

Evaluation of the relationship between vitamin D and calcium levels in serum and the severity of gingival disease in dialysis patients: a case control study

Ocena związku między poziomem witaminy D i wapnia w surowicy a nasileniem choroby dziąseł u pacjentów dializowanych: badanie kontrolne przypadku

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Summary

Aim of the study. The aim of this study was to investigate the relationship between serum levels of vitamin D and calcium and the severity of gingival disease in patients with end-stage renal disease undergoing dialysis.

Material and methods. In this case-control study, 43 patients diagnosed with chronic kidney disease undergoing dialysis were evaluated for probing pocket depth, clinical attachment loss, gingival index, bleeding on probing and plaque index. Then, they were divided into the case group with gingival disease and the control group without gingival disease. Serum levels of vitamin D and calcium were also determined. Data were analyzed using stata11 software using chi-square test and independent t-test with a significance level of 0.05 and a 95% confidence level.

Streszczenie

Cel pracy. Celem badania było sprawdzenie zależności pomiędzy poziomem witaminy D i wapnia w surowicy a stopniem zaawansowania choroby dziąseł u dializowanych pacjentów w schyłkowej niewydolności nerek.

Material i metody. Oceniono 43 pacjentów z przewlekłą chorobą nerek poddanych dializie pod kątem następujących parametrów: sondowanie głębokości kieszonek (PPD), kliniczna utrata przyczepu (CAL), indeks dziąsłowy (GI), krwawienie podczas sondowania (BoP) i indeks płytki nazębnej (PI). Następnie pacjenci zostali przypisani do grupy badawczej (z chorobą dziąseł) i kontrolnej (bez). Ustalono poziomy witaminy D i wapnia w surowicy. Dane poddano analizie przy użyciu pakietu stata11 software, testu chi-square i niezależnego t-te-

Results. The difference between the mean serum levels of vitamin D in the case and control groups was 33.66, which was statistically significant (P -value <0.001). The difference between the mean serum calcium levels in the case and control groups was 0.85, which was statistically significant (P -value > 0.001). There was no statistically significant relationship between the mean age and the body mass index between the case and the control groups (P -value = 0.13 and P -value = 0.39, respectively). There was no significant difference between the two groups in terms of gender (P -value = 0.43).

Conclusion. Serum levels of vitamin D and calcium were lower in dialysis patients with gingival disease than in patients on dialysis without gingival disease, also no significant relationship was observed between age, sex and body mass index with gingival disease in dialysis patients.

Introduction

Gingival disease is an inflammatory disease of the supporting tissues of the teeth caused by specific microorganisms. Gingival disease leads to advanced destruction of the periodontium by the host inflammatory response.¹ Bacterial products and the host immune response to these products lead to the destruction of tooth supporting tissues, including the alveolar bone. Because of this tissue damage, chronic periodontitis is the leading cause of tooth loss in adults.^{2,3}

Major risk factors for periodontal disease are diabetes and smoking. However, other diseases and specific conditions may also constitute potential risk factors for the disease.⁴

Vitamin D and calcium are essential for bone mineralization and prevention of osteoporosis. Vitamin D plays an important role in calcium homeostasis and regulation of calcium and phosphate levels. Severe vitamin D deficiency causes bone defects (osteomalacia). A number

of epidemiological studies have reported a positive association between low bone mass or osteoporosis, and also a positive association between alveolar bone loss and tooth loss.⁵⁻¹⁵ Low bone mass has been recognized as a risk factor for the progression of periodontal disease.¹⁰⁻¹²

Wyniki. Różnica pomiędzy średnim poziomem witaminy D w surowicy w grupie badawczej i kontrolnej wynosiła 33.66, co jest wynikiem statystycznie istotnym ($P < 0,001$). Różnica pomiędzy średnim poziomem wapnia w surowicy w grupie badawczej i kontrolnej wynosiła 0.85, co jest wynikiem statystycznie istotnym ($P < 0,001$). Nie było istotnie statystycznej zależności pomiędzy średnią wiekiem i indeksem masy ciała pomiędzy obiema grupami (odpowiednio $P = 0,13$ i $P = 0,39$). Nie stwierdzono istotnie statystycznej zależności pomiędzy obiema grupami w kategorii płci ($P = 0,43$).

