SCIENTIFIC EMINENCE GROUP

Research Article

Open Access

Journal of Hepatology, Nephrology, Endocrinology Science

jhne@scientificeminence.com

Study of vitamin D3 level in Egyptian Hemodialysis patients and the effect of replacement therapy

Alaa Sabry[1*], Ahmed Abd El Wahab[1] and Mohamed Elazaz[2]

[1]Mansoura Nephrology and Dialysis unit, Faculty of Medicine–Mansoura University

[2]Ministry of Health, Egypt

*** Corresponding Author**

Alaa Abdel Aziz Sabry, Professor of nephrology, Mansoura school of medicine, Mansoura university, Tel: 00201028833213, E-mail: asabry2040@yahoo.com

Citation

Alaa Sabry (2022) Study of vitamin D3 level in Egyptian Hemodialysis patients and the effect of replacement therapy.

Publication Datess

Received date: February 12, 2022

Accepted date: March 12, 2022

Published date: March 14, 2022

Abstract

Background: The ability of extrarenal tissues to convert 25-hydroxyvitamin D [25(OH)D] into 1,25-hydroxyvitamin D [1,25(OH)2D] and its dependence on substrate levels provide the rationale for supplementing vitamin D in dialysis patients who usually have severe depletion of both: calcitriol and vitamin D.

The primary aim of the study was to detect serum Vit d3 levels in cohort of Egyptian Hemodialysis patients and to check the effect of its replacement on serum levels .serum1,25(OH)2D in hemodialysis patients with vitamin D deficiency. Secondary outcomes were changes in serum calcium, phosphate, parathyroid hormone (PTH).

Patients and Methods: 40 patients (25 males and 15 females) with Chronic Kidney Disease CKD (stage V) on regular heamodialysis, attending at Nephrology unit, Internal medicine department, Mansoura University Hospital during the period from January to June 2020. Another 40 persons- Age and sex matched- was selected randomly from the medical workers and served as control group .According to laboratory investigation and clinical examination deficient patients treated with Devarol-S (cholecalciferol) for 3 months and then revaluated. Deficient patients received 50000 IU monthly for 3 Consecutive months.

Results: The study was carried on 80 persons, 27 male patients (73.0%) and 13 female patients (27.0%). Their mean age was (47.16±14.92) years .The mean dialysis duration is (4.68±2.42) years and 40 person as control group.

3 Months after vitamin D replacement significant increase in serum calcium (8.33 to 8.89) mg/dL , phosphorous (4.99 to 5.85) mg/dL and Vit D (4.01 to 28.43) ng/mL levels compared to pretreatment level. There is also significant decrease in parathormone hormone level (419.30 to 377.20) pg/mL.

After 3 months of follow up there was no significant change in the levels of haemoglobin , KT/v, Albumin and alkaline phosphatase in the overall sample (p value = 0.7 ,0.4,0.29 and 0.59 respectively) .

Conclusions: In most patients, treatment with cholecalciferol in a 50000 IU / month dose permits safe correction of vitamin D deficiency and is more effective than small doses of alfacalcidol in rising serum 1,25(OH)2D.

Keywords: Vitamin d level; Egyptians; Hemodialysis; supplementation

Introduction

According to a current knowledge, vitamin D regulates the function of many organs and systems, not only mineral and bone metabolism. Moreover, it has been postulated that its deficiency may be associated with an increased risk for nearly all major human diseases

We know now that both 1-alpha-hydroxylase (CYP27B1) and vitamin D receptor (VDR) are present in almost every human tissue and vitamin D may exert its actions via two general ways. These are: (1) the endocrine way with 1,25-hydroxyvitamin D [1,25(OH)2D] as a hormone produced in kidneys, and (2) paracrine, autocrine and intracrine ways, in which its precursor – 25-hydroxyvitamin D [25(OH)D] is converted locally by CYP27B1 to 1,25(OH)2D in the target cell, which activates the VDR and downstream gene expression in the same or a neighbouring, VDR-expressing cell [1].

