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Salivary Antioxidant Level in Oral Squamous Cell Carcinoma

Najafi Sh [1], Gholizadeh N [2]*, Manifar S [3], Rajabzadeh S [4], Kharazi Fard MJ [5]

1. Tehran University of Medical Sciences, International Campus, Tehran, Iran
2. Tehran University of Medical Sciences, Tehran, Iran.
3. Dental Research Center, Tehran University of Medical Science, Tehran, Iran.
4. Tehran University of Medical Sciences, Tehran, Iran
5. Dental Research Center, Tehran University of Medical Sciences, Tehran, Iran.

***Corresponding Author:** Gholizadeh N, **Email:** n.gholizadeh88@gmail.com*

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Abstract

Background: Oral cancer is among the 10 most common cancers worldwide with an increasing global incidence. Compromised antioxidant defense system plays a role in occurrence of cancer. This study evaluated the salivary antioxidant level of oral cancer patients compared to a control group.

Patients and Methods: This case-control study was conducted on 22 oral squamous cell carcinoma patients presenting to Imam Khomeini Hospital in Tehran, Iran, as the case and 20 healthy controls that matched the case group in terms of age, sex and race. Total salivary antioxidant level was measured in both groups.

Results: The salivary antioxidant level of patients was significantly higher than that of healthy controls (P=0.029).

Conclusion: Salivary antioxidant level of oral squamous cell carcinoma patients was significantly higher than healthy individuals. Saliva increases the anti-oxidant level as a compensatory action, thus, by administration of antioxidants we may help saliva in the fight against free radicals that are considered as predisposing factors for cancer.

Keywords: Saliva, antioxidant, oral cancer, squamous cell carcinoma.

Introduction

Oral squamous cell carcinoma (OSCC) is among the 10 most common cancers worldwide and accounts for approximately 3% of all cancers with a higher prevalence among males [1]. About 95% of all cases of OSCC occur in patients older than 40 years of age with a mean age of approximately 60 years at the time of diagnosis [2]. In a study conducted in south Iran, OSCC accounted for 1.7% of all types of cancer and the mean age of patients with OSCC was found to be 56.9±15.5 years with a male to female ratio of 1.4/1 [3].

OSCC has variable clinical manifestations and may be seen in exophytic (mass, mushroom-like, papillary and verrucous form) or endophytic (invasive or ulcerative) forms or as leukoplakia, erythroplakia or erythroleukoplakia [4]. OSCC mostly involves the tongue, pharynx and floor of the mouth. Lips, gingiva, dorsal surface of the tongue and palate are among the less common sites of involvement [2]. Metastatic dissemination of OSCC is usually done via the lymphatic vessels to the lymph nodes of the same side [4].

The stage of SCC is determined based on the primary size of the tumor in cm, involvement of regional lymph nodes and presence or absence of distant metastasis: the higher the stage of disease from I to IV, the poorer the prognosis. Histopathologically, in grade I or well-differentiated tumors, tumoral cells are mature and have high resemblance to their tissue of origin. In anaplastic or high-grade poorly differentiated tumors, tumoral cells are immature, grow rapidly and metastasize to other organs (grade III or IV). OSCC is a multifactorial condition and no single causative agent has been found to be responsible for its occurrence [4].

Tobacco (smoked or consumed), alcohol and other risk factors such as phenols, radiation, iron deficiency, vitamin A deficiency, syphilis, candidiasis, oncogenic viruses and a compromised immune system have been suggested as possible causes [2]. Diagnosis of OSCC relies on clinical examination along with imaging and immediate live tissue staining technologies with toluidine blue and cytology preparation of specimens [2]. The treatment usually comprises of surgical resection, radiotherapy and chemotherapy as adjunct.

Impaired oxidation and reduction system in body is among the suggested causes for development of many cancers such as OSCC. Free radicals are produced during the inflammatory process in body and have to be neutralized by the enzymatic (glutathione peroxidase, catalase, superoxide dismutase) or non-enzymatic (vitamins A, E and C) anti-oxidant agents [5,6]. Free radicals are molecules with one or more pair of electrons in their external orbit and are therefore highly reactive molecules [7]. Oxidative stress results when the production of oxygen free radicals exceeds their physiologic threshold or body's anti-oxidant defense system is weak [8]. Saliva reacts against these free radicals and increases the level of antioxidants as a compensatory act.

This study sought to assess the salivary antioxidant level among OSCC patients and compare it with that of healthy controls.

Patients and Methods

This study was approved by the Ethics Committee of the Tehran University of medical science. This case-control study was conducted on OSCC patients referred to the Cancer Institute of Imam Khomeini Hospital from 2012 to 2013. Patients whose OSCC had been pathologically confirmed were enrolled as cases and healthy subjects who matched the case group in terms of age, sex and race were selected as the controls. Subjects were thoroughly informed about the study protocol and objectives, and written informed consent was obtained from them.

The inclusion criteria were having a confirmed pathological diagnosis of OSCC and willingness to participate in the study as well as signing the written informed consent. The exclusion criteria were underlying systemic conditions such as diabetes mellitus, liver disease or rheumatoid arthritis, and being under pharmaceutical treatment during the past month (like antioxidant supplementation).

Independent t-test was applied to compare the antioxidant level between the two groups. Levene's test showed that data variances were not equal in the two groups (P=0.011). Thus, for comparison, we used t-test with the hypothesis of inequality of variances.