Wniosek. Poziom witaminy D i wapnia w surowicy był niższy u pacjentów dializowanych z chorobą dziąseł niż u pacjentów dializowanych bez choroby dziąseł. Nie zauważono istotnej zależności pomiędzy wiekiem, płcią i indeksem masy ciała a chorobą dziąseł u pacjentów dializowanych.

of epidemiological studies have reported a positive association between low bone mass or osteoporosis, and also a positive association between alveolar bone loss and tooth loss.⁵⁻¹⁵ Low bone mass has been recognized as a risk factor for the progression of periodontal disease.¹⁰⁻¹²

Optimal levels of vitamin D showed several benefits for oral health.^{16,17}

Sufficient intake of vitamin D can decrease the risk of gingivitis and chronic periodontitis, as it has been shown to have immunomodulatory, anti-inflammatory, anti-proliferative effects, and it initiates cell apoptosis.¹⁸

Severe vitamin D deficiency can lead to decreased mineralization of teeth, resulting in dentine and enamel defects. As a consequence, these lesions may increase the risk of the onset and progression of dental caries. Further, vitamin D deficiency has been associated with higher prevalence of periodontitis and gingival inflammation.¹⁹

In cases of chronic periodontitis, taking

vitamin D supplements is associated with a reduction in the severity of periodontal disease.²⁰

Disorders in vitamin D metabolism are associated with periodontal disease.²¹⁻²³ Serum vitamin D levels were inversely associated with clinical attachment loss and gingivitis. Also, serum levels of vitamin D in patients with periodontal disease were low, compared to healthy individuals.^{24,25} Patients with vitamin D deficiency also do not seem to respond well to periodontal surgery.²⁶

Adequate serum levels of vitamin D can prevent and reduce the progression of periodontal disease.¹⁷ Various studies, including NHANES III, have shown the relationship between periodontal health and calcium and vitamin D intake.^{7,27} Vitamin D has an immunosuppressive effect for periodontal disease. Nowadays, as medical science has advanced, dentists are increasingly faced with systemic diseases and their specific medical complexities, and patients with these problems should be treated by dentists. End-stage renal disease (ESRD) can be included as one of the diseases that affect the periodontium and the mouth.

Epidemiological studies conducted in the United States show that about eight million people in the United States have at least one type of kidney disease disorder, of which 360,000 are reported to have ESRD. In addition, approximately 79,000 people are diagnosed with kidney disease each year.²⁸ Despite many studies, accurate statistics on the incidence and prevalence of kidney disease in Iran are unfortunately not available. According to the IRNA news agency and the head of the Foundation for Special Diseases, the number of dialysis patients in Iran in the year of 2020 was 13,000 with 17,000 kidney transplant patients. He also reported that the number of dialysis patients in Iran is increasing every year by 1,500.

Calcium deficiency and increased phosphorus levels lead to secondary hyperparathyroidism disorder, which ultimately removes calcium from the skeleton, affects the alveolar bone, and reduces periodontal support.^{29,30}

Since vitamin D is reduced in dialysis patients, it causes secondary hyperparathyroidism and alveolar bone resorption. Considering the essential role of these two substances in periodontal health, this study is performed to investigate the relationship between gingival disease and serum levels of vitamin D and calcium in dialysis patients.

Materials and Methods

This case-control study has been approved by the ethics committee of Hamadan University of Medical Sciences IR.UMSHA.REC.1398.717.

The study was carried out in the Department of Nephrology, Beheshti Specialized Hospital of Hamadan, Hamadan, Iran in 2020. A total of 43 patients (including 19 men and 24 women with the average age of 59.09 ± 10.84) suffering from ESRD participated in this study. The nature of the study was explained to the patients, and a written informed consent was obtained from them.

