Frontiers in Dentistry

Association of Serum 25-Hydroxyvitamin D and Chronic Periodontitis in Postmenopausal Women after Non-Surgical Periodontal Therapy

Adileh Shirmohammadi[1], Sanaz Mohammadi[1], Masoumeh Faramarzi[1], Amir Reza Babaloo[1], Mehrnoosh Sadighi[1], Solmaz Maleki Dizaj[2*]

1. Department of Periodontics, Faculty of Dentistry, Tabriz University of Medical Sciences, Tabriz, Iran
2. Dental and Periodontal Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Article Info

Article type:
Original Article

Article History:
Received: 03 May 2022
Accepted:17 Nov 2022
Published: 29 Apr 2023

**** Corresponding author:***
Dental and Periodontal Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Email: maleki.s.89@gmail.com

A B S T R A C T

Objectives: Vitamin D deficiency appears to have a major effect on periodontal tissue health. The present study aimed to assess the association of the serum level of 25-hydroxyvitamin D and chronic periodontitis in postmenopausal women.

Materials and Methods: This research was done on 30 postmenopausal women with chronic periodontitis who all had at least 20 natural teeth. Intravenous blood samples were taken from the study population at baseline and after completion of non-surgical periodontal treatment. This was followed by assessment of serum levels of 25-hydroxyvitamin D. Next, clinical parameters of all teeth except for third molars were measured, which included pocket depth (PD), gingival index (GI), and plaque index (PI). Data were analyzed by paired t-test and its non-parametric equivalent, the Wilcoxon test. $P<0.05$ was considered significant.

Results: The mean PD, PI and GI before and after the intervention were significantly different ($P<0.05$). There was, however, no significant difference between the mean vitamin D concentrations before and after treatment ($P>0.05$).

Conclusion: According to the results obtained in the present study, there is no association between serum vitamin D concentrations and chronic periodontitis in postmenopausal women.

Keywords: Periodontitis; Osteoporosis, Postmenopausal; 25-hydroxyvitamin D

➢ **Cite this article as:** Shirmohammadi A, Mohammadi S, Faramarzi M, Babaloo AR, Sadighi M, Maleki Dizaj S. Association of Serum 25-Hydroxyvitamin D and Chronic Periodontitis in Postmenopausal Women after Non-Surgical Periodontal Therapy. *Front Dent*. 2023:20:08.

INTRODUCTION

Periodontitis is an inflammatory disease caused by bacteria, which destroys the tissue surrounding the teeth [1]. This disorder can ultimately result in bone loss and tooth mobility, if left untreated [2]. Prevention and early diagnosis of periodontal disease are, therefore, important to prevent adverse consequences [2].

Non-surgical periodontal therapy with scaling and root planing is the most common treatment of periodontitis, which results in improvement of clinical and microbiological parameters [3]. Presence of bacteria is essential for development of periodontal disease, but the host's susceptibility may be also equally important. The host's inflammatory response is a defensive mechanism, but failure to respond or overreaction can further aggravate tissue

injury. Vitamin D plays an essential role in several inflammatory diseases by playing a role in their course through pro-inflammatory cytokines. Evidence that vitamin D may have certain antibacterial properties as well [1].

Vitamin D is generated in the skin following sunlight exposure and then in the liver, and converts to 25-hydroxyvitamin D, the serum's most plentiful circulating metabolite, which finally reaches the kidneys. Only 10% to 15% of the calcium in the diet and about 60% of phosphorus are digested, which reduces skeletal mineralization in patients with vitamin D deficiency [1]. In a recent systematic review, Machado et al. [4] stated that 25-hydroxyvitamin D serum levels were significantly lower in chronic periodontitis patients compared with healthy controls. They also concluded that owing to the low number of studies, ascription of periodontitis and vitamin D level after non-surgical periodontal treatment is not simple. Factors that influence 25-hydroxyvitamin D concentration have been evaluated with considerable attention [4,5]. However, inadequate information exists on this topic in women, especially menopaused women. Increasing attention has been paid in recent years to moderate vitamin D deficiency especially in seniors, which contributes to diminished bone mass [6].

