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PREVALENCE OF VITAMIN D DEFICIENCY IN DIFFERENT GROUPS OF CHRONIC RENAL FAILURE PATIENTS

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SUMMARY

Purpose: To determine and compare the vitamin D status of different groups CKD patients on hemodialysis, peritoneal dialysis, or no renal replacement therapy and to evaluate the effect of vitamin D therapy.

Patients and Methods: This pilot study enrolled 40 consecutive CKD patients (21 men, 19 women) divided into three groups: 15 CKD patients in 1,2,3,4 stage of the disease without renal replacement therapy (RRT); 10CKD patients on hemodialysis (HD) and 15 CKD patients on peritoneal dialysis (PD), ten of which were on vitamin D therapy. Vitamin D status was determined by serum 25-xydroxyvitamin D (25OHD).

Results: Ninety percent of patients were in vitamin D deficiency/insufficiency; and only 4 patients (10.0%) reached 25OHD levels above 75nmol/L. The median 25OHD level was 31.15nmol/L (interquartile range: 16.67-48.33nmol/L).Tendency of worse vitamin D status in women than in men was observed. Higher 25OHD levels were found in pre-dialysis patients (median 44.81nmol/L, 25%-75% percentile 16.24-52.21nmol/L) and lower in HD (median 31.15nmol/L, 25%-75% percentile 13.04-64.45nmol/L) and PD patients (median 33.38nmol/L, 25%-75% percentile 23.15-48.49nmol/L), but the difference did not reach statistical significance. Better vitamin D status was found in the PD group of patients receiving vitamin D preparations ($p<0.05$).

Conclusions: 25OHD deficiency/insufficiency is prevalent in renal failure patients with or without renal replacement therapy. It seems that vitamin D therapy improves the vitamin D status of PD patients. Further larger studies are needed to clarify the effect of specific type vitamin D therapy on serum 25OHD levels and clinical outcome in different groups of CKD patients.

Key words: chronic kidney disease, hemodialysis, peritoneal dialysis, vitamin D status, 25-hydroxyvitamin D.

INTRODUCTION

Nowadays the discovery of non-renal vitamin D receptor (VDR) triggers research on extra-mineral functions of vitamin D hormone [1]. Vitamin D deficiency is an increasingly recognized public health problem in the general population, in chronic inflammatory disorders, and in chronic kidney disease (CKD) [2].

CKD is characterized with extremely low levels of both 1,25-dihydroxyvitamin D (1,25OHD) and 25-hydroxyvitamin D (25OHD). A possible reason is the deficient UV-light exposure of CKD patients and the inadequate dietary intake of vitamin D rich food. On the other hand the massive proteinuria in patients with nephrotic syndrome results in loss of vitamin D binding protein (DBP) responsible for vitamin D transfer to tissues [3, 4]. The progression of the disease is accompanied with a decrease of kidney megalin and insufficient tubular reabsorption of 25OHD [5]. Another factor contributing to the decrease of 25OHD levels in CKD is the fibroblast growth factor-23 (FGF-23). FGF-23 inhibits the renal 1-alpha hydroxylase and activates 24-hydroxylase leading to increased catabolism of both 1,25OHD and 25OHD [6]. The combination of these factors results in 25OHD deficiency in CKD patients. Recent studies have found significantly lower serum 25OHD levels in individuals with severe decrease in glomerular filtration rate compared with those with normal renal function [7]. Higher vitamin D levels were established in 1, 2, 3, 4 stages CKD patients when compared with the patients undergoing PD [4]. Prnjavorac et al registered vitamin D deficiency in HD patients despite the course of supplemental therapy [8]. The same study has shown moderate 25OHD deficiency in a half of the pre-dialysis patients. There are a limited number of comparative studies on vitamin D status in different groups of CKD

patients undergoing non renal replacement therapy (RRT) or active RRT.

The aim of the present study was to determine and compare the vitamin D status of patients with different stages CKD 1-5 and to evaluate the effect of vitamin D therapy. Vitamin D therapy effects were observed and analyzed in condition of non RRT and of active RRT by hemodialysis and by peritoneal dialysis.

