EFFECT OF CHOLECALCIFEROL SUPPLEMENTATION ON TLR-7, TLR-9, IL-6 AND IFN-γ EXPRESSION IN B AND T LYMPHOCYTES ON CHRONIC DIALYSIS PATIENTS

FAPESP nº:2012/19314-2

Authors: José Tarcisio Giffoni Carvalho[1], Marion Schneider[1], Lilian Cuppari1 Caren Grabulosa[1], Danilo Takashi Aoike[1], Silvia Regina Manfredi1, Beata Marie Quinto Redublo[1], Marcelo Costa Batista[1,3], Miguel Cendoroglo[1,3], Maria Aparecida Dalboni[1,2]

Institutions:

1.Division of Nephrology- Universidade Federal São Paulo, UNIFESP, São Paulo, SP, Brazil.

2.Universidade Nove de Julho, UNINOVE, São Paulo, SP, Brazil.

3.Hospital Israelita Albert Einstein, São Paulo, SP, Brazil.

INTRODUCTION AND OBJECTIVE

Vitamin D deficiency is highly prevalent among patients in all stages of chronic dialysis (CKD) patients. Previous studies have reported that the Vitamin D deficiency is associated with all causes of mortality and morbidity in CKD patients, which may be linked to an excessive inflammatory state. Toll-like receptors (TLRs) are involved in several immunologic responses and in others diseases, the expression of this receptors can be modulated by vitamin D. However, the impact of low levels of vitamin D on lymphocytes from CKD patients is unclear. The purpose of this study was evaluate the effect of cholecalciferol treatment on IL-6, IFN-γ TLR-7 and TLR-9 expression in lymphocytes B and T in patients on CKD patients.

METHODS

In a randomized, placebo-controlled, double-blind study, we investigated the effect of cholecalciferol (100,000 UI once per week or placebo) for 3 months, in patients on chronic dialysis, who had nutritional vitamin D deficiency (25(OH)D3 ≤20ng/mL). The 25(OH)D3 detection was performed by quimioluminescence; and we use Flow cytometry to evaluate IL6, IFN-γ, TLR7, TLR9, VDR, CYP27 and CYP24 expression on lymphocytes B and T, at baseline and after 3 months.

RESULTS

Figure 1: Effect of cholecalciferol supplementation on 25(OH)D_3 levels (n=16 placebo; 16 cholecalciferol)