The inclusion criteria of the study were:

1. Confirmed ESRD diagnosis.
2. Having at least 10 teeth.
3. Having been on dialysis for at least one year.

The patients having any of the following criteria were excluded from the study:

1. Treatment of scaling, root planing in the last six months.
2. History of periodontal surgery.
3. Use of mouthwashes affecting plaque.
4. Having other systemic diseases.
5. Taking vitamin D and calcium supplements in the past three months.
6. Smoking.

Analysis method

To start with, clinical examinations were performed using a Williams HuFriedy-USA probe and a dental mirror, including examination of clinical attachment loss (CAL), pocket probing depth (PPD), bleeding on probing (BOP), gingival index (GI) and plaque index (PI) were measured and recorded. Gingival index was used to determine the sensitivity and quantity of gingivitis. Using this index, only the gingival tissue is evaluated. All four aspects of the gums (facial, mesial, distal, and lingual) were evaluated for inflammation. According to this index, the degree of gingivitis was scored as follows:

0: healthy gingiva

1: mild inflammation; swelling and slight discoloration without bleeding on probing

2: moderate inflammation; redness and swelling and shining of the surface with bleeding on probing

3: severe inflammation; specific redness and swelling, spontaneous bleeding.³¹

During evaluation of the BOP index, after using a standard probe and inserting it gently into the gingival sulcus, if bleeding occurs up to 30 seconds after probe withdrawal, this index is considered positive, otherwise it is negative.³¹

To check the probing depth (PD), a probe was inserted parallel to the longitudinal axis of the Ramfjord teeth (teeth n° 16-21-24-44-41-36) and moved around tooth (Walking technique) and then the numbers obtained for each tooth are added. The sum was divided by the number of measured areas.³²

To check for the presence or absence of CAL, a probe was inserted into the gingival sulcus and the CEJ distance to the depth of the pocket was obtained.³¹

PI is used to check for plaque on the tooth surface. After administering the disclosing agent, the amount of stained tooth surfaces was counted, which included buccal, mesial, distal and lingual surfaces. The number obtained is

divided by the total number of teeth multiplied by 4 and then the obtained number is multiplied by 100.³¹

Then, according to the data, the patients were divided into the case and control groups based on the following:

Case group (with periodontal disease): GI \geq 2, PD \geq 3 mm, presence of BOP and CAL

Control group (without periodontal disease): GI $<$ 2, PD $<$ 3 mm, no CAL observed

Then, blood samples were taken from the eligible patients by the nurse of the dialysis department of Beheshti Hospital, and they were immediately sent to the laboratory to determine the serum level of vitamin D in these patients. In the laboratory, using the 25-OH vitamin D kit with serial number 98004 made by Pishtaz Teb Iran Company, which has been designed by competitive method and monoclonal antibody, the patients' vitamin D levels were obtained and recorded. Their age, sex, height and weight were also recorded using the information records in the patient file. Serum calcium levels of patients were recorded and collected using the latest routine test recorded in their files and the data were analysed.

Statistical Analysis

Data was entered into an electronic datasheet. Descriptive statistics (mean and standard deviation) at 95% confidence level were used to determine the mean serum levels of vitamin D and calcium. Also, to compare the means of the items, independent t-test and analysis of variance (ANOVA) were used at a significance level of 5%. All results were statistically analysed using Stata11 software to determine the differences.

Results

In this case-control study, 21 patients in the case group (dialysis patients with gingival disease) and 22 patients in the control group

Table 1. Characteristics of qualitative variables in the case and control groups

Variables	Level	Case		Control		P_V
		Number	Percentage	Number	Percentage	
Gender	Male	8	38.10	11	50.00	0.432
	Female	13	61.90	11	50.00	
BOP	Yes	21	100.00	10	45.45	0.001>
	No	0	0.00	12	54.55	

(dialysis patients without gingival disease) participated. In the study, more women were included in the case group, but gender distribution was equal in the control group. However, this difference was not statistically significant and there was no relationship between them (P-value = 0.432).

