EFFECTS OF PARICALCITOL ON HEMOGLOBIN LEVELS IN CKD PATIENTS: A PILOT RANDOMIZED TRIAL

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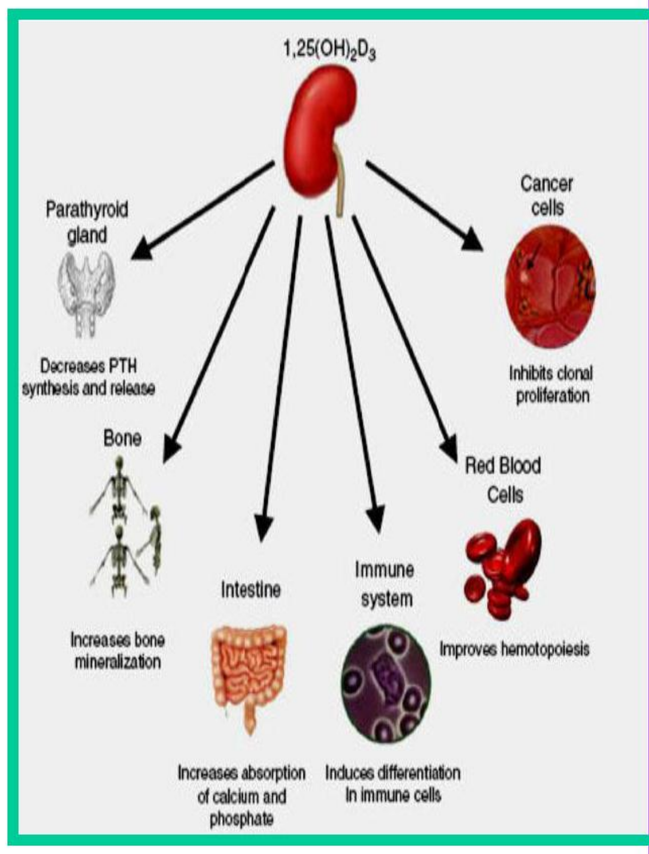
INTRODUCTION

Although current activated vitamin D therapies are approved for secondary hyperparathyroidism treatment in chronic kidney disease (CKD), several experimental data confirm that vitamin D pleiotropic effects extend beyond mineral metabolism[1]. In addition to its role in calcium homeostasis and bone mineralization, in fact, vitamin D is involved in immune defence, cardiovascular function, nflammation and erythropoiesis[2]. In vitro studies of bone marrow red cell precursor cells demonstrate that vitamin D increases erythropoietin-receptor expression and synergistically stimulates proliferation along with erythropoietin[3]. In addition, vitamin D has anti-inflammatory actions that could theoretically improve erythropoietin responsiveness, perhaps by reducing interleukin-6 (IL-6) levels and thus levels of hepcidin[4], and could ameliorate anemia by correcting the secondary hyperparathyroidism[5]. However, there are no data on the direct effect of oral paricalcitol, a newVitamin D Receptor activator, on the anemia in CKD.



Pleiotropic actions of Vitamin D

AIM OF STUDY

Our study aims to determine whether the use of oral paricalcitol leads to improvement in anemia in CKD, and whether this effect is independent from hyperparathyroidism correction.

METHODS

A total of 34 patients with CKD 3-5 stage not on dialysis (eGFR ≤60 ml/min/1.73 m^2) and anemia (Hb 10--12,5 g/dl) were enrolled.

Patients with iron deficiency (ferritin <100 ng/ml; transferrin saturation <20%), severe iperparathyroidism (PTH >300 pg/ml) and inflammation (C-reactive protein >1mg/dL) were excluded. The enrolled patients were randomly assigned to receive either paricalcitol (CASE) or native vitamin D/calcitriol (CONTROL) for 6 months. The end point was the difference in Hb levels from the basal after 6 months of treatment (T3) in the two groups.

