

The Evaluation of Psychological Factor and Salivary Cortisol and IgA Levels in Patients with Oral Lichen Planus

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Article information	Abstract
<p>Article history: Received: 25 Aug 2013 Accepted: 15 Jan 2014 Available online: 3 Feb 2014 ZJRMS 2014 July; 16(7): 31-34</p> <p>Keywords: Cortisol Oral lichen planus Stress</p> <p>*Corresponding author at: Department of Oral Medicine, Genetics of Non-communicable Disease Research Center, Faculty of Dentistry, Zahedan University of Medical Sciences, Zahedan, Iran. E-mail: farbabi@razi.tums.ac.ir</p>	<p>Background: Oral lichen planus (OLP) is a chronic immunological disorder with unknown etiology. The aim of this study was to determine psychological factors and salivary cortisol, IgA level in patients with oral lichen planus.</p> <p>Materials and Methods: In this experimental study 20 patients with OLP and healthy person were admitted to this study. Saliva samples were collected between 9-10 Am. saliva cortisol, IgA level was detected by ELIZA method. In this study, patients with anxiety and depression were measured using the SCL-90 questionnaire. Data analyzed by <i>t</i>-test.</p> <p>Results: The mean salivary cortisol level in patients with OLP was 3.2 ± 1.9 ng/mL and the mean saliva cortisol level in healthy person was 3.5 ± 1.9 ng/mL. Significant difference was observed in the salivary cortisol levels in the 2 study groups ($p=0.04$). The mean salivary IgA level in patients with OLP was 0.69 ± 0.29 ng/mL and the mean saliva IgA level in healthy person was 0.9 ± 0.43 ng/mL but no significant difference was observed in the salivary cortisol levels in the 2 study groups. Results showed that anxiety levels in patients with oral lichen planus were slightly higher than controls but there was no significant difference between healthy subjects.</p> <p>Conclusion: Finding revealed the mean salivary cortisol level in patient with OLP less than healthy persons. Significant difference was observed in the salivary cortisol levels in the 2 study groups. Based on the <i>t</i>-student test, no significant difference was observed in the salivary IgA levels in the 2 study groups. Anxiety levels in patients with oral lichen planus were slightly higher than controls.</p> <p>Copyright © 2014 Zahedan University of Medical Sciences. All rights reserved.</p>

Introduction

Oral lichen planus (OLP) is a chronic immunological disorder. Seventy five percent of the patients with cutaneous lichen planus also experience oral lesions [1]. The etiology of OLP is unknown. In recent years, it has been found that the immune system plays a primary role in causing the disease [2]. On the other hand, we know that OLP is an immune-related disorder, and stress and anxiety are 2 factors causing it [3].

In condition pain, anxiety and stress, many metabolic and endocrine changes occur in the body, the most common effect of which is increased cortisol level in the blood [4]. This hormone is a 21-carbon corticosteroid that is secreted by the adrenal cortex and regulates the metabolism of carbohydrates, fats, proteins, and water. It also plays a role in the regulation of the immune system and vascular reactions. Also known as the stress hormone, cortisol is a decisive index in stressful situations [5].

Following the changes in the blood cortisol level, its level in the saliva also changes. The salivary cortisol is an index of free blood cortisol or biologically active cortisol. Cortisol secretion is regulated through the adrenal-

pituitary-hypothalamus axis. By the 24 h rhythm in response to stress, the afferent fibers of the central nervous system stimulate hypothalamus to release CRH which, in turn, stimulates the production and secretion of ACTH. The plasma cortisol levels increase a few minutes after stimulation [6].

The IgA level measurement is used as a convenient source in determining the immune system performance, and its half-life is approximately 3-6 days [7]. Recent studies show that chronic stress can decrease the immune system performance and suppress the immunoglobulin production [8].

It is a theory that the immunoglobulin level can play a role in the pathogenesis of oral mucosa and its associated clinical changes [9].

Rabiei et al. found that the salivary cortisol and IgA levels are correlated with the incidence of OLP, and one may consider the salivary IgA and cortisol levels as a possible indicator in the creation or development of OLP lesions [10]. Girardi et al. conducted a study to assess the levels of salivary cortisol, dehydroepiandrosterone (DHEA), and psychological factors in patients with OLP.

In that study, 31 patients with OLP were matched with 31 healthy individuals in terms of age and sex. The anxiety and depression level in patients was measured using the Beck test. They observed that there is no significant difference between salivary cortisol in the OLP group and the control group [11].

Tavangar et al. examining anxiety and cortisol levels in patients with OLP on 20 patients with lichen planus and 20 non-infected individuals in Isfahan. For saliva collection, they used the unstimulated spitting method and measured the cortisol level with ELISA. They found that the mean salivary cortisol level in patients with lichen planus was less than non-infected individuals [12].

