Evaluation of Vitamin D Level and its Correlation to Vascular Calcification in Hemodialysis Patients

Mahdieh Hosseini [1] Azadeh Seifadini [2] Mohammad Tamadondar [3] Hamidreza Samimagham [3] Shahram Zare [4]

Internist [1] , Shahid Sadoughi University of Medical Sciences, Yazd, Iran. General Practitioner [2] , Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Assistant Professor Department of Internal Medicine [3] , Hormozgan University of Medical Sciences, Bandar Abbas, Iran. Professor Department of Community Medicine [4] , Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

(Received 22 July, 2013 Accepted 26 Jan, 2014)

Original Article

Abstract

Introduction: Compared with the general population, hemodialysis patients are at increased risk of vascular calcification, which in turn is associated with an increased risk of mortality. Regarding the role of vitamin D in bone formation, regulation of calcium, phosphate and iPTH level and correlation of these variables in survival, this study was performed to evaluate the vitamin D serum level and its correlation with vascular calcification in hemodialysis patients.

Methods: In this analytical, cross-sectional study one hundred hemodialysis patients who referred for dialysis to Shahid Mohammadi hospital in Bandar Abbas were evaluated in 2011. Patients older than 15 years on regular hemodialysis (at least dialyzed for 3 months) were selected as study population and patients who had undergone parathyroidectomy were excluded. Variables such as age, sex, BMI, hemodialysis duration, vitamin D, ferritin, PTH, calcium, phosphate, hemoglobin and CRP were specified. Vascular calcification in lateral x-ray of abdomen determined based on scoring system to abdominal aortic calcification in front of lumbar spines (L1-L4). Data analysis was performed by SPSS software and t-test and Chi-Square test.

Results: In this study 25% of hemodialysis patients had vitamin D deficiency that in male and female were similar. The prevalence of vascular calcification based on plain lateral abdominal x-ray was 52. 2%, that was included 55% women and 45% men. No relationship was found between vascular calcification and Vitamin D serum level, but there was positive correlation between vascular calcification and patients' age, also higher level of serum Ferritin was detected in patients with higher Vitamin D level (P=0.001).

Conclusion: In summary our study results showed the low prevalence (25%) of Vitamin D deficiency in hemodialysis patients as compared to similar studies in other countries that may be related to geographical situation of the region. No relationship was found between Vitamin D serum level and vascular calcification. In this study the vascular calcification has been evaluated with plain x-ray that is not a high sensitive test. For measuring vascular calcification our recommendation is to perform more sensitive tests.

Correspondence:
Azadeh Seifadini, MD.
Shahid Sadoughi University of Medical Sciences.
Yazd, Iran
Tel:+98 9132539289
Email:
azadeh_seifaddiny@yahoo.com

Key words: Vascular Calcification - Vitamin D - Hemodialysis

Citation: Hosseini M, Seifadini A, Tamadondar M, Samimagham HR, Zare S. Evaluation of Vitamin D Level and its Correlation to Vascular Calcification in Hemodialysis Patients. Hormozgan Medical Journal 2016;20(2):74-79.

Introduction:

Vitamin D is one of fat-soluble vitamins which play an important role in bone formation, calcium and phosphate metabolism and will increase calcium reabsorption in kidney (1). Its active form also reduces parathyroid hormone and affects the blood phosphate levels (2).

Vitamin D has great importance in those patients with chronic kidney disease and it is due to direct effect of vitamin D on the cardiovascular system can help to improve blood pressure control and reduce the left ventricular hypertrophy using reduction of vascular tone and activation of the renin-angiotensin system and decrease of cardiac contractility (3). Although vitamin D is prescribed based on serum level of PTH intact, calcium and phosphate in most hemodialysis centers, this form doesn't provide 25 (OH) Vit D which is used as body storage; in fact, the level of 25 (OH) Vit D is related to a person's nutritional status. Regarding nutritional limitations and less contact with sunlight in hemodialysis patients, it can be concluded that most patients with chronic kidney disease are likely to receive less vitamin D (4). Despite these issues, vitamin D level is measured less in hemodialysis patients and levels of vitamin D may have reduced despite of the prescription of active form of vitamin D in these patients (5).The inhibition processes leading to the calcification of intima layer and media of arteries such as the release of pro-inflammatory cytokines, proliferation and migration of vascular smooth muscle cells are among the physiological functions of vitamin D (6).

