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ASCORBIC ACID IN ORAL HEALTH AND DISEASE

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ABSTRACT

Homeostasis and normal metabolic processes within the body are well maintained with the help of vitamines. The requirement of various enzymes varies considerably from individual to individual. Most vitamins are stored minimally in human cells, but some are stored in liver cells to a greater extent. Vitamins A and D, for example, may be stored in sufficient amounts to maintain an individual without any intake for 5 to 10 months and 2 to 4 months, respectively. However, a deficiency of vitamin B complex (except vitamin B12) may be noted within days, and the lack of vitamin C will manifest within weeks and may result in death in 5 to 6 months. The current Recommended Dietary Allowance (RDA) of vitamin C is 75 mg for women and 90 mg for men, based on the vitamin's role as an antioxidant as well as protection from deficiency. High intakes of the vitamins are generally well tolerated, however, a Tolerable Upper Level (TUL) was recently set at 2 g based on gastrointestinal upset that sometimes accompanies excessive dosages. Several populations warrant special attention with respect to vitamin C requirements. These include patients with periodontal disease, smokers, pregnant and lactating women, and the elderly.

KEYWORDS: Vitamin C, oral health, systemic diseases, infections, Recommended Daily Allowance.

INTRODUCTION

Vitamin C is required in human diet for normal physiological functioning. Fruits and vegetables are rich in vitamin C. The intestinal absorption of vitamin C is 80-90% efficient. This efficiency rate, however, declines with increased intake. Vitamin C is actively co-transported with sodium against an electrochemical gradient into intestinal epithelial cells. Once in the cells, a concentration gradient is created by both brush border absorption and intracellular reduction of dehydro-L-ascorbic acid (DHAA) to ascorbate. Facilitated diffusion of ascorbate into the circulation is sodium independent and follows a concentration and electrochemical gradient. A similar transport mechanism is responsible for the near complete resorption of ascorbate in the kidneys.

Mechanisms of Action of Vitamin C

Vitamin C readily undergoes reversible oxidation and reduction and plays an important role as a redox agent in biological systems.[1] Functions of vitamin C includes.[2]

- Synthesis of collagen
- Formation of hydroxyproline
- Wound healing
- Bone healing and prevention of bone fractures

A lack of intracellular cement substance and an inability to form collagen fibrils results in capillary fragility, characterized by petechial, purpuric, ecchymotic skin and mucosal lesions, and subperiosteal and visceral hemorrhages, which lead to anemia.[3] The anemia that accompanies scurvy is of multifactorial origin. It results from acute blood loss related to hemorrhage, decreased absorption of iron, and the concurrent folate deficiency, that is seen in patients with scurvy.[4] Vitamin C appears to function as a buffer against cell damage from free radicals thought to be important in a number of disease processes. As a specific electron donor, vitamin C also appears to participate in the synthesis of brain neurotransmitters and pituitary peptide hormones.[5]

Vitamin C and Oral Health

Scurvy is the classical disease associated with vitamin C deficiency. The earliest symptom is fatigue followed by cutaneous findings such as follicular hyperkeratosis, perifollicular hemorrhage, bent or coiled body hair, petechiae, purpuras, and ecchymoses beginning on the back of the lower extremities, and xerosis. Hemorrhage into the muscles of the arms and legs and joints may lead to phlebothrombosis and pain. In severe deficiency states, hemorrhage in the viscera leads to vomiting of blood and a bloody stool. In terminally scorbutic patients, syncope, cerebral hemorrhage, high fever, convulsions, shock, and death may occur abruptly. Oral manifestations of scurvy include gingival edema, bleeding, and ulcerations, secondary bacterial infections, and the loosening of teeth.[5,6]

