Review / Derleme

MEDICINE PALLIATIVE CARE

DOI: 10.47582/jompac.1208868
J Med Palliat Care 2022; 3(4): 381-385

Relationship between periodontal disease and vitamin D

Periodontal hastalık ve D vitamini ilişkisi

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Cite this article as / Bu makaleye atıf için: Aydoğan T, Karşıyaka Hendek M, Olgun E. Relationship between periodontal disease and vitamin D. J Med Palliat Care 2022; 3(4): 381-385.

ABSTRACT

Vitamin D is a hormone synthesized by human skin cells or consumed through diet with immunomodulatory, anti-inflammatory, and antiproliferative effects. Vitamin D deficiency may increase the risk of periodontal disease by causing decreased bone mineral density, osteoporosis, progression of periodontal diseases, and resorption of the jawbone. In addition, vitamin D is important for bone metabolism, alveolar bone resorption, and the prevention of tooth loss. It increases the antibacterial defense of gingival epithelial cells, reduces gingival inflammation, accelerates postoperative wound healing after periodontal surgery, and is a key supplement functioning as a prophylaxis in periodontology. The present review study aims to highlight the role of vitamin D in periodontal disease.

Keywords: Periodontititis, vitamin D, 25(OH)D3, periodontal treatment, 1.25(OH)2D3

ÖZ

D vitamini, insan deri hücreleri tarafından sentezlenen veya diyet yoluyla tüketilen immünomodülatör, antienflamatuar, antiproliferatif etkilere sahip bir hormondur. D vitamini eksikliği kemik mineral yoğunluğunun azalmasına, osteoporoza, periodontal hastalıkların ilerlemesine ve çene kemiğinde rezorpsiyon oluşmasına neden olarak, periodontal hastalık riskini artırabilir. Ayrıca D vitamini kemik metabolizması, alveolar kemik rezorpsiyonu ve diş kayıplarının önlenmesi için de önemlidir. Diş eti epitel hücrelerinin antibakteriyel savunmasını arttırır ve dişeti enflamasyonunu azaltır, periodontal cerrahi sonrası postoperatif yara iyileşmesini hızlandırır ve periodontolojide profilaksi olarak kullanılan önemli bir takviyedir. Bu derlemenin amacı, periodontal hastalıkta D vitamininin rolünü vurgulamaktır.

Anahtar Kelimeler: Periodontititis, D vitamini, 25(OH)D3, periodontal tedavi, 1,25(OH)2D3

INTRODUCTION

Periodontal diseases are complex disorders resulting in the interaction of biofilm with the host immuno-inflammatory response and subsequent changes to soft and hard tissue hemostasis (1,2). Inıtial human and animal studies to explore the pathogenesis, prevention, and treatment of periodontal diseases in the 1960s concluded that bacteria assume a key role in initiating gingivitis and periodontitis (3,4). Accordingly, the final opinion is that "bacteria lead to periodontal disease." In this model, bacteria-secreted products and metabolism residues cause tissue destruction. Yet, the research in the 1980s revealed that the host immuno- inflammatory response plays a central role in the development of periodontal diseases. The products secreted by polymorphonuclear cells, the very first defense mechanism against bacteria and their products, also cause indirect tissue destruction (5,6). In 1997, it was shown that various genetic, environmental, and acquired risk factors with the bacteria-host relationship play a role in the pathogenesis of periodontitis (7). Among the fat-soluble vitamins, vitamin D is a steroid vitamin that can be synthesized endogenously with hormone-like functions. Vitamin D3 can be taken in two different ways through diet: ergocalciferol (Vitamin D2) and cholecalciferol (Vitamin D3). Cholecalciferol is the primary dietary source of vitamin D and is mainly found in foods of animal origin. Ergocalciferol, on the other hand, is extracted from plant sterols. A significant portion of vitamin D3 (estimated to be about 80%) is produced endogenously in the skin from 7-dehydrocholesterol with the effects of UV rays. After reaching the liver together with vitamin D (D3 or D2) absorbed from food, skin-produced vitamin D3 is hydroxylated by the enzyme 25-hydroxylase and turns into its inactive form, 25(OH) D3, also known as calcidiol. Circulating to the kidneys,

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Received / Geliş: 23.11.2022 **Accepted / Kabul:** 05.12.2022

25(OH)D3 is metabolized by the enzyme 1α-hydroxylase to its active form, 1,25(OH)2D3, also known as calcitriol, or to its inactive metabolite, 24,25-dihydroxyvitamin D3, by the enzyme 24-hydroxylase (8, 9). It is a form of vitamin D with a concentration of about 1000 times that of 1,25(OH)2D3 (10).

