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Perspective

Application of adjunct vitamin D supplementation in the management of periodontal disease: A three-pronged approach

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Chronic inflammatory periodontal disease is caused by microbes in the dental plaque and is accompanied by loss of connective tissue and alveolar bone, resulting in tooth loss and diminished oral function. Endotoxins from the lipopolysaccharides (LPS) in Gram-negative bacteria in the dental plaque induce production of several pro-inflammatory cytokines, such as interleukin 1 (IL-1), Interleukin 6 (IL-6), tumor necrosis factor-alpha (TNF-α), matrix metalloproteinases (MMPs) and prostaglandins (PGs). These are the critical biomarkers of periodontal destruction and oral inflammatory burden transmitted via the hematogenous route to the systemic circulation. The management of periodontal disease encompasses two challenges; first is the control of microbial challenge using mechanical plaque control methods, professional scaling and root planing with adjunct chemical plaque control and antimicrobials agents. The second challenge comes from the host-mediated immune response which requires host modulation therapy to counteract pro-inflammatory cytokines and other biologic mediators involved in periodontal destruction.[1]

Vitamin D is a fat-soluble vitamin derived from sunlight, diet and nutrition. It is converted to 25- hydroxyvitamin D [25(OH)D] in the liver and further to 1,25-dihydroxy vitamin D [1,25 $(OH)_2D3$]; the active form in the kidneys. The vitamin D status is measured by 25(OH)D levels, as it is the major circulating stable biomarker in the serum. The vitamin D deficiency is defined as serum vitamin D levels $\leq$20 ng/ml whereas the range of 21—29 ng/ml comes under vitamin D insufficiency.[2]

Vitamin D has essential roles to play in the health of skeletal as well as extra skeletal organs and tissues of the body. Apart from its role in maintaining adequate bone mineral density and reduced chances of fracture, it is also related to periodontal health. Studies show that serum vitamin D levels in chronic periodontitis are comparatively lower than that in periodontal health. Furthermore, optimum vitamin D status is associated with better healing outcomes of periodontal tissues as compared to insufficient levels, and serum vitamin D levels are inversely related to the clinical attachment loss in periodontal disease.[3—5] However, a recent systematic review of existing literature could not demonstrate the benefit of vitamin D in periodontal disease because of the extreme variability of data, and non-standardized study designs.[5]

The beneficial effect of Vitamin D in periodontitis could be attributed to its anti-inflammatory and host-modulatory actions owing to its active metabolite 1,25 $(OH)_2$ D3, which inhibits pro-inflammatory cytokines. Recently, several studies have demonstrated beneficial effects of vitamin D supplementation (VDS) on the periodontal health. Meghil

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et al.[6] have recently evaluated local and systemic anti-inflammatory effects of VDS as an adjunct to periodontal therapy in periodontitis patients. They observed that VDS regulated immune and host inflammatory response by inhibiting T-cell proliferation, interferon-gamma (IFN-γ), and interleukin-17(IL-17). It also activated interleukin-4 (IL-4), which substantiates the important anti-inflammatory and pro-resolution characteristics of vitamin D.[6] Further, VDS also decreased salivary IL-1, IL-6, TNF-α and IL-10 levels in the periodontitis patients demonstrating its host modulation and immune regulation effects.[6]

Interestingly, VDS was also associated with the release of a greater number of autophagy-related proteins critical for antimicrobial autophagy in the whole blood peripheral blood mononuclear cells (PBMCs).[6] VDS also facilitates the release of antimicrobial peptides LL37 from gingival epithelial cells which are effective against *Aggregatibacter actinomycetemcomitans*.[7]

Moreover, Grenier et al.[8] showed that 1,25(OH)D inhibits the several virulence factor gene expressions of *Porphyromonas gingivalis* with minimal inhibitory concentration (MIC) ranging from 3.125 to 6.25 μg/ml. They also observed a partial synergistic effect of 1,25(OH)D with metronidazole against *P. gingivalis*.[8] In addition to this, 1,25(OH)D also decreased the *P. gingivalis* induced nuclear factor kappa (NF-κB) activation in the monocytes model, decreasing the expressions of various pro-inflammatory cytokines involved in periodontal destruction.[7,8]

