ROLE OF VITAMIN D IN PERIODONTITIS – A NARRATIVE REVIEW

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Abstract:

Vitamin D is a fat-soluble vitamin that primarily aids calcium absorption, promoting growth and mineralization of bones. Recent research on Vitamin D has unravelled the many facets of vitamin D including its role in periodontal health and disease. With larger section of people around the world getting easily afflicted with Vitamin D deficiency as well as chronic periodontitis this review will scrutinize the involvement and nutraceutical importance of vitamin D in periodontal health and disease.

Keywords: Bone mineralization, calcitriol, Periodontitis, Vitamin D.

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1. Introduction:

Vitamin D is seco steroid, a fat soluble vitamin with hormone like action playing key role in calcium and phosphorus homeostasis an metabolism of bone.Vitamin D plays a significant role in bone remodelling and plays a crucial role in both bone mineralisation and demineralisation. The primary source of vitamin D is from 7-dehydrocholesterol during a photochemical reaction under the effect of ultraviolet radiation on the skin,in addition diet and nutritional supplements also contribute to vitamin D.

Vitamin D increases the intestinal absorption of calcium and decreases the secretion of parathyroid hormone, which consequently decreases systemic bone resorption. In addition, vitamin D stimulates osteoblastic bone production and alkaline phosphatase activity, optimizes bone remodeling and covers bone mass by increasing bone matrix proteins [1,2]

Vitamin D deficiency causes rickets, osteopenia, osteoporosis, osteomalacia and in chronic cases it leads to hypertension, autoimmune diseases, certain cancers, type I diabetes, cardiovascular diseases, secondary hyper parathyroidism. In recent studies serum Vitamin D levels has been found to have potential benefits for COVID-19 and in assessing patients' potential of developing severe COVID-19[3,4].

Lower vitamin D levels are also associated with higher periodontal destruction and severe periodontitis stage[5]. Therefore, the present study is aimed to examine the role of vitamin D in periodontitis.

VITAMIN D NORMAL LEVELS IN BODY FLUIDS:

The recommended daily amount (RDA) is 400 international units (IU) for children up to age 12 months, 600 IU for people ages 1 to 70 years, and 800 IU for people over 70 years. Moore et al has reported average daily dietary intake to be between 1000-1200mg/day. The serum and salivary 25 (OH) D level is defined as a deficiency if below 10 ng/mL, insufficiency if between 11–20 ng/mL, and optimal if ≥20 ng/mL. The 1.25 (OH) D serum and saliva are deemed deficient if ≤48 pmol/L and normal if >48 pmol/L [39].Examination of 25 (OH) D and 1.25 (OH) D serum and saliva is carried out using ELISA.

PREVALENCE OF VITAMIN D DEFICIENCY:

It was estimated that 1 billion people worldwide have vitamin D deficiency or insufficiency [2]. 70 - 100% of the general population all over India bear Vitamin D deficiency. [6]. From the study made by Al Zarooni [7] we can observe that Vitamin D deficiency was similar in both male and female (male 83.1%, female 83.8%) as insufficiency (male 12.7%, female 11.2%)[43] and Al Quaiz [8]stated that, younger adults and males are more prone to vitamin D deficiency than the older participants and females .On examining few surveys it's found that Vitamin D deficiency is more among illiterate and non-working women than the literate and working women[9]

Scientific evidences supporting vitamin D deficiency in India even among medical fraternity is reported [10,11].

METABOLISM OF VITAMIN D:

The two significant forms of vitamin D are: Vitamin D2 or ergocalciferol and Vitamin D3 or cholecalciferol. Vitamin D_2 or ergocalciferol is synthesized through the irradiation of ergosterol in the presence of UV light in plants, yeasts and mushroom. UVB irradiation of 7 - dehydrocholesterol, which is an intermediate of cholesterol synthesis, found in malpighian layer of epidermis give rises to secosterol, in which the cis double bond is isomerised to trans bond leading to the formation of Vitamin D_3 or cholecalciferol that is hydroxylated to 25-hydroxycholecalciferol in the liver, which in turn is hydroxylated in kidney to form an active form of vitamin D known as Calcitriol (1, 25-dihydroxycholecalciferol). [12]

BONE MINERALIZATION AND RESORPTION UNDER THE INFLUENCE OF VITAMIN D:

Vitamin D helps to attune skeletal integrity and mineral homeostasis through intestinal, bone, and renal resorption .From the review of Dr. Michael F. Holick we can perceive that decreased serum levels of 25-hydroxyvitamin D, significantly reduces the intestinal absorption of calcium that is associated with increased parathyroid hormone which activates osteoblasts, and stimulates the transformation of pre osteoclasts into mature osteoclasts that can dissolve the mineralized collagen matrix in bone. Thus, intensifying the bones to lose their density and hardness by constant release of calcium into the bloodstream.