Vitamin D deficiency is characterized by low calcium levels and is a stimulus that also elevates parathyroid hormone (PTH) levels. PTH is secreted while serum PTH concentration increases in response to low serum calcium levels. Calcium reabsorption from the kidneys and 1α-hydroxylase activity increase, but 24- hydroxylase activity decreases. Thus, intestinal calcium absorption is boosted with increased production of 1,25(OH)2D3. Along with elevated vitamin D levels, high levels of calcium suppress PTH production. While PTH increases in hypophosphatemia and hypocalcemia, it is inhibited by 1,25(OH)2D3 and FGF-23 (11). Along with PTH, 1,25(OH)2D3 stimulates osteoclasts by osteoblasts and induces the release of calcium from bones to blood (12). Nevertheless, 1,25(OH)2D3 does not robustly inform about vitamin D levels due to its short half-life. With a half-life of 12-19 days, 25(OH)D3 is considered the most accurate indicator of vitamin D in serum.

It was reported that about one billion people worldwide suffer from vitamin D deficiency or insufficiency (13). The 2019 guideline by the Turkish Society of Endocrinology and Metabolism (TEMD) suggests measuring serum 25(OH)D3 levels to assess vitamin D status. In this measurement, serum 25(OH)D3 level > 30 ng/mL is accepted as adequate vitamin D level, 20-30 ng/mL as vitamin D inadequacy, < 20 ng/mL as vitamin D deficiency, and < 10 ng/mL as severe vitamin D deficiency. The TEMD Osteoporosis and Metabolic Bone Diseases Working Party determines the minimum daily vitamin D requirement for bone and muscle health of adults (19-70 years) as 600 IU and the need to keep the serum 25(OH) D3 level at 30 ng/ml as 1500-2000 IU. Satisfying daily vitamin D needs requires food consumption and sun exposure, as well as vitamin D supplementation. People at risk for vitamin D deficiency need to be supplemented with vitamin D at the recommended doses. The safe upper limit of vitamin D is known to be 4000 IU per day, and every 100 IU (2.5 micrograms) of vitamin D increases serum 25(OH)D3 level by 0.7-1 ng/ml (14). Sufficient vitamin D levels allow the formation of the appropriate calcium-phosphorus compound, resulting in adequate bone mineralization. Yet, low vitamin D levels are associated with type 2 diabetes mellitus (T2DM), insulin resistance, hypertension, and endothelial dysfunction. In addition to its role in bone mineralization and calcium balance, vitamin D has antioxidant, anti-inflammatory, antiangiogenic, immunomodulatory, and antiproliferative properties. Vitamin D level is key in bone development since boosting the absorption of magnesium, calcium, and phosphate. Osteomalacia, a severe metabolic end-stage disease, may develop in adults due to low (< 4-10 ng/ml) vitamin D levels. Renal 1-alpha hydroxylation has strict control mechanisms in the synthesis of vitamin D. When being sufficient, vitamin D allows intestinal calcium absorption to reach 30-40% of dietary intake; however, vitamin D deficiency may lead to the inability to absorb more than 10-15% of dietary calcium (15,16).

Current evidence demonstrates the immunomodulatory effect of 1,25(OH)2D3, particularly in innate immunity, can be acknowledged as anti-inflammatory and immunomodulatory, including up-regulation of expression of antimicrobial peptides, promotion of phagocytic killing of pathogenic microorganisms, down-regulation of inflammatory factor release, and reduction of inflammation (15,17). Thanks to its key role in calcium/phosphorus homeostasis and bone physiology, vitamin D also holds a central place in the optimal functioning of the cardiovascular, endocrine, and immune systems. It also helps reduce the risk of many chronic diseases (e.g., cancer, autoimmune disease, infectious disease, hypertension, and cardiovascular diseases). Moreover, vitamin D supports immune regulation and function by controlling more than 200 genes responsible for cellular proliferation, differentiation, and apoptosis (18, 19, 16).

Relationship between Vitamin D and Periodontal Disease

Previous research reported that periodontal ligament cells and human gingival fibroblasts have the ability to synthesize vitamin D (20). It was also found that both 1,25(OH)D3 and 25(OH)D3 regulate inflammatory responses in periodontal ligament cells through the VDR and may affect inflammatory processes in periodontal disease (21). Moreover, it was shown that 25(OH)D3 suppresses the expression of IL-1ß, IL-6, and TNF-α and improves alveolar bone loss (22, 23). The "perio protective" effects of vitamin D were documented to be related to human gingival fibroblasts' ability to regulate inflammatory cytokine production following the AGE-RAGE interaction (24). In vitro studies showed that vitamin D can reduce the number of Porphyromonas gingivalis through active autophagy (25) and the inflammatory burden of periodontitis in rodent models (26, 27). Vitamin D may affect periodontal disease through both its immunomodulatory effects and its effects on bone mineral density. A meta-analysis study concluded an association between specific VDR polymorphisms and susceptibility to periodontitis in humans (28). It was also shown that there are significant relationships between vitamin D and calcium and

