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Vitamin D and Dentistry

Elif Gül Aydın and Öner Özdemir

Abstract

Vitamin D deficiency is a pandemic issue due to decreased vitamin D intake from food and lessened sunlight exposure. Attention is drawn to vitamin D and its role learned in notable clinical disorders such as diabetes, cardiovascular disease and cancers including oral ones. Vitamin D is also very effective along with minerals in the protection of oral health. Vitamin D helps maintain the calcium-phosphate balance and contributes to the shaping of the bone. It is reported that with sufficient vitamin D level, the onset and progression of caries in the tooth structure can be stopped, the formation of caries can be reduced and enamel loss can be prevented. Vitamin D also affects the disease and health conditions of the periodontium. Anti-inflammatory and immunomodulatory functions have a role in the pathogenesis of periodontal disorders. It can reduce bone resorption and suppress the inflammatory outcome related to periodontal diseases by increasing mineral density. Vitamin D has been linked with tooth decay, gingivitis, and tooth loss. Vitamin D, in particular, as a promising oral health-protective agent, is said to lessen the incidence of caries and periodontitis.

Keywords: Vitamin D, periodontitis, gingivitis, caries

1. Introduction

Vitamin D deficiency (VDD) owing to significant sunlight decrease in today's conditions and the use of sunscreens that increase in both summer and winter months is considered as a pandemic issue [1–3]. The amount of vitamin D (vitD) intake from food is very low. This amount cannot meet the daily vitD requirement for both adults and children [1].

Some of the oldest phytoplankton in the world (species that have existed for more than 750 years) have been reported to produce vitD when exposed to sun exposure. Among the species existing in the world, all species containing vertebrae need the sun for their vitD production [1]. The definition of rickets, which showed devastating bone deformities in children lack of sunlight, was made by Sniadecki in 1822. After approximately 100 years later, The US government had arranged an organization to explain and provide recommendations to parents about the favorable effects of sunlight exposure in order to prevent this disease. In those years, fortification of milk by adding vitD has been found to be quite effective in preventing rickets in the USA. However, they continued to supplement vitD into milk that expired due to the shortage in milk supply after the Second World War in Great Britain. The reason for this, they thought that the vitD added to the milk had extended the shelf life of the milk. Subsequently, vitD supplementation was banned in dairy products in Europe as a result of increasing hypercalcemia cases in infants [1].

It is recognized that vitD levels in serum begin to decrease with age. The reason for this is explained as the decline in endogenous vitD synthesis and the surge in the time spent indoors due to the limitation of physical activity [2, 4].

2. Sources of vitamin D

The key source of vitD is the sunlight, and the level of 25-hydroxy vitD (25 (OH) D) in serum varies depending on the seasonal change of sunlight. Fatty fish like salmon, mackerel and herring, and fats from fish, containing cod liver oil, are among the rare foods that naturally comprise vitD. Milk, some juice products, some bread, yogurts and cheeses are supplied with vitD in the US. Furthermore, commercially available multivitamin preparations contain varying amounts of vitD and are offered for daily use to individuals [1, 2].

3. Synthesis of vitamin D

One of the fat-soluble secosteroids recognized as vitD is in control of the increased absorption of phosphate, magnesium and calcium in the gut. In humans, vitD3 (defined as cholecalciferol) and vitD2 (named as ergocalciferol) are identified as the most significant elements in this group. There are two varied ways of obtaining vitD: dietary and non-dietary substance by exposure to sunlight [1, 4].

Ultraviolet (UV)- B rays regulate vitD synthesis. Initially, pro- vitD 3 is formed by converting cholesterol to 7- dehydrocholesterol in the intestinal epithelium by oxidation. Then, it is transformed into pro- vitD 3 and transferred to the skin and pre- vitD 3 is produced by UV rays at wavelengths of 270 to 300 nm. The pre- vitD 3 isomerizes to vitD 3 and cholecalciferol in the heat-dependent reaction. Activation of vitD 3 occurs by two hydroxylations and $1\alpha, 25$ -dihydroxy vitD 3 (calcitriol, the biologically active type of vitD) is formed [5].

4. The effects of VDD on musculoskeletal system

Vitamins are organic compounds that play a role in basic metabolic reactions in our body. Serious problems can occur in the deficiencies of vitamins, since the mechanisms of basic metabolic events will be disrupted.

