Research Paper

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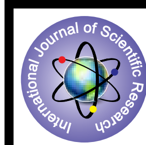
Vitamin D and Oral Health: A Review



Medical Science

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ABSTRACT

Vitamin D has an array of impact on human body physiological processes such as bone and calcium metabolism, cell growth and differentiation, immunity and cardiovascular function. Through its various mechanism of action it not only maintains musculoskeletal health but also has an important role in prevention of infectious and chronic inflammatory diseases. Vitamin D plays an important role in oral health not only by maintaining bone mass but also through its anti-inflammatory, anticancer and anti-infectious effects.

Introduction
The two main forms of vitamin D are vitamin D3 or cholecalciferol and ergocalciferol or vitamin D2 .Vitamin D3 is formed in the skin after exposure to sunlight or ultraviolet light. Vitamin D2 is obtained from foods. Vitamin D3 or cholecalciferol is hydroxylated in the liver into 25-hydroxyvitamin D3 (25(OH) D3) and subsequently in the kidney into 1,25-dihydroxyvitamin D3 (1,25(OH)2 D3). This is the active metabolite, which stimulates the calcium absorption from the gut. Vitamin D is important for calcium and phosphate homeostasis. Through its various mechanism of action it maintains musculoskeletal health, prevent infectious and chronic inflammatory diseases. It also maintains oral health by maintaining bone mass, decreasing bone resorption and preventing inflammatory and infectious diseases. This review presents bioavailability, transport of vitamin D and role in general and dental health.

Bioavailability and Transport
The vitamin D metabolites are bound in the circulation to vitamin D binding protein. The active metabolite 1,25(OH)2 D3 enters the cell and binds to the vitamin D receptor. Then this complex forms a heterodimer with the retinoid receptor and binds to a vitamin D responsive element on a responsive gene, such as that of osteocalcin, calcium binding protein or 24-hydroxylase. After this transcription and translation occurs and proteins are formed such as the calcium binding protein or osteocalcin. The classic effect of 1,25(OH)2D3 on active calcium transport occurs in the intestinal cell. In intestine, Calcium enters the cell through membrane proteins. In the intestinal cell, 1,25(OH)2D3 binds to the vitamin D receptor and the calcium binding protein is synthesized and this regulates the active transport through the cell. The calcium transport to the extracellular fluid is by an ATP dependent mechanism. Passive transport also occurs through paracellular diffusion of calcium. The 1,25(OH)2D3 has its effect on the classic target organs which includes bone, intestine and kidney and stimulates calcium transport from these organs to the blood. The production of 1,25(OH)2D3 is stimulated by parathyroidhormone (PTH). There is a negative feedback through calcium which decreases parathyroidhormone (PTH) and a direct negative feedback from 1,25(OH)2D to PTH. The active metabolite 1,25(OH)2D also shows rapid actions through a membrane receptor. [1]

Bone metabolism
Vitamin D plays an important role in calcium and phosphate homeostasis. It augments bone mineralization. Vitamin D deficiency results into low bone mineral density, osteoporosis and osteopenia. There is a relationship between alveolar bone density, osteoporosis and tooth loss. Low bone mass is a risk factor for teeth loss and periodontal disease. [2,3]

Post menopausal women are at high risk for periodontal disease, tooth loss due to progressive bone loss and inflammatory processes because of oestrogen deficiency. Calcium and vitamin D therapy along with hormone replacement therapy increases bone mass in these women. [4] Calcium and vitamin D supplements prevents osteoporosis and enhance tooth retention in elderly persons. [3] There are many target genes for vitamin D in the ameloblasts and odontoblasts of developing tooth germ. There is alteration in enamel and dentin in vitamin deficient children. [5]

Immunomodulatory effects
Vitamin D has potent immunomodulatory effects .VDR (Vitamin D receptor) is widely expressed in various immune cells of both innate and adaptive immunity. VDR ligand decreases expression of various pro-inflammatory molecules like IL-2, IFN, IL-6,8 in T cells and proliferation of T lymphocytes and keratinocytes. It increases expression of anti-inflammatory cytokines IL-10. VDR ligands prevent differentiation, maturation, activation of antigen presenting cells and dendritic cells. Vitamin D deficiency results in to variety of autoimmune disorders like IBD, multiple sclerosis. VDR polymorphisms are associated with increased susceptibility to both Crohn's disease and ulcerative colitis in human subjects. [6]

