CALCIUM ACETATE/MAGNESIUM CARBONATE THERAPY IS ASSOCIATED WITH LOWER PROGRESSION OF LEFT VENTRICULAR MASS INDEX AND VALVULAR CALCIFICATIONS IN HAEMODIALYSIS PATIENTS

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Introduction and Aim

- Magnesium (Mg) is the second most abundant intracellular cation. In haemodialysis (HD) patients, its balance depends on the intake and most importantly on its dialysate concentration[1,2].
- Hypomagnesaemia seems to play a role in the pathogenesis of arterial hypertension, endothelial dysfunction and vascular calcifications in dialysis patients[1-4].
- Calcium acetate/ magnesium carbonate (CaMg) is a recent phosphate binder whose effects in the cardiovascular (CV) system remain to be determined.
- The aim of this study was to evaluate the relationship between CaMg therapy and CV risk markers like pulse pressure (PP), left ventricular mass index (LVMI) and valvular calcifications in chronic HD patients.

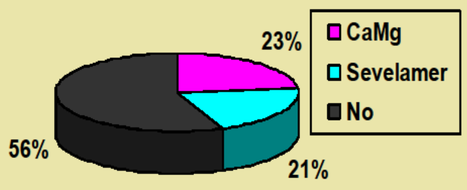
Patients and Methods

- Prospective study performed in 206 prevalent HD patients.
- Baseline demographic, clinical, biochemical and ecocardiographic parameters were evaluated and repeated after a 48-month period. Patients started CaMg therapy during the study and were under this phosphate binder for at least 36 months.
- Clinical data included aetiology of renal failure, presence of diabetes mellitus, hypertension and coronary artery disease, PP, interdialytic weight gain and therapy with ACE inhibitors, vitamin D and phosphate binders. Laboratory data considered were pre dialysis haemoglobin, albumin, C-reactive protein (CRP), calcium, phosphorus, intact PTH and serum Mg.
  LVMI was calculated using the Devereux formula and indexed to body surface area. Aortic and mitral valvular calcifications were classified in mild (1), moderate (2) and severe (3).
  In multivariate analysis, progression of LVMI and of valvular calcification was considered when there was an increase of 5% from baseline value.
- Statistical analysis was performed with SPSS 19.0 and a $p<0,05$ was considered significant.

Results

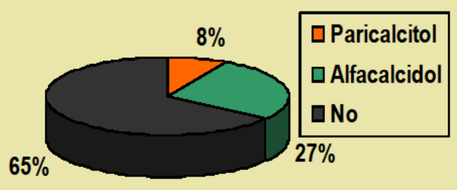
Population:
- 206 chronic HD patients
- all submitted to post dilution on-line haemodiafiltration, with a dialysate Mg concentration of 0.5 mmol/L.
- ultrapure water dialysate and high flux helixone filter (Fresenius®) were used.
- mean age: 63.6 ± 14.3 years
- 45% female
- mean HD time: 42.3 ± 38.6 months
- 26% diabetics, 34% hypertensive and 28% with coronary artery disease.

Phosphate binders therapy



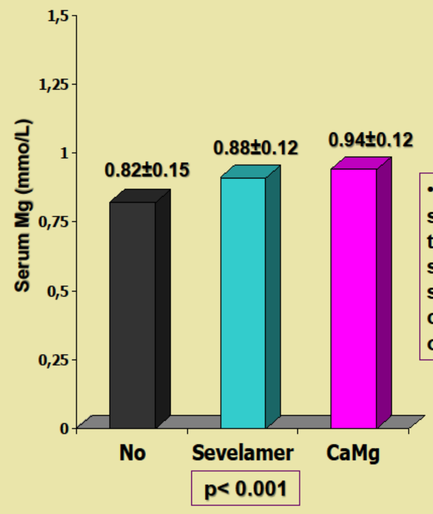
- 23% (n=48) of the patiens were taking CaMg – mean dose: 1876 ± 791 mg/day
- 21% (n=43) of the patients were under sevelamer – mean dose: 3412 ± 2025 mg/day
- 56% (n=115) were not taking phosphate binders.

Active vitamin D therapy



- 8% (n=17) of the patients were under paricalcitol – mean dose: 8.1 ± 4.8 µg/week
- 27% (n=55) of the patients were taking alfacalcidol – mean dose: 2.7 ± 1.9 µg/week
- 65% (n=134) were not under active vitamin D therapy.

Serum Mg and type of phosphate binder



- At the end of the study, patients taking CaMg showed higher serum Mg compared with the other two groups.

