Cholesterol HDL, mg/dl	44 ± 15	36 ± 10
Cholesterol LDL, mg/dl	81 ± 37	76 ± 26*

Table 5. Clinical characteristics in patients without (A) and with cardiovascular events (B)

CVE n° patients	A (n=149)	B (n=31)
C-reactive protein, mg/L	3.77 ± 4.69	5.21 ± 4.85
Homocysteine, µMol/L	31.6 ± 29.1	31.4 ± 29.1
Albumin, gr/dl	4.0 ± 0.3	3.9 ± 0.3
SBP, mmHg	135 ± 22	143 ± 23
DBP, mmHg	78 ± 12	77 ± 11
CIMT, mm	1.27 ± 0.62	2.08 ± 0.91*
LVMi, gr/m^2	147 ± 44	177 ± 57°
CaCO3, g/d (n° pts)	1.7 ± 0.8 (70)	1.9 ± 0.8 (16)
Vitamina D, µg/w/t (n° pts)	3.4 ± 2.6 (75)	2.7 ± 2.2 (16)
rHhEPO, IU/Kg/p.c./w (n° pts)	145 ± 110 (135)	138 ± 85 (29)

°P<.05; *P < .01

CONCLUSIONS

-In addition to some traditional and non-traditional risk factors for atherosclerotic process, even lower sMg were closely and independently associated with risk of carotid artery alteration, including mean CIMT, suggesting that a low sMg level represents an independent risk factor or predictor of carotid artery alteration.

-Our results suggest a hypothetical interrelationship between sMg, CIMT and LVMi.

- Further investigations are needed to examine the relationship between sMg levels, and the incidence of cardiovascular disease, and then of morbidity and mortality.

DOI: 10.3252/pso.eu.51era.2014