Vitamin D_3 modulates inflammatory response and expression of vitamin D-regulatory proteins in circulating monocytes of patients on dialysis with hypovitaminosis D

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Category: Chronic Kidney Disease (Nutrition, inflammation and oxidative stress)

Introduction

✓ Vitamin D may exert pleiotropic effects on several complications of CKD, such as chronic inflammation which is highly prevalent in patients on dialysis.

✓ Although a potential benefit of the vitamin D repletion on inflammation has been suggested, this issue has still been poorly investigated in patients on dialysis.

Objectives

To investigate the effects of vitamin D_3 supplementation on vitamin D-regulatory proteins expression in monocytes and on circulating markers of inflammation in patients on dialysis with hypovitaminosis D.

Methods

Study design: Randomized double-blind placebo-controlled trial of 12 weeks

Sample: Patients with CKD undergoing hemodialysis or peritoneal dialysis

Inclusion criteria:

- 25(OH)D < 20 ng/mL
- Age 18-80 years
- Dialysis vintage ≥ 3 months

Exclusion criteria:

- Use of vitamin D or analogues
- Liver failure, intestinal malabsorption
- Cancer, autoimmune disease
- Infection in activity and positive HIV

Groups:

Vitamin D_3	Control
50 drops/twice weekly 1.000 IU/drop → **100.000 IU/wk**	50 drops/twice weekly **Placebo solution**

Laboratory assessment:

Fasting blood samples

Serum:

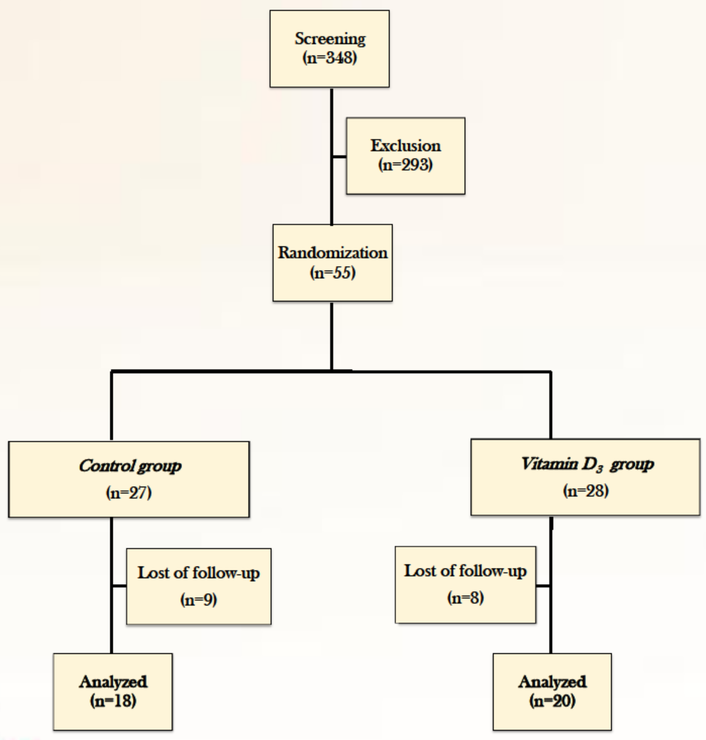
- 25(OH)D: Chemiluminescence
- PTH: Chemiluminescence
- CRP: Immunoturbidimetry
- IL-6, TNF-α, FGF-23: ELISA

Isolation of monocytes

Flow citometry:

- IL-6
- Vitamin D receptor (VDR)
- 1-α hydroxylase enzyme
- 24-hydroxylase enzyme

Flow diagram of patients enrolled in the study:



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Results

Main characteristics of the patients at baseline according to the groups.

Parameters	Control (n = 18)	Vitamin D_3 (n = 20)	p
HD/PD (n)	12/6	11/9	0.463
Gender, male/female (n)	9/9	11/9	0.758
Diabetes Mellitus [n(%)]	8 (44.4)	8 (40.0)	0.782
Hypertension [n(%)]	16 (88.9)	18 (90.0)	1.000
Age (years)	56.5±12.9	55.5±14.2	0.831
BMI (kg/m²)	25.25±6.40	25.49±4.96	0.898
Dialysis vintage (months)	32.5 (15.2-62.2)	28 (8.7-49.7)	0.534
Creatinine (mg/dL)	10.0±3.2	10.6±5.0	0.659

