Original paper

The association of 25-hydroxyvitamin D levels with secondary hyperparathyroidism in end-stage renal failure patients undergoing regular hemodialysis

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Abstract

Introduction: To investigate the role of 25-OHD as a marker of nutrition and its association with mineral metabolism and serum parathormone secretion in end-stage renal failure patients undergoing regular hemodialysis (HD), a cross sectional study was carried out on a group of maintenance hemodialysis patients.
Material and methods: Serum 25-hydroxy (25-OH vitamin D) levels, Intact serum PTH (iPTH) and also serum C-reactive protein(CRP), calcium, phosphorus and alkaline phosphatase (ALP) were measured.
Results: In the study, significant differences of serum 25-OH vitamin D between diabetic and non-diabetics of male dialysis patients with more values in nondiabetic HD patients and a significant positive correlation of serum 25-OH vitamin D with BMI and also a near significant inverse correlation of serum 25-OH vitamin D with serum phosphorus were found, also a significant inverse correlation of serum 25-OH VitD with serum calcium was seen, too. Moreover, a weakly significant inverse correlation of serum 25-OH vitamin D with serum iPTH was seen, too. In this study no significant association between serum 25-OH vitamin D with serum albumin, CRP, ALP, dialysis adequacy and ages of the patients, duration and sessions of dialysis were found.
Conclusions: In hemodialysis patients, low serum 25-OHD levels could be a risk factor for secondary hyperparathyroidism. Serum 25-OHD could show the nutritional status of HD patients. In dialysis patients, we suggest that the plasma levels of 25-OHD are maintained around the upper limit of the reference range of sunny countries.

Key words: 25-hydroxy vitamin D, end-stage renal failure, secondary hyperparathyroidism, nutritional status, regular hemodialysis , parathormone.

Introduction

25-hydroxyvitamin D (25-OH vitamin D) is the major circulating metabolite of vitamin D. Although the biological active form of vitamin D is $1,25(OH)_2$ vitamin D, synthesised in the kidney, it is widely accepted that the measurement of circulating 25-OH vitamin D provides better information with respect to the patients vitamin D status and is used for diagnosis of hypovitaminosis [1, 2]. The concentration of 25-OH vitamin D decreases with age and deficiency is common among the elderly [3, 4]. Recently, some authors have emphasized the role of plasma 25(OH) vitamin D levels in

mineral metabolism dysregulation in chronic kidney diseases [5, 6]. It has been demonstrated that a moderate reduction in plasma 25-OHD levels plays a role in the development of secondary hyperparathyroidism (SHPTH) in hemodialysis patients [7], whereas a greater reduction in plasma 25-OHD levels is associated with osteomalacia and with the risk of developing osteoporosis [7]. Furthermore, K-DOQI clinical practice guidelines emphasize the importance of monitoring plasma levels of the hormone and suggest, even though as "an opinion", vitamin D administration when plasma 25-OHD levels are <30 ng/mL [8]. Furthermore, to date little attention has been paid to 25-OHD metabolism abnormalities as a marker of nutritional status in maintenance hemodialysis patients (MHPs). This cross-sectional study was aimed to better understand the role of 25-OHD as a marker of nutrition as well as its association with mineral metabolism and serum parathormone secretion in end-stage renal failure patients undergoing regular hemodialysis.

Material and methods

Patients

This cross-sectional study was conducted on patients with end-stage renal disease (ESRD), who were undergoing maintenance hemodialysis treatment with acetate basis dialysate and polysulfone membranes. According to the severity of secondary hyperparathyroidism, each patient being treated for secondary hyperparathyroidism was given oral active vitamin D3 (Calcitriol; Rocaltrol) (Roche Hexagon; Roche Laboratories Inc, New Jersey, USA), calcium carbonate capsule , and Rena-Gel (sevelamer; Genzyme Europe B.V.; United Kingdom/Ireland) tablet at various doses.

