ORIGINAL RESEARCH

Estimation of Serum Cortisol Levels in Oral Lichen Planus Patients and its Relation to Stress

Muhaseena[1], Vishnudas Prabhu[2], Maji Jose[3], Muhamood Moothedath[4]

ABSTRACT

Introduction: Oral lichen planus is a chronic mucocutaneous disease which manifest in the oral mucosa. Its pathogenesis is multifactorial and as stress being one of the psychological factor in its etiology, the present study correlating anxiety and depression with the serum cortisol levels in oral lichen planus patients, will further elucidate the pathogenesis of the disease.

Material and method: A case control study was conducted on 26 oral lichen planus cases and 26 healthy controls. Serum cortisol levels of all 52 subjects were estimated using electrochemoluminiscence. Hospital anxiety and depression scale questionnaire was administered for psychometric analysis.

Results: The mean serum cortisol value was 9.265 ± 2.349 µg/dl in the test group. The mean anxiety score and the mean depression score in test group was calculated to be 9.538 ± 2.404 and 10.385 ± 2.061 respectively.

Conclusion: The mean serum cortisol level of the oral lichen planus group showed a highly significant difference (P = 0.001) from the controls. When mean anxiety score was analyzed, a highly significant difference (P = 0.001) was noted between the two groups. A statistically significant difference was noted when mean depression score was analyzed between the oral lichen planus and control group (P = 0.013). These findings suggest that psychological factors play a role in the pathogenesis of oral lichen planus and cortisol estimation could be a valuable indicator in stressful conditions like in oral lichen planus.

Keywords: Oral Lichen Planus; Serum Cortisol; Anxiety; Depression; Stress.

How to cite this article: Muhaseena, Vishnudas Prabhu, Maji Jose, Muhamood Moothedath Estimation of serum cortisol levels in oral lichen planus patients and its relation to stress. International Journal of Contemporary Medical Research 2015;2(4):856-860

[1]Post graduate student, [2]Professor, [3]Professor & HOD, Department of Oral Pathology and Microbiology, Yenepoya Dental College, Mangalore, Karnataka, [4]Associate Professor & HOD, Department of Public Health Dentistry, Century International Institute of Dental Sciences and Research Centre, Kasaragod, Kerala, India

Corresponding author: Dr Muhaseena, Post Graduate Student, Dept. of Oral & Maxillofacial Pathology, Yenepoya Dental College, Mangalore, Karnataka, India.

Source of Support: Nil

Conflict of Interest: None

INTRODUCTION

Lichen planus is a relatively common chronic inflammatory disorder of the stratified squamous epithelia[1] that typically affects the skin and /or oral cavity and also other non-oral mucosal surfaces.[2] It is estimated to affect 1-2% of the general population and women are more commonly affected than men in a ratio of 1.4:1.[3] Oral lichen planus (OLP) is a disease of the adulthood and are mostly seen in the fifth and sixth decades of life.

Oral cavity is one of the target areas to psychological state of the human life. It can reflect the general health of the individual. Stress is one of the commonest psychological factors, which causes alteration of the body tissues in general and oral cavity in specific. OLP is often referred to as "stress-related" or "stress-associated" disorder of the oral mucosa.

Although various factors are suggested to be involved in the pathogenesis of this disease, its exact etiology is still not clear. It appears to be complex interactions with genetic, environmental and life style factors. Stress is considered to be one of the important etiological factors in OLP. Patients with OLP often relate the onset and aggravation of oral symptoms to increased levels of stress.[4,5] cortisol production is often regulated with the stress levels in humans. Chemically cortisol is a 21 –carbon glucocorticoid secreted by adrenal cortex. This hormone regulates carbohydrates, protein, lipid and fluid metabolism and maintains vascular reactivity. Cortisol affects sensitivity of nervous system, regulates blood cell numbers and all these together affects the human stress response. Adrenocorticotrophic hormone is produced in the anterior pituitary gland and it regu-

lates the production of cortisol. Stress and the diurnal rhythm are modulating factors that can up regulate the production of cortisol.[6]

It has been supported that there is an increased level of stress in patients with OLP and stressful life events aggravate the condition, hence stress is considered as an etiological factor for OLP. Most of the studies have used the different type of psychological stress scale to evaluate the stress level in OLP. But there is little documentation about the cortisol level to determine the stress level in patients with OLP, as cortisol level is increased in stress.