Univariate analysis:

	No phosphate binders	CaMg	p
Age (years)	68.7±14.4	69.2±15.8	NS
Time on HD (months)	49.9±39.2	48.5±41.1	NS
Diabetes mellitus (%)	42.3	40.1	NS
Hypertension (%)	32.3	35.1	NS
Coronary disease (%)	31	28	NS
Interdialytic weight gain (g)	1861±1115	1747±968	NS
ACE inhibitors therapy (%)	59.1	62.3	NS
Vitamin D therapy (%)	29.2	40.0	< 0.001
Haemoglobin (g/dL)	11.4±1.2	11.2±1.1	NS
CRP (mg/dL)	1.1±0.5	0.8±0.6	0.02
Albumin (g/dL)	3.2±0.4	3.6±0.3	0.03
Calcium (mg/dL)	8.6±0.6	8.8±0.5	NS
Phosphorus (mg/dL)	3.7±1.1	4.7±1.3	0.01
iPTH (pg/mL)	257±161	306±224	0.02
ΔPP (mmHg)	5.2±4.9	- 9.7 ±4.8	< 0.001
ΔLVMI (g/m²)	7.4±5.4	- 10.1 ±3.9	0.004
Δ Aortic valve calcifications	0.83±0.53	- 0.05 ±0.22	0.003
Δ Mitral valve calcifications	0.53 ±0.42	0.08 ±0.25	0.03

- Compared with patients who did not take phosphate binders, patients taking CaMg showed a significant reduction in PP ($p < 0.001$), LVMI ($p=0.004$) and aortic ($p=0.003$) and mitral ($p=0.03$) valvular calcifications at the end of the study.

	Sevelamer	CaMg	p
Age (years)	54.3±15.6	69.2±15.8	< 0.001
Time on HD (months)	51.1±39.4	48.5±41.1	NS
Diabetes mellitus (%)	14.3	40.1	< 0.001
Hypertension (%)	36.8	35.1	NS
Coronary disease (%)	25	28	NS
Interdialytic weight gain (g)	1913±883	1747±968	NS
ACE inhibitors therapy (%)	64.6	62.3	NS
Vitamin D therapy (%)	46.9	40.0	0.03
Haemoglobin (g/dL)	11.3±1.2	11.2±1.1	NS
CRP (mg/dL)	0.6±0.5	0.8±0.6	NS
Albumin (g/dL)	3.7±0.4	3.6±0.3	NS
Calcium (mg/dL)	8.9±0.8	8.8±0.5	NS
Phosphorus (mg/dL)	5.0±0.9	4.7±1.3	0.01
iPTH (pg/mL)	420±303	306±224	0.03
ΔPP (mmHg)	5.3±4.3	- 9.8 ±4.7	< 0.001
ΔLVMI (g/m²)	8.8±5.9	- 8.7±3.6	0.02
Δ Aortic valve calcifications	0.06±0.17	- 0.21 ±0.12	0.03
Δ Mitral valve calcifications	0.19 ±0.34	0.05 ±0.18	NS

- Compared with patients under sevelamer, patients taking CaMg showed a significant reduction of PP ($p <0.001$), LVMI ($p=0.02$) and aortic valve calcifications ($p=0.03$) at the end of the study.

Multivariate analysis:

dependent variable	independent variables	OR	CI 95%	p	R^2
LVMI progression	time on HD	2.18	1.22 - 3.43	0.002	0.452
	albumin	0.19	0.08 - 0.24	<0.001	
	serum phosphorus	1.19	1.11 - 2.09	0.006	
	serum Mg	0.17	0.03 - 0.09	0.003	
	PP	2.35	1.21 - 2.93	<0.001	
	interdialytic weight gain	1.37	1.09 - 2.94	0.007	
	CaMg therapy	0.17	0.02 - 0.13	0.02	

dependent variable	independent variables	OR	CI 95%	p	R^2
Aortic valve calcification progression	time on HD	2.13	1.18 - 2.41	0.003	0.477
	diabetes mellitus	1.21	1.01 - 3.32	0.02	
	albumin	0.19	0.05 - 0.11	<0.001	
	serum phosphorus	1.27	1.09 - 1.94	0.02	
	serum Mg	0.18	0.04 - 0.08	0.02	
	CaMg therapy	0.16	0.02 - 0.08	0.01	

- In multivariate analysis, CaMg therapy was associated with less progression of LVMI ($p=0.02$) and aortic valve calcification ($p=0.01$).

Conclusions

- In this 48-month study, we observed that the use of CaMg was associated with a reduction of both PP and LVMI and a stabilization of aortic valvular calcifications in prevalent HD patients.
- These results need to be confirmed in randomized controlled trials.

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