DOES CHOLECALCIFEROL CORRECT SECONDARY HYPERPARATHYROIDISM IN NON-DIALYSIS CHRONIC KIDNEY DISEASE PATIENTS?

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BACKGROUND AND AIMS

Since native vitamin D supplementation was reported to improve biochemical parameters in chronic kidney disease (CKD) patients[1], even at a smaller degree than active vitamin D analogs[2], but the data originated from low-to-moderate quality studies and conflicting opinions still exist[3], we aimed to compare the effects of medium-term cholecalciferol and paricalcitol therapy on the biochemical calcium-phosphate metabolism parameters in non-dialysis CKD patients.

METHODS AND SUBJECTS

STUDY DESIGN:

- Multicenter, open-label, active comparator controlled, 1:1 randomized (stratified by the CKD stage).

THERAPEUTIC INTERVENTIONS:

- Oral cholecalciferol 1000 UI/day (C)
- Oral paricalcitol 1 mcg/day (P)

} For six months (compliance verified by drug accountability).

PRIMARY STUDY PARAMETERS:

- Efficacy - Median changes after 6 months vs. baseline in serum calcidiol (25OHD), parathyroid hormone (iPTH), and alkaline phosphatase (AlkP) (Δ=6Mo-Bas);
- Safety - The incidence of hyperphosphatemia (>5 mg/dL) and hypercalcemia (>10.5 mg/dL) episodes.

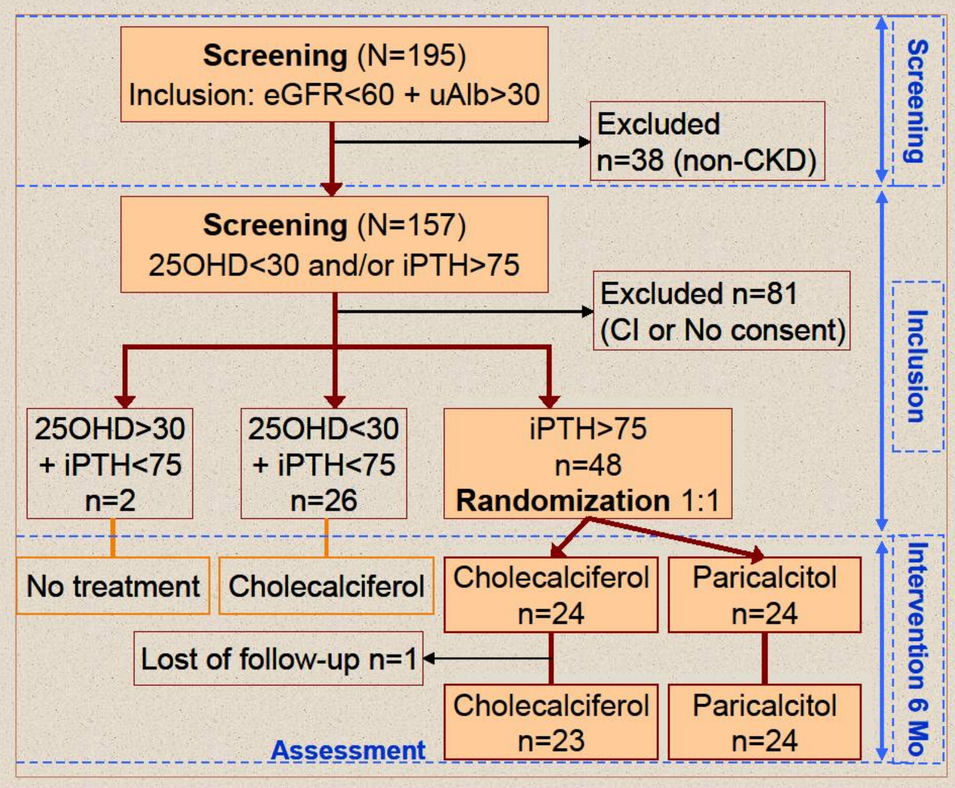
SECONDARY STUDY PARAMETERS:

- Median values of the studied variables at the assessment moments (baseline, 2, 4 and 6 months);
- Percentages of patients with the studied variables in target, as defined by the KDIGO guidelines[4];
- Percentages of patients with decrease in iPTH / increase in 25OHD.