PATIENTS AND METHODS

Patients

The present pilot study enrolled 40 consecutive CKD patients, 21 men (52.5%) and 19 women (47.5%). The patients were investigated at the Clinic of Nephrology and Dialysis, University Hospital of Varna during June-October, 2014. The mean age of the studied group was 52.3±14.4 years (men 53.0±16.2, women 51.8±14.5 years). Patients with CKD in pre-dialysis stage as well as patients undergoing HD or PD with or without vitamin D therapy were included in the study. Individuals with acute intercurrent disease, diabetes mellitus, cancer or on cytostatic/corticosteroid therapy were excluded from the study. All patients were tested for 25OHD during the summer season. According to the type of therapy the patients were divided into three groups: CKD group comprised of 15 CKD patients in 1, 2, 3, 4 stages; HD group – 10 patients on hemodialysis; PD group – 15 patients on peritoneal dialysis. The average duration of PD was 2.18±0.88 years, and of HD 4.33±2.18 years. Rocaltrol 0.25mcg (Roche) and One-Alpha® 0.25mcg (LEO Pharma) were used as supporting therapy in ten of the PD patients.

METHODS

BMI was calculated as weight (kg)/height2 (m2).

Routine biochemical tests. Intact parathyroid hormone (iPTH) was determined on Immulite 2000 Immunoassay System (Siemens Healthcare Diagnostics, USA).

25OHD assay. For all studied patients serum samples for measuring the levels of 25OHD were collected only once – at the time of their admittance to the Nephrology Clinic. All serum samples were frozen, and stored at -80°C until analysis. Serum 25OHD was assayed by a validated LC-MS/MS method. The vitamin D status was defined as absolute deficiency (25OHD <25nmol/L), severe insufficiency (25OHD 25-50nmol/L), insufficiency (25OHD 50-75nmol/L), and sufficiency (25OHD >75nmol/L).

STATISTICAL ANALYSIS

Categorical variables were presented as frequencies (%). GraphPad Prism v. 6.00 for Windows (GraphPad Software, La Jolla, CA, USA) was used for statistical analysis of continued variables. Median values, 25-th and 75-th percentiles were calculated. Mann Whitney statistics was used for evaluation of differences between groups. The level of significance was $p<0.05$.

The study was approved by the local Ethics Committee, following the guidelines of the Declaration of Helsinki and the International Ethical Guidelines for Biomedical Research Involving Human Subjects. Written informed consent was obtained from each subject prior the participation in the study.

RESULTS

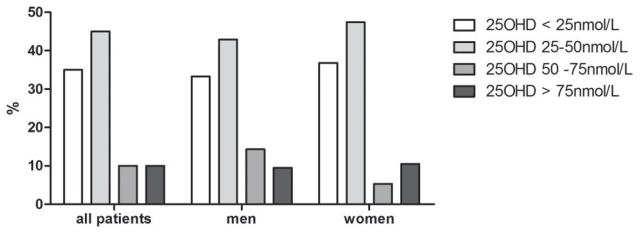
Table 1 shows the median values for demographic, anthropometric, and biochemical parameters.

Table 1. Characteristics of the studied group.

Parameter	Value
Total number of studied patients (N)	40
Gender	
men, (%)	21 (52,5%)
women, (%)	19 (47,5%)
Age, years, median (25%- 75% percentile)	54.0 (42.0-65.0)
men	54.0 (42.8-65.5)
women	55.5 (36.0-69.0)
BMI, median (25%- 75% percentile)	24.95 (23.0-26.0)
normal, (%)	52.5%
overweight + obese, (%)	47.5%
iPTH, ng/L, median (25%- 75% percentile)	384.0 (239.8 – 699.3)

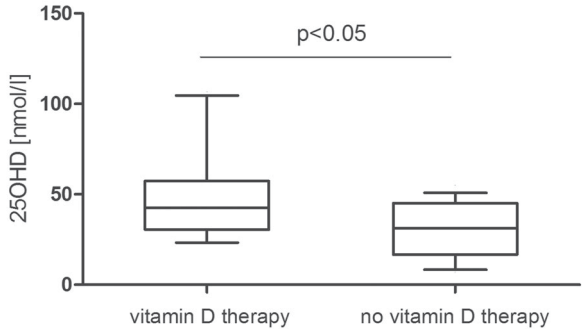
All studied patients revealed median 25OHD levels (31.15nmol/L, 16.67-48.33 nmol/L) below the cut-off value of 50.0nmol/L, defining severe vitamin D insufficiency. Fourteen patients (35.0%) were in absolute vitamin D deficiency (25OHD<25nmol/L), 18 subjects (45.0%) show severe vitamin D insufficiency (25OHD between 25.0 and 50.0nmol/L); 4 patients (10.0%) were vitamin D insufficient (25OHD between 50.0 and 75.0 nmol/L). Only 4 patients (10.0%) reached 25OHD levels above the desirable threshold of 75nmol/L. Categorization by gender showed worse vitamin D status in women than in men. Absolute vitamin D deficiency was detected in 36.8% of women vs 33.3% in men. Severe vitamin D insufficiency was detected in 47.4% of women vs 42.9% of men, while 5,3% of women showed vitamin D insufficiency vs 14.3% of men. These differences in 25OHD levels between genders were not statistically significant (Fig. 1).

