LONG TERM CHOLECALCIFEROL SUPPLEMENTATION IN HAEMODIALYSIS PATIENTS: EFFECTS ON MINERAL METABOLISM, INFLAMMATION AND CARDIAC DYSFUNCTION

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Introduction and Aim

❑ Native vitamin D deficiency is very common in patients with chronic kidney disease[1]. However, few studies have been performed in this population with long term vitamin D supplementation.

❑ Besides the known effects of vitamin D in mineral metabolism, pleiotropic effects of this vitamin on immunitary and cardiac systems have also been described [2,3].
Our group showed in haemodialysis (HD) patients negative associations between 25-vitamin D [25(OH)D_3] levels and cardiovascular risk factors, like brain natriuretic peptide (BNP), pulse pressure (PP), left ventricular mass index (LVMI) and vascular calcifications[4].
In 2010, we published the first results of this prospective study with 6 months of cholecalciferol supplementation and its benefits on mineral metabolism, inflammation and cardiac dimension parameters[5].

❑ The aim of this study was to evaluate the effects of long term oral cholecalciferol supplementation on mineral metabolism, inflammation markers and cardiac dysfunction in chronic HD patients.

Patients and Methods

❑ This was a 5-year prospective study performed in 97 prevalent HD patients.

❑ Supplementation with oral cholecalciferol (Vigantol®) was done during 60 months, thrice weekly, after each HD session, assuring 100% compliance. Supplementation was given according to [25(OH)D_3] levels in the first 6 months (mean dose of 21.000 IU/week) and afterwards 8.000 IU/week.

❑ Clinical data included presence of diabetes mellitus, hypertension and coronary artery disease. PP was evaluated. Therapy with active vitamin D, phosphate binders and darbepoetin was also assessed.
Laboratory data considered were [25(OH)D_3], calcium, phosphorus, intact parathormone (iPTH), haemoglobin, albumin, C-reactive protein (CRP) and plasma BNP.
All patients were submitted to an echocardiographic evaluation and LVMI was calculated using the Devereux formula and indexed to body surface area.

❑ For statistical analysis the arithmetic media of the two measurements of [25(OH)D_3] at baseline (after winter and after summer) was used. Demographic, laboratory and echocardiographic data were compared at baseline and after 60 months of cholecalciferol supplementation. Comparison between two groups was performed using paired T-test. A $p<0.05$ was considered statistically significant.

Results

❑ Population data:
- 97 patients on chronic HD

- All submitted to on-line haemodiafiltration, with ultrapure water and high flux helixone filter (Fresenius®).

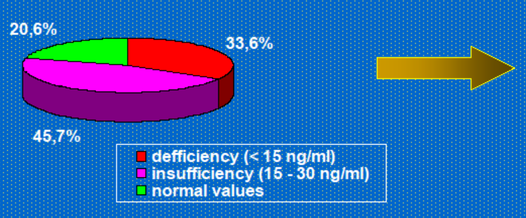
- Mean age (± SD): 63.2 ± 14.1 years

- 40.6% female

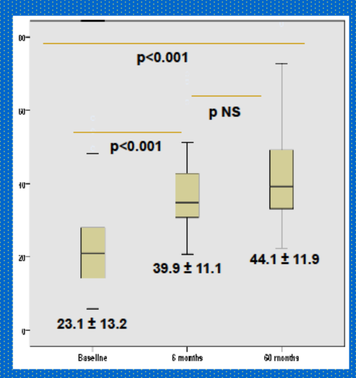
- Median HD time at baseline: 25 months

- 27% diabetics, 36% with hypertension and 31% with coronary artery disease

25-hydroxyvitamin D_3



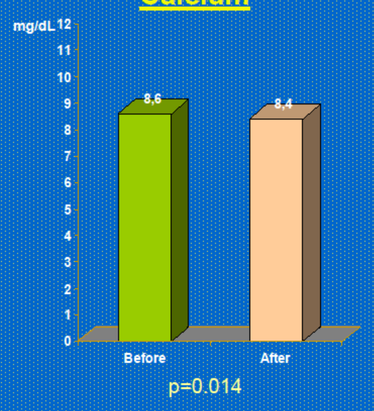
Mean baseline value (after winter and after summer): 23.1 ± 13.2 ng/mL



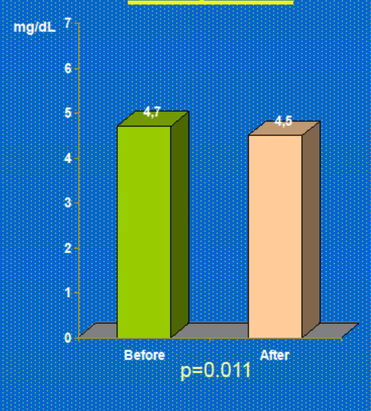
There was a significant increase in [25(OH)D_3] levels. The highest increase was observed in the first 6 months.