According to the severity of anemia, the patients were prescribed intravenous iron therapy with Iron Sucrose (Venofer; International Inc. St. Gallen/ Switzerland) at various doses after each dialysis session. All patients received treatments of 6 mg folic acid daily, 500 mg Acetyl-L-Carnitine (Jarrow Formulas, Inc™ Los Angeles, CA) daily, oral vitamin B-complex tablets daily, and 2,000 U intravenous Eprex (recombinant human erythropoietin (Janssen-Cilag; CILAG- AG International 6300 Zug/Switzerland) after each dialysis session. Exclusion criteria were active or chronic infection and using NSAID or ACE inhibitor drugs. The study was done in the hemodialysis section of Hajar Medical Educational & Therapeutic Center of Shahrekord University of Medical Sciences in Shahrekord of Iran.

Laboratory methods

Serum 25-hydroxy (25-OH vitamin D) level (normal range of values is 25 to 125 nmol/L) and intact serum PTH (iPTH) were measured as follows. Blood samples were drawn after an overnight fast, blood samples were centrifuged within 15 min of venepuncture, and were measured by enzyme-linked immunosorbent assay (ELISA) method using DRG kits from Germany. Intact serum PTH (iPTH) was measured by the radioimmunoassay (RIA) method using DSL-8000 kits from the USA (normal range of values is 10-65 pg/ml). Also peripheral venous blood samples were collected after an overnight fast, for biochemical analysis including serum predialysis creatinine (Creat), post and predialysis blood urea nitrogen (BUN), albumin (Alb) as well as serum C-reactive protein (CRP), serum calcium (Ca), phosphorus (P) and alkaline phosphatase (ALP) were measured using standard methods. Body mass index (BMI) calculated using

Table I. Mean ±SD, minimum and maximum of age, duration, sessions and also laboratory results of total hemodialysis patients

Total patients N=36	Minimum	Maximum	Mean ±SD	Median
Age (years)	18	80	47±17	43
DH* (months)	2	156	32±36	19
Dialysis sessions	54	216	123±54	156
URR (%)	39	76	59±9	57.5
Ca (mg/dl)	5	10	7.7±0.9	8
P (mg/dl)	3.4	10	6.4±1.8	6.2
Alp (IU/L)	150	5487	533±890	444
25-OH vit. D (nmol/l)	1.3	105	10.5±18.7	3.5
Alb (g/dl)	2.4	4.8	3.8±0.5	3.95
CRP (mg/l)	3	40	8.7±6.7	8
iPTH (pg/ml)	16	1980	434±455	309
BMI (kg/m^2)	16	34	22±4.4	21.5

**Duration of hemodialysis*

Table II. Mean ±SD, minimum and maximum of age, duration, sessions and also laboratory results of nondiabetic hemodialysis patients

Non-diabetic patients N=25	Minimum	Maximum	Mean ±SD	Median
Age (years)	16	80	44±17	41
DH* (months)	2	156	40±40.8	22
Dialysis sessions	36	1584	370±452	156
URR (%)	60	76	61±7.5	60
Ca (mg/dl)	6	15	7.8±0.75	8
P (mg/dl)	4	10	6.6±1.8	6.5
ALP (IU/L)	190	5478	760±1044	478
25-OH vit. D (nmol/l)	1.3	105	12.6±21	6
Alb (g/dl)	2.4	4.7	3.8±0.50	4
CRP (mg/l)	2	20	7.4±3.8	6
iPTH (pg/ml)	22	1980	537±483	340
BMI (kg/m^2)	16	33	21±4.6	19

**Duration of hemodialysis*

Table III. Mean ±SD, minimum and maximum of age, duration, sessions and also laboratory results of diabetic hemodialysis patients

Diabetic patients n=11	Minimum	Maximum	Mean ±SD	Median
Age (years)	27	75	53±15.8	55
DH* (months)	6	24	14.5±6	12
Dialysis sessions	54	216	123±54	108
URR (%)	39	75	53.5±9.8	54
Ca (mg/dl)	5	10	7.4±1.3	7.5
P (mg/dl)	3	10	5.9±2	6
ALP (IU/L)	175	584	327±148	295
25-OH vit. D (nmol/l)	1.5	36	5.8±10	2.8
Alb (g/dl)	3	4.8	3.8±0.50	3.9
CRP (mg/l)	4	40	12±10	10
iPTH (pg/ml)	16	840	201±277	41
BMI (kg/m^2)	20	34	23.3±4	23