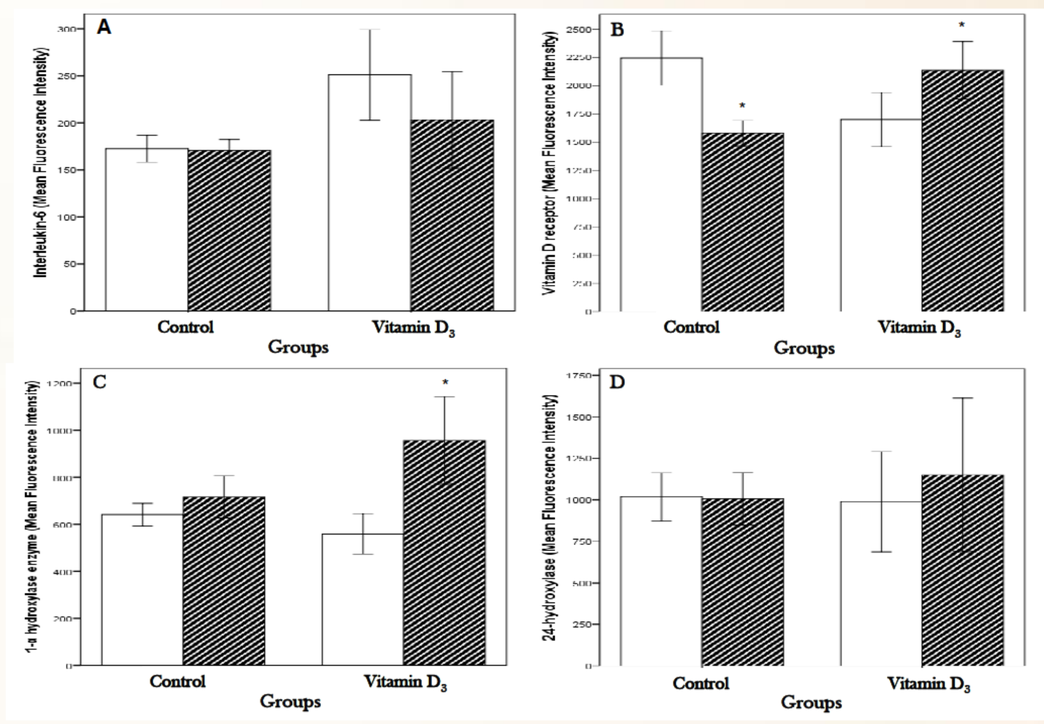
Data are expressed as number, mean ± s.d. or median (interquartile range). HD: hemodialysis, PD: peritoneal dialysis, BMI: body mass index. Wilcoxon, t test or χ^2 as appropriate.

Laboratory parameters at baseline and after 12 weeks of intervention according to the treatment group.

Parameters	Control group (n=18)			Vitamin D_3 group (n=20)			*Group-by-time interaction p*
	Baseline	*12-week*	*p*	*Baseline*	*12-week*	*p*	
25(OH)D (ng/mL)	13.9±4.2	13.5±4.3	0.562	14.3±4.7	43.1±11.0	<0.001	< 0.001
CRP (mg/dL)	0.57 (0.19-1.73)	0.48 (0.21-1.71)	0.845	0.50 (0.10-1.27)	0.28 (0.09-0.62)	0.010	0.097
IL-6 (pg/mL)	9.0±5.2	9.6±5.6	0.673	8.1±6.6	4.6±4.1	0.012	0.033
TNF-α (pg/mL)	5.5 (4.3-5.8)	4.7 (3.8-5.7)	0.223	6.0 (4.0-6.7)	5.1 (3.7-7.1)	0.985	0.377
PTH (pg/mL)	276.0(168.5-392.5)	278.5(126.2-521.7)	0.156	432.0(225.5-558.5)	331.5(243.2-504.0)	0.033	0.018
FGF-23 (ng/mL)	2220 (696-9475)	1620 (980-7895)	0.896	930 (522-3800)	980 (347-3260)	0.324	0.828
Phosphorus (mg/dL)	5.3±1.4	5.6±1.7	0.351	5.1±1.5	5.2±1.4	0.571	0.593
Calcium (mmol/L)	1.24(1.18-1.28)	1.23(1.19-1.28)	0.176	1.24(1.19-1.28)	1.27(1.21-1.31)	0.116	0.063
AP (U/L)	83.5(59.5-142.7)	83.5(58.5-123.0)	0.395	84.5(71.7-130.7)	85.0(70.2-126.0)	0.711	0.355

Data presented as mean ± s. d. or median (interquartile range). CRP: C-reactive protein; IL-6: interleukin-6; TNF-α: tumor necrosis factor-α; PTH: parathyroid hormone; FGF-23: fibroblast growth factor-23. AP: Alkaline phosphatase. General linear model test or Wilcoxon signed-rank test as appropriate.

Monocytes expression of Interleukin-6 (A), Vitamin D receptor (B), 1-α hydroxylase enzyme (C), 24-hydroxylase enzyme (D) at baseline and after 12 weeks of intervention according to the treatment group.



Baseline; 12 weeks. * p < 0.05 within groups.

Conclusion

Vitamin D repletion led to an upregulation in the expression of 1-α hydroxylase enzyme and vitamin D receptor (VDR) in monocytes and a decrease of circulating IL-6 and CRP in patients on dialysis with hypovitaminosis D.

References

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