Periodontal Disease

Periodontal disease is a chronic inflammatory disease affecting the tooth supporting structures and results from complex interaction between microbes and host immune response. Vitamin C deficiency has been shown histologically to result in a lack of collagen formation by affecting the hydroxylation of proline and increasing the permeability of the oral mucosa to endotoxins.[7] Vitamin C also enhances the mobility of polymorphonuclear leukocytes, and a deficiency of vitamin C is associated with decreased host immune responses.[8,9] Animals placed on a diet deficient in vitamin C exhibit adverse changes in the periodontium related to a lack of collagen formation characterized by degenerative soft and hard tissue changes, distorted nuclear morphology of polymorphonuclear leukocytes, and reduced chemotactic responses.[10,11,12,13] Vitamin C has long been a candidate for modulating periodontal disease.[14] A study which evaluated the role of dietary vitamin C as a contributing factor for periodontal disease, has shoswn a relationship between reduced dietary vitamin C and increased risk for periodontal disease in the general population (odds ratio [OR] = 1.19; 95 % Cl: 1.05 to 1.33).[14] The study has also shown current and former tobacco users who were taking less dietary vitamin C had an increased risk of periodontal disease with an OR of 1.28, 95 % Cl: 1.04 to 1.59 for former smokers, and an OR of 1.21, 95 % Cl: 1.02 to 1.43 for current tobacco users. The dietary intake of vitamin C showed a weak but statistically significant relationship to periodontal disease in current and former smokers as measured by clinical attachment. Those taking the lowest levels of vitamin C, and who also smoke, are likely to show the greatest clinical effect on periodontal tissues. Since smokers already are at a greater risk for periodontal disease independent of vitamin C intake and oxidants from cigarette smoking lower vitamin C concentrations in blood, it can be hypothesized that smokers require higher levels of dietary vitamin C intake.

Dental Caries

Ascorbic acid affects growth of bacteria *in vitro* and may also act to decrease caries activity *in vivo*. A double blind study has evaluated the possible association between vitamin C in plasma, the number of carious lesions, the relative numbers of selected species of the oral cariogenic flora, and the rate of salivary secretion.[14] The study concluded that the amount of visible plaque and the number of decayed tooth surfaces were significantly higher in the low vitamin C group.

Primary and Secondary Dentin Formation

Collagen is the major organic matrix component of dentin. It has been shown *in vitro* that the treatment with ascorbate enhanced the formation of mineralized nodules and collagenous proteins.[15] Calcium threonate may be one of the metabolites influencing the mineralization process.[16] Studies have also suggested that ascorbic acid deficiency hampers dentin Formation.[17]

Bone Healing

The initial inflammatory stage of bone healing is characterized by the formation of granulation tissue and the induction of precursor cells that differentiate into fibroblasts, chondroblasts, chondroclasts, osteoblasts, osteoclasts, and cells essential for capillary proliferation. The major difference between calcifying and non-calcifying cartilage is the amount of type II and type IV collagen. In non-calcifying cartilage, type II collagen predominates because it is the major component of cartilage matrix. In calcifying cartilage, type X collagen predominates under the influence of alkaline phosphatase, which is induced by ascorbate.[18] In an animal study, it was found that vitamin C supplemented group progressed through the various stages of bone healing faster than the control group.[19]

Vitamin C deficiency has also been associated with decreased bone density in a number of animal studies.[20,21] In a recent human study, low intake of vitamin C was found to be a risk factor for hip fractures in the elderly. Dietary ascorbic acid intake was independently associated with bone density among premenopausal women.[22]

Vitamin C and Oral Cancer

The possible anticarcinogenic effect of vitamin C appears to be related to its ability to detoxify carcinogens or block carcinogenic processes through its action as an antioxidant or as a free radical scavenger.[23] Other proposed mechanisms of action of vitamin C in the prevention and treatment of cancer include enhancement of the immune system, stimulation of collagen formation, necessary for "walling off" tumors, inhibition of hyaluronidase which may keep the ground substance around the tumor intact and prevent metastasis, inhibition of oncogenic viruses, improved wound healing after cancer surgery, enhancement of the effect of certain chemotherapy drugs, reduction in the toxicity of chemotherapeutic agents such as adriamycin, prevention of free radical damage, and neutralization of carcinogenic substances.[24,25]