In retrospective studies that have been conducted on hemodialysis patients, the treatment with vitamin D analogues has been associated with reduced mortality; on the other hand, high doses of vitamin D may exacerbate vascular calcification by increasing the absorption of calcium and phosphate (7) while lower doses of vitamin D which is commonly used to suppress PTH can have a protective effect on vascular calcification (8). After vascular calcification, the increase in systolic pressure and pulse pressure may have both resulted in an increased risk of myocardial infarction and cardiovascular mortality (9,10). By early detection of vascular calcification, it can be hoped to reduce the likelihood of cardiovascular disease in hemodialysis patients using direct therapeutic intervention. Risk factors such as age, sex, Tobacco Use, reduced GFR, hyperphosphatemia, PTH disorder, duration of dialysis, and having diabetes before have been listed for vascular calcification (11). There wasn't enough information about the level of 25 (OH) Vit D. On the other hand, 17% of hemodialysis patients don't get vascular calcification and it seems it's due to vascular calcification inhibitors in the body (12).

Vascular calcification can be measured by various methods including plain radiography, computed tomography (CT), Electron Beam CT or Multi Slice CT Scan (13 & 14).Various studies have shown that vascular calcification on a plain x-ray radiograph may show the presence of coronary artery calcification (15).

Considering the essential role of vitamin D in bone formation and regulation of calcium, phosphate and iPTH and the effectiveness of each of these parameters on the survival of kidney patients as well as direct effect of vitamin D on the hemodialysis patients' cardiovascular status and given the fact that there was no study on this issue in Iran until now, the present study tried to examine vascular calcification level of the abdominal aorta and its relationship with vitamin D serum levels in hemodialysis patients.

Methods:

In this Analytical, cross-sectional study all hemodialysis patients who referred for dialysis to Shahid Mohammadi hospital in Bandar Abbas in 2011 were evaluated prospectively. The samples consist of one hundred hemodialysis patients who referred for dialysis to Shahid Mohammadi hospital in Bandar Abbas and include 51 males and 49 females.

Criteria for inclusion included patients who are older than 15 years old and have been dialyzed for at least 3 months and exclusion criteria included having history of hyperparathyroidism or parathyroid surgery before. After obtaining the consent of all patients to participate in this study, the information was recorded in questionnaires.

It should be noted that some of the tests were conducted in the laboratory outside Shahid Mohammadi hospital while the rest was conducted in the hospital. CBC, CRP, hemoglobin, calcium

and phosphate tests were conducted in the laboratory of Shahid Mohammadi hospital and other tests such as vitamin D and serum ferritin test were performed in another laboratory. (It should be noted that wherever vitamin D serum is used in the article, it means 25 (OH) Vitamin D serum). Variables include age, sex, BMI, serum ferritin, the level of aortic calcification on lateral abdominal x-ray, CRP, PTH, Hb, calcium, phosphate, as well as diseases such as diabetes and hypertension. (Hypertension in patients with chronic kidney disease without proteinuria is higher than 130/80 and is 125/75 in patients with proteinuria).

Evaluation of the level of aortic calcification was done by lateral abdominal x-ray and all the graphs were taken with one device in the department of radiology in Shahid Mohammadi Hospital. It should be noted that due to lack of cooperation of 4 patients and the death of 6 hemodialysis patients, only 90 patients of the total number of these samples were examined. Scoring was done using lateral abdominal x-ray at the level of the lumbar vertebrae in the way that in lateral abdominal x-ray, calcification in each of the anterior or posterior walls of abdominal aorta in lumbar vertebrae was measured from L1 to L4 and then the length of calcification was scored in front of each of these vertebrae; i.e. the length of calcification of the aortic for each 1.3 vertebrae was considered as one point and this score is given separately to the anterior and posterior walls of abdominal aorta.

Scoring the vascular calcification in hemodialysis patients ranging from zero to 24 is based on Abdominal X-ray Score which is categorizedas follows:

1. Patients who have not achieved artery calcification scores (zero).
2. Patients who have achieved artery calcification scores from 1 to 12.
3. Patients who have not achieved artery calcification scores from 13 to 24.

