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ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2021;10(3):694-7

Prevalence and predictors of 25-OH vitamin D deficiency in peritoneal dialysis patients: A single center study

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Received 04 December 2020; Accepted 01 February 2021
Available online 11.06.2021 with doi: 10.5455/medscience.2020.11.244

Abstract

Vitamin D has a critical role in bone-mineral disorders in chronic kidney disease (CKD) and its deficiency is further associated with increased cardiovascular morbidity and mortality among CKD patients. We aimed to evaluate prevalence of vitamin D deficiency and investigate the laboratory and clinical parameters associated with 25-OH vitamin D deficiency in peritoneal dialysis (PD) patients. Sixty-four (33M/31F) peritoneal dialysis patients were enrolled in this retrospective single center study. Clinical and laboratory data were obtained from patient charts. Prevalence of 25-OH vitamin D deficiency and its associations were analyzed. The patients' mean age was 49.7±13.3 years and the mean duration of PD was 61.0±55.0 months. The mean 25-OH vitamin D level was 8.9±2.4 ng/ml and none of the patients were on 25-OH vitamin D therapy. All of the patients had lower than normal 25-OH vitamin D levels according to KDOQI guidelines. Levels of 25-OH vitamin D were deficient and insufficient in 84.4% (57.8% mild; 26.6% severe) and 15.6% of the patients, respectively. There was no association between 25-OH vitamin D levels and sex, age, BMI, duration of PD and cause of ESRD. There was a negative correlation between 25-OH vitamin D levels and uric acid and parathyroid hormone. Uric acid was an independent predictor of 25-OH vitamin D deficiency in the logistic regression analysis [OR (95%CI): 0.139 (0.029-0.667), p: 0.014]. We conclude that 25-OH vitamin D deficiency is very common in PD patients. Serum uric acid is an independent predictor of 25-OH vitamin D deficiency which should further be investigated in larger studies.

Keywords: 25-hydroxyvitamin D, parathyroid hormone, peritoneal dialysis, uric acid, vitamin D deficiency

Introduction

Vitamin D is a fat-soluble vitamin that plays an important role in calcium homeostasis and bone metabolism. Vitamin D has potent anti-inflammatory, anti-angiogenic and anti-fibrotic properties. Total 25-OH vitamin D remains the best indicator of total body vitamin D stores and its availability for biologic functions. Vitamin D status is best evaluated by measuring the serum concentration of 25-OH vitamin D. The 25-OH vitamin D is converted to calcitriol, its active form, in the kidney and plays a significant role in the immune response. Low 25-OH vitamin D levels have been associated with malignancy, auto-immune diseases, diabetes mellitus and high cardiovascular mortality [1,2].

Vitamin D deficiency is common in chronic kidney disease (CKD) and dialysis patients due to factors such as limited intake of dairy products, inadequate exposure to sunlight, impaired photo-transformation of vitamin D due to uremia, loss of vitamin D-binding protein (VDBP) in urine [3,4] hyperphosphatemia and secondary hyperparathyroidism. The incidence of 25-OH vitamin D deficiency is about 97% in dialysis patients and 86% in patients with stage 3-4 CKD [5,6]. It has been linked with various CKD-related disease processes such as mineral bone disorder, anemia, inflammation, infection, high blood pressure, and proteinuria [7-10].

Data on prevalence of deficiency in Turkish peritoneal dialysis patients are scarce [5,11]. The aim of this study is to investigate the prevalence of 25-OH vitamin D deficiency among peritoneal dialysis patients and to evaluate its associations with laboratory and clinical parameters.

Materials and Methods

Consecutive patients admitted to the peritoneal dialysis outpatient clinic between June 2018 and June 2020 were enrolled in this retrospective study. We included patients who were on successful peritoneal dialysis for at least 3 months. Patients under the age of 18 years or those receiving 25-OH vitamin D supplementation were excluded. Medical history and demographical data were recorded.

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Duration of peritoneal dialysis (PD), type of PD, primary kidney disease, urine volume and medications were determined. Serum 25-OH vitamin D, calcium, phosphorus, and PTH, CRP, uric acid, serum albumin, lipid profile, ferritin and complete blood count were measured on the same day as a part of routine care.

