

Assessment of salivary antioxidant status and immunoglobulin E in patients with geographic tongue

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ABSTRACT

Objective: One of the possible ways of changing human health might be through the oral mucosa. One of tongue disorders is geographic tongue (GT), which classic manifestation is an area of erythema, with atrophy of filiform papillae of the tongue, surrounded by a serpiginous, white, hyperkeratotic border. Saliva is a rich source of antioxidant and fulfills an important role in maintaining the normal function of the oral cavity. The purpose of the present study was to investigate the status of salivary antioxidant and immunoglobulin E in patients with GT and healthy people. **Materials and Methods:** In this case-control study, samples were gathered from high school students in three municipal regions of Kermanshah, Iran by using multistage random cluster sampling method. The samples included 30 patients with GT (15 men and 15 women with the mean age of 17.6 ± 0.72) and 30 healthy volunteers (15 men and 15 women with the mean age of 17.1 ± 0.61). Saliva samples were collected through standard method, and total antioxidant capacity (TAC), catalase (CAT), and salivary immunoglobulin E were measured. **Results:** In patients with GT, unstimulated salivary shows increased level of immunoglobulin compared with that of control group ($P = 0.013$). However, there was no significant relationship between control and GT patient groups regarding TAC of saliva ($P = 0.91$) and CAT ($P = 0.83$). **Conclusion:** It seems that the activity of CAT enzyme and TAC of saliva does not play primary role in the pathogenesis of GT. However, the level of immunoglobulin E present in saliva can function as an indicator of increased sensitivity in GT.

Keywords: Anti-oxidants, geographic tongue, immunoglobulin E, saliva

Introduction

Benign migratory glossitis or geographic tongue (GT) is a benign inflammatory and relatively common disorder which affects dorsal surface and lateral borders of the tongue^[1] and is characterized by an erythematous zone with yellow-white or gray elevated margin and irregular spiral pattern (like geographic maps), indicating atrophic changes of filiform papillae of the tongue.^[2,3] Depending on the rate of the activity of the lesion, there may be one or more lesions present in the clinical manifestation; these lesions move over the surface of the tongue and heal without leaving scar. The clinical features of

this mucous disorder are clear, and pathological investigation is rarely required.^[4,5]

Saliva, a complex combination of oral fluids, plays important roles in maintaining oral health and is produced by major and minor salivary glands.^[6] Followings are some of the most common physiologic and pathologic criteria which can change quality and quantity of saliva: odor, taste, chewing, hormonal and mental status, medications, age, inheritance, oral hygiene, and sport activities.^[7] Oxidative stress is a state of imbalance between the production of free radicals and rate of present antioxidants which causes oxidative damage to macromolecules such as lipids and proteins.^[8] Reactive oxygen species include free radicals and derivatives of non-radicals oxygen (derivatives with the ability to produce oxygen radicals). Hydrogen peroxide (H_2O_2), superoxide anion ($O_2^{\cdot-}$), and hydroxyl (OH^{\cdot}) radicals present in the body

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fluids, such as saliva, are main oxidative factors which affect the incidence of systemic and oral diseases.^[9,10] Body is provided special systems, known as antioxidant systems, to deal with damage which results from the activity of free radicals. The sum of all materials present in body fluids with antioxidant activity is known as total antioxidant capacity (TAC).^[11]

Body antioxidants originate from external sources (food, drinks, sunlight) and internal production. Internal production includes enzymatic and nonenzymatic systems: the enzyme systems include metalloproteinase enzymes which are dependent on food. Although the main role of enzyme systems is in intracellular environment, they perform various activities outside the cell.^[12] Enzymatic systems include superoxide dismutase, catalase (CAT), and glutathione peroxidase; nonenzymatic system contains vitamins A, E, C, and uric acid.^[13]

CAT is one of the most efficient oxidation enzymes which attends to active site in the presence of Fe and is mainly in the peroxisomes. This enzyme has the potential of catalyzing H_2O_2 into oxygen and water. Otherwise, H_2O_2 might change into radical hydroxyl, which is one of the most active and harmful radicals for living cells.^[14]

Immunoglobulins are protein molecules produced by specific cells in the immune system in response to external factors that are recognized by surface antigens. These molecules are produced in saliva in order to protect oral cavity.^[15] Immunoglobulin E is one of the five Ig isotypes which plays an important role in pathogenesis of allergic and inflammatory reactions.^[16] The aim of this study was to measure some parameters of oxidative stress, such as CAT activity, TAC of saliva, and evaluation of saliva IgE level in patients with GT compared to control group in order to attain a clear view of GT etiopathology.

Materials and Methods

This case-control study was carried out after obtaining the consent of the Department of Research of the University of Medical Sciences, Kermanshah, Iran. The study included 30 patients with GT (15 females, 15 males) and 30 healthy subjects (15 males, 15 female) with the same age and gender. In this study, samples were obtained from the male and female high school (second and third grade) students in three municipal regions of Kermanshah, Iran, through observing the tongue of the students by a general dentist (researcher). The written consent of all participants was taken from their parents before collecting the samples and the study was approved by the Ethics Committee, School of Dentistry. Medical history and oral examinations including dental and periodontal condition and mucosal lesions were recorded. People with the following features were excluded from the study: those with systemic disease, history of allergy, medication consumption in recent 3 months, periodontal disease and any pathological lesions in the mouth, severe decay, and mouthwash consumers. The tongue was examined using gloves, tongue blade, gauze pad, and flashlight.

