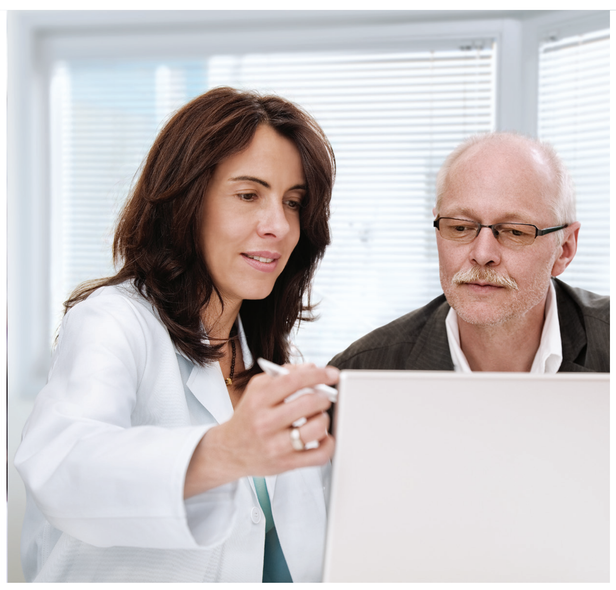


Evaluation of vitamin D supply in relation to binding proteins and PTH levels, and in correlation with types of dialysis

L. Kovács[1,2] | D., Z. Lőcsei[2] | B. Kalman[2,3] | I. Kulcsár[1,2] | E. Toldy[2,3]

[1]B. Braun Avitum 6 th Dialysis Centre

[2]Department of Internal Medicine, Markusovszky Teaching Hospital, Szombathely, Hungary

[3]Faculty of Health Science, University of Pécs, Hungary

Background

The total 25-hydoxy-vitamin-D (t-25OHD) level reflects the vitamin-D supply, but is also influenced by the levels of vitamin-D-binding-proteins (DBP) and albumin. The type of dialysis influences the levels of serum proteins.

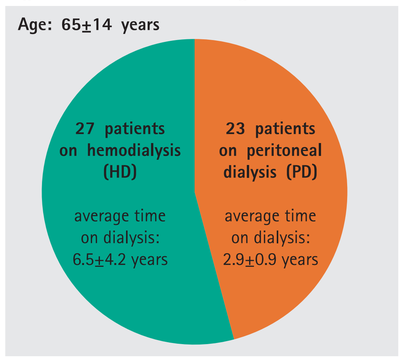
Aims

To examine and monitor the vitamin-D supply on the bases of t-25OHD and bioavailable vitamin-D (Bio-25OHD) levels, parathyroid hormone intact (PTHi), biointact 1-84-PTH (bioPTHi) and ionized calcium (Ca^{2+}) concentrations in patients on peritoneal- (PD) and hemodialysis (HD) before and after taking 1000 IU/day cholecalciferol (D_3).

Patients

Altogether 50 dialyzed patients (26 males, 24 females) were included in two dialysis groups matched by gender and age *(Figure 1)*. The average time period spent in dialysis was 4.8±3.6 years.

Figure 1: The 50 investigated cases



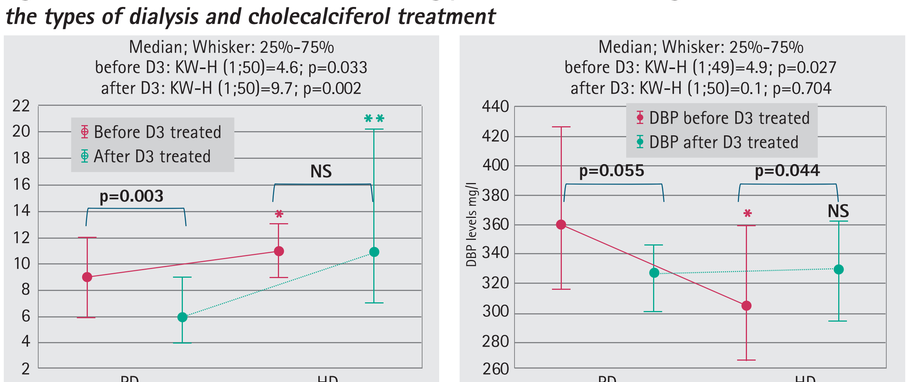
The duration of native vitamin D supplementation in the study was 6.0±3.5 months. Twenty-six patients received active forms of vitamin D before (7 HD and 19 PD) and after (8 HD and 18 PD) taking native D_3.