Sistig et al. reported increased levels of IgA and IgG in patients with lichen planus [9]. Ghalayani et al. evaluated the IgA and IgG levels in patients with OLP and lichenoid reaction Lesions. The results showed that the IgA and IgG levels are higher than normal individuals in both groups [13].

Although stress is considered as a possible factor in the development of OLP, the association of increased salivary IgA and cortisol with OLP is still disputed. Due to conflicting results in previous studies, the following study aimed to compare the salivary IgA and cortisol levels in patients with OLP and normal subjects.

Materials and Methods

In this experimental study, the patient group consisted of 20 patients with OLP diagnosed by oral disease specialists and the control group included healthy individuals from the general population matched with patients with OLP in terms of age and sex. Patients with clinical and histopathological diagnosis of OLP were enrolled in this study. Prior to entering the study, patients signed an informed consent form. Then intraoral examinations were done by a supervision of an oral disease specialist on the dental unit in the vertical position using a disposable mirror under good light. The results of these examinations were recorded in the related information form. The following were excluded from the study: Patients with history skin lesions and genital, people with a history of neoplasia malignancies, patients undergoing radiotherapy or chemotherapy, or patients with autoimmune disease such as lupus erythematosus, rheumatoid arthritis, Sjogren's syndrome or metabolic diseases such as diabetes, patients taking any systemic medication (including benzodiazepines, antidepressants, anabolic steroids, OCP, corticosteroids suppressing the immune system) within the last 30 days and smokers. The unstimulated spitting method was used to collect saliva samples in the 2 groups. In this method, the participants evacuated 2 mL of their saliva into a tube with 1-cm opening without the application of any stimulating substances every 60 seconds during 2-5 minutes. The samples were collected between the 9-10 AM because the cortisol level in blood and saliva is at a high level of the circadian cycle cortisol. After collection, the samples were immediately sent to the laboratory, frozen at 20°C and centrifuged in 1500 rpm. Using the ELISA method,

the salivary cortisol and IgA levels were then measured. Psychosocial factors of study and control groups were measured by depression anxiety and stress using a questionnaire SCL-90 (symptom checklist-90)

Results

In this study, 20 patients with OLP aged 23-71 years and a mean age of 45.8±14, and 20 healthy subjects aged 21-67 years with a mean age of 42.8±11.9 were studied.

Among the 20 patients with OLP, 13 cases (65%) were female and 7 cases (35%) were male. The most common site of involvement was chick (13 cases, 65%), followed by tongue, gum (20% and lips 19%) and palate (5%). The most common form of OLP was reticular and papular (55%).

Based on the ELISA test results, table 1 shows the salivary cortisol and IgA level in patients with OLP and healthy subjects. Based on the *t*-student test, a significant difference was observed in the salivary cortisol levels in the 2 study groups ($p=0.04$). Based on the *t*-student test, no significant difference was observed in the salivary IgA levels in the 2 study groups.

Table 1. Comparison of the mean salivary cortisol and IgA in healthy subjects and patients with OLP

Groups	Healthy Mean ±SD	Patient Mean±SD	<i>p</i> -Value
Cortisol level (ng/mL)	3.5±1.9	3.2±1.9	0.04
IgA level (ng/mL)	0.69±0.29	0.90±0.43	0.08

Discussion

In this study, 20 patients with OLP aged 23-71 years mean age and 20 healthy subjects aged 21-67 years were studied. Results showed the mean salivary cortisol level in patient with OLP less than healthy persons and no significant difference was observed in the salivary IgA levels in the two study groups. Anxiety levels in patients with oral lichen planus were slightly higher than controls. Wilson first described lichen planus as a disease that involves the skin, nails, and oral mucosa [14]. OLP is a chronic inflammatory skin-mucous disease mediated by T cells and unknown etiology. OLP has periods of remission and relapse. It is a cell-dependent safety condition that T lymphocytes are accumulated under the epithelium of oral mucosa and increase the differentiation of stratified squamous epithelium leading to hyperkeratosis, redness with or without a wound.

This disease involves 2-5% of the general population with predominance in women. Its onset is in the decade 4-5 [15]. In the present study, a total of 20 patients with OLP (13 women and 7 men) with a mean age of 45.8±1 years, and 20 healthy subjects (13 women and 7 men) with a mean age of 42.8±11.9 years were studied. Lichen planus may involve different places in the oral mucosa. The buccal mucosa is the most common site as bilateral lesions. The floor of the mouth is the rarest incidence site [15]. Our study reported the most common site of involvement as follows: buccal mucosal (65%), tongue

and gum (20%), lips (10%), palate (5%). The most common form in our study is the reticular form with 11 cases (55%). The cortisol production level in different periods varies by several factors, including the circadian rhythm, diet and stress. The normal cortisol level was 10-20 mg/dL early in the morning and 3-10 mg/dL in the afternoon. The urinary excretion is about 3-8 mg in 24 hours [16].