The recognition of the ability of extrarenal tissues to produce calcitriol, and the suggestions that many of the significant biological consequences of dysregulated vitamin D balance may be associated with changes in the extracellular concentration of substrate 25(OH)D together with the fact of severe deficiency of both, 1,25(OH)2D and 25(OH)D, in patients with end-stage renal disease especially those on long-term dialysis therapy provided a rationale to the study.

In addition, since oral alfacalcidol is a popular active vitamin D analogue in many countries, in some cases given in a small dose [2-3], we decided to examine if this therapy has any advantage over nutritional vitamin D supplementation.

The primary outcome of the study was the effect of 12-week therapy of cholecalciferol in comparison with low-dose alfacalcidol or placebo on serum 1,25(OH)2D in vitamin D naïve hemodialysis patients with vitamin D deficiency.

Materials and Methods

This interventional study was carried out on 40 patients (25 males and 15 females) with Chronic Kidney Disease CKD (stage V) on regular heamodialysis attending at Nephrology unit, Internal medicine department, Mansoura University Hospital during the period from January to June 2017.

Ethical approval had been obtained from Medical Research Ethics Committee of Faculty of Medicine, Mansoura University. Patients signed their written consents after detailed explanation of the study protocol.

- We excluded the following patients; Those with cognitive impairment, Cancer, active hepatitis or any liver disease, and those who have inflammation or active infection.

Patients were subjected to the following investigations : Complete blood picture by automated cell counter CD 1800 (USA) using the 1ml EDTA blood sample. Serum albumin, Parathormone Hormone (PTH) by commercially available ELISA kits, serum Calcium (Ca++) and Phosphorus.

Results

Forty patients were included in our study, 29 were males (72.5.0%) and 11 were females (27.5%) , their mean age (47.16±14.92) years. The mean dialysis duration is (4.68±2.42) years. The original renal disease percentage of hypertension, diabetes and both diseases is 70.3%, 18.9% and 10.8% respectively. Data are shown in Table (1).

Table 1: Demographic data

Age by year		**47.16±14.92**	
Sex	**Male**	**29**	**72.5%**
	Female	**11**	**27.5%**
Dialysis duration		**4.68±2.42**	
Original renal disease	**hypertensive**	**26**	**70.3%**
	diabetic	**7**	**18.9%**
	Both	**4**	**10.8%**

Data expressed either as mean±SD or as frequency

At the end of the study there were significant increase in serum calcium level (8.33 to 8.89) mg/dL , serum phosphorous level (4.99 to 5.85) mg/dL and Vit D3 serum level (4.01 to 28.43) ng/mL levels compared to pretreatment level. There was also significant decrease in parathormone hormone level (419.30 to 377.20) pg/mL. Data are shown in Table 2 (Tables 2,3, and 4).

After 3 months of follow up there was no significant change in the levels of haemoglobin , KT/v, Albumin and alkaline phosphatase in the overall sample (p value = 0.7 ,0.4,0.29 and 0.59 respectively).

Table 2: Comparison between pre & post treatment

	Pre-treatment		**Post-treatment**		**P**
	Mean	**±SD**	**Mean**	**Standard Deviation**	
Ca	**8.33**	**±.89**	**8.89**	**±.96**	**0.008***
Po4	**4.99**	**±.1.73**	**5.85**	**±.1.10**	**0.01***
PTH	**419.30**	**242.30-951.40**	**377.20**	**206.00-626.00**	**<0.001***
Vit D	**4.01**	**.79**	**28.43**	**23.64**	**<0.001***

Data expressed as mean±SD or as median(IQR)

SD: standard deviation IQR: interquartile range P:Probability

*:significance <0.05

Test used: Student's t-test(Paired) for data expressed as mean±SD and Wilcoxon signed rank test for data expressed as median(IQR)

Table 3: Comparison between pre & post treatment

	Pre-treatment		**Post-treatment**		**P**
	Mean	**±SD**	**Mean**	**±SD**	
HB	**9.91**	**1.61**	**10.00**	**1.37**	**0.7**
KT/v	**1.14**	**.36**	**1.20**	**.23**	**0.4**
ALB.	**3.68**	**.50**	**3.80**	**.46**	**0.29**
Alk.Phosph.	**18.80**	**5.70**	**19.43**	**4.71**	**0.59**

