

Review Article

The Impact of Vitamin Deficiencies in Oral Cavity: A Review

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ABSTRACT:

Vitamins are organic compounds and are derived from diet. They are required for proper growth, development and normal activity of body tissues. They play an important role in maintenance of oral health of an individual. They can be fat soluble or water soluble. The initiation, pathogenesis and increase in severity of oral and periodontal diseases, depends on the presence of vitamins in the body. Deficiency of vitamins can lead to increased risk of dental caries. They have a significant impact on the development of enamel, dentin and bone formation in the oral cavity. They affect the periodontal health of an individual.

KEYWORDS: vitamins, energy, growth, development vitamins

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INTRODUCTION:

Vitamins are organic compounds that regulate metabolism, growth and energy supply of the body. Proteins, carbohydrates and fats influence the functioning of vitamins. They are of two types, fat soluble vitamins which include vitamin A, C, D, E, and K whereas water soluble vitamins include vitamin B and C.^[1] Vitamins affect the initiation, pathogenesis and increase in severity of oral diseases, such as dental caries, gingivitis and periodontitis.^[2] Casimir Funk, in the year 1912, named these organic substances "vitamine". They are either obtained from food, where they are present in small amount, or they are derived from provitamin. The maintenance of appropriate growth, development and wellbeing of a person depends upon the presence of vitamins.^[3] This detailed review shall highlight the importance of Vitamins in health and oral diseases.

VITAMIN A (retinol):

Vitamin A is absorbed into intestinal luminal cells, where the precursors (beta carotene) are activated and transferred to chylomicrons. These chylomicrons consists of carotenoids, retinyl esters, triglycerides and unesterified retinol, and they travel through lymphatic system and reach extra hepatic tissues, where triglycerides are produced. Vitamin A remnants are moved to liver and retinol can be obtained from liver with the help of specific carrier. It is essential for normal vision, normal growth, development and regulation of epithelial cellular integrity, immunity and reproduction. Night blindness can occur due to its deficiency.^[4] Oral manifestations caused due to its deficiency are enamel hypoplasia, reduced odontoblast differentiation and impairment of dentin production.^[1] Deficiency of this vitamin can also lead to gingivitis, periodontitis, dental caries, xerostomia, white patches which are hyperkeratotic and impairment in tooth morphogenesis.^[4] In some experiments, it was observed

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that deficiency of vitamin A can lead to increased cell production (indicating precancerous changes) and hyperkeratosis of gingiva. There is increased risk of formation of periodontal pockets and atrophy of salivary gland in such patients. Retinoids can enhance the immune response of the body, activate cellular differentiation process and trap the free radicals preventing them from causing damage to healthy cells of the body, thus, preventing development of tumors. The major sources include milk, eggs and green vegetables.^[3]

VITAMIN D:

Vitamin D acts as prohormone. On exposure to sunlight, 7-dehydrocholesterol is converted into cholecalciferol and 25-hydroxycholecalciferol is generated. Calcitriol is active form of this vitamin. The major actions include bone formation, development of teeth and initiation of enamel mineralization. It connects to vitamin D receptor (VDR), which is present in teeth and bones and regulate differentiation of ameloblasts and odontoblasts. The rise in calcium absorption and suppression of inflammation are also some of its actions.^[5] If there is less calcium and phosphate levels in the body, it results in rickets in infants and children and osteomalacia in adults, due to deficiency of vitamin D. Clinical features of rickets include tetany, cranio tabes, swelling of wrists and ankles, short stature and distortion of the limbs. Oral manifestations include enamel hypoplasia, defect in tooth eruption, blurring of lamina dura, thinning of mandibular canal and decrease in number, density and thickness of trabeculae with radiolucent radiographic appearance. Osteomalacia shows pain in bones, muscular weakness and tetany. Oral manifestations include thinning of lamina dura and decrease in trabeculae with radiolucent radiographic appearance.^[6]

