Role Of Vitamin E In Prevention Of Oral Cancer

Vitamin E is an umbrella term for a group of 8 fat soluble antioxidants including alpha-, beta-, gamma-, and delta-tocopherol, and alpha-, beta-, gamma-, and delta-tocotrienol, though alpha-tocopherol is believed to be the primary form used by the human body.1 Vitamin E prevents production of reactive oxygen species by fat oxidation and is important for immune/endothelial cell function.

Oral cancer is one of the major global threads to public health. The most common way a person can get oral cancer is directly correlated to the consumption of tobacco. Vitamin-E can stop the reaction of the tobacco`s nitrosamine which undergoes activation followed by detoxification process. Dietary supplement such as vitamin-E can prevent oral cancer at a very early stage that is in premalignant lesions, in premalignant conditions. Main action of vitamin E includes increasing immunity, controlling free radicals mediated cell disturbances, maintaining membrane integrity, inhibition of cancer cell growth, cytotoxicity. Vitamin-E as an antioxidant helps in prevention and slow the growth of Head and Neck cancer, improve the effects of cancer chemotherapy and reduce the side effects from both chemotherapy and radiation therapy for cancer patients.

Introduction

Discovery of Vitamin-E in 1922 is credited to Herbert Evans and Katherine Scott Bishop when they found that “antisterility factor-x” was essential for reproduction in rats [1]. The pair showed that rats fed a purified diet of casein (18%), cornstarch (544%), lard (15%), butterfat (9%), salts (4%), adequate Vitamin-A (as cod liver oil), Vitamin-B (as yeast), and Vitamin-C (as orange juice) lost their ability to reproduce [2]. Two year later Barnett Sure confirmed Evans and Bishop’s observations after performing similar experiments; he called the substance “Vitamin-E” because vitamins A, B, C, and D were then already known to the scientific community [2]. In 1936 Evans first published the chemical formula of Vitamin-E in the Journal of Biological Chemistry [1].

Vitamin-E is the collective term for a family of chemical substances that are structurally related to alpha-tocopherol. Vitamin E occurs naturally in eight different forms: four tocopherols, alpha (?)-, beta (?)-, gamma (?) - and delta (?) tocopherol and four tocotrienols, alpha-, beta-, gamma- and delta-tocotrienol. All of these forms consist of a chromanol ring with a long aliphatic side chain, bound to the chromanol ring at the second position. Tocotrienols differ from their corresponding tocopherols in that the saturated phytyl side chain is replaced with an unsaturated isoprenoid side chain. The Greek characters refer to the number and position of the methyl groups at the 5, 7 and 8 positions [3].

Vitamin-E exhibit antioxidant properties by acting as a lipid-soluble free radical scavenger in cell membranes. Thus, Vitamin-E may involve in both initiation and promotion stages. Among the other potentially anticarcinogenic effects of Vitamin E are its ability to inhibit formation of the carcinogenic chemical nitrosamine from nitrites in some foods, and its ability to promote immune system function [4].

The Role of Vitamin-E in Cancer Chemoprevention Can Be Summarized As:

1. Inhibits oral cavity carcinogenesis.
2. Reduces the risk of developing oral cancer.
3. Causes reversal of premalignant lesion like oral leukoplakia.

Oxidative damage is recognized as playing a role in the pathogenesis of cancer which could arise from incorrect nutritional habits and lifestyle practices. This process can cause DNA damage, which is a basic mechanism in cancer induction [5]. Sufficient antioxidative status is crucial in free radical defence. To reduce the risk of oral and pharyngeal cancer, especially oral cell carcinoma, diet must be optimized, primarily to reduce calorie intake, monosaturated fat and red or processed meat. The important dietary micronutrients that are antioxidant in action include vitamin A, ?-carotene, lycopene, Vitamin C, vitamin E (alpha- tocopherol), Zinc and Selenium. Considerable evidence exists suggesting a role for nutrients, particularly the so-called antioxidants vitamin A, ?-carotene, vitamin C, vitamin E, lipoic acid, zinc, selenium and spirulina in the prevention of this disease [6]. Antioxidants are group of chemical compounds that can deactivate the free radicals and prevent their formation. Free radicals are oxidants which are single unpaired electron that bombard and destroy cells and other molecules in their search for another electron [7]. A recent study has suggested that these anti-oxidant nutrients act to inhibit the development of cancer cells and to destroy them through apoptosis (programmed cell death), by their stimulation of cytotoxic cytokines, by their action on gene expression, by preventing the development of tumour's necessary blood supply or by cellular differentiation [8]. A report has also shown a reduction in adverse effects of chemotherapy when given concurrently with antioxidants [9].