Measured biochemical markers

t-25OHD (protein bindig assay, Roche), PTHi bioPTHi (ECLIA, Cobas, Roche), c-reactive protein (CRP), DBP (Immuno-turbidimetry, Dako), albumin (colorimetry, Modular Roche), and Ca^{2+} (ion-selective electrode, Nova) were measured prior to and after vitamin D supplementation. The Bio-25OHD values were calculated using a mathematical model (Vermeulen et al, 1999, Bhan et al, 2012).

Results

Figure 2: Differences of albumin and binding protein levels according to the types of dialysis and cholecalciferol treatment



Both before and after vitamin D supplementation, lower albumin levels were detected in PD than in HD. The DBP was significantly higher in PD than HD, but only before D_3 treatment. After D_3 supplementation, the DBP level rose in HD, while decreases in PD *(Figures 2)*.

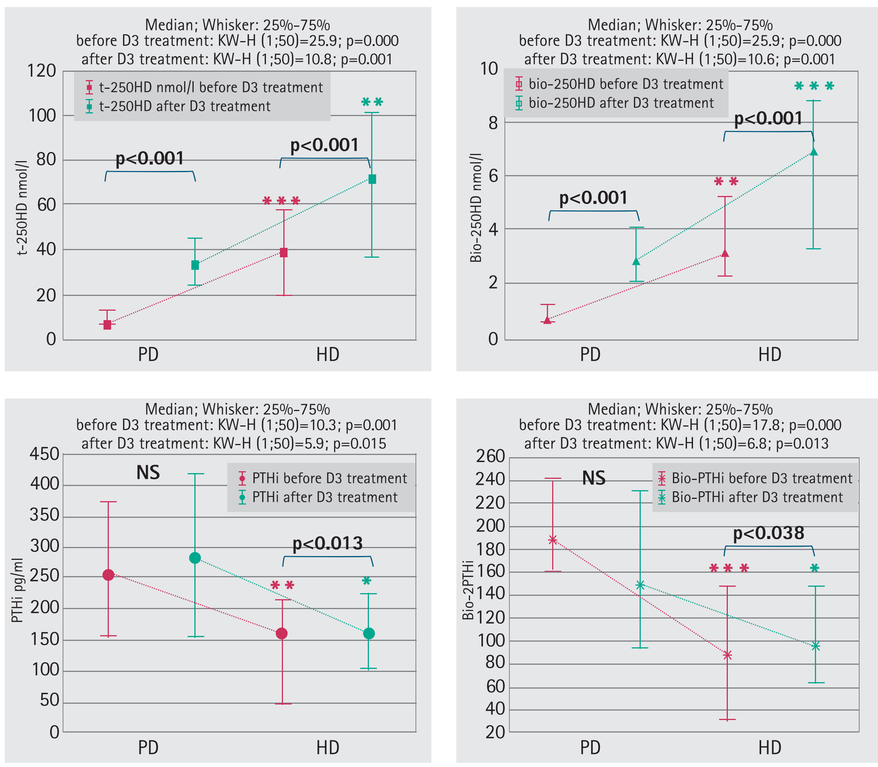
*Legend to Figure 2 and 3: The stars above the whiskers indicate levels of significance when the PD and HD groups are compared (*p<0.05; **p<0.01,***p<0.001). The blue bars and blue p values depict the Wilcoxon Matched Pairs test p-values for concentrations compared before and after vitamin D_3 treatment within the PD and HD groups.*

Conclusions

- There are considerable interactions between t-25OHD and DBP/albumin in PD patients, thus evaluation of the vitamin D supply is more reliable based on the bio-25OHD levels. The t-25OHD values overestimate the vitamin D supply particularlyin the lower ranges of measurements.
- In contrast, the t-25OHD measurements appear sufficient to reliably assess the vitamin D supply in HD.
- Cholecalciferol 1000 IU/day supplementation is not enough to sufficiently raise 25OHD levels in either group of dialysis patients. PD patients suffer from more serious vitamin-D deficiency than HD patients, and therefore, need much higher doses of cholecalciferol. Different protein interactions in PD than in HD may explain this observation.
- The lower serum albumin and higher DBP levels in PD may explain the particularly low 25(OH)D levels, and the loss of protein during PD.
- The significant negative correlations between BioPTHi and 25OHD underscores that the normal and abnormal values of bioPTHi should be determined taking into consideration the vitamin D supply in patients undergoing dialysis, independent of the type of dialysis.

