ROLE OF SALIVARY VITAMIN C IN ORAL MALIGNANT AND POTENTIALLY MALIGNANT DISORDERS

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ABSTRACT

Oral cancer is reported as the sixth most frequent malignant neoplasm in the world. Among all malignancies 25% are found in the oral cavity. Early diagnosis of malignant and potentially malignant disorders may help in reducing mortality. Clinical efforts in cancer therapeutics were concentrated mainly on invasive cancer. Such an approach has limited effect. A refocus on carcinogenesis is important with prime aim for cancer prevention. Plasma concentrations of ascorbate have been shown to be inversely associated with risk for developing cancer. The objective of study was to estimate and correlate the salivary levels of vitamin C in oral malignant and potentially malignant disorders. 20 subjects with oral cancer and 20 subjects with potentially malignant disorders were selected and salivary levels of vitamin C were compared with controls. 1ml of whole saliva was collected from each subject. The samples were collected in micro centrifuging tube and were frozen at less than minus 20°C. The samples were analyzed in a spectrophotometer for vitamin C levels. It is observed that salivary levels of vitamin C were very much reduced in oral malignant and potentially malignant disorders when compared to control (p<0.001). In the control group salivary vitamin C levels were maintained in all the age groups. Low levels of vitamin C causes increased cell damage. There is an inverse association of vitamin C and development oral cancer. Thus this study suggests that Vitamin C may have a strong association in inhibiting initiation and promotion of oral cancer.

INTRODUCTION

Oral cancer is reported as the sixth most frequent malignant neoplasm in the world. Among all malignancies 25% are found in the oral cavity. Even though tobacco is the major cause of oral cancer, alcohol synergistically acts causing malignant changes. Tobacco, either smoked or smokeless form is responsible for 75% of oral cancer (Harinder Garewal, 1995). Most cancers of oral cavity are squamous cell carcinoma. Early diagnosis of malignant and potentially malignant disorders may help in reducing mortality. In a World Health Organization (WHO) Workshop, held in 2005, the terminology of oral lesions predisposing to malignant transformation was discussed.
Promotion is generally reversible. Since it takes long time, it is ideal for intervention with chemopreventive agents. A potentially malignant disorder can be either made to regress, or the rate of conversion to malignancy can be slowed down. Vitamins are essential nutrients that are required for various biochemical and physiological processes in the body. It is known that most vitamins cannot be synthesized in the body. Hence dietary supplementation is necessary. Vitamin C is a water soluble vitamin. It was first isolated in 1923 by Hungarian biochemist and Nobel laureate Szent-Gyorgyi and synthesized by Howarth and Hirst (Shailja Chambial et al., 2013). Since the discovery of vitamin C, the number of its known biological functions are expanding. The body requires vitamin C for normal physiological functions. It increases the absorption of iron in the gut by reducing ferric to ferrous state.

Nitroso compounds which are known to induce carcinogenesis are reduced by vitamin C. It acts as co-antioxidant with vitamin E to protect low density lipoprotein (LDL) from oxidative damage induced by aqueous peroxy radicals.

The chemopreventive role of vitamin C was 1st proposed by Cameron et al in 1949. Vitamin C is also known to inhibit N-Nitroso compounds which are known to induce carcinogenesis (Sotiriou, 1987). Various studies showed that consumption of vitamin C rich foods reduces the risk of developing cancer. Plasma concentrations of ascorbate in plasma of healthy humans is about 40-80μM. These levels of ascorbates functions as an endogenous antioxidant. It acts as co-antioxidant with vitamin E to protect low density lipoprotein (LDL) from oxidative damage.

Vitamin C is a water soluble vitamin. It is a strong antioxidant. It protects the body from various toxic effects of free radicals. The recommended dietary intake for vitamin C is 75-125 mg daily. Ascorbate is essential for the full function of an array of enzymes. Adequate intake of vitamin C will optimize the metabolism and prevent cancer and other degenerative diseases. The concentration of ascorbate in plasma of healthy humans is about 40-80μM.

**RESULTS**

A total of 60 patients were included in this study. Analysis of variance (ANOVA) test was used to analyze the statistical significance of salivary vitamin C levels in oral cancer and potentially malignant disorders with the control. ‘P’ value < 0.01 was considered to be statistically highly significant at 1% level, ‘P’ value between 0.011-0.05 was considered to be statistically significant at 5% level and the ‘P’ value of greater than 0.05 was considered to be statistically not significant at 5% level. The mean salivary vitamin C levels in control group were 231.45μmol/l. In oral cancer and potentially malignant disorders, the mean salivary vitamin C levels were 35.15 and 68.82μmol/l. The results were statistically highly significant (p < .001) when vitamin C levels in oral cancer and potentially malignant disorders were compared with control (Table.1).

In the age group up to 30 years, the mean salivary vitamin C levels in control group were 240.03μmol/l and in potentially malignant disorders the vitamin C levels were 150.24μmol/l. No oral cancer patients were present in this age group. In the age group of 31-40 years, the mean salivary vitamin C levels in control group were 301.08μmol/l and in oral cancer and potentially malignant disorders it was 68.21μmol/l and 31.97μmol/l respectively. In 41-50 years age group the salivary vitamin C levels were 187.55μmol/l in control group. In oral cancer the vitamin C levels were 15.88μmol/l and in potentially malignant disorder the mean salivary vitamin C levels were 41.05μmol/l. In this age group the difference in salivary vitamin C levels were highly significant (p<.001) between control group and others. Age group of 51-60 years showed salivary vitamin C levels of 189.60μmol/l in control group and 43.49 μmol/l and 73.97μmol/l in oral cancer and potentially malignant disorders respectively. Above 60 years of age the vitamin C levels were 182.22μmol/l in control group.12.44μmol/l in oral cancer and 119.94μmol/l in potentially malignant disorders (Table.2).