Tocoferol (AT) is the commonest and most active form of vitamin-E. It is found in plant oil, margarine, and green leaves. Tocoferol is an effective antioxidant at high levels of oxygen, protecting cellular membranes from lipidic peroxidation. Main actions of AT includes;

- Free radical scavenging
- Maintenance of membrane integrity
- Immune function
- Inhibition of cancer cell growth/differentiation
- Cytotoxicity
- In hibits mutagenicity and nitrosamine formation
- In hibition of DNA and RNA, protein synthesis in cancer cells.

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Chandra Mouli PE et al., [10] recommended use of Vitamin-E as an antioxidant in oral lesions. Vitamin-E can inhibit reactions of the tobacco specific nitrosamine (carcinogens) which undergo specific activation and detoxification process. Antioxidants such as ? carotene, provitamin A, vitamin-C, vitamin-E, zinc, selenium and spirulina are believed to have a preventive role against oral cancer.

Recent studies by Balwant Rai et al., [11] have proved that antioxidants such as Vitamin-C and Vitamin-E may be utilized in oral Lichen planus patients to counteract free radical mediated cell disturbances.

T.N. Uma Maheswari [12] highlighted the role of Vitamin-E in the treatment of leukoplakia. Antioxidant combinations [Vitamin A, E, and C] had proved to be most effective with maximum clinical resolution [90%] recorded [13] and regression of dysplasia recorded as 97.5% [14].

According to Uplabdhi Raghuwanshi et al., [15] the low levels of ?-tocopherol in patients could be either a cause or effect of oral carcinoma.

Vikas Fotedar et al., [16] states the role of Vitamin-E in oral cancer and chemoprevention. The term vitamin-E describes a family of light antioxidants, four tocopherols (alpha-, beta-, gamma and delta-). Alpha-tocopherol is the only form of vitamin E that is actively maintained in human body. Vitamin-E (alpha-tocopherol) is a potent antioxidant that neutralizes free oxygen radicals and inhibits carcinogenic nitrosamine formation. They have been reported to block the in vivo formation of N-nitroso compounds and suppress chemical carcinogenesis in animals. They may inhibit cancer development through several mechanisms like stimulation of wild-type p53, down regulation of mutant p53, activation of heat shock proteins, and an antiangiogenic effect mediated by blockage of transforming growth factor-alpha. The antioxidant vitamin E (?-TF) prevented the development of cancers in oral cavities in animal studies. A phase II study showed that among 43 patients with oral leukoplakia who took 400 IU of vitamin E twice daily for 24wks, 46% had clinical responses and 21% had histological responses. The treatment was well tolerated, without any toxicity, and with good compliance.

Rai Balwant [17] reported in his study, the role of Vitamin-E in oral cancer. Antioxidant defences (vitamin-E and C) are compromised and oxidative stress is increased in patients with oral cancer. A weak antioxidant defense system makes the mucosal cells more vulnerable to the cytotoxic effect of reactive oxygen species. This creates in intracellular environment more favourable for DNA damage and disease progression. So, antioxidant supplement (vitamin C and E) may have role in oral cancer patients.

Sumit Bhateja [18] highlighted the role antioxidants in oral mucosal lesions. The evidence in support of a chemopreventive role for the so called antioxidant nutrients, beta-carotene and Vitamin-E, against oral cavity cancer.

S Chitra and C S Shyamala Devi [19] highlighted the effect of Vitamin-E on oral submucous carcinoma patients. Serum glycoproteins were evaluated in oral squamous cell carcinoma patients treated with radiotherapy and also the effect of vitamin-E on these patients. The levels of glycoconjugates were significantly decreased in radiation treated patients having vitamin-E supplementation. This measurement may be useful in assessing disease progression and identifying patients resistant to therapy and the role of vitamin-E on reduction in glycoconjugate levels of radiation treated oral squamous cell carcinoma patients.

Soma Gupta et al., [20] highlighted the role of Vitamin-E in oral submucous fibrosis. Plasma Vitamin-E level was found to be decreased in grade II and III OSMF cases but not in grade I cases. However, mean Vitamin-E level was found to be decreased (9.3 ± 0.3 mg/L) as compared to healthy controls (mean = 10.1 ± 1.2 mg/L). Enzymatic antioxidant defense was assessed by SOD activity, which did not show any significant change in any stage of the disease.

Maher et al., [21] evaluated the role of multiple micronutrients consisting of retinol, vitamin-E, vitamin-D, vitamin-B complex and some minerals in the management of OSMF and reported

clinical improvement.

Other work has indicated a possibly beneficial role for supplemental vitamin-E in diabetes based on lowered serum levels of glycosylated hemoglobin and triglyceride [22]. Supplemental vitamin-E at a dose of 60-800 ID/day reportedly improves immune function in elderly subjects [23] while a single dose of 1g helped to prevent oxidative damage of DNA [24].