**Duration of hemodialysis*

the standard formula (postdialyzed weight in kilograms/height in square meters; kg/m^2). For the efficacy of hemodialysis the urea reduction rate (URR) was calculated from pre- and post-blood urea nitrogen (BUN) data. Duration and the amount of sessions of hemodialysis treatment were calculated from the patients' records. The duration of each hemodialysis session was 4 hours.

Statistical analysis

Results are expressed as the mean ±SD and median values. The comparison between the groups was done using the Student's t-test. Statistical correlations were assessed using a partial correlation test. The statistical analysis was performed on total hemodialysis (HD), females, males, diabetics and non diabetics populations separately. All statistical analyses were performed using SPSS (version 11.5.00). The statistical significance was determined at a p-value below 0.05.

Results

The total number of patients was 36 (F 15, M 21), consisting of 25 (F 11, M 14) non-diabetic HD patients and 11 (F 4, M 7) diabetic HD patients. Tables I, II and III show the Mean ±SD, minimum and maximum and median of age, duration and sessions of hemodialysis and also laboratory results of total hemodialysis (HD) patients. The mean patient's age was 47 (±17) years. The value of serum predialysis creatinine in total

patients was 9.5±3.6 mg/dl. The value of serum 25-OH vitamin D of total HD patients was 10.5±18.7 (median: 3.5) nmol/L, the value of serum 25-OH vitamin D of diabetic and nondiabetic dialysis patients were 5.8±10 (median: 2.8) and 12.6±21 (median: 6) nmol/L, respectively. The value of serum iPTH of total HD patients was 434±455 (median: 309) pg/ml, the value of serum iPTH of diabetic and nondiabetic-dialysis patients were 201±277 (median: 41) and 537±483 (median: 340) pg/ml, respectively. There were no significant differences of serum 25-OH vitamin D between diabetic and non-diabetics or male and females of total HD patients was seen (p NS), however a significant differences of serum 25-OH vitamin D between diabetic and non-diabetics of male dialysis patients was found (r=0.014; Figure 1). In non diabetic HD patients, there was a significant positive correlation of serum 25-OH vitamin D with BMI (r=0.51, p=0.011; Figure 2) was seen (adjusted for age). In this group also there was a near significant inverse correlation of serum 25-OH vitamin D with serum phosphorus (r=- 0.39, p=0.057) and also a significant inverse correlation of serum 25-OH vitamin D with serum calcium (r=-0.42, p=0.040; Figure 3) was found, too (adjusted for dialysis sessions for two above correlations). In male HD patients a near significant inverse correlation of serum 25-OH vitamin D with serum iPTH (r=-0.43, p=0.057) (adjusted for duration dialysis) was seen. In this study no significant association between serum 25-OH vitamin D with serum albumin, CRP, ALP, URR and age, duration and sessions of dialysis were found (p=ns).

Discussion

In this study we found a significant difference of serum 25-OH vitamin D between diabetic and non-diabetics of male dialysis patients with more values in nondiabetic HD patients and a significant positive correlation of serum 25-OH vitamin D with BMI and also a near significant inverse correlation of serum 25-OH vitamin D with serum phosphorus were seen, also a significant inverse correlation of serum 25-OH vitamin D with serum calcium were found, too. Moreover, a near significant inverse correlation of serum 25-OH vitamin D with serum iPTH was seen, too. In a study conducted by Gonzalez et al. on 103 patients undergoing hemodialysis, it was found that 97% of the patients had vitamin D levels in the suboptimal range, and there was no correlation of 25(OH)D levels with either PTH or serum albumin values [9]. In agreement with this study we also could not show the correlation of 25(OH)D with serum albumin. Interestingly, we showed a positive correlation of 25(OH)D with BMI, implies that serum 25(OH)D have an association with nutritional status in MHPs. In contrast to the mentioned study we showed a near significant inverse correlation of serum 25-OH vitamin D[25(OH)D] with serum iPTH