RDAs of Vitamin C

The current daily recommended dietary allowance (RDA) of vitamin C is 75 mg for women and 90 mg for men, based on the vitamin's role as an antioxidant as well as protection from deficiency.[26,27] Pharmacological doses (> 100 mg/ day) of vitamin C may reduce the risk of chronic diseases such as cancer, cardiovascular disease, and cataracts, probably through antioxidant mechanisms. The totality of the reviewed data suggests vitamin C, 100 mg/day, may be required for the optimum reduction of chronic disease risks in non smoking men and women.[28] Several populations warrant special attention with respect to vitamin C requirements. These include patients with periodontal disease, smokers, pregnant and lactating women, and the elderly.

Patients with Periodontal Disease

There is a significant relationship between dietary vitamin C intake and periodontal disease after adjusting for age, gender, gingival bleeding, and tobacco consumption. A dose-dependent relationship between dietary vitamin C intake and periodontal disease has been seen.[14] Therefore, patients with periodontal disease may benefit from a dietary analysis and, when appropriate, from daily vitamin C supplementation.

Smokers

Smokers have a higher requirement for vitamin C than nonsmokers.[29,30] This is most likely due to increased demand as a result of increased oxidative stress.[31,32,33,34] The current RDA for smokers is 110 mg/day for women and 125 mg/day for men[27], although it has been proposed that smokers require 120 to 180 mg/day to maintain plasma vitamin C concentrations comparable to nonsmokers.[34]

Pregnant and Lactating Women

Pregnant or lactating women also require a higher intake of vitamin C to maintain optimal plasma vitamin C concentrations.[30,35] The higher requirement is due to active placental vitamin C transport, whereby vitamin C concentrations are significantly higher in cord blood and in newborn infants than in the mothers, and the loss of vitamin C through milk.[30,36] The current RDA for women during pregnancy and lactation is 85 and 120 mg/day, respectively.[27]

The Elderly

The elderly are prone to vitamin C deficiency because of dietary habits.[29,30,36] The RDA for those over 70 years of age is the same as for young adults (75 mg for women and 90 mg for men).[27] Oxidative processes have been implicated in aging and it has been proposed that antioxidants may have beneficial effects on cognitive functions in the elderly.[37]

Vitamin C Toxicity

Vitamin C appears to be relatively nontoxic, although intake levels above 1 gram/day can cause nausea and diarrhea.[27,38] The tolerable upper intake level for adults is 2000 mg.[27] Potential problems with pharmacological doses may also include "rebound scurvy," which occurs when the intake of high levels is abruptly stopped. In excess states (>4 gram/day), high levels of ascorbate and, significantly, one of its metabolites, oxalates, are found in urine and may increase the risk of renal-oxalate stone formation. The latter is pertinent, as it accounts for one of the few potential clinical toxicities of systemic vitamin C supplementation.]

SUMMARY

The current RDA of vitamin C for non-smoking women and men is 75 mg and 90 mg, respectively. The totality of the reviewed data suggests these dosages of vitamin C are optimal in this population both as an essential nutrient as well as an effective antioxidant. Several populations warrant special attention with respect to vitamin C requirements. These include patients with periodontal disease, smokers, pregnant and lactating women, and the elderly. However, even in these subpopulations, the data do not support recommending the routine daily intake of more than 200 mg of vitamin C. While higher dosages are generally well tolerated, the tolerable upper level of vitamin C is 2 g. In response to the aggressive promotion and advertising by health food advocates related to the use of nutritional supplements and antioxidants, patients may seek information from their dentist, a trusted source, about holistic issues. Clinicians should be cognizant about such issues and should be prepared to provide their patients with evidence-based recommendations. In their comprehensive approach to patient care, clinicians should base the need for recommending dosages in excess of the RDA on sound data supported by a nutritional analysis and the patients' plasma vitamin C concentration (normal:>0.2 mg/dl) levels.

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