As stress being one of the possible factor related to the development of OLP, this study correlating anxiety and depression with the serum cortisol levels in such patients, will further elucidate the pathogenesis of the disease.

MATERIALS AND METHODS

Ethical clearance

The study protocol was reviewed and ethical clearance was provided by the Institutional Review Board of Yenepoya University.

The study group consisted of 26 clinically and histopathologically confirmed oral lichen planus patients and 26 age and sex matched healthy controls visiting the department of Oral Medicine and Radiology. Patients suffering from any systemic disease(s) such as cardiovascular disease, renal dysfunction, and liver disorders, oral mucosal or muco-cutaneous lesions, lichenoid reactions were excluded in the study.

The purpose of the study and the procedures to be carried out were clearly explained to the chosen group of people and only those who agreed to give a written consent were included in the study. After recording a detailed case history, oral examination of the patients was carried out using diagnostic instruments (mouth mirror & probe) in order to clinically diagnose OLP. The clinical diagnosis was confirmed histopathologically after performing an incisional biopsy under local anesthesia. The tissue thus obtained was fixed in formalin solution, tissue processing and staining was performed and the sections were evaluated histopathologically.

The selected subjects were recalled during the morning hours (9-11AM) for the study due to the diurnal variation of cortisol. After obtaining a written consent, Hospital Anxiety and Depression Scale (HADS) questionnaire was given to each subject included in the study. Later, blood samples were collected for analysis.

ANXIETY AND DEPRESSION SCORES

Each of the subjects was administered a HADS questionnaire. The questions were translated into the regional language for patients unable to read English. Scores were added separately for anxiety and depression and they were assigned as normal (0-7), borderline abnormal (8-10) and abnormal (11-21). The scores were analyzed in order to analyze the anxiety and depression levels of both the OLP patients and healthy controls.

BLOOD SAMPLE COLLECTION

5ml of venous blood sample was collected from each subject (study group and control group) with disposable syringe under aseptic conditions through venipuncture of the median cubital vein. Serum was separated by centrifugation at 3000 rpm for 15 minutes. The sample thus collected was stored below zero degrees until analyzed for cortisol or sent immediately within 1 hour for serum cortisol estimation.

SERUM CORTISOL ESTIMATION

Serum cortisol levels were estimated using fully automated electrochemoluminiscence (ECL) method as per the manufacturer's instructions.

Statistical Methodology

The obtained data was coded and entered into Microsoft excel sheet. The data was then fed in to SPSS (Statistical Package for Social Studies) software-16 for analysis.

RESULTS

In the test group, the age of the subjects ranged from 24 to 56 years with a mean of 36.6923 ± 9.97103 years. In the control group, the age of the subjects ranged from 25 to 52 years with a mean of 34.4615 ± 7.33882 years. When comparison of age was done between the test group and the control group using t test, the difference in age was not found to be significant (P=0.363).

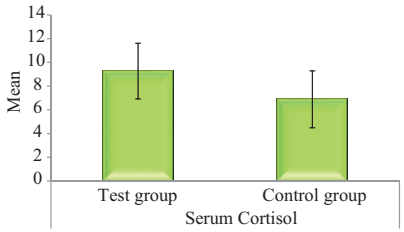
Among the 26 patients with OLP, 10 (38.5%) were females and 16 (61.5%) were males. In the control group, 14 (53.8%) were females and 12 (46.2%) were males. Statistical analysis by Chi-Square test showed no significant difference among the gender in the test group and control group with the P value of 0.266.