The serum level required for vitD (25 (OH) D) to be identified as deficient is 50 nmol/L or 20 ng/mL. Concentrations of 25 (OH) D between 51 and 74 nmol/L or 21–29 ng/mL are considered insufficient, while levels of 80 nmol/L or 30 ng/mL are thought to be sufficient [1, 6]. It is presumed that children require the same doses as adults. It is stated that vitD toxicity will not occur until 25 (OH) D levels reach up to 375 nmol/L or 150 ng/mL [1, 4].

The most lately reported recommendations for vitD consumption are 200 IU/day for children and adults up to the age of 50, 400 IU/day for 50–70 years, and 600 IU/day afterward. The increase in recommendations with age is a clear reflection of the fact that the efficiency of this synthesis decreases with age, although cutaneous synthesis appears to happen in most individuals [4].

Vitamin D has a vital biological role in the human body and helps continue normal growth and mineralization of bone and other calcified tissues, including teeth [2]. Vitamin D deficiency will result in growth delay and the characteristic signs and symptoms of rickets in children. In adults, VDD will accelerate and aggravate both osteopenia and osteoporosis and amplify the risk of fractures of bones. Muscle

weakness has long been thought to be related with VDD. Vitamin D receptor (VDR) is available in skeletal muscle, and VDD has been linked with proximal muscle weakness, enhanced body sway, and an augmented risk of falling. Vitamin D deficiency can also end up with skeletal mineralization disorder [1].

Vitamin D and VDR have increasing importance in recent years as they produce an important role in calcium and phosphorus metabolism as well as homeostasis. Furthermore, attention is drawn to vitD and VDR's role learnt in notable clinical disorders such as diabetes, cardiovascular disease and cancer [5, 7].

5. The effect of vitamin D and VDR in oral cancer

Oral cancer is defined as malignant neoplasia that occurs in the lips or oral cavity. Oral squamous cell carcinomas (OSCC) are important types consisting of more than 90% of all oral cancers [8]. In recent years, OSCC has generally been observed at increasing rates around the world. Widespread studies on the main risk factors for the development of oral cancers indicate that alcohol consumption and tobacco use increase the risk of oral cancer by 80%. Oral infection due to human papilloma virus (HPV) is defined as another important risk factor for oral infection, pharyngeal and oral cancers [9]. Eliminating significant risk factors, even after diagnosis of oral cancer, can improve prognosis and reduce the risk of recurrence [5].

OSCC growth is a multi-step progress that affects vital cellular pathways implicated in tumor development and growth. Various exogenous and endogenous incitements have been shown to lead to multifaceted molecular changes that contribute to cancer development. The anti-neoplastic activity of vitD (calcitriol) has been demonstrated in *in vitro* and *in vivo* studies in a wide variety of cancer-associated defects, containing head and neck cancer, and particularly in OSCC [10]. Also, it has the capacity to affect cytostatic chemotherapy and augment apoptosis induction in OSCC cells. Examination of the association between serum vitD level and VDR seems appropriate to guide supportive therapy for patients with pre-cancerous lesions and OSCC [5]. Although the anticancer influences of vitD have been demonstrated by various *in vitro* and *in vivo* studies, new data suggests that these influences are controlled by some other elements. Further studies are needed to assess the effects of the vitD system (both ligand and receptor) on the growth of oral cancer and the potential benefits of improving VDD on tumor growth and progression [5].

6. Vitamin D relation of oral and dental health

A balanced and good diet is necessary and essential for maintaining general body health as well as improving oral health [6]. While the importance of vitamins in general health has been highly researched and developed, their relationship with oral and dental health has not been fully elucidated. Vitamins act as a catalyzer for basic metabolic events in the body that are essential for growth, development, energy, and cell maintenance [11].

Minerals such as magnesium, calcium, and phosphorus, the basic structural components of the tooth, should be taken in sufficient levels with the diet. These minerals play a role by interacting with vitamins in strengthening the tooth structure. Especially vitD is related with calcium, magnesium, and zinc [6]. Several possible mechanisms have been suggested to clarify the role of vitD in decreasing the risk of caries.

One of these mechanisms is the regulation of serum calcium, phosphate and parathyroid hormone, which are necessary for the formation, calcification, mineralization and protection of teeth. Calcium and phosphate homeostasis is necessary for the formation, calcification, mineralization and maintenance of oral bone and teeth, as well as bone and hard tissue. Enamel and dentin defects- hypoplasia have been linked with hypocalcemia and hypophosphatemia [2, 7].