In the case group, all 21 patients had bleeding on probing recorded. The index among the control group was that 10 patients had BOP and 12 patients did not have BOP. The difference was statistically significant (P-value <0.001) (Table 1).

The mean age of the case group was 59.09 years and the mean age of the control group was 54.36 years and the age difference between the two groups was 4.73 years, which was not statistically significant using independent t-test (P-value = 0.131)

The mean serum level of vitamin D in the case group was lower than in the control group (28.20 vs. 61.87) and the difference between them was 33.66, which was statistically significant using the independent t-test (P-value 0.0001).

The mean serum calcium level in the case group was 8.45 and in the control group was 9.30 and the difference between the two was 0.852, which was statistically significant using independent t-test (P-value <0.001).

The mean value of gingival index in the case

group was 2.33 and in the control group was 1.13 and the difference between the two was 1.19, which was statistically significant using independent t-test (P-value <0.001).

The mean value of plaque index in the case group was 0.77 and in the control group was 0.62 and the difference between the two was 0.15, which was statistically significant using independent t-test (P-value <0.001).

The mean amount of CAL in the case group was 1.42 and in the control group was 0.04 and the difference between the two was 1.38, which was statistically significant using the independent t-test (P-value <0.001).

The mean values of probing depth in the case group and the control group were 4.54 and 2.22, respectively, and the difference between them was 2.32, which was statistically significant using independent t-test (P-value <0.001).

The mean value of body mass index in the case group and the control group were 23.66 and 23.87, respectively. This difference was not statistically significant (P-value = 0.397) using independent t-test, and no correlation it was found (Table 2). The analysis showed that with increasing severity of periodontitis, serum calcium and vitamin D levels decreased in patients undergoing hemodialysis and increased in the severity of periodontitis with increased severity of kidney disease.

Table 2. Comparison of quantitative variables between the case and control groups

Variables	Case		Control		Difference		P_V
	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard error	
Age (years)	59.09	10.84	54.36	15.85	-4.73	4.16	0.13
Serum level of vitamin D (ng/ml)	28.20	4.45	61.87	17.07	33.66	3.84	< 0.001
Serum calcium level (ng/ml)	8.45	0.574	9.30	0.55	0.852	0.17	< 0.001
Gingival Index	2.33	0.48	1.13	0.46	-1.19	0.14	< 0.001
Plaque Index	0.77	0.07	0.62	0.06	-0.15	0.02	< 0.001
Clinical Attachment Loss (CAL) (mm)	1.42	0.81	0.04	0.213	-1.38	0.17	< 0.001
Probing Depth (mm)	4.54	0.72	2.22	0.52	-2.32	0.19	< 0.001
Body Mass Index (weight/height squared)	23.66	2.50	23.87	2.82	0.21	0.81	0.39

Discussion

It is now accepted that periodontitis can be an important risk factor for chronic kidney disease and kidney failure for the following reasons.³³

(a) Systemic inflammation is affected by periodontal inflammation.

(b) Periodontal bacteria or bacterial products can enter the bloodstream.³⁴

In addition, the oral health of dialysis patients is often poor due to poor oral hygiene, because of their poor condition.

Due to the role of periodontal disease in the development of systemic inflammation and the effectiveness of some serum factors as an indicator of kidney function, the aim of this study was to investigate the relationship between serum levels of vitamin D and calcium.

Numerous studies have attempted to show a relationship between periodontal disease and kidney disease, but the results were contradictory.³⁵

In the study of *Naghsh et al.*, there was a

significant relationship between serum levels of calcium and phosphorus and clinical attachment loss. They observed that with increasing severity of periodontitis, serum levels of calcium and phosphorus increased in patients on hemodialysis. Elevated serum calcium and phosphorus levels in hemodialysis patients is an important risk factor for mortality.³⁶ In the present study, the average amount of CAL in dialysis patients with gingival disease was 1.42 and in dialysis patients without gingival disease was 0.04 and the difference between the two was 1.38. The observation was statistically significant (P-value <0.001).