Bone is resorbed by osteoclasts, and is deposited by osteoblasts by the process called ossification. Receptor activator of nuclear factor kappa-B ligand (RANKL) and Osteoprotegerin [OPG](RANKL antagonist) are produced by osteoblasts and other

cells such as activated CD4 + T lymphocytes to regulate the bone remodelling. Binding of RANKL to RANK results in the differentiation of osteoclast progenitor cells into mature osteoclast. These mature osteoclasts remove calcium and phosphorus from the bone, maintaining calcium and phosphorus levels in the blood.

Whereas, OPG (osteoprotegerin) acts as a soluble receptor for RANKL, inhibiting RANK‑RANKL interaction and the maturation of osteoclast progenitor cells. Therefore, the mature osteoclast formation is determined by the relative ratio of RANKL to OPG in the osteoclast precursor microenvironment. The RANKL gene promoter contains vitamin D and glucocorticoid response elements. Studies have shown that vitamin D‑VDR stimulates RANKL expression in cells such as osteoblasts and bone marrow‑derived stromal cells.

Vitamin D down regulates OPG, increased RANKL expression and decreased expression of OPG caused by vitamin D would favour the differentiation and activation of osteoclasts that eventually causes increased bone resorption. However, Hofbauer et al. stated a sparking effect of vitamin D on OPG, and Kondo et al. stated that vitamin D initially represses OPG, but long-term exposure to vitamin D leads to a recovery of OPG expression. This suggests that the catabolic effects of vitamin D can be ephemeral. Anabolic effects of vitamin D on osteoblasts, includes stimulation of osteopontin and alkaline phosphatase [13-17].

VITAMIN D AND PERIODONTITIS:

Vitamin D has a significant role in the modulation of the immune system, inflammation system and ossification process. All these characteristics show significant associations between periodontal health and intake of vitamin D.A study by Madi et al has shown that vitamin D status is found to be positively correlated with periodontal health in a Saudi population [37]. various studies done by several authors shows a positive association between vitamin D status and periodontal health correlating serum and salivary levels of VitD with pocket depth and alveolar bone loss [5,22,35,36]. A study Dietrich et al has shown the relationship between serum levels of Vitamin D and periodontal inflammation [33].

Nathalia Gracia et al in a systematic review as concluded that there is probably little correlation between vitamin and periodontitis [38].Also, study by Zhan et al contradicts the role of vitamin D in periodontal health[39]. In spite of the perplexing reports available vitamin D is considered as a nutraceutical component playing a key role in periodontal health. The most important characteristics of vitamin D in periodontal health are reported as follows.

ANTI-INFLAMMATORY PROPERTY OF VITAMIN D IN PERIODONTAL HEALTH:

It is far and wide known that periodontitis is a chronic host mediated response causing periodontal destruction by the release of pro‑inflammatory cytokines by local tissues and immune cells in response to the bacteria of dental plaque and their products and metabolites which results in destruction of connective tissue and alveolar bone. Vitamin D has anti‑inflammatory properties that can inhibit the inflammatory cytokines and makes the monocyte/macrophages to secrete molecules that have a strong antibiotic effect.

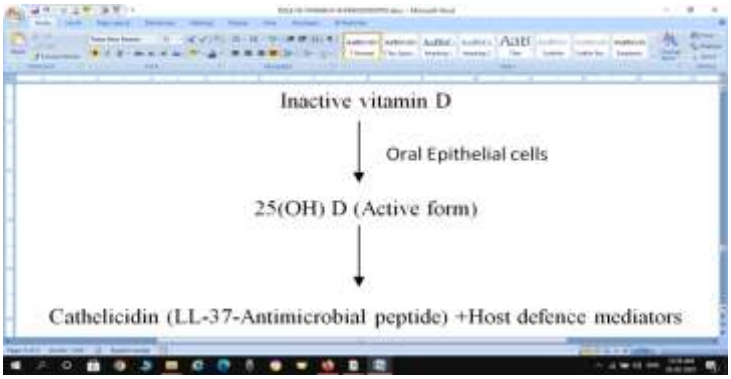
VITAMIN D AS AN IMMUNO MODULATING AGENT:

Activation of vitamin D is enabled in gingiva under inflammation and microbial plaque accumulation as gingival fibroblasts produce 25hyroxylase and the cell receptors 1 alpha hydroxylase due to which 1,25(OH)D3 is formed. This in turn activates the VDR gene and participate expression of genes that produces proteins facilitating tight junction in epithelial cells. Ginigival cells under the influence of Vitamin D also secrete antimicrobial peptides such as beta defensins [30,31,32].

Human B defensin (hBD) and cathelicidin are two naturally occurring antimicrobial peptides that are expressed by gingival epithelial cells as host response to microbial stimuli.They are seen in gingiva,buccal mucosa and epithelial cells.Wang et al,2004 has reported that vitamin D upregulates the expression of the aforementioned antimicrobial peptides in periodontitis[28] .In line with this a recent study by Bayirli,2020 has also concluded that serum deficiency of vit D is associated with low GCF levels of hBD and cathelicidin in GCF of periodontitis subjects[29].

The vitamin D receptor (VDR) is widely expressed in immune cells such as antigen – presenting cells, natural killer cells, T cells and B cells [18]. Beta-Defensins (anti-microbial peptide) exhibit antimicrobial activity against oral microbes including periodontitis-related bacteria like Actinobacilusactinomycetemcomitans, Porphyromonasgingivalis, Fusobacterium nucleatum, Candia and Papilloma virus.Several studies reveals the relation between the polymorphism of VDR gene and periodontitis[19]. Due to lack of appropriate immune response in vitamin D deficient patients, they fail to respond

properly to invading pathogens in periodontal diseases. Figure represent the mechanism of Vitamin D against the periodontitis-related bacteria [20].



Vit D also plays a significant role by influencing T and B lymphocytes [21].A meta analysis by Vannessa et al shows that the level of vitD3 to be less in chronic periodontitis when compared to that of healthy controls[22]

VITAMIN D IN BONE METABOLISM:

As discussed earlier, Vitamin D has a significant role in bone metabolism. It increases mineralization of bone in the mandible and inhibit the resorption of alveolar bone [23,24]. One of the conspicuous feature of periodontal disease is resorption of alveolar bone caused by the host immune response to bacterial insult, in due course leads to loss of teeth. From the previous studies, we can observe that alveolar bone loss due to periodontitis is more prevalent in osteoporosis which occurs in vitamin D deficiency condition.

Prevalence of periodontal disease increases with age. According to the Global Burden of Disease Study (2016), severe periodontal disease was the 11th most prevalent condition in the world. Study done by Muhammad Nazir shows that Hundred percent of older persons in China, India, and Croatia have periodontal disease [25].

VITAMIN D THERAPY IN PERIODONTITIS:

Periodontitis is mainly caused by bacterial invasion that give rise to inflammation and in severe cases resorption of alveolar bone and eventually loss of teeth. [26,40]. Vitamin D has anti-microbial actions, anti-inflammatory properties and increases the calcium absorption thereby reducing the resorption of alveolar bone thus, teeth are held tight in the alveolar process. Hence, proper intake of Vitamin D can help in treating periodontitis. It was found that vitamin D offered effective outcome in wound healing and periodontal surgeries [27]. Vitamin D receptors (VDR) are helpful in the treatment of periodontitis through its anti-microbial peptides against periodontopathic bacteria, immunomodulatory effects against pro inflammatory cytokines and bone anabolic effects against the alveolar bone loss.

2. Conclusion:

Vitamin D, beyond its potential in preventing bone related diseases like rickets, osteoporosis, osteopenia and osteomalacia by increasing calcium absorption and bone mineralization, numerous study reports supports the present review and explains its significant role in periodontitis. Major problems of periodontitis are pathogenic bacteria, inflammation and alveolar bone loss, which can be counteracted by the unique properties of vitamin D like immune response, anti-inflammatory and calcification of bone. Vitamin D deficiency also leads to poor oral health and aggravates periodontitis. On the whole, the current review suggests that vitamin D plays a crucial role in periodontal health.

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