Dental caries and VDD affect children around the world. In children who had a VDD, changes in both enamel and dentin are observed. Therefore, vitD has a significant role in the formation of oral hard tissue, comprising tooth enamel and dentin, and affects primary teeth development [2].

Vitamin D has a significant role in odontogenesis [2, 12]. The mechanism by which vitD excites the mineralization of tooth enamel involves binding to VDR expressed in both tooth and bone cells. Vitamin D receptors direct the transcription of several target genes, most expressed by ameloblasts and odontoblasts [2, 7, 13]. VDR stimulates the formation of structural gene products in dentin, together with calcium-binding proteins and diverse extracellular matrix proteins. The gene encoding VDR is positioned on chromosome 12q13.11 and comprising several polymorphisms [14]. The VDR gene adjusts the biological role of major vitD metabolites, thus having a key role in the configuration of teeth, particularly in the mineralization of dentin and enamel. Consequently, enamel developmental deficiencies e.g., enamel hypoplasia, can take place in consequence of VDD. It was decided that vitD and VDR at the molecular level influence the tooth germ formation; supplies to the regulation of enamel and dentin structure and maturation; and organizes the phases of dental crown growth [2, 6].

Moreover, vitD adjusts and adapts both the innate and adaptive immune system. The immunological role of vitD is stimulation of the arrangement of some anti-microbial peptides, e.g. defensins and cathelicidin (LL-37), which defend against many pathogens, counting oral bacteria [2, 15]. Cathelicidin (LL-37 or hCAP-18) is controlled by vitD, which has both anti-endotoxin and antimicrobial properties [3].

In mineral deficiencies due to absorption disorders, increased tendency to bleeding, bone resorption, and early tooth loss occur [6]. The chewing process ensures that the person receives the highest possible amount of nutrients, and the number and distribution of teeth affect chewing efficiency. Since diet selection and nutritional status are affected in early tooth loss, deficiency occurs in the intake of vitamins, that is, the two situations create a synergistic effect on each other. During the development of the tooth, the hard tissues of the tooth are strongly affected by nutritional status and thus vitamin deficiency. It is stated that there is a positive correlation between malnutrition and enamel hypoplasia and caries in the primary dentition period in children [11]. In addition, deficiencies of these minerals cause delayed tooth eruption, bleeding gums, destruction patterns in alveolar bone, periodontal disease, enamel or dentin hypoplasia [6, 11].

Vitamin D is also very effective along with minerals in the protection of oral health. Vitamin D helps maintain the calcium-phosphate balance and contributes to the shaping of the bone. It also has important functions by showing anti-inflammatory effects. It is reported that with sufficient vitD level, the onset and progression of caries in the tooth structure can be stopped, the formation of caries can be reduced and enamel loss can be prevented [2, 6, 16].

In the formation of tooth decay, the acid that is produced by bacterial fermentation of the residues on the tooth surface that are not brushed after eating sugary foods lowers the pH below 7 and plays a role in the destruction of the tooth hard tissues. However, it has been recently revealed that dental caries can be reduced with UV- B rays and vitD supplements. Considering the helpful effects of vitD on dental caries, it is thought to be effective in reducing the overall prevalence, especially in

children at risk of early caries [2, 6]. Early childhood caries (ECC) were described as the presence of one or more caries, missing (due to caries) or filled (DMFT: decay, missing, filled) tooth surface in any primary teeth in young children under six years old, is one of the most common chronic diseases and can have adverse effect on individual's overall health [2, 17].

Early childhood caries affect the nutritional status and general health of the child. It is stated that children with ECC may have malnutrition, iron deficiency anemia and VDD [2, 16]. When the relationship between vitD intake and caries is evaluated, it is determined that the incidence of tooth decay is higher in children with low vitD or children of mothers with low vitD during pregnancy. There is an association between vitD levels in early childhood (up to 8 years old) and DMFT scores. When serum vitD concentrations are more than 50 nmol in early adolescents (10–11 years) considerably less caries is detected in permanent first molars has been found. Similarly, in children aged 6 to 17 years, they found a 0.66 decrease in DMFT for every 10 ng/ml of serum vitD level increase. In general, malnutrition and shortage in vitamin intake due to malnutrition augments the incidence of enamel hypoplasia in children [2, 11, 18].