SD: standard deviation P:Probability *:significance <0.05

Test used: Student's t-test (Paired)

Table 4: Comparison between pre-treatment of patients & Control

	Pre-treatment		**Control**		**P**
	Median	**IQR**	**Median**	**IQR**	
VitD	**4.01**	**2.79-8.17**	**4.49**	**3.08-10.35**	**0.34**

IQR: interquartile range P:Probability

*:significance <0.05

Test used: Mann whitney

Discussion

The rapidly aging dialysis population with a high burden of comorbid illnesses, insufficiently exposed to the sun, or affected by malnutrition, is particularly vulnerable to bone fractures due to profound disturbances in mineral metabolism. From the same reasons together with defective cutaneous cholecalciferol synthesis and the effects of a variety of medications that prevent its intestinal absorption or interfere with its metabolism [4-6], vitamin D deficiency is a common finding in this population, ranging from 38 to 95%, depending on the definition, geographic latitude, and season of the year [7-9].

This single center study , aimed to prospectively assess vitamin D levels in a cohort of 40 vitamin D naive hemodialysis patients, and compare levels with a control groups and to examine the effect of weekly supplementation on both serum vitamin D level and Parathormone, serum calcium and phosphorus levels.

Vitamin D affects significantly the bony skeleton and extra skeletal tissues. That can be noticed in its regulation to calcium and phosphorus absorption from the intestine. Vitamin D deficiency will elevate level of parathormone which in turn increase bone turnover and reduce the mineralization, these factors increase bone softening diseases such as osteoporosis and osteomalacia [10].

In the past decade, multiple information spotlighted the pluripotent effects of vitamin D on different tissues of the human body. There is also underestimation of the real size of deficient individuals in general population and chronic kidney patients [11-12].

Chronic kidney disease patients having Vitamin D deficiency will end up developing 2ry hyperparathyroidism and mineral bone disease syndrome [13].

Our work aim was to assess vitamin D levels among patients with chronic kidney disease(CKD5) treated by hemodialysis and the prevalence of patients with vitamin D deficiency and insufficiency and the effect of replacement therapy on serum Calcium ,phosphorus ,PTH and Vitamin D levels .

Results from our study showed that all patients were Vit D deficient (100%). Vitamin D deficiency is defined as serum 25 (OH) D <20 ng/ml. [14]. All patients did not exceed 13.5 ng/ml and most of them (70%) were below 7 ng/ml when they were assessed before the replacement therapy. This observation agrees with what was reported previously by ***(Ngai et al., 2014)*** that >80% of CKD non-transplant patients had low serum 25(OH) D levels. [15].

(Kim et al., 2014) reported that the prevalence of vitamin D deficiency 85.7% in Stage 5 CKD. [16].(Restrepo Valencia and Aguirre Arango, 2016) from Colombia showed that 70.1% were insufficient and 8.8% were within deficit range in CKD patient (stage2-5). Our results also showed that control cases who are healthy individuals were also deficient in agreement with[17]. (Mitchell et al., 2012) who did a study showed that 39% of subjects had 25(OH)D ≤20 ng/mL and 64% had 25(OH) D ≤30 ng/mL. [18]. (Guessous et al., 2014) who also reported that vitamin D deficiency is similarly observed in CKD patients and in the general population. [19].

Despite the alarming results of the studies evaluating vitamin D deficiency in dialysis Populations worldwide, the current nephrology societies leave us without a clear guideline on that issue. In 2009 and 2017, KDIGO proposed, with a low quality of evidence, measuring 25(OH)D serum and treating its deficiency as in the general population, however, without any suggestion concerning the dosing and the target threshold [20, 21]. With such a weak and imprecise recommendation, many patients undergoing dialysis remain without vitamin D supplementation.

The main argument for neglecting vitamin D supplementation in patients on dialysis has been the fact of a weak 1,25(OH)2D production by severely damaged kidneys. However, the discoveries of the last decades showing a presence of high extrarenal synthesis of calcitriol point anew to the importance of vitamin D supplementation in those with end-stage kidney disease undergoing dialysis [22].