About duration of lesions, recovery and recurrence, ulcer, and change the location of lesion on the tongue due to the immigrant nature of GT to confirm the diagnosis and rule out other oral mucosa diseases were questions. This study was approved by the Ethic Committee of Kermanshah University of Medical Sciences, Kermanshah, Iran.

Unstimulated saliva samples were gathered in the morning while the patients were fasting. Participants were asked not to drink any beverage, except for water. Sample gathering was done in sitting position with their heads bent toward. After washing mouth with distilled water, saliva collected on the floor of the mouth was gathered and evacuated into disposable tubes. Then, the samples were placed in ice at 4°C, transported to the laboratory,^[17] centrifuged (200 rpm) for 10 min to remove debris, and frozen at -80°C.

Nonenzymatic TAC of saliva used in this study was measured through ferric reducing antioxidant power method and expressed in terms of $\mu\text{mol/L}$. This method is based on the capability of plasma in the reduction of ferric ions (Fe^{3+}) into down (Fe^{2+}) in the presence of a substance called TPTZ (Tripyridyl-s-Triazine). As a result of reaction between Fe^{3+} with the reagent TPTZ (made by Merck, Germany) Fe^{2+} -TPTZ blue complex is produced with maximum absorption at 593 nm wavelength. The power of revival was measured and recorded using a spectrophotometer device.^[18] The activity of CAT enzyme was measured according to Aebi method, the basis of which is decrease of optical absorption of hydrogen peroxide at a wavelength of 240 nm. The decomposition rate of the enzyme-substrate (H_2O_2) was measured for 30 s in intervals of 5 to 10 s using a spectrophotometer device. CAT activity is expressed in International Units.^[19] IgE of saliva was measured according to Elisa method, using human IgE kits made by EUROIMMUN Germany (order NO: EV 3840-9601 E) based on IU/ml.

For the data analysis, independent sample *t*-test and correlation coefficient between variables were used. SPSS 16 software was used to analyze all collected data. The significance level was considered $P < 0.05$ in this study. The results were presented as mean \pm Deviation Standard ($X \pm D$).

Results

The patient group included 15 men and 15 women with mean age of 17.6 ± 0.72 ; control group, as well, included 15 men and 15 women mean age of 17.1 ± 0.61 . Table 1 shows average TAC, CAT, and IgE in both case and control groups.

As shown in Table 1, the comparison between patient and control group showed that the level of IgE of saliva of patient group was significantly higher than normal group ($P = 0.013$). There was not a statistically significant difference between two groups in CAT ($P = 0.83$) and TAC ($P = 0.91$).

There was a positive correlation between CAT and TAC and IgE of control group, and a correlation between CAT and TAC was significant ($P = 0.019$). There was a negative correlation between CAT and TAC and IgE of GT group [Table 2].

Discussion

Saliva has functioned as a mirror of the body healthiness for a long time and presented strong potential to be used instead of blood test.^[20] Saliva is a unique liquid, and interest in it as a tool for detection of diseases has experienced considerable progress in the last 10 years. Saliva contains a wide variety of proteins, peptides, nucleic acids, hormones, and electrolytic excreted from various sources. However, because of lack of information about biological molecules present in saliva and their relationship with the causes of diseases, and lack of highly sensitive diagnostic system, saliva is rarely used as a diagnostic fluid.^[21]

Changes in human health may be reflected through oral mucosa.^[22] The prevalence of GT, also known as geographic stomatitis, is 1–2.5% and it has equal distributions in both sexes; however, some reports have shown the prevalence of the lesion to be higher in men.^[2,23] The etiology and pathogenesis of GT is still unknown and its relationship with genetic factor reported. Some common factors associated with GT include psoriasis, Reiter's Syndrome, stress, and fissured tongue. Stability of this lesion causes concern of malignancy in these patients.^[2] Attenuation of the antioxidant system may lead to inflammation and hypersensitivity and autoimmune conditions; the main role of the immune system against free radicals in allergic patients in detoxification of blood cells has been demonstrated.^[24]