	Before supplementation	After 60 months of supplementation	p
25(OH)D_3 (ng/ml)	23.1 13.2	44.1 11.9	<0.001
Calcium (mg/dl)	8.6 0.8	8.4 0.3	0.02
Phosphorus (mg/dl)	4.7 1.5	4.5 1.3	0.018
iPTH (pg/ml)	267 156	227 118	0.03
Vitamin D therapy (%)	38	29	<0.001
Phosphate binders (%)	66	48	<0.001
Darbepoetin (µg/week)	33.2 21.9	26.4 19.9	0.02
Haemoglobin (g/dl)	11.6 1.2	11.5 1.4	NS
Albumin (g/dl)	3.8 0.5	4.1 0.3	<0.001
CRP (mg/dl)	0.9 1.1	0.7 0.9	0.01
PP (mmHg)	71 11	64 14	0.007
BNP (pg/ml)	443 211	336 182	<0.001
LVMI (g/m²)	135 71	122 56	0.02

Calcium

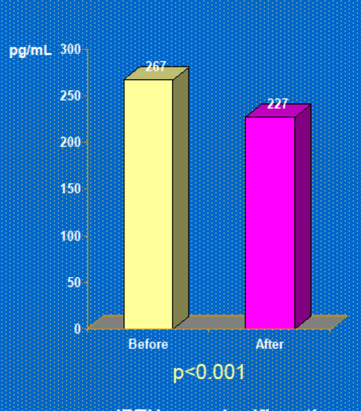


Phosphorus



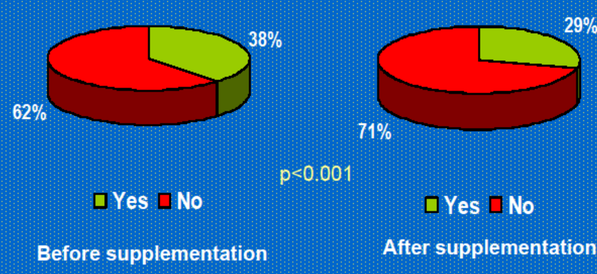
Serum calcium and phosphorus showed a significant decrease with supplementation.

iPTH

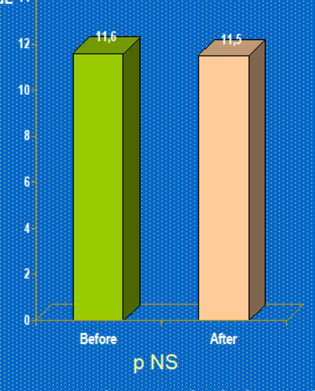


iPTH was significantly reduced during the study in spite of a lower consume of active vitamin D.

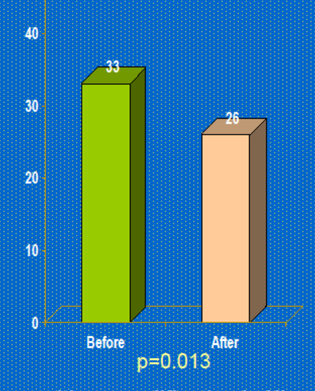
Active vitamin D therapy



Haemoglobin

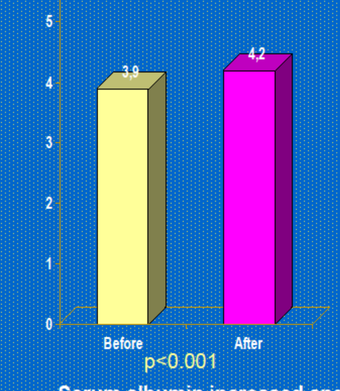


Darbepoetin

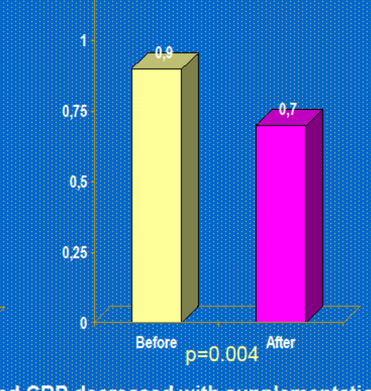


There was a decrease in darbepoetin use, with no modification in Hb values.

Albumin

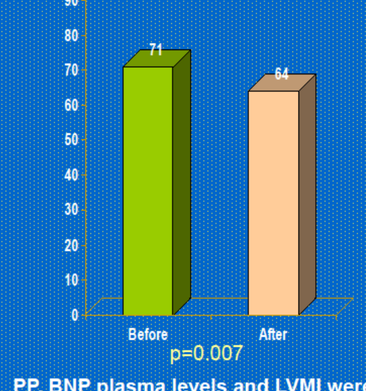


CRP

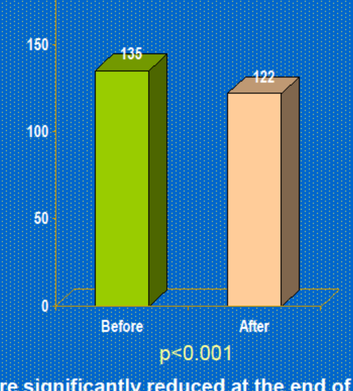


Serum albumin increased and CRP decreased with supplementation.

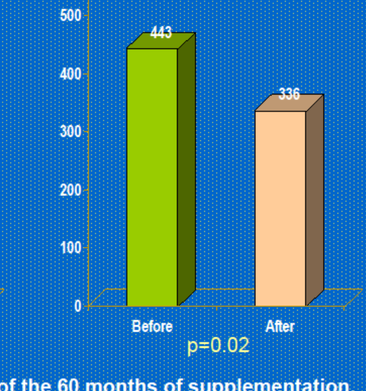
PP



BNP



LVMI



PP, BNP plasma levels and LVMI were significantly reduced at the end of the 60 months of supplementation.

Conclusions

❑ Our results show that long term oral cholecalciferol supplementation in HD patients appears to be an easy, simple and cost-effective therapeutic measure. It allows correction of vitamin D deficiency, better control of mineral metabolism with less use of active vitamin D, attenuation of inflammation, reduced dosing of erythropoiesis stimulating agents, and possibly, improvement of cardiac dysfunction.

❑ Based in this study we propose cholecalciferol supplementation in all dialysis patients, although the very promising effects in morbi-mortality still need to be confirmed in randomized studies.

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52 ERA
L6) Dialysis. Bone disease.
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