Furthermore, gingival and junctional epithelium have specific vitamin D receptors that enhance host defense against the microbial insult by improving the epithelial barrier function, thereby augmenting the innate barrier immunity.[7] In an animal model, topical vitamin D application led to inhibition of interleukin-1α (IL-1α), a major cytokine involved in periodontal tissue destruction.[9]

Recently, Gao et al.[10] evaluated the efficacy and safety of VDS in moderate to severe periodontitis subjects after three months of nonsurgical periodontal therapy in a double-blind clinical trial. The subjects were randomly assigned to three groups; VDS 2000 international unit (IU), VDS 1000 IU, and placebo. They found vitamin D to be well tolerated and without any side effect in the doses of 2000 international units (IU) and 1000 IU. VDS increased serum 25(OH)D levels along with a significant decrease in clinical attachment loss and pocket probing depth in both doses as compared to the placebo.[10]

Thus, adjunct VDS is a *three-pronged approach* in tackling periodontal disease progression by *anti-inflammatory, host modulatory,* and *antimicrobial effects*. The innovative uses of adjunct vitamin D in systemic as well as the local mode of delivery appear to have potential clinical benefits and can be supplemented with antimicrobial therapy.[8–10]

Looking at the preliminary findings, vitamin D could be a promising game-changer in the prevention and management of periodontal disease. Prospective longitudinal studies with robust study designs, multivariate models to rule out confounders with standardized selections of subjects are necessary, particularly in vulnerable patients with various comorbidities like post-menopausal osteoporosis and diabetes to validate the efficacy of adjunct vitamin D supplementation in terms of dosage, frequency, and its effect on periodontal, inflammatory and systemic health outcomes.

Declaration of Competing Interest

The authors declare no conflicts of interest.

References

1. Kim J, Amar S. Periodontal disease and systemic conditions: a bidirectional relationship. *Odontology* 2006;94:10—2.
2. Dawson-Hughes B, Heaney RP, Holick MF, Lips P, Meunier PJ, Vieth R. Estimates of optimal vitamin D status. *Osteoporos Int* 2005;16:713—6.
3. Bonnet C, Rabbani R, Moffatt MEK, Kelekis-Cholakis A, Schroth RJ. The relation between periodontal disease and vitamin D. *J Can Dent Assoc* 2019;85:j4.
4. Antonoglou GN, Knuuttila M, Niemelä O, et al. Low serum level of 1,25(OH) D is associated with chronic periodontitis. *J Periodontal Res* 2014;50:274—80.
5. Pinto JPNS, Goergen J, Muniz FWMG, Haas AN. Vitamin D levels and risks for periodontal disease: a systematic review. *J Periodontal Res* 2018;53:298—305.
6. Meghil MM, Hutchens L, Raed A, et al. The influence of vitamin D supplementation on local and systemic inflammatory markers in periodontitis patients: a pilot study. *Oral Dis* 2019;25:1403—13.
7. McMahon L, Schwartz K, Yilmaz O, Brown E, Ryan LK, Diamond G. Vitamin D-mediated induction of innate immunity in gingival epithelial cells. *Infect Immun* 2011;79:2250—6.
8. Grenier D, Morin MP, Fournier-Larente J, Chen H. Vitamin D inhibits the growth of and virulence factor gene expression by *Porphyromonas gingivalis* and blocks activation of the nuclear factor kappa B transcription factor in monocytes. *J Periodontal Res* 2016;51:359—65.
9. Menzel LP, Ruddick W, Chowdhury MH, et al. Activation of vitamin D in the gingival epithelium and its role in gingival inflammation and alveolar bone loss. *J Periodontal Res* 2019;54:444—52.
10. Gao W, Tang H, Wang D, Zhou X, Song Y, Wang Z. Effect of short-term vitamin D supplementation after nonsurgical periodontal treatment: a randomized, double-masked, placebo-controlled clinical trial. *J Periodontal Res* 2020. https://doi.org/10.1111/jre.12719.