Some studies show a link between geographical tongue and sensitivity or allergy; according to these studies, patients with a personal or family history of allergies or sensitivities such as asthma (5), eczematous dermatitis, and hay fever, generally all those with high levels of immunoglobulin E serum, are more likely to have geographical tongue than those without these

features.^[25,26] In another study, carried out by Voros-Balog, on the relation of GT with age, gender, systemic diseases, and allergies, no significant association with systematic disease was observed, while there was evident relationship with a history of tendency of hypersensitivity.^[27] Järvinen and his colleagues proved strong tendency allergy in patients with GT.^[28] Recent research has indicated a wider pathophysiological role for IgE in various diseases, including metabolic diseases, auto-immune diseases, nociception, and anxiety. The function of IgE is carried out through binding to FcεRI receptors on the mast cell. Because of synthesis and release of a variety of inflammatory mediators, mast cells are prone to make pathophysiological changes in different organs and cause the development of various diseases mentioned above.^[29] However, few studies have investigated the change of IgE subtypes in serum and saliva of GT patients.^[30,31] Based on the findings of present study that level of IgE increases in the saliva of patients with GT and considering the role of IgE in allergic and inflammatory reactions and risk factors associated with GT, we can confirm the relationship between GT and hypersensitivity and consider IgE as an influential factor in the appearance and severity of disease. Therefore, antihistamines and corticosteroids are appropriate in the treatment of this disease. Probable relationship between inflammatory process and metabolism of free radicals has been reported in several studies.^[32] It is claimed that the imbalance between the level of free radicals and some reactive species of oxygen with antioxidant might play significant role in the initiation and development of the pathology of oral inflammatory diseases.^[33] Antioxidants found in saliva are the first line of defense against oxidative stress caused by free radicals.^[20] Antioxidants are found in the bodies of all living creatures and protect them against the harmful effects of excessive oxidative materials.^[34] However, since free radicals and reactive oxygen species and antioxidant systems seem to interact with each other, and antioxidant acts collectively rather than alone, individual studies of antioxidant activity might be misleading and reductive and size of any antioxidant may be less indicative of the overall situation of body antioxidants. The present studies are moving toward a method called “total antioxidant capacity” of biological fluids such as saliva.^[6]

Table 1: Comparison of total antioxidant capacity of saliva (TAC), catalase (CAT), and IgE among healthy students and those with geographical tongue

	Sex: male/female	Age	TAC μmol/L	CAT U/L	IgE
Geographic tongue	15/15	17.6±0.72	416.2±146	116.5±74	0.663±0.49
Control	15/15	17.1±0.61	421±156	112.4±76.6	0.4±0.27
P	P=1	P=0.6	P=0.91	P=0.83	P=0.013

T-Test. ($P < 0.05$)

Table 2: Pearson correlation between catalase antioxidant activities (CAT), total antioxidant capacity (TAC), and immunoglobulin E (IgE) of geographic tongue (GT) and control group

Variable	Geographic tongue			Control		
	TAC	CAT	IgE	TAC	CAT	IgE
TAC	1	-0.044 (0.817)	-0.244 (0.194)	1	0.427 (0.019)	0.14 (0.459)
CAT	-0.044 (0.817)	1	-0.193 (0.308)	0.427 (0.019)	1	0.045 (0.814)
IgE	-0.244 (0.194)	-0.193 (0.308)	1	0.14 (0.459)	0.045 (0.814)	1

P-values are presented in parenthesis

Therefore, TAC may be the most relevant parameter to assess the ability of defense.^[35]

CAT is a type of antioxidants enzyme which is found in almost all aerobic organisms. Since red blood cells are exposed to high concentrations of oxygen, they produce a large amount of hydrogen peroxide; CAT carries more than half of this hydrogen peroxide and protects hemoglobin in this way. CAT is influential in ethanol metabolism, inflammation, apoptosis, aging, and cancer and its lack might cause genetic disease.^[36] In this study, CAT and TAC of GT patients and a control group were measured to assess their antioxidant status; the study showed slight decrease of TAC and increase of CAT; however, these changes were not statistically significant. Given these results, we can conclude that antioxidant system is not affected in the saliva of GT patients and it seems that CAT activity and TAC do not play significant role in the pathogenesis of GT.

Kullaa-Mikkonen *et al.* revealed increased levels of substances in saliva, such as lysozyme, myeloperoxidase, and IgA, G, M in the fissured tongue and interpreted this change as reflecting inflammatory conditions in fissured tongue.^[30] Jia *et al.*, showed reduced salivary flow, PH, and increase NA/K and SIgA ratio and introduced following factors as significant in the appearance of fissured tongue: in saliva and in shaping electrolytic disorder, malnutrition, and endocrine and safety performance of the patients.^[31]

Given the positive correlation between TAC and CAT in control group, and the negative correlation between them in GT group, it can be concluded that antioxidant balance may be affected in GT patients.

The results of recent study can demonstrate that a correlation between antioxidant status and increasing of sensitivity maybe existed.

Conclusion

TAC and CAT in patients with GT do not show significant difference compared to those without this lesion. IgE level of saliva of GT patients showed a significant difference compared to that of control group.

Suggestions

It is first time that these elements in saliva (TAC, CAT, and IgE) were measured; therefore, it cannot be determined that impaired antioxidant system is a cause for GT or vice versa; neither increase of IgE can be considered a diagnostic tool for GT. We recommend further studies to be multicenter, with a larger number of patients. The effects of antihistamines and anti-allergy medications on treatment of this disease need to be worked upon in further studies, as well.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients/parents have given

their consent for their images and other clinical information to be reported in the journal. The patients/parents understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflict of Interest

There is no conflict of interest.

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