Levels of 25-OH vitamin D was assessed by the National Health Laboratory Services by chemiluminescent immunoassay. Serum levels of uric acid, phosphorus, calcium, lipid profile and ferritin were analyzed using standard laboratory methods and expressed as milligrams per deciliter. CRP levels were determined using the nephelometric method (Date Behring Siemens, Marburg, Germany) and expressed as milligrams per liter. Intact PTH serum levels were measured by enzyme amplified sensitive immunoassay (Roche Diagnostics, IN, USA) expressed as picograms per milliliter.

Status of 25-OH vitamin D was defined according to KDOQI guidelines: Levels <5 ng/mL were considered severely deficient, 5-15 ng/mL as mildly deficient, and levels 16-30 ng/mL as insufficient [12].

The study was approved by the Ethics committee of Marmara University School of Medicine (Protocol no: 09.2020.644). The investigation conforms to the principles outlined in the Declaration of Helsinki. All participants gave written informed consent.

Statistical Analysis

Categorical variables were presented as numbers and percentages and compared with the Chi-square test. All variables that are distributed normally presented as mean ± standard deviation. Continuous variables were compared with independent samples T-test, or Mann-Whitney U-test where appropriate. Kolmogorov-Smirnov was performed to determine whether continuous variables were normally distributed. The Spearmen correlation test was used to identify the correlation between 25-OH vitamin D levels and demographical and laboratory parameters of patients. Logistic regression analyses were performed to determine independent predictors of 25-OH vitamin D deficiency in patients with ESRD. We considered p values less than 0.05 as statistically significant. Statistical analysis was performed using SPSS for Windows, version 22.0 software (SPSS Inc, Chicago, IL).

Results

The present study included 64 (33 male) PD patients. The demographic features and baseline laboratory findings of the study population are summarized on Table 1 and Table 2. The mean patient age was 49.7±13.3 years and the mean duration of PD was 61.0±55.0 months. Forty-two patients were treated with continuous ambulatory PD while 22 patients were on automated PD.

Causes of kidney disease were diabetic nephropathy in 5 patients, hypertensive nephropathy in 11 patients, glomerulonephritis in 19 patients, polycystic kidney disease in 9 patients and vesico-ureteral reflux in 4 patients; the etiology was unknown in 14 patients. At study inclusion, 73.4% of the patients were being treated with calcium carbonate, %23.4 with sevelamer, 48.4% with calcitriol and 15.6% with cinacalcet. The mean urine volume was 1030±965 ml. According to KDOQI guidelines, 25-OH vitamin D levels were deficient in 84.4% (57.8% mild; 26.6% severe) and insufficient in 15.6% of the patients (Figure 1).

Table 1. Clinical features of peritoneal dialysis patients

Variables	All patients (n:64)
Age, years	49.7±13.3
Sex, male (%)	33 (51.6%)
BMI, kg/m²	26.8±6.3
Duration of PD, months	61.0±55.0
CAPD/APD, n	42/22
Cause of kidney disease	
Diabetes Mellitus, n(%)	5 (7.8%)
Hypertension, n (%)	11 (17.2%)
Glomerulonephritis, n (%)	19 (29.7%)
Polycystic kidney, n (%)	9 (14.1%)
VUR, n (%)	4 (6.3%)
Unknown, n (%)	14 (21.9%)
Urine volume, ml	1030±965
Drugs	
Calcium carbonate, n(%)	47 (73.4%)
Sevelamer, n(%)	15 (23.4%)
Cinacalcet, n(%)	10 (15.6%)
Calcitriol, n(%)	31 (48.4%)

APD: Automated PD; CAPD: Continuous ambulatory PD; PD: Peritoneal dialysis; VUR: Vesico-ureteral reflux. Data presented as mean±std deviation

