

# Association of Vitamin D Deficiency with Renal Anaemia and Erythropoietin Hyporesponsiveness in Haemodialysis Patients

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## Introduction

Nearly one tenth of hemodialysis (HD) patients exhibit erythropoietin (EPO) hyporesponsiveness/resistance: inability to achieve or maintain target hemoglobin despite escalating EPO doses. An inverse association has been found between vitamin D levels and EPO requirements in chronic kidney disease patients. Vitamin D supplementation may improve response to EPO either by suppression of the chronic inflammatory status, control of hyperparathyroidism, or direct stimulation of erythroid progenitors. A prospective clinical study is needed to assess the potential therapeutic role of vitamin D supplementation on EPO response in HD patients and explore its possible mechanisms.

## Methods

30 anemic patients on regular HD for  $\geq 6$  months were included. They were on standard anemia therapy with SC EPO 4000 U and IV iron sucrose 100 mg once or twice weekly. 20 matching healthy subjects were included as controls. Baseline laboratory studies included complete blood picture, calculation of EPO resistance index (ERI) (weekly EPO dose/ body weight in Kg / hemoglobin increment in 2 weeks), serum iron, TIBC, ferritin, hepcidin, calcium, phosphorus, alkaline phosphatase, iPTH, 25(OH)vit D (Vit D3), CRP and IL-6. These studies were repeated after 3 months of oral alfacalcidol therapy (2 micrograms thrice weekly, with each dialysis session).

## Results

Hemoglobin level increased significantly from a median of 8.4 to 9.5 gm/dL ( $P < 0.001$ ), ERI decreased significantly from  $7.46 \pm 1.47$  (median 7.37) to  $6.53 \pm 1.22$  (median 6.34) U/Kg/gm/dL ( $P < 0.001$ ). Inflammatory markers (serum CRP, IL-6, ferritin and hepcidin) decreased significantly ( $P < 0.001$  for all). Serum iPTH and alkaline phosphatase decreased significantly ( $P = 0.007$ ,  $P < 0.001$ , respectively). At the start of the study, there was a significant positive correlation between ERI and serum ferritin ( $P = 0.026$ ), and a significant negative correlation between serum vitamin D3 level and alkaline phosphatase ( $P = 0.004$ ). At the end of the study, there was a significant negative correlation between serum vitamin D3 level and each of serum ferritin ( $P = 0.005$ ) and IL-6 ( $P = 0.019$ ).

## Conclusions

A three months course of oral alfacalcidol supplementation of HD patients significantly increases hemoglobin and decreases EPO resistance. This improvement is associated with, and possibly mediated through, amelioration of the chronic inflammatory status and control of hyperparathyroidism prevalent in these patients. Within the limits set by CKD-MBD guidelines, vitamin D supplementation of HD patients has the added benefit of improving EPO response and increasing its cost effectiveness.