The kidneys play an important role in regulating serum calcium and phosphorus levels.³⁷ As mentioned earlier, inflammation following the exacerbation of periodontal disease causes gradual damage to the kidneys and compromises their function.³⁴ Therefore, it can be stated that as a result of decreased renal function due to periodontal disease and the role of the kidneys in the regulation of

serum calcium and phosphorus, these values increase with the exacerbation of periodontitis. The relationship between periodontal disease and chronic kidney disease is reciprocal in that chronic kidney disease has oral manifestations and periodontal disease also affects renal function.³⁸ In the present study, the mean serum levels of vitamin D and calcium in the case group were 28.20 and 8.45, respectively, and in the control group were 61.87 and 9.30, respectively. The difference in serum levels of vitamin D and calcium between these two groups was 33.66 and 0.852, respectively, which was statistically significant (P-value <0.001).

Rodrigues et al. reported that serum calcium levels were not significantly associated with periodontal disease in hemodialysis patients, which is not consistent with the present study.³⁹

Botelho et al. investigated the relationship between serum vitamin D levels and periodontal disease and indicated that compared with healthy controls, 25 (OH) D serum levels were significantly lower in chronic periodontitis patients, which is in line with the present study.¹⁹

Isola et al. investigated the relationship between serum vitamin D levels and periodontal disease and showed that patients with periodontitis and periodontitis plus coronary heart disease (CHD) presented significantly lower serum levels of vitamin D compared to CHD and healthy controls. Moreover, the presence of periodontitis negatively influenced serum vitamin D levels; the results of this study are in accordance with the results of the present study.⁴⁰

Millen et al.⁴¹ studied the relationship between serum vitamin D levels and periodontal disease in 920 postmenopausal women and found that vitamin D status was inversely associated with periodontal disease, which can be confirmed by the present study.

The results of a study showed evidence of

an association between low serum vitamin D levels and periodontal disease. They found that the association between low levels of vitamin D and an increased risk of gingivitis was significant, which can be similar to the results of the present study.²⁵

Antonoglou et al. also reported no significant association between vitamin D and selected indicators of periodontal disease among 1262 Finnish patients in their cross-sectional study, which is not in concordance with the results of the present study.⁴²

In the present study, the mean value of gingival index in dialysis patients with gingival disease was 2.33 and in dialysis patients without gingival disease was 1.13 and the difference between them was 1.19, which is statistically significant (P-value <0.001).

In the present study, the mean values of plaque index, probing depth and body mass index in case group were 0.77, 4.54 and 23.66, respectively, and in the control group they were 0.62, 2.22 and 23.87, respectively. In all the cases except in the body mass index category, the difference between the two groups was statistically significant (P-value <0.001).

Although cross-sectional studies have provided strong evidence for the serum status of vitamin D in periodontal disease, the largest and longest longitudinal study⁴⁰ as well as a recent cross-sectional study⁴² have failed to establish a link between them.

Considering the relationship between periodontal diseases and some of serum level factors in hemodialysis patients, it seems that periodontal treatment and promotion of oral health in these patients can help control the serum level of inflammatory cytokines. To achieve more definite results and compare patients undergoing hemodialysis with healthy patients without hemodialysis, clinical trials are needed to assess serum levels of these factors before and after periodontal treatment.

Conclusion

In the present study, which aimed to investigate the relationship between serum levels of vitamin D and calcium with the severity of gingival disease in dialysis patients, it was observed that the severity of gingival disease was associated with serum levels of vitamin D and calcium in hemodialysis patients. Mean serum levels of vitamin D and calcium were lower in the dialysis group with gingival disease than in the dialysis group without gingival disease.

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