STATISTICAL ANALYSIS: Data were expressed as median with 95%CI or percentages, and compared with Mann-Whitney, Wilcoxon and Chi^2 tests. A p value <0.05 was considered statistical significant.

SUBJECTS: Forty-eight vitamin D naïve subjects with increased serum parathyroid hormone (iPTH) were selected from a cohort of 157 stage 3 to 5 CKD patients (Figure 1).

Figure 1. STUDY FLOW CHART



RESULTS

At baseline, demographic and general characteristics were similar, except for higher iPTH in P group:

	Cholecalciferol (n=23)	Paricalcitol (n=24)	*p*
Age (y)	60 (54 to 66)	61 (54 to 67)	0.80
Gender (men) (%)	48	67	0.19
Cause of CKD (%)			
Vascular nephropathies	44	46	0.87
Primary glomerulopathies	22	25	0.79
Interstitial nephropathies	22	13	0.65
Hereditary kidney disease	4	13	0.63
Secondary glomerulopathies	4	4	0.99
eGFR (mL/min/1.73m²)	30.0 (25.4 to 37.6)	24.6 (21.9 to 33.9)	0.40
iPTH (pg/mL)	81 (65 to 192)	161 (155 to 320)	0.001
25OHD (ng/mL)	12.5 (9.9 to 15.1)	14.8 (12.9 to 19.3)	0.06
Alkaline phosphatase (UI/L)	68 (66 to 92)	101 (91 to 129)	0.05
Serum calcium (mg/dL)	9.1 (8.4 to 9.6)	9.1 (8.7 to 9.3)	0.60
Serum phosphate (mg/dL)	3.5 (3.2 to 4.5)	3.5 (3.4 to 4.2)	0.50