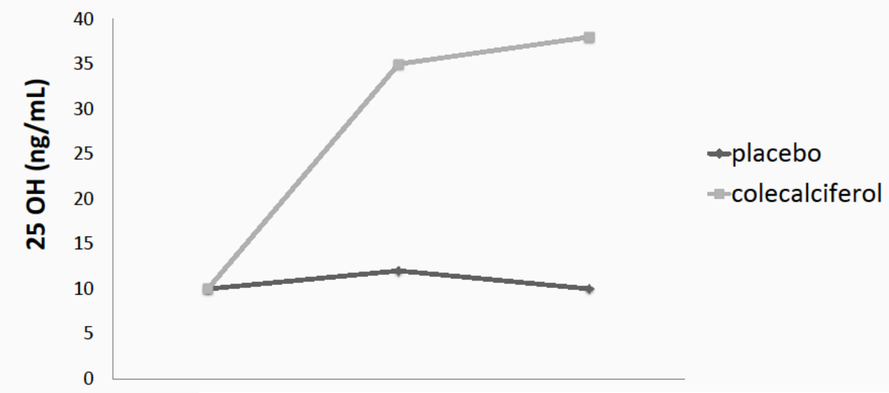


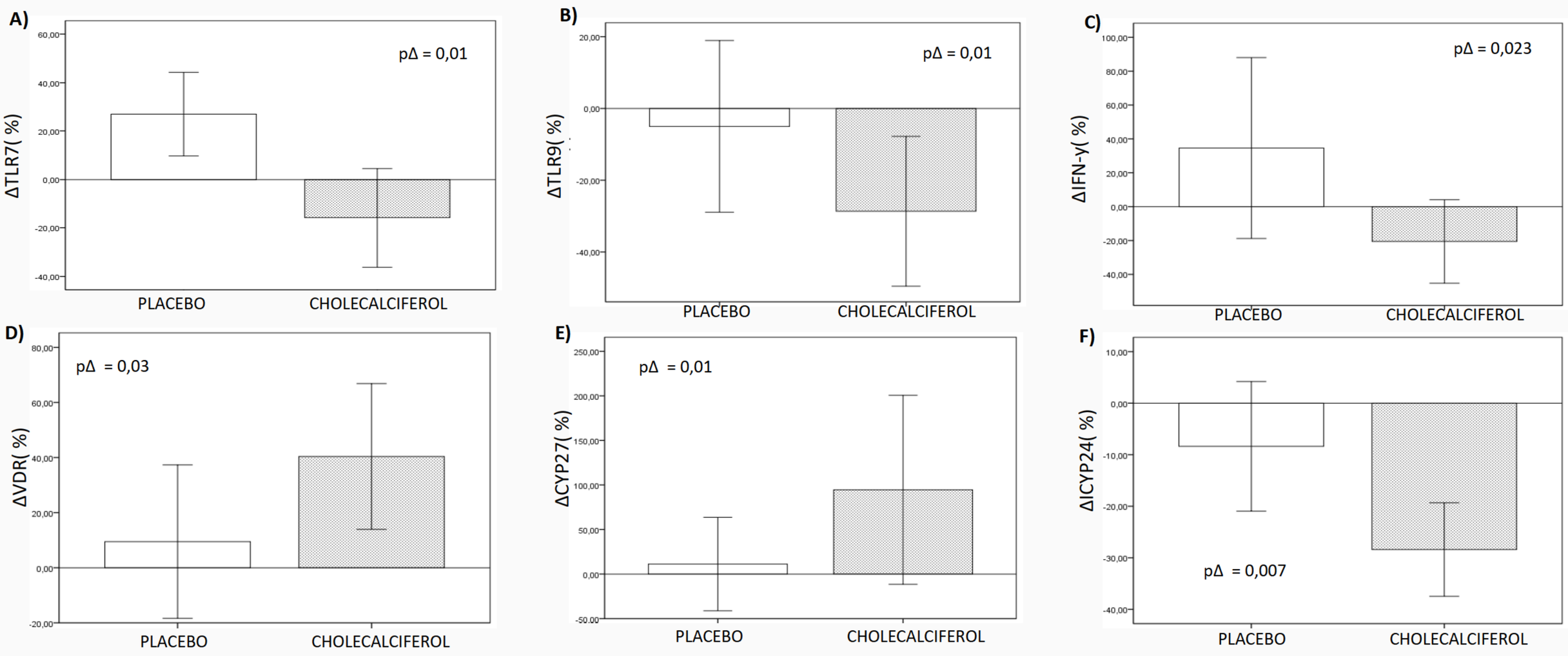
Table 1: : Effect of cholecalciferol supplementation on Calcium (Ca), 25(OH)D_3, Phosphorus (P) and PTH (n=16 placebo; 16 cholecalciferol)

	PLACEBO			CHOLECALCIFEROL			
	PRE	POS	p*	PRE	POS	p#	pΔ
Ca (mg/dL)	8,76±,59	8,86±,78	0,46	8,64±,81	8,74±0,74	0,26	0,52
25(OH)D_3 (ng/L)	13±4	15±9	0,41	16±4	43±13	0,01	0,01
P (mg/dL)	5,37±1,45	5,57±1,83	0,45	5,19±1,66	5,32±1,68	0,50	0,60
PTH (pg/mL)	260 (70-510)	330(28-595)	0,04	385 (128-640)	300 (85-520)	0,03	0,01
FGF-23 (pg/mL)	2215 (220-7720)	1870(240-6140)	0,30	1360 (204 - 3960)	1470 (180-5200)	0,40	0,01

General Lineares Model

***pos≠pre placebo group ; # pos≠pre cholecalciferol group ; Δ diference between groups**

Figure 2 A-F: : Effect of cholecalciferol supplementation on TLR7 , TLR9, IFN-Y , VDR, CYP27 and CYP24 (n=16 placebo; 16 cholecalciferol)



CONCLUSION

Cholecalciferol treatment in dialysis patients showed to be safe and efficient to correct hipovitaminosis D. In addition, we observed impact of 25(OH)D_3 repletion on reduction of expression of the TLR7, TLR9, IFN-γ and improve of regulatory mechanisms associated with intracellular production of vitamin D on lymphocytes from CKD patients. These results suggests that cholecalciferol treatment play an important role on TLRs expression as an anti-inflammatory and that this may contributed to a better systemic inflammation response in CKD patients

REFERENCES

1.Dickie et al Rheumatology 2010; 49, 1466–1471
2.Khoo et al Cytokine. 201155(2):294-300.
3. Rodriguez et al J Leukoc Biol. 2012 91(5):829-38.
4. Stubbs et al. J Am Soc Nephrol. 2010 Feb;21(2):353-61
5. Alvarez et al. Eur J Clin Nutr. 2013 Mar;67(3):264-9

DOI: 10.3252/pso.eu.52era.2015