This is extremely important in postmenopausal women, since the bone mineral mass is decreased leading to a reduction in estrogen [7]. Increased bone resorption due to decreased sex hormones in the first decade after menopause is a common problem in women. Periodontitis in women with osteoporosis is more prevalent due to relatively low serum level of this vitamin [8,9]. Vitamin D affects both the immune system and the bone mineral mass, which may lead to progression or prevention of periodontal disease. Lee et al. [7] observed that vitamin D was correlated with periodontal wellbeing. In a report, individuals with lower concentrations of 25-(OH)D were more often in the periodontal community [6]. Cheng et al. [8] stated that the key circulating metabolite of vitamin D or 25-(OH)D was high in patients with generalized aggressive periodontitis. A cross-sectional study of non-smokers and non-diabetics in Finland confirmed that there was no definitive link between the serum concentrations of vitamin D and development of a pocket deeper than 4 mm and gingival bleeding in individuals at low risk of periodontal diseases [10]. There is limited data on variations of 25-hydroxyvitamin D levels in postmenopausal women after non-surgical therapy for chronic periodontitis. Therefore, this study aimed to assess the association of serum level of 25-hydroxyvitamin D and chronic periodontitis in postmenopausal women before and after receiving non-surgical periodontal treatment.

MATERIALS AND METHODS

Sample size and sampling:

Based on a pilot study, the serum 25-hydroxyvitamin D levels were measured in 5 postmenopausal women with chronic periodontitis before and at 3 months after non-surgical periodontal treatment. According to the results and by considering α=0.05 and statistical power of 80%, the sample size was estimated to be 30 patients.

Participants:

Participants were chosen from postmenopausal women with chronic periodontitis referred to the Department of Periodontology, Faculty of Dentistry, Tabriz University of Medical Sciences. The statistical population of this study included 30 postmenopausal women aged 50 years and over.

Inclusion criteria:

This study was undertaken on postmenopausal women over 50 years with radiographic confirmation of alveolar bone loss who had at least 20 natural teeth.

Exclusion criteria:

The exclusion criteria consisted of history of using non-steroidal anti-inflammatory drugs and antibacterial agents in the past 1 month before the trial, history of periodontal procedures during the past 1 month before

the trial, all systemic conditions and infectious diseases except for periodontitis, invasive periodontitis, systemic disorders including kidney failure, diabetes mellitus and bone defects, which would interfere with bone metabolism and immune system, and consumption of mouthwashes and vitamin supplements in the past 3 months before the study.

Intervention:

Five milliliters of blood samples were collected from patients at baseline and transferred into sterile vacuum tubes lacking anticoagulant to determine the serum concentration of 25-hydroxyvitamin D. A dental mirror and a UNC-15 periodontal probe were used to measure clinical parameters, including pocket depth (PD) of mesiobuccal, distobuccal, distolingual, lingual, and mesiolingual areas around the teeth, gingival index (GI) and plaque index (PI) [11]. All assessments were conducted by one examiner (a periodontist) to prevent inter-examiner disagreements. Next, non-surgical periodontal therapy, which involves oral health instruction, dental prophylaxis, precise manual scaling and root planing, and 2-week administration of 0.12% chlorhexidine mouthwash was performed [12-14].

The patients received phase I periodontal therapy and were followed-up during the maintenance phase following the completion of the procedure. In cases requiring surgery, appropriate treatment was performed and they were followed afterwards. Intravenous blood samples were collected again from the participants after 3 months of follow-up to measure the serum level of 25-hydroxyvitamin D, and subsequently the clinical parameters were measured again. The response to phase I periodontal therapy is assessed during a span of 3 months in most periodontal trials [12].

The protocol of this study was approved by the Ethics Committee of Tabriz Dental School (code: IR.TBZMED.REC.1396.919) and it was registered at IRCT.ir under IRCT20110726007128N10).

Statistical analysis

SPSS 20 was used for statistical analysis of data at $P<0.05$. The Kolmogorov-Smirnov test was used to assess normal distribution of data. The Wilcoxon test was used to analyze values with non-normal distribution while paired t-test was used to analyze normally distributed data.

RESULTS

Among 30 patients, three patients were lost to follow-up. Table 1 presents the mean values of the studied parameters. As shown, the mean of all variables other than vitamin D decreased after the intervention. The greatest change was noted in PI in an amount of 39% and the minimum in vitamin D in an amount of 9%. The level of vitamin D slightly improved after the intervention but not significantly ($P>0.05$).

The Kolmogorov-Smirnov test indicated that all values except for vitamin D level had a non-normal distribution ($P\leq0.05$). To compare the mean PD, PI, and GI before and following an intervention, the Wilcoxon test was used while the mean level of vitamin D was compared by paired t-test (Table 1).