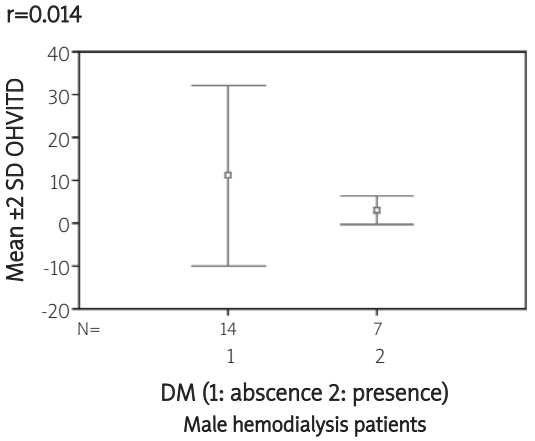

Figure 1. Significant differences of serum 25-OH vitamin D between diabetic and non-diabetics of male dialysis patients

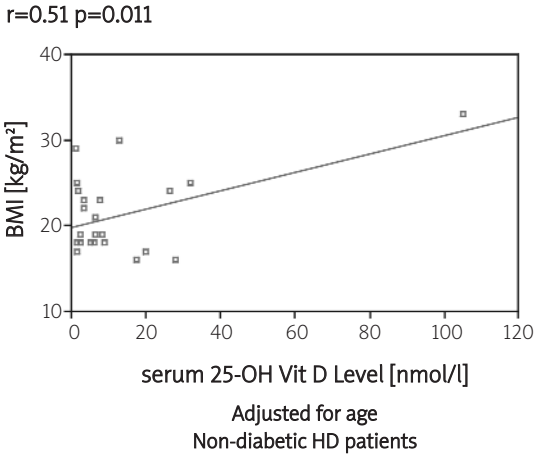

Figure 2. A significant positive correlation of serum 25-OH vitamin D with body mass index

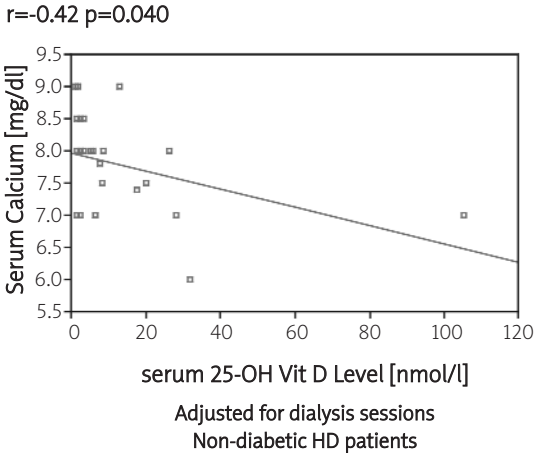

Figure 3. A significant inverse correlation of serum 25-OH Vitamin D with serum calcium

also negative association of serum 25(OH)D with Ca and P, showed that low levels of serum 25(OH)D clearly aggravate the secondary hyperparathyroidism of regular HD patients. In this regard Ghazali et al. in a study to evaluate the plasma 25(OH)D levels as a risk factor for parathyroid hormone hypersecretion and radiological bone disease, on 113 patients who were not taking supplements of alphacalcidol or calcitriol, found that plasma PTH was correlated negatively with plasma 25-OHD. They concluded that low plasma 25-OH vitamin D is a major risk factor for hyperparathyroidism and Looser's zones [10]. Therefore, our study strengthens the suggestion that low serum 25-OH vitamin D levels could be a risk factor for secondary hyperparathyroidism in hemodialysis patients as well as serum 25-OH vitamin D could show the nutritional status of HD patients. In summary, we think that our results are of interest for two reasons: first, because there is limited previous data concerning this topic and, secondly, because our results indicate the importance of monitoring plasma 25-OH vitamin D levels in HD patients. In dialysis patients, we suggest that the plasma levels of 25-OH vitamin D are maintained around the upper limit of the reference range of sunny countries.

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