Based on serum vitamin D levels, classification of patients is as follows:

Vit D＜10ng/ml shows high vitamin D deficiency, Vit D＝10-30ng/ml is mild vitamin D deficiency and Vit D＞30ng/ml shows the normal amount of vitamin D. Finally, the data were analyzed through Chi-square test, ANOVA and test-t using 17 SPSS software

Results:

In this study, the frequency distribution of the level of serum vitamin D have been defined based on age and sex (high vitamin D deficiency of Vit D ＜10ng/ml, high vitamin D deficiency of Vit D＝10-30ng/ml and normal levels of vitamin DVit D＞30ng/ml) in table 1 in which the highest percentage of the high and mild vitamin D deficiency are 66.7% and 61.5% for the ages of 51-70 years, respectively. According to chi-square test (P=0.486), no significant relationship was found between serum vitamin D and age in hemodialysis patients. And also based on chi-square test (P=0.501), there was no significant relationship between serum vitamin D and gender in hemodialysis patients. The frequency distribution of vascular calcification scores in hemodialysis patients have been defined based on age and sex in table 2 in which the highest level of vascular calcification was based on scores between 51-70 years. Using the chi-square test (P=0.002), a significant correlation was observed between vascular calcification and age in hemodialysis patients so that vascular calcification will increase with increase of age. And also based on chi-square test (P=0.533), no significant relationship was found between vascular calcification and gender. Following the study, the level of serum vitamin D and its relationship with vascular calcification were studied in hemodialysis patients (table 2), and according to chi-square test, there was not a significant correlation between vascular calcification and serum vitamin D in comparison of high and normal deficiencies with P=0.90, and in comparison of mild and normal deficiencies with P=0.44. Then the level of serum vitamin D and its relationship with some variables such as BMI, ferritin, CRP, hemoglobin, calcium, phosphate were studied (table 3), and using t-test in comparison of high and normal vitamin D deficiencies, and in comparison of mild and normal vitamin D deficiencies, P=0.004 and P=0.001 were obtained respectively and there was a significant relationship between the average level of ferritin and serum vitamin D in comparison between high and normal deficiencies and also in comparison between mild and normal deficiencies so that the average level of ferritin is multiplied by 2.4 when the level of vitamin D increases from 10-30 ng/ml to over than 30 ng/ml.

Table 1. Frequency distribution of serum vitamin D based on age and general

Vitamin D		High deficiency	Mild deficiency	Normal
Age	15-30	1 (8.3%)	2 (15.4%)	18 (24%)
	31-50	2 (16.7%)	3 (23.1%)	22 (29.3%)
	51-70	8 (66.7%)	8 (61.5%)	30 (40%)
	71-90	1 (8.3%)	0 (0%)	5 (6.7%)
Gender	Male	4 (33.3%)	7 (53.8%)	38 (50.7%)
	Female	8 (66.7%)	6 (46.2%)	37 (49.3%)

Table 2. Frequency distribution of vascular based on gender, age and serum vitamin D level

Calcification		Zero	1-12	13-24
Age	15-30	15 (34.9%)	5 (13.5%)	0 (0%)
	31-50	12 (27.9%)	7 (18.9%)	8 (80%)
	51-70	12 (27.9%)	23 (62.2%)	8 (80%)
	71-90	1 (2.3%)	2 (5.4%)	2 (20%)
Gender	Male	16 (43.2%)	24 (55.8%)	5 (50%)
	Female	21 (56.8%)	19 (44.2%)	5 (50%)
Serum vitamin D	High deficiency	5 (11.6%)	5 (13.5%)	1 (10%)
	Mild deficiency	6 (14%)	5 (13.5%)	0 (0%)
	Normal	32 (74.4%)	27 (73%)	9 (90%)

Table 3. Frequency distribution, mean and standard deviation of the variables of hemodialysis patients separated by the levels of serum vitamin D