Vitamin D controls both innate and adaptive immune responses of the body. The synthesis of defensins and cathelicidin, which are antimicrobial peptides, is controlled by vitamin D and this immunological function provides protection against diseases caused by oral bacteria. Vitamin D protects teeth and gums by controlling calcium phosphate balance in the body. It also obstructs the development of dental caries because it plays an important role in digestion and absorption of calcium, magnesium and phosphorus, which are required for normal development of bones and teeth. In premalignant lesions and oral cancer, VDR expression was found to be increased, so administration of vitamin D can cause decrease in therapy related toxicities in later stages of oral malignancies. This leads to reduction in morbidity.

During orthodontic treatment, controlled mechanical stimulus is required for tooth movement, so that it can cause bone resorption at pressure site with the help of osteoclastic action and bone formation at tension site with the help of osteoblastic action. The increase in speed of tooth movement can result due to this process, and it was observed that administration of vitamin D can facilitate the increase in speed of tooth movement. The antiproliferative, immunomodulatory and anti-inflammatory activity of vitamin D, along with its capacity to stimulate cell apoptosis, results in prevention of resorption of alveolar bone. It also reduces the progression of gingivitis and chronic periodontitis.^[5]

VITAMIN E:

Vitamin E comprises of eight different compounds, which are four tocopherol and four tocotrienols, out of which alpha tocopherol is most active.^[1] It is a free radical scavenger in cell membranes and is lipid soluble. This vitamin has antioxidant and anticarcinogenic properties. It obstructs generation of nitrosamine, which is carcinogenic, and enhances immune response of the body. It helps in prevention of premalignant lesions of oral cavity.^[2] It saves the cell membrane from oxidative damage. Deficiency causes disturbance in red blood cells, muscular dystrophy, disturbance in blood vessels, pigmentation loss and deterioration of enamel organ. Green leafy vegetables, plant oils and egg yolk are some of the major sources.^[3]

VITAMIN K:

It is a fat soluble vitamin and has two natural forms vitamin K1 and vitamin K2. The functions of vitamin K include maintenance of calcium metabolism, cell growth, oxidative stress, inflammatory actions, bone stability and blood clotting.^[2] The generation of blood clotting factors require vitamin K, which acts as a catalyst. This is required for maintenance of prothrombin levels.^[1] The calcification of bone matrix, improvement of bone regeneration ability and transformation of dental pulp stem cells into osteoblasts, are enhanced by this vitamin. In vitro studies were conducted, in which it was found that vitamin K can prevent dental caries. There is elevation in reactive oxygen species and oxidative stress in the hypothalamus due to increased consumption of sugar. It leads to obstruction in normal flow of dentinal fluid and oral bacteria can damage the tooth surface by generating acid which has the tendency to demineralize the enamel. This can cause damage to dentin and the matrix metalloproteinases of the body show dentin breakdown. The preservation of endocrine regulated

normal flow of centrifugal dentinal fluid is caused by vitamin K2. It occurs due to its capacity to generate antioxidant activity in the brain. It plays a major role in buffering of the saliva.^[2] Deficiency can cause defect in production of prothrombin. The risk of gingival bleeding is common in such cases. Sources of this vitamin include green leafy vegetables and milk.^[3]

VITAMIN C:

Vitamin C is also called ascorbic acid. It is a water soluble vitamin and is present in diet. It is a hydrophilic antioxidant.^[7] It plays an important role in collagen production. It enhances strength of blood vessels and body tissues, thus playing an important part in the process of wound healing. It promotes evolution of erythrocytes by increased absorption and utilization of iron.^[1] It facilitates calcium deposition and mineralization, which decreases the possibility of development of dental caries. Eydou et al conducted a study which demonstrated that there is inhibitory effect, which is concentration dependent, between vitamin C and *Streptococcus mutans*. *Streptococcus mutans* is a bacteria which is associated with initiation of dental caries. The deficiency of vitamin C causes scurvy, a disease identified by the presence of bleeding and swelling in gingiva, increased tooth mobility, damage of periodontal ligament and deterioration of ameloblasts and odontoblasts. Defective wound healing, fatigue and depression can occur due to deficiency of this vitamin. Vitamin C obstructs the progression of inflammation caused due to periodontal disease. It can decrease deposition of supragingival calculus. It can obstruct the beginning of carcinogenesis due to its antioxidant property. A study was conducted in which patients suffering from oral cancer were observed and it was found that there is reduction in vitamin C levels in the saliva of patients suffering from oral cancer, when they were compared with control group. In a case control study, it was observed that the initiation and progression of oral premalignant lesions was obstructed in individuals consuming vitamin C in diet.^[7] Citrus fruits and vegetables are some of the sources.^[3] Cigarette smoking decreases vitamin C level in plasma because of elevated turnover. During exercise or in conditions associated with metabolic stress, there is theoretical proof for increased demand of vitamin C. In cases of patients who have undergone surgical management or patients who are suffering from infection, plasma concentration of vitamin C is decreased as the utilization by body tissues is increased.^[7]

VITAMIN B1 (THIAMINE):

Vitamin B1, also known as thiamine, plays an important role in energy metabolism, cerebral metabolism and generation of neurotransmitters. It helps in maintenance of cell membrane, cellular differentiation, axonal development, synapse synthesis and prevents cytotoxicity. Thiamine pyrophosphate is active form and plays an important role in energy metabolism by acting as cofactor for enzymes. These enzymes play a crucial role in carbohydrate catabolism. Beriberi disease, dry and wet beriberi, can result due to its deficiency. The clinical features of dry form include pain in calf muscle, atrophy of calf and thigh muscles, burning sensation in feet, muscle cramps, pain in legs, and paresthesia of toes causing absence of vibratory and position sensation in toes. The wet form features include peripheral vasodilation, tachycardia, high cardiac output, lactic acidosis and heart failure. Wernicke encephalopathy affects mostly alcoholics due to improper diet and diet consisting of excessive carbohydrates as it increases metabolic requirements of thiamine. Clinical features include nystagmus, ptosis, aphonia, hypothermia, ophthalmoplegia, loss of muscle control and lack of vibratory sensation and coordination.^[8] Oral manifestations include increased sensitivity of oral mucosa, deterioration of oral mucosa, and presence of vesicles in the oral cavity.^[3] There can be presence of erythematous and edematous tongue.^[1] The sources of this vitamin include cereals, beans and nuts.^[3]

VITAMIN B2 (RIBOFLAVIN):

Riboflavin is a water soluble and heat stable vitamin. It comprises of antioxidant activity and can alleviate lipid peroxidation. It can function as photosensitizer. Fortified grains, cereals, peas and dairy products are some of the sources where this vitamin is found. Aerobic cells generate free radicals causing ageing and chronic diseases. This leads to destruction of cellular macromolecules like DNA, damage to body tissues, inflammation and cellular apoptosis. Malignancies such as cancer are accompanied by oxidative stress. Several studies have been done which showed the antioxidant activity of riboflavin as it protects the body from damage caused by free radicals. Reactive oxygen species (ROS) is a term given to oxygen metabolites. An in vitro study was conducted which showed that riboflavin reduction in intestinal cells can cause excessive generation of ROS. An animal study was conducted in which MDA (malondialdehyde), which is an indicator of lipid peroxidation is reduced after riboflavin is given in rat model associated with renal toxicity. Riboflavin has prooxidant activity. When it absorbs ultraviolet radiation and blue light, it

functions as photosensitizer. Although it is not toxic in darkness but the photoreactivity of riboflavin is due to the isoalloxazine moiety. As a result, it plays an important role in anticancer photodynamic therapy.^[9] It plays an important role in the metabolism of carbohydrates, proteins and fats, causing generation of cellular energy.^[1] It facilitates normal vision and plays an important role in maintenance of healthy skin.^[3] Deficiency can cause angular cheilosis, anaemia and dermatitis. The lips become erythematous and smooth. There is deterioration of fungiform papillae, which becomes mushroom shaped. There is atrophy of tongue. The tongue can attain magenta colour because of proliferation of blood vessels and reduced blood supply.^[1]