As shown, all periodontal parameters significantly improved after the intervention ($P<0.05$) but the change in serum level of vitamin D was not significant.

Table 1. Comparison of the parameters measured in this study before and following an intervention

Index	Mean±SD Before treatment	Mean±SD After treatment	Mean differences	%	Relationship coefficient	P
Pocket depth (mm)	2.78±1.52	2.31±0.75	0.47	16	-2.67	0.007
Plaque index	0.88±0.81	0.52±0.22	0.35	33	-2.36	0.018
Gingival index	0.95±0.81	0.62±0.24	0.32	39	-2.37	0.018
Vitamin D (ng/mL)	28.49±15.5	31.17±12.4	-2.68	9	-0.73	0.471

SD: standard deviation

DISCUSSION

Menopause constitutes an important change in the life of a woman and is related to anatomical changes in the ovarian tissue, contributing to decreased estrogen secretion. Reduced blood level of this hormone induces bone degradation and subsequent osteoporosis. Vitamin D and its metabolites play a significant role in preserving the bone integrity. Extreme deficiency of vitamin D in adults leads to clinical osteomalacia [15]. Also, moderate vitamin D deficiency causes secondary hyperparathyroidism and bone loss [16]. This is particularly significant in postmenopausal women because of the reduction in bone mineral density caused by estrogen reduction [17]. The interactions of the intestines, parathyroid gland, kidneys, and bone by preserving extracellular amounts of calcium are necessary for proper bone metabolism [18]. Furthermore, vitamin D modulates the adaptive and innate immune response and influences the proliferation, differentiation and activity of immune cells directly and indirectly. Consequently, low blood concentrations of vitamin D are linked to some autoimmune and inflammatory disorders, including rheumatoid arthritis, lupus erythematosus, inflammatory bowel syndrome, type 6 diabetes and multiple sclerosis [19]. Previous data have also indicated that serum concentrations of vitamin D are correlated with periodontitis [19].

Periodontitis is a bacterial disease triggered by multiple oral microorganisms that form pockets which may contribute to osteoporosis or tooth mobility in severe types. While microbiota is crucial for periodontal disease, the host status is another important factor [19]. Several studies have found that serum concentrations of vitamin D in patients with type 1 diabetes, pregnant mothers, osteoporotic patients, menopausal women, and patients with chronic obstructive pulmonary disease are correlated with periodontal deterioration [20, 21].

A previous study demonstrated little beneficial effects on periodontal health in users of a one-year supplement of calcium (less than 1000mg/day) plus vitamin D (less than 10 micrograms/day) [22]. Based on the bone defense ability and anti-inflammatory characteristics of vitamin D, we carried out a study to assess the effect of non-surgical periodontal therapy in postmenopausal women with chronic periodontitis on serum concentrations of 25-hydroxyvitamin D. In this study, non-surgical periodontal therapy increased the serum concentrations of 25-(OH)D in chronic periodontitis patients. The findings of this study indicated that non-surgical periodontal therapy resulted in a substantial improvement in PD in postmenopausal women with chronic periodontitis.

The serum level of vitamin D was associated with inflammation and gingival bleeding in a study conducted by Millen et al, [19] on 920 postmenopausal women. There was no correlation between serum concentrations of vitamin D and chronic periodontitis marked by alveolar bone loss and dental problems. This observation confirms the results of the present study that vitamin D serum levels did not significantly improve in postmenopausal women following treatment of chronic periodontitis.

There was no direct correlation between the serum concentrations of vitamin D and PD of less than 4mm and gingival bleeding in patients with low risk of periodontitis in a cross-sectional study of Antonoglu et al, [23] on non-smokers and non-diabetics in Finland. They observed that the association between 25(OH)D serum concentrations and PD did not significantly differ between males and females.

In a study carried out by Dietrich et al. [9] to evaluate the correlation of serum 25(OH)D concentrations and gingivitis on non-smoker patients between 13-90 years, an inverse linear correlation was found between 25(OH) D concentration and inflammation. Disparity in statistical population is one explanation for the differences between the findings of their study and the current study.

Hagenau et al. [24] observed an inverse correlation between the serum level of vitamin D and periodontal problems, including tooth loss in a study on 780 postmenopausal

women who had tooth loss attributed to periodontal disease. The findings of their study were different from the results of the present study, which may be due to substantial reductions in participants throughout the experiment. The number of participants dropped from 781 to 471 during the follow-up period in their study. Whereas; in the present study only 3 patients were lost to follow-up. Significant improvements occurred in PD. PI, and GI after the intervention in postmenopausal females in the present study.