Vitamin D variable	High deficiency			Mild deficiency			Normal		
	No.	Mean	Standard deviation	No.	Mean	Standard deviation	No.	Mean	Standard deviation
BMI	12	22.64	2.55	13	22.54	4.73	75	21.73	5.36
Ferritin	12	152.95	120.55	13	153.58	204.5	75	369.18	318.51
iPHT	12	127.23	115.84	13	180.68	196.74	75	315.82	338.59
Hb	12	8.09	2.05	13	9.25	1.78	75	8.54	1.84
CRP	12	16.95	27.87	13	18.19	28.48	75	19.31	28.87
Calcium	12	8.57	0.89	13	9.36	0.74	75	8.91	0.98
phosphor	12	5.66	1.38	13	4.78	1.26	75	6.14	2.25

Regarding the level of P-value which is higher than 0.05 and with the use of t-test, no significant relationship was found between variables of CRP, BMI, Hb, calcium and phosphate and serum vitamin D level in two groups of hemodialysis patients having high and normal deficiencies and mild and normal deficiencies. According to table 4, the level of vascular calcification was analyzed based on the average age of hemodialysis patients and the highest level of vascular calcification is for the highest average age. Based on ANOVA test (P=0.002), the vascular calcification and age have a significant relationship with each other in hemodialysis patients; i.e. the level of vascular calcification will increase with the increase of age in hemodialysis patients.

Table 4. The frequency distribution of vascular calcification based on the average age of hemodialysis patients

Calcification score	Number	Mean	Standard deviation
Zero	43	40.51	16.42
1 to 12	37	53.51	14.37
13 to 24	10	62.80	10.8
Total	90	-	-

Conclusion:

Based on the results in this study, among 100 patients studied, 12 patients (12%) suffered from high vitamin D deficiency and 13 patients (13%) suffered from mild vitamin D deficiency and all other patients had normal level of vitamin D. The level of serum vitamin D was the same for males and females and totally 25% of vitamin D deficiency was found in these patients and it is less prevalent in comparison with similar studies. For example, Tokmark et al reported that vitamin D deficiency was 95% (15). In a similar study, Del Valle et al reported that the vitamin D deficiency was 76% (16). But the results of present of study is more similar to the study of Cuppari L et al in which the lack of vitamin D in hemodialysis patients is related to geographical conditions and better exposure to sunlight. The level of vascular calcification was 52.2% which is high based on the methods of the present study in comparison with other expensive methods such as EBCT or sonography. The results of previous studies about the increase of vascular calcification with the increase of the age were confirmed (17); however, no significant relationship was found between the prevalence of vascular calcification and gender. In the present study, there was no significant relationship between serum vitamin D and vascular calcification and this is consistent with the results of studies of Chang JH et al (18), Lee SY et al (19) and Cesar Garcia (20). On evaluation of the relationship between other variables and serum vitamin D, there was a relationship between serum ferritin and vitamin D so that with increase of vitamin D level, the level of serum ferritin increased which requires further researches on this issue. Saab G et al showed there is a relationship between response to treatment of simple iron deficiency anemia with vitamin D and Erythropoietin in hemodialysis patients so that there would fewer need for Erythropoietin and ferritin would increase if vitamin D deficiency was treated (21). Perhaps the main reason for better treatment of anemia in hemodialysis patients is the treatment of iron level deficiency or increase of iron level and help for its absorption and this may lead to treatment of vitamin D level.

Recommendation

Regarding the high prevalence of vascular calcification in hemodialysis patients which is confirmed in the present study, it is recommended that in addition to treatment of disease factors and precise regulation of the calcium and phosphate, iPHT, Dyslipidemia should also be treated as risk factors in order to prevent the side effects of vascular calcification. It is also recommended to measure the vitamin D level annually and conduct another study to evaluate the effect of vitamin D deficiency on hemodialysis patients.

References:

1. Van de Graaf SF, Hoenderop JG, Bindels RJ. Regulation of TRPV5 and TRPV6 by associated proteins. Am J Physiol Renal Physiol. 2006;290(6):1295-1302.
2. Silver J, Naveh-Many T, Mayer H, Schmelzer HJ, Popoutzer MM. Regulation by vitamin D metabolites of parathyroid hormone gene transcription in vivo in the rat. J Cline Invest. 1986;78(5):1296-1301.
3. Levin A, Li YC. Vitamin D and its analogues: do they protect against cardiovascular diseasein patients with kidney disease? Kidney Int. 2005;68(5):1973-1981.
4. Daggirdas JT, Blake PG, Ing TS. Handbook of dialysis 4th ed. Lippincott; Wiliams and Wilkins Press; 2007.
5. Sakuma M, Endo N, Oinuma T. Serum 25- OHD insufficiency as a risk factor for hip fracture. J Bone Miner Metab. 2007;25(3):147-150.
6. Zitterman A, Schleithoff SS, Koerfer R. Vitamin D and Vascular calcification. Curr opin lipidol. 2007;18(1):41-46.
7. Mizobuchi M, Finch JL, Martin DR, Slatopolsky E. Differential Effects of Vitamin D Receptor Activators on Vascular Calcification in Uremic Rats. Kidney Int. 2007;72(6):709-715.
8. Mathew S, Lund RJ, Chaudhary LR, Geurs T, Hruska KA. Vitamin D receptor activators can protect against vascular calcification. J Am Soc Nephrol. 2008;19:1509-1519.

9. Lehto S, Niskanen L, Suhonen M, Rönnemaa T, Laakso M. Medial artery calcification: a neglected harbinger of cardiovascular complications in non-insulindependent diabetes mellitus. Arterioscler Thromb Vasc Biol. 1996;16(8):978-983.

10. London GM, Guérin AP, Marchais SJ, Métivier F, Pannier B, Adda H. Arterial media calcification in end-stage renal disease: impact on all-cause and cardiovascular mortality. Nephrol Dial Transplant. 2003;18(9):1731-1740.

11. Hutchison JA. Vascular calcification in dialysis patients. Prilozi. 2007;28(1):215-224.

12. Jean G, Bresson E, Terrat JC, Vanel T, Hurot JM. Peripheral vascular calcification in long-haemodialysis patients: associated factors and survival consequences. Nephrol Dial Transplant. 2009;24(3):948-955.

13. Braun J, Oldendorf M, Moshage W, Heidler R, Zeitler E, Luft FC. Electron beam computed tomography in the evaluation of cardiac calcification in chronic dialysis patients. Am J Kidney Dis. 1996;27(3):394-401.

14. Goodman WG, Goldin J, Kuizon BD, Yooh C, Gules B, Sider D, et al. Coronary-artery calcification in young adults with end-stage renal disease who are undergoing dialysis. N Engl J Med. 2000;342(20):1478-1483.

15. Tokmak F, Quack I, Sehieren G, Sellin L, Rattensperger D, Holland-Letz T, et al. High-dose cholecalciferol to correct vitamin D deficiency in haemodialysis patients. Nephrol Dial Transplant. 2008;23(12):4016-4020.

16. Del Valle E, Negri AL, Aguirre C, Fradinger E, Zanchetta JR. Pervalence of 25 (OH) Vitamin D Insufficiency and deficiency in Chronic Kidney disease stage 5 patients on hemodialysis. Hemodial Int. 2007;11(3):315-321.

17. Cuppari L, Carvalho AB, Draibe SA. Vitamin D Status of Chronic Kidney disease Patients Living in a sunny Country. J Ren Nutr. 2008;18(5):408-414.

18. Chang JH, Ro H, Kim S, Lee HH, Chung W, Jung JY. Study on relationship between serum 25-hydroxyvitamin D levels and vascular calcification in hemodialysis patients with consideration of seasonal variation in vitamin D levels. Atherosclerosis. 2012;220(2):563-568.

19. Lee SY, Kim HY, Gu SW, Kim HJ, Yang DH. 25-hydroxyvitamin D levels and vascular calcification in predialysis and dialysis patients with chronic kidney disease Kidney Blood Press Res. 2012;35(5):349-354.

20. Garcia-Canton C, Bosch E, Ramirez A, Gonzalez Y, Auyanet I, Guerra R, et al. Vascular calcification and 25-hydroxyvitamin D levels in non-dialysis patients with chronic kidney disease stages 4 and 5. Nephrol Dial Transplant. 2011;26(7):2250-2256.

21. Saab G, Young Do, Gincherman Y, Giles K, Norwood K, Coyne Dw. Pervalence of Vitamin D deficiency and the safety and effectiveness of monthly ergocalciferol in hemodialysis patient. Nephron Clin Part. 2007;105(3):132-138.