Table 2. Laboratory findings of the peritoneal dialysis patients

Variables	All patients (n:64)
Blood urea nitrogen, mg/dl	56.0 ± 15.6
Creatinine, mg/dl	9.0 ± 2.5
Albumin, g/dl	3.7 ± 0.5
Calcium, mg/dl	9.1 ± 0.9
Phosphorus, mg/dl	4.8 ±1.1
Sodium, mg/dl	135.9 ± 2.9
Potassium, mg/dl	4.4 ±0.75
Uric acid, mg/dl	5.7 ± 1.2
LDL cholesterol, mg/dl	124.7 ± 38.6
Triglyceride, mg/dl	160.0 ± 87.0
Hemoglobin, g/dl	10.8 ± 1.5
Leucocyte, 103 uL	7.3 ± 2.1
Platelet, 103 uL	251.0 ± 95.0
C-reactive protein, mg/L	9.07 ± 9.33
Ferritin, mg/dl	346.0 ± 318.0
Parathyroid hormone, pg/mL	389.0 ± 325.0
25-OH vitamin D, ng/ml	8.9 ± 2.38

LDL: Low density lipoprotein; Data presented as mean±std deviation

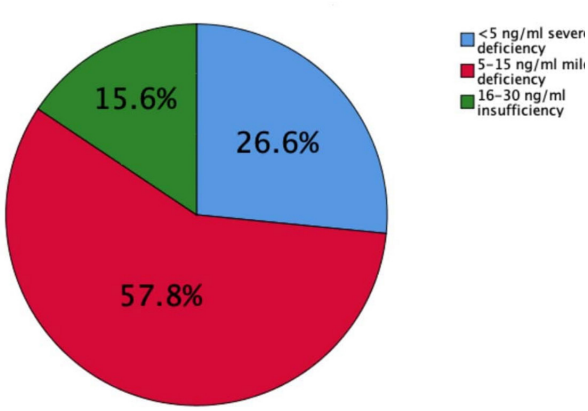

Figure 1. 25-OH vitamin D status according to KDOQI guidelines

There were no association between 25-OH vitamin D levels and age, sex, BMI, time of PD, type of PD and cause of ESRD. The Spearman correlation test revealed that serum 25-OH vitamin D level was negatively correlated with serum uric acid (r: -0.351, p:0.005) and parathyroid hormone levels (r: -0.326, p:0.009) (Figure 2). Age, gender, uric acid and parathyroid hormone level were added into model for logistic regression. Uric acid was an independent predictor of 25-OH vitamin D deficiency in logistic regression analysis [OR (95%CI): 0.139 (0.029-0.667), p: 0.014] (Table 3).

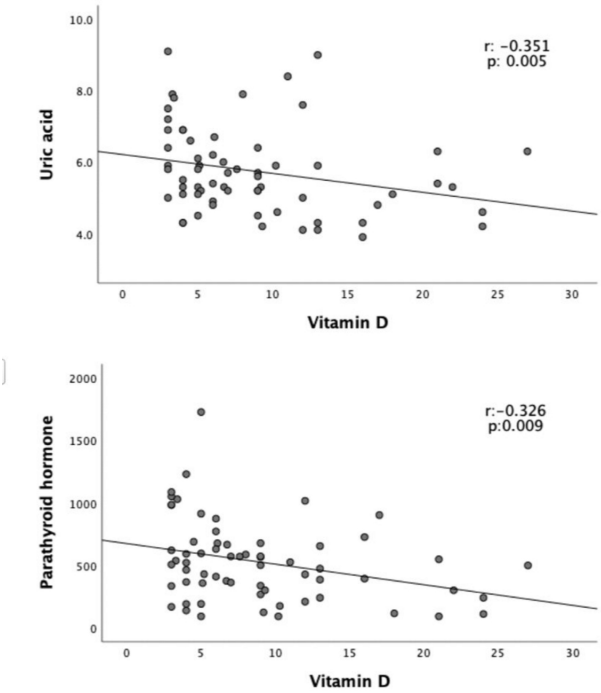

Figure 2. Correlation analysis of 25-OH vitamin D with serum uric acid and parathyroid hormone levels

Table 3. Independent predictors of vitamin D deficiency

	OR (95%CI)	P value
Age	0.996 (0.934-1.063)	0.915
Gender (male)	0.441 (0.083-2.355)	0.338
Uric acid	0.139 (0.029-0.667)	0.014
Parathyroid hormone	0.997 (0.994-1.000)	0.080

OR: Odd's ratio, CI: Confidence interval

Discussion

Vitamin D deficiency is a global public health issue. About 1 billion people worldwide have vitamin D deficiency, while 50% of the population has vitamin D insufficiency. In the adult population, 35% of adults in the United States are vitamin D deficient whereas over 80% of adults in developing countries are vitamin D deficient [13]. A meta-analysis from Turkey revealed that the prevalence of 25-OH vitamin D deficiency was 63.5% in adults [14]. Investigation of 25-OH vitamin D deficiency in specific patient groups in Turkey is still in progress. In this study, we aimed to determine the current prevalence of 25-OH vitamin D deficiency in our PD cohort.