Vitamin D use may have a role in the protection of caries early in life. It is thought to be a promising caries prevention agent, given that vitD supplementation is connected with a 47% reduction in caries in children according to meta-analysis studies [16]. Vitamin D deficiency during pregnancy (a vital period for tooth growth) is related with developmental defects; especially enamel hypoplasia and caries susceptibility. Also, vitD intake during pregnancy diminishes the risk of enamel defects and hypoplasia in babies and is associated with better eruption of deciduous teeth [2, 11].

Improving vitD levels in children from an early stage of life appears to be an important task. This requires awareness from pregnancy. Pregnant women should have their vitD levels tested routinely during the first trimester of pregnancy and the risk of VDD, VDD and vitD ingestion should be evaluated. Prenatal vitD levels appear to influence the development of primary dentition and ECC [2, 11, 18].

Vitamin D is an essential hormone for the absorption of calcium, magnesium and phosphorus from the intestine, which is necessary for the appropriate mineralization of bones and teeth. In addition, covering the surfaces of the implants with vitD during implant application, which is one of the dental procedures, increases osteointegration. Moreover, applying vitD3 intraperitoneally speeds up orthodontic tooth movement, and even patients receiving vitD and bisphosphonate therapy can obtain orthodontic treatment [6].

7. Vitamin D and periodontal health

Vitamin D also affects the disease and health conditions of the periodontium. Anti-inflammatory and immunomodulatory functions have a role in the pathogenesis of periodontal disorders [3]. It can reduce bone resorption and suppress the inflammatory outcome related to periodontal diseases by increasing mineral density [6, 11].

There is a positive correlation between increased mineral density and decreased bone resorption in the mandibular bone and taking vitD and calcium and magnesium supplements. It is also reported that loss of attachment level is associated with decreased serum vitD levels. It is stated that in individuals with sufficient vitD, periodontal tissues are healthier, and accordingly, gingivitis formation, bleeding during probing, attachment, bone and tooth loss are reduced [11].

In studies conducted on women's level of vitD in their saliva and serum, a statistically significant relationship was found between gingivitis and periodontitis during their life, pregnancy, menopause and postmenopausal periods [19, 20]. The prevalence of periodontal disease was higher in individuals with low vitD levels [11].

Besides these beneficial effects on bone metabolism, it has been found that periodontitis accelerates the healing with its direct antibiotic effect on periodontal pathogens. Vitamin D reduces inflammatory mediators causing periodontal destruction. Having a diet rich in vitD after periodontal surgical procedures contributes to the faster and easier recovery of periodontal tissues. The quality of the host immune response is highly correlated with healthy and proper nutrition. It plays an important role not only in the prevention of periodontal diseases, but also in facilitating the recovery of tissues in the existing periodontal disease conditions. One of the most important functions of vitD in the immune system is that it has a stimulating effect on human cathelicidin (LL-37). LL-37 has both antimicrobial and anti-endotoxin functions. Vitamin D excites cathelicidin in oral epithelial cells and children with high dental caries activity had low LL-37 levels. Many epithelial antimicrobial peptides, including LL-37, have been termed the guardian of the oral cavity and detected to play important roles in oral health. LL-37 also has significant benefits in decreasing the risk of gingivitis. Maternal VDD also increases the DMFT score in children of 12–35 months old. As a result, vitD may be useful in the treatment of periodontitis due to its direct effects on bone metabolism and potential anti-inflammatory effects on periodonto-pathogens [6, 15].

As diet plays a dominant modifier in the development of periodontal disorders, dentists should inform patients on how good diet influences the supporting the formation of teeth, e.g. the significance of ingesting healthy foods rich in magnesium and vitD in thwarting dental caries [6].

There is common agreement on the effects of vitamin deficiencies or supplementation on oral health, but scientific data is still at a level that needs to be investigated. In particular, multivitamin supplements or the mixture of two or more vitamins lead to more bias as it is not likely to determine the single help of each vitamin.

8. Conclusion

Vitamin D has been linked with tooth decay, gingivitis, and tooth loss. Vitamin D, in particular, as a promising oral health-protective agent, is said to lessen the incidence of caries and periodontitis, leading to a low-precision result. In order to prevent tooth decay, which is a serious public health problem, existing structural defects in teeth (enamel and dentin hypoplasias) and to maintain oral health, the awareness of health care providers should be increased. It seems to be an issue that should not be overlooked, especially from the early stages of life, to control vitD levels for oral health.

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