Figure 2. CHANGES IN SERUM CALCIDIOL AFTER 6 MONTHS OF THERAPY

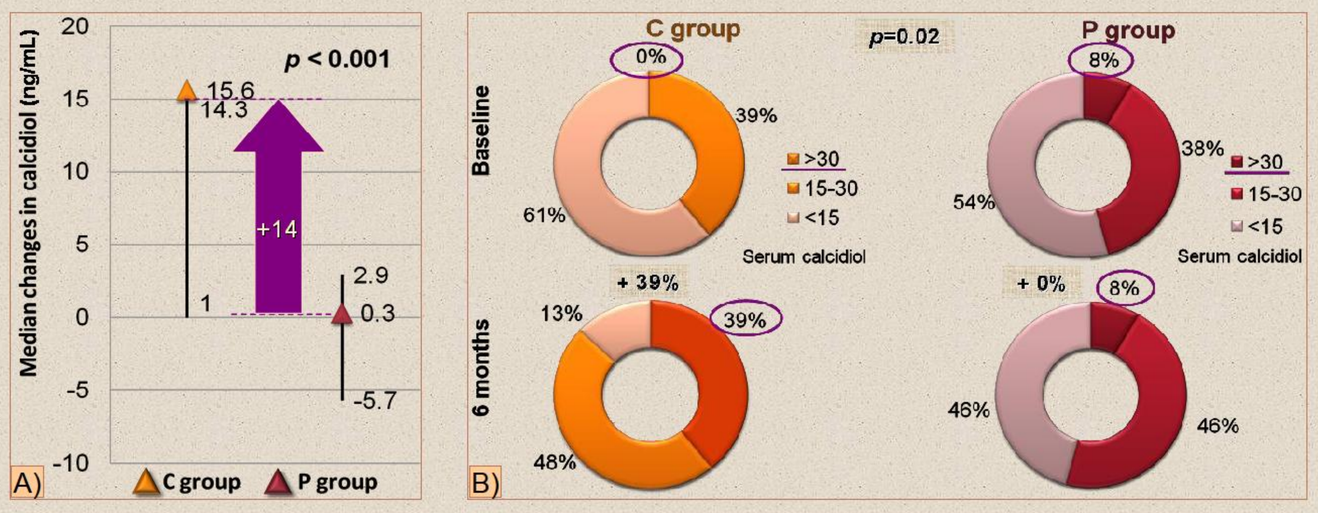
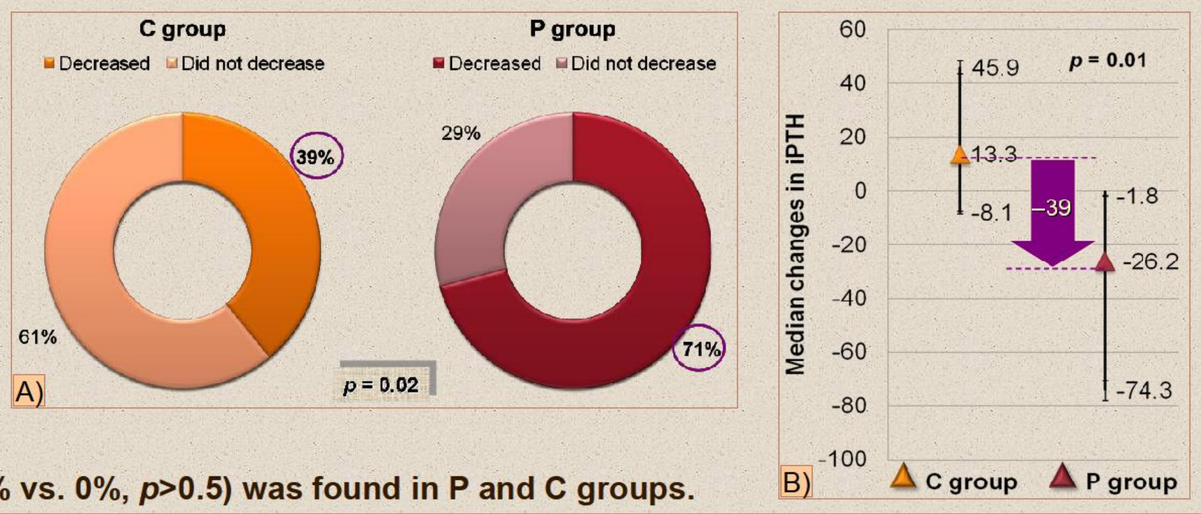


Figure 3. CHANGES IN SERUM INTACT PTH AFTER 6 MONTHS OF THERAPY



In C-treated subjects, higher increase in serum calcidiol was seen (Fig. 2A), and more subjects reached optimal levels (>30ng/mL; Fig. 2B). Conversely, more patients from P-treated group had a decrease of iPTH (Fig. 3A) and the decline in serum iPTH was found only in this group (Fig. 3B).

However, the proportions of subjects whith 3 and 4 mineral metabolism parameters concomitantly in the reference range were not influenced by the type of vitamin D therapy (+9% vs. +8% and +13% vs. +4%, respectively, *p*=0.6 for both).

Similar incidence of hyperphosphatemia (16.6% vs. 13%, *p*=0.9) and hypercalcemia (4% vs. 0%, *p*>0.5) was found in P and C groups.

CONCLUSIONS

1. Six months of cholecalciferol therapy partially corrected the calcidiol deficiency, but did not improve secondary hyperparathyroidism in non-dialysis CKD, at least in a rather small dosage.

On might speculate that:

- Higher doses would be required to reveal beneficial systemic effects of native vitamin D;
- Combined native and active vitamin D therapy could be useful for non-dialysis CKD patients.

} Both these hypothesis should be tested in future studies.

2. Hypercalcemia and hyperphosphatemia were not a concern, at least at this rather small doses of both drugs.

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