We showed that all of our PD patients had levels of 25-OH vitamin D less than 30 ng/mL, which is the threshold for sufficient 25-OH vitamin D according to KDOQI guidelines. Peritoneal dialysis patients may especially be prone to 25-OH vitamin D deficiency due to loss of vitamin D binding protein in the peritoneal dialysate [15]. Ulutas et al. reported that 94.7% of patients on peritoneal dialysis had 25-OH vitamin D deficiency. In another study Shah et al. measured 25-OH vitamin D levels and found 25-OH vitamin D deficiency in 97% of PD patients [11,16]. Similar to previous reports, we also showed a very high prevalence of 25-OH vitamin D deficiency. Indeed, almost 85% of our patients had levels <15 ng/mL, similar to that reported by Marinelli et al in chronic dialysis patients [17].

The most common cause of mortality in dialysis patients is cardiovascular disease [18]. Reduced 25-OH vitamin D levels are linked to all-cause and cardiovascular mortality in the PD population [19]. Furthermore, low 25-OH vitamin D levels are also associated with the development of vascular calcifications in hemodialysis patients [20]. Furthermore, apart from suppressing parathyroid hormone levels, vitamin D therapy, such as calcitriol, 25-OH vitamin D and paricalcitol, has immunomodulatory and cardio-protective effects in dialysis patients [21]. In our study, there was a negative correlation between 25-OH vitamin D levels with uric acid and PTH. It can be hypothesized that low 25-OH vitamin D levels combined with high uric acid could could have an additive effect, accelerating cardiovascular events in PD patients.

Several studies have reported on the association between vitamin D levels and uric acid with conflicting results. Fayed et al. demonstrated a negative correlation between 25-OH vitamin D and PTH and serum uric acid, similar to our study [22]. On the contrary, another study has shown that lower levels of uric acid predict lower 25-OH vitamin D levels [23]. The exact mechanisms involved in the association between 25-OH vitamin D, PTH and uric acid levels are not known. Serum uric acid levels increase as renal function is impaired due to decreased renal excretion. Several studies support the influence of parathyroid hormone on uric acid levels [24,25]. Low 25-OH vitamin D levels induce the release of PTH [26], which in turn is thought to raise serum uric acid levels [24,25,27]. In a previous study, PTH increased the incidence of higher levels of uric acid in postmenopausal women [27]. Another study demonstrated that insufficiency of 25-OH vitamin D was significantly associated with elevated uric acid in postmenopausal women [28]. The reduced serum 25-OH vitamin D levels, commonly encountered in chronic kidney disease population, stimulates the secretion of parathyroid hormone and may thus cause uric acid retention. However, uric acid may also have an inhibitory

effect on 25-OH vitamin D. These findings suggest a reverse relationship between 25-OH vitamin D and serum uric acid levels. Several studies have shown an independent association between parathyroid hormone levels and hyperuricemia [27], although the mechanism is not clear. Furthermore, the effect of 25-OH vitamin D therapy in reducing uric acid levels and cardiovascular events in PD patients is not known. There is a need for prospective studies regarding this intervention.

The major limitations of the study are its retrospective nature and small sample size. Larger, prospective studies are needed to explore the potential effects of 25-OH vitamin D deficiency and determine whether treatment decreases cardio-vascular morbidity and mortality in the peritoneal dialysis population.

In conclusion, patients undergoing PD treatment may have mild to severe 25-OH vitamin D deficiency. Insufficiency of 25-OH vitamin D was significantly associated with uric acid levels in PD patients. However, the effect of 25-OH vitamin D therapy on hyperuricemia should be investigated in future prospective studies.

Conflict of interests
The authors declare that they have no competing interests.

Financial Disclosure
All authors declare no financial support.

Ethical approval
The Marmara University ethics committee approved the study (09.2020.644)

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