VITAMIN B3 (NIACIN):

Redox and adenosine diphosphateribosylation reactions need niacin. The NAD (nicotinamide adenine dinucleotide) pool exists in oxidized condition and it plays an important role in oxidative pathways, like glycolysis and tricarboxylic acid cycle (Krebs cycle). There is reduced state of NADP (nicotinamide adenine dinucleotide phosphate) pool and it plays an important role in anabolic pathways like generation of fatty acid and oxidant defense.^[10] The deficiency leads to pellagra, whose clinical features include photo distributed rash transforming into chronic dermatitis, gastrointestinal, neurologic and psychiatric problems. The main features include dermatitis, diarrhea, dementia and even death. Initially, the lesion is erythematous but in advanced stages it becomes dry, dark and scaly. Lesions on the neck are called "castle's necklace". It can occur in all ages but 30-40 years old male patients are mostly found.^[11] Oral manifestations include painful stomatitis. There is edematous, smooth and shiny tongue, where pain can be felt by the patient. There is destruction of filiform and fungiform papillae.^[1] Meat, cereals and pulses are some of the sources of this vitamin.^[3]

VITAMIN B6 (PYRIDOXINE):

Vitamin B6 plays an important role in the metabolism of carbohydrates, amino acids, lipids and nucleic acids. It helps in cellular signaling and has antioxidant property.^[12] Green leafy vegetables, meat and fish are some of its dietary sources.^[3] Pyridoxal phosphate (PLP) is its active form and is synthesized by yeasts and bacteria. It plays an important role in glycogen breakdown. It is also involved in transformation of amino acid, where it acts as a coenzyme in transamination and reactions causing decarboxylation. It influences the functioning of

inflammasomes, so, it has anti-inflammatory action. It controls blood pressure by acting on rennin angiotensin system and regulates blood clotting, causing stability of endothelium and platelet aggregation. Mikkelsen conducted a study and found that vitamin B2 (riboflavin), vitamin B6 (pyridoxine), and vitamin B9 (folic acid) can produce antitumor action on promonocytic lymphoma cell lines. The result indicated that vitamin B can obstruct development of malignancy. It was found that vitamin B2, B6 and B9 increased the production of interleukin 8 and interleukin 10 by the cells of the monoblastic leukemia cell line compared to control groups. Vitamin B6 is a cofactor of the enzyme kynureninase and leads to the synthesis of anti-inflammatory molecules. This can obstruct the development of cancer in vivo.^[12] Depression, mental confusion, hypochromic microcytic anaemia and leucopenia are some of the deficiency features.^[3] Glossitis is common causing erythema and hypertrophy of filiform papillae. Scalded sensation of tongue is observed. Pain can be felt by such patients.^[1]

VITAMIN B9 (FOLIC ACID):

Folic acid plays an important role in synthesis of blood cells, protein metabolism and formation of DNA. Green leafy vegetables, fortified grain products and milk are major sources of folate.^[3] Less thymidine can cause folate deficiency, hypomethylation of DNA and destruction of DNA. Folate metabolism is essential for cell replication and cell existence. It helps in treatment of megaloblastic anaemia. Folate deficiency can cause macrocytic anaemia, memory loss, confusion, weakness, difficulty in breathing, peripheral neuropathy, malignancy and difficulty in pregnancy.^[13] Oral manifestations include glossitis and chronic periodontitis. There is increased mobility of teeth in such patients.^[1]