This study was in line with the results of Papalsi et al, [25] regarding PD. They assessed the association of osteoporosis and periodontitis in 31 women between 45 and 71 years, and demonstrated that in senior females with osteoporosis, PD was more frequent than in those without osteoporosis [25]. The current results regarding PI was similar to that reported by Shen et al [26] who analyzed 94 menopausal osteoporotic patients and showed that there was significantly higher PD in the interproximal regions of teeth in postmenopausal women compared to their osteoporosis-free controls. The results obtained regarding GI in the present study were similar to those reported by Alves et al [27]. They assessed the correlation between menopause and periodontal disease in 611 Portuguese women with chronic periodontitis in postmenopausal and premenopausal states. Alves et al. [27] indicated that the number of teeth in postmenopausal women was lower than in younger individuals. However, after adjusting for age, smoking and plaque index, the difference was no longer statistically significant. In another study, Lee et al. [28] analyzed the association between plasma 25-(OH)D levels and periodontitis in people aged ≥60 years. The results showed that periodontitis was not significantly associated with plasma 25(OH)D levels.

Small sample size due to small number of patients who only required phase I periodontal therapy was a limitation of this study. Future studies with a larger sample size and at least two follow-ups are suggested to further assess the serum level of vitamin D after periodontal therapy over longer periods of time.

CONCLUSION

This study sought to evaluate the potential correlation between 25-hydroxyvitamin D serum levels and chronic periodontitis in postmenopausal women. Based on the results there was no significant relationship between the two variables.

ACKNOWLEDGMENTS

This study was based on a thesis (No. 57715) registered at the Faculty of Dentistry, Tabriz University of Medical Sciences, Tabriz, Iran. It was financially supported by the Vice-Chancellor for Research at Tabriz University of Medical Sciences, Tabriz, Iran, which is greatly appreciated.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Eshghi R, Rashidi Maybodi F, Khabazian A, Shahhosseini S. Association between serum levels of vitamin D and chronic periodontitis in premenopausal women in Yazd. Caspian J Dent Res. 2016 Mar 10;5(1):47-51.
2. Penoni DC, Torres SR, Farias ML, Fernandes TM, Luiz RR, Leão AT. Association of osteoporosis and bone medication with the periodontal condition in elderly women. Osteoporos Int. 2016 May;27(5):1887-96.
3. Camargo GA, Abreu MG, Cordeiro Rdos S, Wenderoscky Lde F, Duque C. Prevalence of periodontopathogens and Candida spp. in smokers after nonsurgical periodontal therapy - a pilot study. Braz Oral Res. 2016 Aug 22;30(1):e92.
4. Machado V, Lobo S, Proença L, Mendes JJ, Botelho J. Vitamin D and Periodontitis: A Systematic Review and Meta-Analysis. Nutrients. 2020 Jul 22;12(8):2177.
5. Mazahery H, von Hurst PR. Factors Affecting 25-Hydroxyvitamin D Concentration in Response to Vitamin D Supplementation. Nutrients. 2015 Jun 25;7(7):5111-42.
6. Fu XM, Fan SG, Li SL, Chen YS, Wu H, Guo YL. Low 25(OH) D serum levels are related with hip

