International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Original Research Article

Serum α-Tocopherol Levels Indicating Status of Oral Carcinoma Patients

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Received: 19/11//2012 *Revised: 23/12/2012* *Accepted: 27/12/2012*

ABSTRACT

Background: Epidemiological studies suggest that antioxidants may play a major role in the progression of oral cancer. Oxidative processes contribute in promoting stages of carcinogenesis, at this stage the level of antioxidants are very crucial in prevention & progression of carcinogenesis. Studies have suggested that deficiencies in antioxidant nutrient level are likely to be important risk in progression of cancer. Antioxidant nutrients, which play a crucial role against defense of pro oxidants, can be measured quantitatively. If they are reduced from the normal levels they can be supplemented.
Objective: The study was planned to evaluate the levels of non-enzymatic antioxidant, particularly vitamin E, in serum of oral cancer patients (n=100) & control subjects (n=50) in order to study its possible role in prediction & prevention of oral cancer.
Materials & Methods: Serum vitamin E levels were estimated colorimetrically (520 nms) by method of Baker & Frank (1968).
Results: A concomitant decline in vitamin E levels was noted in oral cancer patients w r t control group ($p < 0.001$). Similar results were obtained when grade I & II patients were compared with control ($p < 0.001$). Risk of oral cancer was 5.80 times more in patients with low vitamin E levels [2.588 to 12.8025 at 95% CI].
Conclusion: The low levels of α-tocopherol in patients could be either a cause or effect of oral carcinoma. Measurement of vitamin E in circulation of oral cancer patients may thus be a useful index in assessing tumor grades of patients. Further studies using a larger sample size & long-term follow-up of subjects are desirable.
***Key words*:** α-tocopherol, oral squamous cell carcinoma, non-enzymatic antioxidant.

INTRODUCTION

Tocopherol appears to be the first line of defense against peroxidation of PUFAs contained in cellular & subcellular membrane phospholipids. Vitamin E is a sacrificial antioxidant that can donate hydrogen atoms. It is localized in membranes & lipoproteins, where it can interrupt the radical chain reaction of lipid peroxidation. Therefore, vitamin E is also called a chain-breaking antioxidant. Plasma levels of anti-oxidants are reliable indicators of the antioxidant status, because they reflect the bioavailability as well as

increased utilization to counter lipid peroxidation. Furthermore anti-oxidants levels in plasma are also influenced by life style factors such as diet & tobacco.

Etiology of oral cancer is rather a complex, multi-factorial, ill-defined, & incomplete concept. Tobacco is a major risk factor in pathogenesis of this disease. Oral cancer is the fifth most common cancer worldwide (Parkin et al., 1993) & is one of the most common malignancies in India accounting 30-40% of all cancers.[1] Males, particularly over 40 years, are affected twice as often as females. Though several studies have been made which attempt to evaluate the levels of vitamin E, only a few are available w r t different grades of oral cancer. This aspect is studied in present work.

MATERIALS AND METHODS

Eligible cases were 50 healthy subjects & 100 histopathologically-diagnosed cases of OSCC (91 males & 9 females), particularly grade I (well differentiated, n = 63) & grade II (moderately differentiated, n = 37). All of them were in either age group 25-50 years (n = 85) or 51 & above years (n = 15). Blood samples were collected from the O.P. Department of Surgery, Sasoon Hospital, B.J. Medical College, Pune, Maharashtra, India. A detailed history of patients was assessed by an oral questionnaire which included age, sex, duration of disease, duration of chewing habits, socioeconomic background, dietary habits over last six months, etc.

Inclusion Criteria:

1. Histopathologically-diagnosed & confirmed cases of squamous cell carcinoma of oral cavity [grade I & grade II].
2. Control cases were healthy, i.e. free from any disease/abnormality/or any habit including tobacco chewing.
3. All cases had a well-known history of tobacco-chewing habit.

Exclusion Criteria:

1. Grade III & IV patients;
2. Those with carcinoma of lip, pharynx, & larynx, tonsils, minor salivary gland tumors, etc;
3. Those with any concomitant disorder such as diabetes mellitus, liver diseases, rheumatoid arthritis, etc;
4. Patients taking vitamins/antioxidants supplements.
5. Those having previous history of smoking or alcohol abuse.

Method: Taking aseptic precautions, approximately 5 ml of blood samples were collected, from in appropriate sterile vials by venous arm puncture after overnight fasting & sera were separated by centrifugation at 3000 rpm for 10 minutes. Serum vitamin E was estimated by the method of Baker and Frank (1968), [2] which is based on reduction of ferric to ferrous ions by α-tocopherol, which then forms a red colored complex with 2, 2'-dipyridyl that is read at 520 nm. Values for serum vitamin E levels were calculated as mgs/dL.

Statistical Analysis

Data were expressed as (mean ± SD) & calculations were performed using Microsoft Excel 2010. Statistical analysis [patient Vs control] was done using students' t test & comparison between groups was performed with one-way analysis of variance (ANOVA). Odds ratio (ORs) & 95% confidence intervals (CIs) were calculated to determine the risk of oral cancer associated with levels of serum antioxidant. P-value of less than 0.05 was considered as statistically significant.

RESULTS

Alpha-Tocopherol levels showed a highly significant ($p < 0.001$) decline in oral cancer patients w r t control group [Table I].