Some observational studies were conducted which indicated that hyperhomocysteinemia can cause cardiovascular related disorders. There is increased plasma homocysteine levels in such patients and it can lead to atherosclerosis and coronary artery diseases. Homocysteine can cause atherogenesis and thrombogenesis which can result in the development of fibrosis and hyperplasia of muscle cells. Folic acid can decrease plasma homocysteine levels in the body. Larger scaled randomized trials should be done for better observation. Qin et al conducted a study in which it was observed that there is decrease in progression of cardiovascular disease, when folic acid was given in such patients. But trials involving large sample sizes should be done. Title et al conducted a

study on patients suffering from type 2 Diabetes Mellitus, who were given folic acid, versus placebo and it was found that folic acid improved endothelial dysfunction. Folic acid can cause better glycemic control.^[13]

VITAMIN B12 (COBALAMIN):

Vitamin B12 plays an important role in the synthesis of erythrocytes, nucleic acids and myelin. It plays an important role in catabolism of specific amino acids and fatty acids.^[1] Bacteria, yeasts, molds are the sources of this vitamin. Deficiency of vitamin B12 can lead to pernicious anaemia, breathlessness, fatigue, weakness, dementia, macrocytosis, sclerosis of spinal cord, jaundice, Hunter's glossitis, ataxia, mucocutaneous ulcers and increased levels of bilirubin. Oral manifestations include burning sensation of tongue, glossitis, angular stomatitis, angular cheilitis, recurrent oral ulcers, oral candidiasis, distortion of oral mucosa and defect in taste sensation.^[14]

VITAMIN B5 (PANTOTHENIC ACID):

Pantothenic acid is a water soluble B complex vitamin and is also known as vitamin B5. It blends into coenzyme A and acyl carrier protein. It is produced by plants, bacteria and fungi. Some of the dietary sources include eggs, yeast, oats, tomato, potato, beef and chicken. Royal bee jelly has very high amount of this vitamin. Coenzyme A participates in several enzymatic process including oxidation of fatty acid, amino acid catabolism, carbohydrate metabolism, pyruvate breakdown, heme formation and generation of acetylcholine. Acyl carrier protein plays an important role in elongation of fatty acid because it is a part of structure containing fatty acid synthase.^[15] In some experimental animals, it was observed that deficiency of pantothenic acid leads to anaemia, reduction in production of steroid and fatty liver but no features, associated with deficiency, were observed in human beings.^[3]

VITAMIN B7 (BIOTIN):

Biotin is a water soluble vitamin. It is an important cofactor for carboxylase enzymes which start functioning as soon as they are connected by holocarboxylase synthase. Various metabolic processes like production of fatty acid, gluconeogenesis and amino acid catabolism require these enzyme complexes. Biotin plays an important role in generation of keratin and helps in development of nails and hairs. Unpolished rice, whole grains, egg yolk and nuts are some of the dietary sources of this vitamin. Deficiency symptoms include eczematous skin rashes,

conjunctivitis, alopecia, seborrheic dermatitis, seizures, hypotonia, depression and lethargy.^[16] The use of raw egg whites for long duration can cause biotin deficiency. Oral manifestations include paleness of tongue and destruction of lingual papillae.^[1]

CONCLUSION:

There is increased requirement of water soluble vitamins as coenzymes due to high metabolic rate. There can be increase in requirement of antioxidant vitamins, for example vitamin E and vitamin C, due to rise in oxidative metabolism causing more generation of reactive oxidant species. Also, there is variation in spread of vitamins in body fluids. The decrease in carrier proteins can cause less concentration of vitamins in plasma. If there is decrease in plasma concentration of retinol binding protein, the concentration of vitamin A is decreased. In patients undergoing renal dialysis, there is loss of water soluble vitamins. Laboratory analysis of vitamins is not common but some tests, involving intracellular measurement of vitamins, can be done for research work.

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Conflicts of Interest

There are no conflicts of interest.

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