The cortisol level can be measured in plasma, urine, and saliva. The salivary cortisol collection is the most sensitive one. In fact, the salivary cortisol is an index of free blood cortisol or biologically active cortisol. The salivary cortisol collection has advantages and disadvantages.

Advantages: its measurement technique is simple, non-invasive, and inexpensive, and its analysis does not require a complex process.

Disadvantages: since the salivary cortisol concentration is low, its assessment separation is sensitive (ELISA method), and sometimes blood can also be associated with saliva that makes a false report [17].

Based on the ELISA method, the mean salivary cortisol level was 3.2 ± 1.9 ng/mL in patients with OLP, and 3.5 ± 1.9 ng/mL in the control group. Based on the *t*-student test, a significant difference was observed between the 2 groups in terms of salivary cortisol.

In the most recent study in this area by Girardi et al. on 31 patients with lichen planus and the control group, the mean salivary cortisol level showed no difference between the 2 groups. The obtained result could be due to the low sample size in this study [11].

Ivanovski et al. attributed the possible cause of variability in the cortisol measurement to differences in breed and food absorption. These factors increase the possibility of variation and inaccuracy in the cortisol measurement [18].

About the reason for differences between studies, one can say that since some patients with lichen planus require histopathological and biopsy examinations for the final diagnosis, this will lead to increased stress and anxiety in patients and ultimately will affect both serum and salivary cortisol. This change is different in individuals and can be the reason for differences in the salivary cortisol.

Given our results in this study and consistent studies such as Rabiei et al., Tavangar and Ghalayani, Rodstrom et al. [10, 12, 19] and inconsistent studies such as Shah et al., Koray et al. [20, 21], one can say that any stress, whether physical or mental, leads to the rapid increase in ACTH. Then the cortisol level in the blood increases within a few minutes, stressors arrive at the hypothalamus through the brain stem and increase the CRF hormone (corticotropin releasing factor) in the pituitary. Within some minutes, all these stages lead to the high secretion of cortisol in the blood.

This time does not exceed 1-2 hours. Therefore, it can be justified that high cortisol levels in the blood or saliva is not a reason for increased anxiety in the individual, but it can be an indicator of momentary stress in the individual or it can be explained that in the lichen planus

disease, there is a high activity of T cells, Langerhans cells, lymphocytes, and cytotoxicities against epithelial cells. Moreover, since cortisol leads to a reduction in the number of lymphocytes and other immune cells, it can be concluded that any dysfunction in the HPA (Hypothalamic-pituitary-adrenal axis) and reduced blood cortisol secretion, and subsequently reduced salivary cortisol secretion, cause diseases affecting the immune system like lichen planus.

Moreover, since the most common form of OLP was reticular and papular and this form of lesions are asymptomatic and the patient feels no burning pain, the blood cortisol and subsequently the salivary cortisol remained unchanged in the normal range. Based on the ELISA test, the mean salivary IgA level was 0.9 ± 0.43 ng/mL in patients with oral lichen planus and 0.69 ± 0.29 ng/mL in the control group. An increase in the salivary IgA level was observed in the case group compared to the control group. Based on the *t*-student test, a significant difference was observed in the salivary cortisol in the studied groups.

Similar to our study, Sistig et al. and Sato studies compared the salivary IgA level in patients with different oral diseases and healthy subjects with the ELISA method. An increase in the salivary IgA level was observed in patients with oral leukoplakia, OLP and carcinoma of the oral cavity [9, 22]. Higher IgA levels facilitate the antigen supply by Langerhans cells, make changes in the basal layer destruction and dispatch immune cells to the area. Rabiei et al. reported a decrease in IgA which is different from our study. They practically considered this change as a reduction in the host's superficial defense [10].

In this study, patients with anxiety and depression were measured using the SCL-90 questionnaire. Anxiety level in patients with oral lichen planus was higher than the control group but no significant difference was observed between the 2 groups.

One purpose of the study was to investigate the level of anxiety in 2 groups using a questionnaire SCL-90 that its validity and reliability has been proven. Results showed that anxiety level in patients with oral lichen planus was slightly higher than controls but there was no significant difference between healthy subjects. This is similar to, Girardi et al. [11], Ghalayani et al. [13] studies and in contradiction with Lundqvist et al. [23] study. These differences could be due to enrolled patients with ulcerative oral lichen planus. However, our study evaluated all pattern of oral lichen planus.

In this study, the mean level of salivary cortisol in patients with OLP was lower than healthy individuals and the mean IgA level in patients with OLP was higher than healthy individuals. To prove this hypothesis, we require further research with higher sample sizes for different types of lichen planus, especially erosive type

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Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

The authors declare no conflict of interest.

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