Fig. 1. Stratification of 25OHD levels by gender of CKD patients.



Stratification by the type of therapy revealed higher 25OHD levels in pre-dialysis patients (median 44.81nmol/L, 25%-75% percentile 16.24-52.21nmol/L) and lower in HD (median 31.15nmol/L, 25%-75% percentile 13.04-64.45nmol/L) and PD patients (median 33.38nmol/L, 25%-75% percentile 23.15-48.49nmol/L), not reaching statistical significance. Not surprisingly, better vitamin D status was found in the group of patients receiving vitamin D preparations. Among them 16.7% were absolute deficient in vitamin D vs 32.1% in the non-supplemented group. The differences in 25OHD levels between these two groups were statistically significant ($p<0.05$) (Fig. 2).

Fig. 2. Effect of vitamin D therapy on 25OHD levels of PD patients.



DISCUSSION

Interest in vitamin D has increased considerably in recent years due to discovering of its non-calcitropic effects on various organs and systems [9].

Multiple studies have shown the helpful effect of vitamin D therapy in patients on dialysis and with CKD [10]. A recent study in HD patients on 1,25OHD therapy revealed reduced serum levels of IL8, TNF-alpha and C-reactive protein (CRP) [11]. Beneficial effect of alfacalcidol on acute phase inflammatory markers such as beta2-microglobulin in HD patients was shown also by others [12].

Despite the long use of various forms of vitamin D in CKD, there are still many open questions [13]. Sufficient amount of data demonstrate that CKD is associated with a high prevalence of vitamin D insufficiency/deficiency. It may be suggested that the improvement of vitamin D status would provide appropriate levels of serum 25OHD as a substrate for the remaining renal 1-alpha hydroxylase to reach maximum activity for adequate production of physiologically active 1,25OHD [14]. According to KDOQI guidelines supplementation of vitamin D is recommended for dialysis patients as well as for those with stage 3 and 4 of CKD, if basal level of 25(OH)D is less than 30 ng/ml [14, 15].

A systematic review and meta-analysis of prospective observational studies on 6853 patients with CKD reveals that higher 25OHD levels were associated with significantly improved survival in patients with CKD [16]. The same study estimated a decrease of the relative mortality risk in CKD patients by 14% per 25-nmol/L increase in 25(OH)D level. Another prospective study on the prognostic impact of 25OHD levels on mortality and hospitalization of HD patients had shown that low 25OHD concentration is an independent predictor for survival and it is linked to significantly increased mortality rate in HD patients [17].

We also found severe vitamin D insufficiency with 25OHD values slightly higher than 25nmol/L in all studied patients. Moreover we found significantly higher 25OHD concentrations ($p<0.05$) in patients undergoing vitamin D therapy and their 25OHD levels almost approach the cut-off value of 50nmol/L for mild vitamin D insufficiency. Our data are in agreement with the hypothesis for the supportive role of higher 25OHD levels on the functional activity of renal 1-alpha hydroxylase in renal failure patients. Until now, comparative data on the vitamin D status and the effect of vitamin D therapy of different groups CKD patients in Bulgaria are very scarce.

CONCLUSIONS

25OHD deficiency or insufficiency is prevalent in renal failure patients with or without renal replacement therapy. It seems that vitamin D therapy improves the vitamin D status of PD patients. Further larger studies are needed to clarify the effect of specific type vitamin D therapy on serum 25OHD levels and clinical outcome in different groups of CKD patients.

FUNDING

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CONFLICT OF INTERESTS

We declare no conflict of interests.

ABBREVIATIONS

CKD - chronic kidney disease
DBP - vitamin D binding protein
FGF-23 - fibroblast growth factor-23
RRT - renal replacement therapy
VDR - vitamin D receptor
1,25OHD - 1, 25-dihydroxyvitamin D
25OHD - 25-hydroxyvitamin D

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