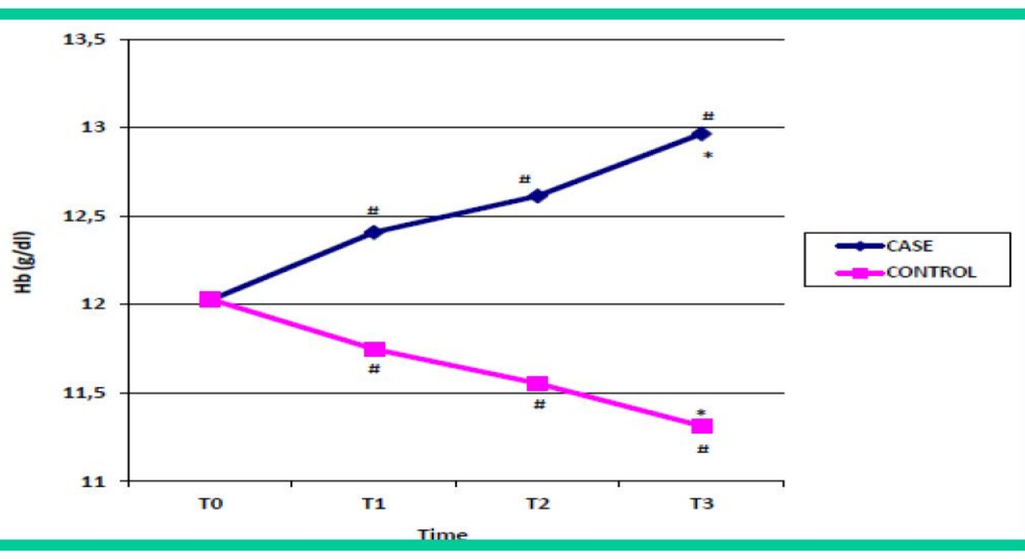
RESULTS

The patients of the case group (n=17) showed a significant increase in Hb levels after 6 months of therapy (p=0,03). In control group (n=17), Hb progressively decreased (p=0,01). Moreover, after only 2 months (T1) the difference in Hb levels between the groups was significant (p=0,012), and remained stable until the end of the study (p=0,015). No significant change was reported in PTH and PCR levels.

	All (34 pt)	Case (N=17)	Control (N=17)
Hb (g/dL)	12,03±0,66	12,02±0,7	12,03±0,65
Ferritine (ng/mL)	203,74±127,75	191,18±146,64	216,29±108,74
TSAT (%)	29,03±8,09	27,72±7,67	30,33±8,53
Vit B12 (pg/mL)	26,32±10,81	25,58±9,99	27,06±11,83
Folic acid (ng/mL)	481,95±201,07	450,54±204,47	513,36±198,71
Ca (mg/dL)	9,37±0,35	9,36±0,34	9,38±0,38
P (mg/dL)	3,66±0,58	3,51±0,59	3,81±0,56
PTH (pg/mL)	147,2±80,78	147,84±81,16	146,56±82,89
Albumine (g/dL)	4,45±0,35	4,4±0,33	4,51±0,38
hsPCR (mg/L)	1,71±1,57	1,67±1,39	1,75±1,76
Prot^u (g/24 h)	1,14 ± 1,63	1,24±1,89	1,05±1,37

Baseline characteristics of the patients

	CASE				CONTROL			
	T0	T1	T2	T3	T0	T1	T2	T3
Hb (g/dL)	12,02	12,40$^{\#}$	12,61$^{\#}$	12,96$^{*\#}$	12,03	11,75$^{\#}$	11,55$^{\#}$	11,31$^{*\#}$
GFR (mL/min)	25,58	26,48	23,89	23,60	27,06	26,49	27,14	25,11
Ferritine (ng/mL)	191,18	164,4	131,38	155,71	216,29	199,47	186,53	186,88
TSAT (%)	27,72	25,29	27,48	26,51	30,33	30,82	27,55	27,33
Ca (mg/dL)	9,36	9,37	9,44	9,46	9,38	9,29	9,29	9,14
P (mg/dL)	3,51	3,83	3,72	3,78	3,81	3,86	3,53	3,88
PTH (pg/mL)	147,84	119,80	96,37	97,00	146,56	164,47	152,20	142,18
hsPCR (mg/L)	1,67	1,88	1,98	1,53	1,75	1,68	1,24	1,70
Prot^u (g/24 h)	1,24	1,39	1,35	1,16	1,05	1,04	1,17	1,07



RESULTS

*p< 0,05 vs T0
# p< 0,05 between groups

CONCLUSIONS

Oral paricalcitol could improve anemia in CKD patients. The increase in Hb levels is likely due to a direct stimulation of erythroid precursors as reported *in vitro* for calcitriol and it could be no related to hyperparatiroidism correction.

REFERENCES

1) Lin R, White JH. Pleiotroic actions of Vitamin D. BioEssays, 2003; 26: 21-28.
2) Nagpal S, Na S, Rathnachalam R. Noncalcemic actions of Vitamin D Receptor Lignads. Endocrine Reviews, 2005; 26(5): 662-687.
3) Alon DB, Chaimovitz C, Dvilansky A et al. Novel role of 1,25(OH)(2)D(3) in induction of erythroid progenitor cell proliferation. Exp Hematol 2002; 30: 403–409.
4) Turk S, Akbulut M, Yildiz A et al. Comparative effect of oral pulse and intravenous calcitriol treatment in hemodialysis patients: the effect on serum IL-1 and IL-6 levels and bone mineral density. Nephron 2002; 90: 188–194.
5) Neves PL, Trivino J, Casaubon F et al. Elderly patients on chronic hemodialysis with hyperparathyroidism: increase of hemoglobin level after intravenous calcitriol. Int Urol Nephrol 2006; 38: 175–177.