**DISCUSSION**

This study was done to evaluate and compare the salivary vitamin C levels in malignant and potentially malignant disorders in oral cavity. Three groups with 20 subjects were considered in this study. Group1 with histologically proven oral cancer. Group 2 with histologically proven potentially malignant disorders and group 3 control with no mucosal changes. After obtaining an informed consent from each patient included in the study, a detailed clinical examination was done and 1ml of whole saliva was collected in a MCT.
The samples were stored in a plasma freezer at a temperature less than -20 degree Celsius. The samples were transported and centrifuged for the analysis of salivary vitamin C in a spectrophotometer. The salivary levels of vitamin C were compared in each group.

When salivary vitamin C levels were compared with age group, there were highly significant results above the age of 40 years. The mean salivary levels of vitamin C were very much reduced in oral cancer and potentially malignant disorders when compared with control group. These results again favor the role of vitamin C in initiation and promotion of oral cancer. When control group is taken alone, there was no significant difference in vitamin C levels in different age groups. This suggests that there may be no significant relationship between vitamin C levels and age. The same is for oral cancer and potentially malignant disorders. But as the age increases there is a strong relationship between reduced vitamin C levels and incidence of oral malignant and potentially malignant disorders. In our study the salivary levels of vitamin C were reduced in smokers when compared to the non smokers in the control group. This is in favor of Vitamin C, a known antioxidant which plays a vital role in many physiological functions of body including prevention of cancer. In our study the results showed that there may be strong relation with reduced vitamin C and oral malignant and potentially malignant disorders. Even though vitamin C levels cannot independently predict oral cancer, our study showed that vitamin C may play an important role in inhibiting initiation and promotion of malignant changes of oral cavity. Our study also suggests that vitamin C may not play a role in the progression of malignancy since there was no correlation between the levels of vitamin C and degree of dysplasia.

The result suggested that the salivary levels of vitamin C in malignant and potentially malignant disorders were highly reduced when compared to the control group. The vitamin C levels in oral cancer were reduced when compared to the potentially malignant disorders but there was no statistical significance. In this study the prevalence of malignant and potentially malignant disorders were high in males when compared to females. There were no oral cancer patients below 40 years of age and the average age was 54 years. This is in accord with the statement of Greenberg and Glick in 2003 that oral cancer is a disease of older age group and 95% of cases occur in people above 40 years with an average of 60 years of age (Greenberg, 2003). This study suggests that there is a strong inverse association between vitamin C levels and oral cancer which is in favor of statement by Alexander J Michels in 2013 that many cohort study have observed the inverse association between Vitamin C intake or plasma levels and incidence of cancer which is in favor of statement by Alexander J Michels (1999). When compared with control group, the salivary vitamin C levels were significantly reduced in potentially malignant disorders including OSMF. This is in accord with the study of R Guruprasad in 2014. In his study the serum vitamin C was significantly reduced in oral submucous fibrosis compared to control group. Though in this study there was no significant association of vitamin C levels and clinical staging of OSMF (Guruprasad, 2014). There was no significant difference in salivary vitamin C levels in the histological grading of oral cancer and in degree of dysplasia, which is contradictory to the study of Balwant Rai in 2008. He concluded that the salivary levels of Vitamin C were significantly decreased in patient with advanced grade of oral cancer (Balwant Rai, 2008). Even though the mean vitamin C levels in oral cancer were less when compared to potentially malignant disorders, they were not statistically significant. This study suggests that there is no correlation between degree of dysplasia and vitamin C levels in potentially malignant disorders. Also there was no much significant difference in the salivary levels of vitamin C between males and females in oral cancer and potentially malignant disorders. In control group the mean levels of salivary vitamin C were less in females.

**Table 1. Mean age and salivary vitamin C levels**

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<th>Age</th>
<th>Mean</th>
<th>SD</th>
<th>Female</th>
<th>Mean</th>
<th>SD</th>
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<td>11.37</td>
<td>46.33</td>
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<td>Oral Cancer</td>
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<td>13.72</td>
<td>59.00</td>
<td>6.52</td>
<td>55.40</td>
<td>12.34</td>
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<tr>
<td>Potentially malignant Disorders</td>
<td>48.38</td>
<td>11.16</td>
<td>42.50</td>
<td>15.59</td>
<td>47.20</td>
<td>11.94</td>
<td>0.87</td>
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<tr>
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<td>2.41</td>
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<td>0.003**</td>
<td>0.124</td>
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**Table 2. Salivary vitamin C levels in different age group**

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<th>SD</th>
<th>ANOVA</th>
<th>P</th>
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<tbody>
<tr>
<td>Control</td>
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<td>41.00</td>
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<tr>
<td>Oral Cancer</td>
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<td>55.40</td>
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<tr>
<td>Potentially malignant Disorders</td>
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<td>11.94</td>
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</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>47.87</td>
<td>13.55</td>
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<tr>
<td>Salivary Vitamin C</td>
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<td>&lt; 0.001**</td>
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**REFERENCES**


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