Basing on the available studies as a minimal dose of cholecalciferol which could effectively replenish vitamin D deficits in studied subjects, we assumed 50.000IU per week, given during every hemodialysis.

However, it remains to be verified in clinical studies if these serum 25(OH)D concentrations are sufficient to fully capture the effect of the localized, tissue-specific conversion to 1,25(OH)2D in ESRD with their specific mineral-bone and other uremia-related disorders.

Our observation of a marked (p<0.0001) increase of serum 1,25(OH)2D concentrations confirms the significance of that effect and is consistent with the findings of the other authors [23-26]. The treatment was safe; there were no episodes of hypercalcemia. In none of patients serum 25(OH)D concentrations exceed 60 ng/ml.

These results question the usefulness of the small doses of alfacalcidol in HD patients as ineffective: it has a weak influence on serum 1,25(OH)2D and no effects on serum PTH concentrations.

This practice should be abandoned, and instead, the low-dose cholecalciferol supplementation should be introduced since it raises serum 1,25(OH)2D more effectively, replenishes 25(OH) D stores and is safe and cheap.

The study showed significant increase in Vitamin D25 OH Vit D from (4.01 ± .97 to28.43 ± 23.64 ng/mL p<0.001) after monthly dose of 50.000 IU of cholecalciferol for 3 consecutive months which agrees with *Matias et al., 2010* who reported increase in 25OH VitD form ±22.3 to ±42.0 ng/ml) after 6 months of cholecalciferol supplementation with dose of 50.000 iu once to thrice weekly according to the previous status of vitD deficiency . [27]. who also reported increase of 25OH Vit D after two doses of 300,000 IU 8 weeks apart, which effectively replenished the stores up to 70 ng/ml) after 16 weeks . [28]

Results of our study showed that Serum PTH concentrations significantly decreased from baseline after the replacement therapy from (±419.30 to ±377.20 p<0.001) pg/mL. This observation agrees with what was reported by .*Okša et al., 2008* who administered cholecalciferol treatment with either 5,000 or 20,000 IU/week for 12 months in patients with CKD stages 2–4. and also agree with[29]. *(Alvarez et al., 2012)*who showed reduction in PTH with cholecalciferol replacement therapy after 12 weeks (mean PTH concentration: 89.1 ± 49.3 to 70.1 ± 24.8 pg/mL) ,but we are not in agreement with what reported by[30]. *(Mose et al., 2014)* who showed that there was no change in the level of PTH concentration before and after replacing vitamin D probably due to potential changes in plasma concentrations of PTH which are most likely concealed by medication changes. [31]

Results of our study showed significant increase in serum calcium (±8.33 to ±8.89 p=0.008) mg/dL which was in accordance with *(Bansal et al., 2014)* who showed that calcium levels increased significantly at 6 weeks in intervention group, no patient developed hypercalcemia despite being on active vitamin D analogues as well [32] . In contrast [13]. [13].*(Chandra et al., 2008; Kandula et al., 2011; Massart et al., 2014)* showed no significant difference in serum calcium level from the baseline mostly because they were on non-calcium containing phosphate binders. [33-35].

Regarding phosphorous, it showed significant increase from (±4.99 to ±5.85 p=0.01) mg/dl Which disagree with *(Hewitt et al., 2013)*. They reported that there was no change in bone-related minerals including serum phosphorus because patients were on calcium-based phosphate binders. [36].

Our study has certain limitations; Small patients number ,absence of bone biopsy, lack of assessment of dietary intake calcium and phosphorous, the short duration of intervention and follow-up and small patient groups that will be considered in a future work.

In conclusion, the results of our study allow us to conclude a high prevalence of Vit D deficiency in both hemodialysis patients and healthy general population and this alarming finding should be investigated in Egypt on a wide scale.

It also showed us the cost effectiveness of a cheap product as cholecalciferol in replenishing the stores of Vitamin D and its possible role in treating its deficiency without serious side effect in one of the most vulnerable categories of patients such as hemodialysis patients.