Cancer and vitamin D
VDR is present in a wide variety of other cells including malignant cells. Recently it has been recognized that calcitriol exerts antiproliferative and prodifferentiating effects in many malignant cells and retards the development and growth of tumours in animal models raising the possibility of its use as an anticancer agent. Mechanism of anticancer action is growth arrest and differentiation. Calcitriol inhibits the proliferation of many malignant cells by inducing cell cycle arrest and the accumulation of cells in the G0/G1 phase of the cell cycle, Apoptosis, Inhibition of Invasion and Metastasis, Antiinflammatory Effects, Regulation of prostaglandin metabolism and signalling, Induction of mitogen-activated protein kinase phosphatase-5 (MKP5) and inhibition of stress-activated kinase signalling. [7]

Vitamin D receptor (VDR) are present in keratinocytes and Vitamin D induces the differentiation and inhibits the proliferation of keratinocytes. Various studies have shown that vitamin D inhibit the growth of squamous cell carcinoma cells both in vivo & vitro. Vitamin D also inhibits leukemic cells growth. Leukemia is also manifested in oral cavity .In leukemia there is uncontrolled proliferation of haemopoietic cells occurs and these cells are

unable to differentiate into mature cells. Vitamin D induces differentiation of these myelomonocytic leukemic cells. Various studies have also shown that vitamin D also have an additive effect on other treatment modalities for cancer treatment like retinoids ,Vitamin K and chemotherapeutic agents, for differentiation of leukemic cells. [8]

Antimicrobial effects
Vitamin D has potent antimicrobial activity against bacteria, virus and fungi. Various mechanism of antimicrobial activity are activation of various immune cells like B lymphocytes, T lymphocytes, monocyte, macrophage. Vitamin D boosts innate immunity by modulating production of antimicrobial peptides (A MPs) and cytokine response. Vitamin D exerts its antibacterial activity by the production of various peptides like B-defensins and cathelicidin. These peptides have antibacterial action against various strains of streptococcus, staphylococcus, klebsella, pneumonia, E coli. Vitamin D also has antiviral and antifungal activity. As all these microbial diseases have oral manifestations therefore Vitamin D because of its antimicrobial action can be used as an therapeutic agent alone or as an adjunct to various antimicrobial agents. [9]

Vitamin D and Oral Health
Vitamin D can reduce risk of dental caries because it induces production of peptides like cathelicidin and defensins and these have both antimicrobial and anti-endotoxin activity. [9] Oral Candidiasis is most prevalent lesion of immunocompromised individuals. A strong association between vitamin D deficiency and oral Candidiasis has been observed. Vitamin D modulates immune system and down regulates expression of calptoprotein (which is an immune regulatory protein complex which down regulates neutrophil recruitment and inhibits neutrophil oxidative function). Vitamin D deficiency results in increased expression of this immune-regulatory protein complex and this ultimately results in decreased neutrophil functions and hence increased chances of opportunistic infections like oral candidiasis. [10]

Vitamin D prevents acute and chronic gingivitis. There is negative association between serum concentration of vitamin D and prevalence of bleeding on probing. It reduces susceptibility to gingival inflammation through anti-inflammatory effects. [11] Vitamin D deficiency leads to disorder of immune system, promotes infection and inflammation resulting into periodontitis.

Vitamin D deficiency
There are various risk factors for vitamin D deficiency including old age, female sex, non-white race, malabsorption (inflammatory bowel disease and cystic fibrosis), obesity, low dietary intake, less outdoor physical activity, exclusive breast-feeding, sunscreen use, clothing, higher latitude season of year. [12] According to the United States Institute of Medicine, the recommended dietary allowances of vitamin D are:

Infants 0–6 months: 400 IU/day*

Infants 6–12 months: 400 IU/day*

1–70 years of age: 600 IU/day (15 μg/day)

71+ years of age: 800 IU/day (20 μg/day)

Pregnant/lactating: 600 IU/day (15 μg/day)

Asterisk for infants indicates Adequate Intake (AI) for infants, as an RDA has yet to be established for infants. [13]

Conclusion
Vitamin D plays an important role in oral health by maintaining bone mass, preventing tooth loss, caries, gingivitis and periodontitis, prevention of malignancy, prevention against infection by boosting immunity and having antimicrobial properties.

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