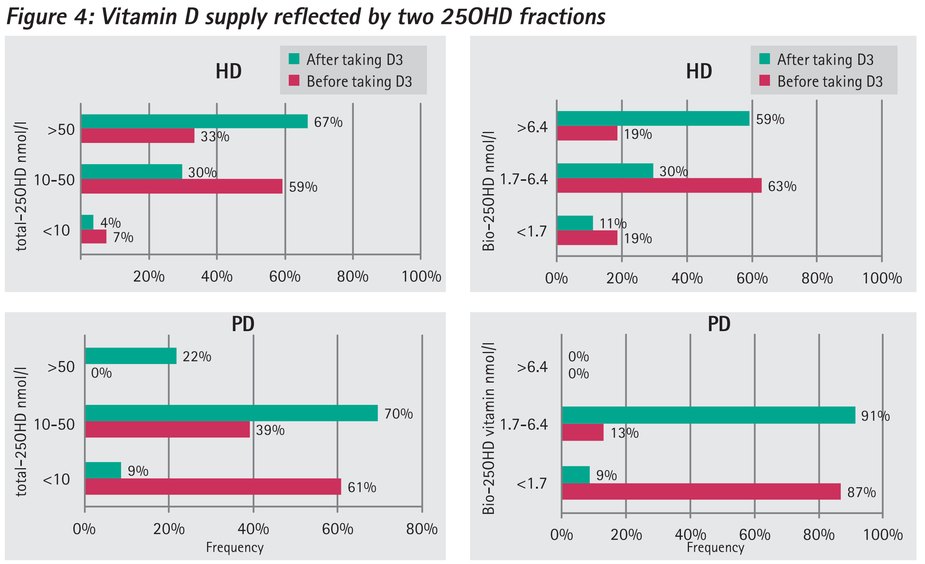
B. Braun Avitum Hungary Zrt. | 1023 Budapest, Felhévízi u. 5. | Tel.: +36 (1) 346-9700 | Fax: +36 (1) 438-4900 | www.bbraun.hu

Figure 3: 25OHD fractions and PTHi, bioPTHi levels before and after taking cholecalciferol



Cholecalciferol 1000 IU/day supplementation caused significant increases in the serum levels of vitamin D fractions in both dialysis groups. The t-25OHD levels were significantly lower, while bioPTHi and iPTH levels were significantly higher in PD than HD group both before and after taking cholecalciferol. However, cholecalciferol 1000 IU/day supplementation was insufficient to raise levels of t-25OHD beyond 50 nmol/l and of Bio-25OHD beyond 6.4 nmol/l, particularly in PD *(Figure 3)*.

Figure 4: Vitamin D supply reflected by two 25OHD fractions



According to the t-25OHD measurements, 100% of PD patients and 67% of HD patients were vitamin D deficient before cholecalciferol treatment. Deficiency remained in 79% of PD and 34% of HD subjects after D_3 supplementation on the bases of t-25OHD concentrations *(Figure 4, left side)*.

According to the Bio-25OHD levels, vitamin deficiency remained in 100% of PD and 41% of HD patients after vitamin D3 supplementation. Serious deficiency was more frequent in PD than in HD (87% vs. 19%) on the bases of Bio-25OHD levels. Significant ($p<0.05$) differences were noted between the two fractions of 25OHD in PD (87% vs. 61%), but not in HD *(Figure 4, right side)*.

Results of the Sperman Rank Order Correlations

The correlations between the total and bio 25OHD levels were excellent (r=0.93) in HD, but weaker in PD (r=0.73). The significant ($p<0.001$) correlations among the biomarkers, irrespective of vitamin D3 supplementation are summarized in the table.

Correlations among biologically related markers

	Albumin		DBP		bio-PTHi		Ca^+	
	HD	PD	HD	PD	HD	PD	HD	PD
t-25OHD	-	+0.51	-	+0.52	-0.55	-0.59	-	-
Bio-25OHD	+0.51	+0.47	-	-	-0.42	-0.37	-	+0.51

Positive correlations were observed between levels of t-25OHD and DBP and t-25OHD and albumin only in PD. All fractions of 25(OH)D showed similar negative correlations with the bioPTHi levels in both groups. Significant positive correlations between Ca^{2+} and Bio-25OHD levels, but not between t-25OHD and Ca^{2+} were found only in PD.