Sampling method

After confirming the diagnosis of OSCC through biopsy, 5ml salivary samples were collected using stippling technique. The patients were placed in a seated position and were asked to hold their saliva for one minute and then spit into a Falcon tube. This process was repeated 5 times (for a total of 5 minutes). Salivary samples were obtained with subjects fasted and they were asked to refrain from eating, drinking or smoking for 2 hours prior to sampling.

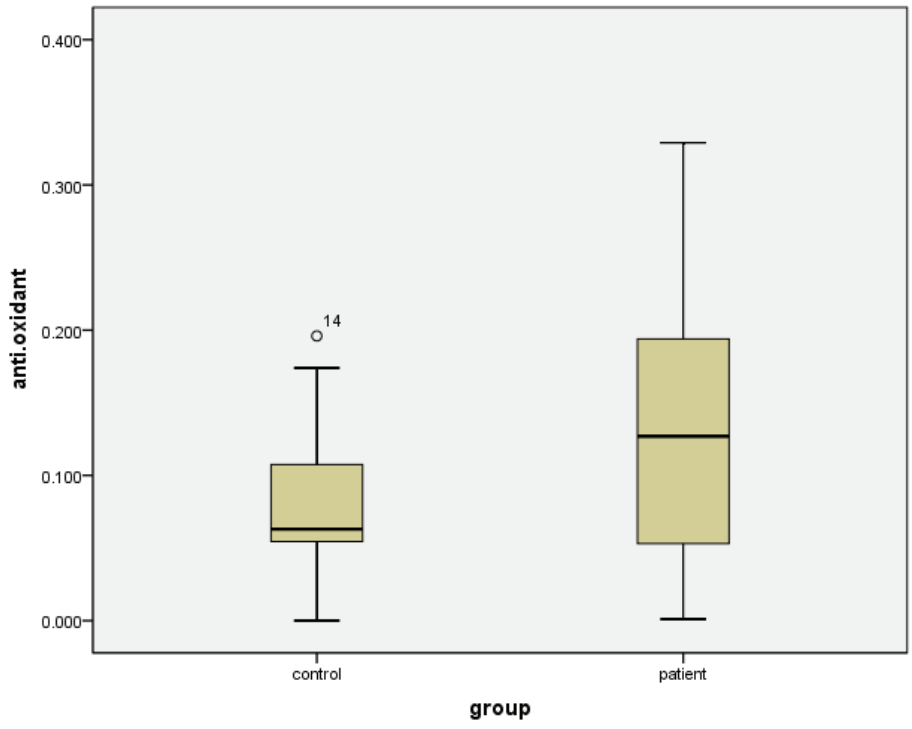
Instruments and tools

Disposable instruments like wooden tongue depressor and dental explorer were used for clinical examination of patients and 15ml Falcon tubes were used for collection of salivary samples. Data including age, sex and definite diagnosis were extracted from patient records and recorded in a specific form. Salivary samples were centrifuged at 2,400 rpm for 10 minutes and transferred to new tubes using a sampler. Specimens were stored at -70°C in the Oncology Laboratory of Imam Khomeini Hospital until the total salivary antioxidant level was measured.

Results

A total of 22 OSCC patients including 16 males and 6 females in the age range of 22-82 years were evaluated. About 40% of patients had a history of cigarette smoking. The mean of total salivary antioxidant level was 0.101±0.137 in the case and 0.051±0.081 in the control group. Independent t-test showed a significant difference in this respect between the two groups and found that the salivary antioxidant level of patients was significantly higher than that of controls (P=0.029) (Figures1).

Figure 1: Salivary antioxidant level of oral cancer patients compared to a the control group.



Discussion

This study demonstrated that the salivary antioxidant level in OSCC patients was significantly higher than in the control group.

In a study on level of antioxidant vitamins and lipid peroxide in saliva and serum of patients with recurrent aphthous ulcers conducted in Turkey in 2005, it was revealed that the concentration of some non-enzymatic antioxidants namely vitamins A, E and C as well as malondiable-hyde was higher in patients with recurrent aphthous ulcers compared to controls [9]. Ziobro and Bartosz[10] in 2003 compared the total antioxidant capacity of some body fluids and reported that the total salivary antioxidant capacity was higher than plasma antioxidant capacity in a specific age range. Astaneie et al. [11], evaluated the total serum and salivary antioxidant level of diabetic patients and found that salivary antioxidant capacity of type I diabetic patients was higher than that of the control group.

Chemical composition and the quality and quantity of salivary and serum antioxidants are different [12]. Saliva is the first defense line against free radicals and also plays a role in chewing and digestion of food and causes several enzymatic reactions such as lipid peroxidation. Therefore, antioxidant capacity of serum and saliva is different [13]. Saliva shows a compensatory reaction against free radicals and increases the antioxidant level.

It should be noted that primary and secondary prevention are highly important in OSCC. Our results showed that a compromised antioxidant system may be responsible for occurrence of OSCC. Thus, healthy individuals might benefit by reinforcing their antioxidant system in order to prevent this condition (primary prevention). OSCC patients might also prevent the adverse consequences of disease by reinforcing their antioxidant system. Further studies are required to evaluate the diagnostic value of salivary antioxidants in oral cancer.

Conclusion

Salivary antioxidant level of oral squamous cell carcinoma patients was significantly higher than healthy individuals. Saliva increases the anti-oxidant level as a compensatory action, thus,

by administration of antioxidants we may help saliva in the fight against free radicals that are considered as predisposing factors for cancer.

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