periodontal diseases (29). Another study reported a negative correlation between serum vitamin D levels and attachment loss, suggesting that increased vitamin D levels have a positive effect on periodontitis (30). It was previously found that low serum 25(OH)D3 levels are associated with periodontitis and gingival inflammation (31). In another study, high serum 25(OH)D3 level was associated with a lower prevalence of periodontal disease (32). It was also reported that daily calcium and vitamin D supplementation of more than 800-1000 IU can reduce the severity of periodontal disease (33). In addition, it was discovered that 25(OH)D3 levels increase in patients with chronic periodontitis following a dental cleaning and root surface straightening (34). In the literature, periodontal treatment with vitamin D supplementation was reported to improve periodontal health; therefore, vitamin D can be used as a supplement in the treatment of moderate and severe periodontitis (35).

A previous study identified defects in dental and mandibular bone mineralization In mice deficient in 1,25(OH)D3 and reported that vitamin D assumes a dominant role in hard tissue formation than PTH (36). In an animal study, it was found that mice deficient in 1,25(OH)D3 had greater alveolar bone loss, that gene expression levels of IL-1β, TNF-α, MMP-3, and MMP-8 markedly increased, and bone mineral density decreased significantly independent of extracellular calcium and phosphorus levels and age (37). In the same study, it was shown that the reduced bone volume in vitamin D-deficient mice was due to decreased formation rather than increased resorption, as the number and surface of TRAP-positive osteoclasts did not change between groups, and that vitamin D exhibited an anabolic effect. In addition, it was stated that the impact of vitamin D on alveolar bone is directly intrinsic regardless of diet. In another study, 1,25(OH)D3 deficiency induced a higher inflammatory response in gingival tissues with greater numbers of NF-κB p65 and CD3+ cells, which is consistent with reports showing the anti-inflammatory effect of 1,25(OH)D3 by regulating the biosynthesis of pro-inflammatory molecules via NF-κB, which mediates oral infections and periodontitis (38, 39). As a result, 1,25(OH)D3 deficiency accelerated bone loss by inhibiting the osteoblastic bone formation and boosting periodontal tissue degeneration regardless of phosphorus and age. The above- mentioned findings bring novel insights into the deleterious effects of vitamin D deficiency on the periodontium, thereby promoting the idea that vitamin D plays a protective role in periodontal tissues (37). Possible underlying biological mechanisms are that vitamin D has the function of regulating calcium maintenance, which is key in bone metabolism, and its anti-inflammatory or antimicrobial effects (40). Despite increased scholarly interest in the relationship between vitamin D and the development and progression of periodontal diseases, the literature hosts inconsistent findings on uncertainties about whether vitamin D deficiency contributes to the severity of periodontitis (31,32,41-44). In their randomized, double-blind, placebo-controlled clinical study comparing systemic vitamin D and calcium administration with calcium-only administration, Schulze-Spate et al. (2016) found no difference between the groups by graft resorption or bone formation following the maxillary sinus augmentation procedure and reported a higher bone remodeling activity associated with higher vitamin D levels (45). Supplementation with vitamin D was shown to have a dose-dependent anti-inflammatory impact on gingivitis (46). Following periodontal treatment, the healing of intraosseous defects was found to be better in patients with adequate 25(OH)D3 levels compared to those with insufficient 25(OH)D3 levels (47). It was also shown that the use of vitamin D3 in diabetic mice significantly reduces the destruction of periodontal tissues and is a convenient and effective method in modulating immune function thanks to its effect of promoting cathelicidin production (48). The literature documented that patients with chronic periodontitis have lower 25(OH)D3 levels compared to healthy periodontal individuals (49). Recently, low serum vitamin D concentrations have been demonstrated in T1DM and T2DM patients (50, 51) and found to be associated with an increased risk of cardiovascular mortality. In addition, serum 1,25(OH) D3 levels were found to be significantly increased following anti-infective periodontal therapy in T1DM patients (52). Moreover, the previous studies uncovered an increase in PTH after periodontal treatment in T1DM patients with moderate or severe periodontitis and that the increase in serum 1,25(OH)D3 is largely independent of serum PTH (53). Some studies also suggested that vitamin D is inversely related to gingival bleeding and probing depth rather than tooth and alveolar bone loss (32) and that patients with low 25(OH)D3 levels can be kept periodontally stable for five years, which may imply no relationship between vitamin D and tooth loss (43,44).

CONCLUSION

Assuming significant functions in the bodily systems, Vitamin D is essential for adequate calcium absorption in bones. Vitamin D deficiency is often shown to be associated with periodontal disease. Vitamin D supplementation can improve periodontal health in periodontal therapy, and it can be utilized as a supplement in the treatment of moderate to severe periodontitis. In periodontal diseases, vitamin D levels should be checked and supplemented if deficient considering that vitamin D level is related to periodontal health.

ETHICAL DECLARATIONS

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest do declare

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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