fracture in postmenopausal women: a matched case-control study. J Transl Med. 2015 Dec 23;13:388.
7. Lee HJ, Je DI, Won SJ, Paik DI, Bae KH. Association between vitamin D deficiency and periodontal status in current smokers. Community Dent Oral Epidemiol. 2015 Oct;43(5):471-8.
8. Cheng TY, Millen AE, Wactawski-Wende J, Beresford SA, LaCroix AZ, Zheng Y, et al. Vitamin D intake determines vitamin d status of postmenopausal women, particularly those with limited sun exposure. J Nutr. 2014 May;144(5):681-9.
9. Dietrich T, Joshipura KJ, Dawson-Hughes B, Bischoff-Ferrari HA. Association between serum concentrations of 25-hydroxyvitamin D3 and periodontal disease in the US population. Am J Clin Nutr. 2004 Jul;80(1):108-13. doi: 10.1093/ajcn/80.1.108.
10. Antonoglou GN, Suominen AL, Knuuttila M, Ylöstalo P, Ojala M, Männistö S, et al. Associations between serum 25-hydroxyvitamin d and periodontal pocketing and gingival bleeding: results of a study in a non-smoking population in Finland. J Periodontol. 2015 Jun;86(6):755-65.
11. Preshaw PM. Detection and diagnosis of periodontal conditions amenable to prevention. BMC Oral Health. 2015;15 Suppl 1(Suppl 1):S5.
12. Farooqi OA, Wehler CJ, Gibson G, Jurasic MM, Jones JA. Appropriate Recall Interval for Periodontal Maintenance: A Systematic Review. J Evid Based Dent Pract. 2015 Dec;15(4):171-81.
13. Zarandi A, Salahaddin S, Faramarzi M. Efficacy of different concentrations of chlorhexidine mouthwash on plaque accumulation and periodontal parameters. J Periodontol Implant Dent. 2016;8(1):8–11
14. Quirynen M, Mongardini C, Pauwels M, Bollen CM, Van Eldere J, van Steenberghe D. One stage full- versus partial-mouth disinfection in the treatment of chronic adult or generalized early-onset periodontitis. II. Long-term impact on microbial load. J Periodontol. 1999 Jun;70(6):646-56.
15. Parfitt AM, Gallagher JC, Heaney RP, Johnston CC, Neer R, Whedon GD. Vitamin D and bone health in the elderly. Am J Clin Nutr. 1982 Nov;36(5 Suppl):1014-31.
16. Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. Endocr Rev. 2001 Aug;22(4):477-501.
17. Khosla S, Atkinson EJ, Melton LJ 3rd, Riggs BL. Effects of age and estrogen status on serum parathyroid hormone levels and biochemical markers of bone turnover in women: a population-based study. J Clin Endocrinol Metab. 1997 May;82(5):1522-7.
18. As, D., Vitamin D. Am J, Physiol Renal Physiol, 2005. 289: p. F8-F28.
19. Millen AE, Hovey KM, LaMonte MJ, Swanson M, Andrews CA, Kluczynski MA, et al. Plasma 25-hydroxyvitamin D concentrations and periodontal disease in postmenopausal women. J Periodontol. 2013 Sep;84(9):1243-56.
20. Bolland MJ, Grey A, Gamble GD, Reid IR. The effect of vitamin D supplementation on skeletal, vascular, or cancer outcomes: a trial sequential meta-analysis. Lancet Diabetes Endocrinol. 2014 Apr;2(4):307-320.
21. Ghorbani F, Haghgoo R. Evaluation of the effect of magnolia herbal mouth wash on O'leary plaque index. Daneshvar Medicine, 2015. 1: 61-66.
22. Garcia MN, Hildebolt CF, Miley DD, Dixon DA, Couture RA, Spearie CL, et al. One-year effects of vitamin D and calcium supplementation on chronic periodontitis. J Periodontol. 2011 Jan;82(1):25-32.
23. Antonoglou GN, Suominen AL, Knuuttila M, Ylöstalo P, Ojala M, Männistö S, et al. Associations between serum 25-hydroxyvitamin D and periodontal pocketing and gingival bleeding: results of a study in a non-smoking population in Finland. J Periodontol. 2015:86(6), 755-765.
24. Hagenau T, Vest R, Gissel TN, Poulsen CS, Erlandsen M, Mosekilde L, et al. Global vitamin D levels in relation to age, gender, skin pigmentation and latitude: an ecologic meta-regression analysis. Osteoporos Int. 2009 Jan;20(1):133-40.
25. Pepelassi E, Nicopoulou-Karayianni K, Archontopoulou AD, Mitsea A, Kavadella A, Tsiklakis K, et al. The relationship between osteoporosis and periodontitis in women aged 45-70 years. Oral Dis. 2012 May;18(4):353-9.
26. Shen EC, Gau CH, Hsieh YD, Chang CY, Fu E. Periodontal status in post-menopausal osteoporosis: a preliminary clinical study in Taiwanese women. J Chin Med Assoc. 2004 Aug;67(8):389-93.
27. Alves RC, Félix SA, Rodriguez-Archilla A, Oliveira P, Brito J, Dos Santos JM. Relationship

between menopause and periodontal disease: a cross-sectional study in a Portuguese population. Int J Clin Exp Med. 2015 Jul 15;8(7):11412-9.
28. Lee MR, Han SJ, Kim HE, Choi JS. Relationship between Vitamin D Deficiency and Periodontitis in Korean Adults Aged ≥60 Years: Analysis of Data from the Korea National Health and Nutrition Examination Survey (2013-2014). Int J Environ Res Public Health. 2021 Apr 15;18(8):4181.