Low levels were noted in Grade II patients as compared to Grade I patients & the difference ($p < 0.001$) w r t control, i.e. F cri (7.41) < F cal (27.042) at $\alpha = 0.001$, so results are significant at 0.1% level. Most patients (59%) had low levels of vitamin E [< 1.0 mgs/dL] than control (20%). The risk of oral cancer was 5.80 times more in patients who had lower serum vitamin E levels [Table III].

Table I: Mean ± S.D. Values:-

Group	Control	Patient	Grade I	Grade II
Mean ± S.D. [mgs/dL]	0.71 ± 0.33	0.45 ± 0.24**	0.54 ± 0.24	0.30 ± 0.15[a]**

** $p < 0.001$, [a]F cri $0.001_{(2, 147)} = 7.41$ ($p < 0.001$)

Table II: Mean ± SD Values According to Tumor Location:-

Tumor Location	Tongue (8)	Buccal Mucosa (88)	Hard Palate (4)
Mean ± S.D. [mgs/dL]	0.33 ± 0.17	0.45 ± 0.24	0.30 ± 0.16

Table III - Association Between Low Vitamin Levels & Risk of Oral Cancer:-

Serum Indices	Patient [n=100]	%	Control [n=50]	%	OR	95.0 % CI for OR
Low Vitamin E [< 1.0 mgs/dl]	59	59	10	20	5.80*	2.69 to 12.80

*p = 0.001 [Fischers' exact test], OR = Odds Ratio [median of control was taken as cut-off point], CI = Confidence Interval

DISCUSSION

The highly significant decline in oral cancer patients w r t control group concluded an inverse relationship with the severity of disease, also indicating defective non-enzymatic antioxidant mechanism in oral cancer patients. Similar results were obtained by Syed Sultan Beevi et al (2004).[3] Low levels of vitamin E could be due to increased utilization of antioxidants by tumor tissues or to counteract free-radical mediated cell disturbances. This finding correlated with the findings of previous studies.[3-5, 6] Thus determination of serum levels of tocopherol will indicate the status of oral cancer patients. The lower serum vitamin E levels in oral cancer patients could be either a cause or an effect of the oral cancer.

Although dietary factors have been identified as having a possible association with oral cancer, accumulated scientific evidence that use of tobacco increases oral cancer risk far outweighs any evidence linking a deficient diet to increased risk.[5] A low intake of vitamin E has been associated with an increased risk of cancers of the oral cavity. A study by Mirvish SS found that patients with low serum levels of vitamin E had more than double the general risk of gastrointestinal cancers.[7] In another study, which evaluated more than 2,000 cases, the use of vitamin E supplements correlated with a diminished risk for oral & pharyngeal cancer.[8] The most consistent dietary findings across multiple cultural settings are that high fruit consumption has a protective effect & that high alcohol consumption has a carcinogenic effect.[9]

Low levels were noted in Grade II patients may be due to shifting of tocopherol from blood to site of malignancy & thereby decreasing serum levels, possibly due to increased requirement in higher grades. The decline in vitamin E levels in serum of patients seemed to be disease related because as the disease advanced from the immuno-competent grade to immuno-compromised grade, the serum concentrations of these vitamins decreased progressively. Study was similarly demonstrated by S. Manoharan et al (2005)

w r t different cancer stages. [10] This decline could be attributed to tumor progression from lower to a higher grade which in turn reflects the significant increase of oxidative stress in the stages of oral cancer development.

The risk of oral cancer was 5.80 times more in patients who had lower serum vitamin E levels. The results were in absolute correlation with study by AO Lawal et al (2012).[11] These significant low levels may be due to, low or improper consumption of vitamin-containing foods thereby reducing the protective effect of antioxidants against cancer, & loss of appetite that may be caused by TNF [tumor-necrosis factor] as well as IL-6 [interleukin-6] produced in cancer patients consequently leading to general malnutrition, including reduced intake of vitamins.[12]

Lower levels of plasma & erythrocyte membrane vitamin E have been reported in various pathological conditions including oral cancer.[13,14] Enhanced lipid peroxidation with decline in antioxidants has been reported in venous blood of oral cancer patients & patients with oral squamous cell carcinoma at different intraoral sites.[13,15] Kolanjiappan et al have reported an increase in vitamin E and glutathione levels in tumor tissues of patients with various clinical stages of oral squamous cell carcinoma.[16] Buzby et al suggested that host tumor cells sequester essential nutrients from the circulation to meet the demand of growing tumor.[17] Thus observed decrease in serum vitamin E of oral cancer patients can be due to utilization of these antioxidants by tumor or to compromise the excessive oxidative stress in circulation.

CONCLUSION

The study showed low levels of antioxidant vitamin E in oral cancer patients than those of healthy volunteers, indicating defective non-enzymatic antioxidant mechanism in patients. The risk of oral cancer was higher in patients with low levels of antioxidant vitamin E. Also levels of vitamin E were found to be associated with tumor grades of patients, thus measurement of vitamin E in circulation of oral cancer patients may be helpful in assessing the tumor grades of oral cancer. An optimized diet rich in vegetables & fruits, which are rich in antioxidants like vitamin E, as well as therapeutic measures to increase antioxidants are warranted for effective control of its complications. However studies with more patients are required to explore the relationship of non-enzymatic antioxidants with promotion & malignant conversion stages of oral cancer.

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How to cite this article: Raghuwanshi U, Choudhari SC, Patil R. Serum α-tocopherol levels indicating status of oral carcinoma patients. Int J Health Sci Res. 2012;2(9):60-64.

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