The mean serum cortisol value in test group was 9.265 ± 2.349 µg/dl and was higher than the mean serum cortisol value of control group 6.879 ± 2.402 µ/dl, highly

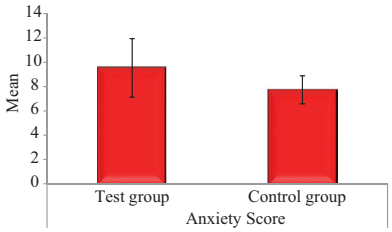
significant difference ($P = 0.001$) was noted. [Graph 1] The mean anxiety score in test group was found to be 9.538 ± 2.404 and was higher than the mean anxiety score in control group 7.731 ± 1.151. [Graph 2,4]. When the results were statistically analysed with t test, a highly significant difference ($P = 0.001$) was noted. In the test group, anxiety scores of 5 (19.2%) subjects were normal, 14 (53.8%) were borderline, 7 (26.9%) were abnormal. In the control group, 12 (46.2%) were normal, 14 (53.8%) were borderline, 0 (0%) were abnormal. Statistical analysis by Fishers exact test showed highly significant difference among the test group and control group with the P value of 0.006.

The mean depression score in test group was found to be 10.385 ± 2.061 which was higher than the mean depression score in control group 9.115 ± 1.451. [Graph 3,4] A statistically significant difference was noted when the results were subjected to t-test ($P = 0.013$). In the test group, depression score of 1 (3.8%) subject was normal, 14 (53.8%) were borderline, 11 (42.3%) were abnormal. In the control group, depression score of 3 (11.5%) subjects were normal, 21 (80.8%) were borderline, 2 (7.7%) were abnormal. Statistical analysis by Chi-Square test showed significant difference among the test group and control group with the P value of 0.013.

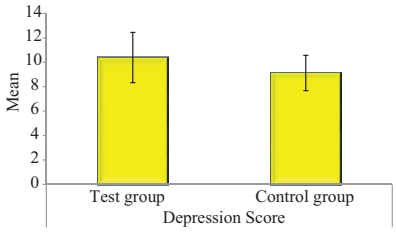
Different parameters in the study (serum cortisol, anxiety & depression) were compared using Karl pearson correlation coefficient. In test group, a statistically significant difference was found between serum cortisol – depression score and depression score – anxiety score. In the control group, highly significant difference was found between anxiety score – depression score.



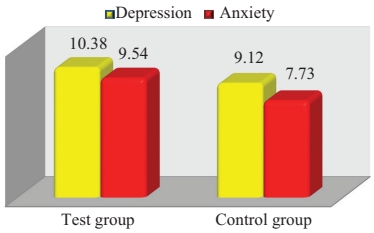
Graph-1: Mean Serum Cortisol Levels of study subjects



Graph-2: Mean Anxiety Scores



Graph-3: Mean Depression Scores



Graph-4: Combined HADS Scores

DISCUSSION

The present study was undertaken to determine any possible association between stress and OLP. In order to assess the stress levels in OLP patients, serum cortisol levels were estimated along with HADS questionnaire. Numerous studies have been done on the prevalence rates of lichen planus in various populations. The age distribution in our study was within the range of 24 to 56 years (mean of 36.69) which is similar to that reported by Singh OP & Kanwar AJ[7] in their study of 441 patients with lichen planus in which majority of the patients belonged to the third decade of life. Our results were also consistent with that obtained by Bhattacharya M et al[8] who reported the age range to be 20-49 years. However studies conducted by Brown RS et al[9] and Gorouhi F et al[10] showed the development of the lesion in the sixth decade of life.

Analyzing the gender distribution in the present study, it was noted that out of 26 lichen planus subjects majority were males (61.5%) which is similar to the one observed by Singh OP & Kanwar AJ[7] where the ratio was 3:2 in favor of males. Silverman S Jr et al[11] and Brown RS et al[9] in their study observed an increased female predilection which is not in par with our study. Bhattacharya M et al[8] reported an equal predilection for both males and females.

When anxiety and depression scores were statistically analysed, a significant difference was obtained between the study group and control group. The test group showed significantly higher anxiety scores (9.538 ± 2.404) and depression scores (10.385 ± 2.061) when compared to anxiety scores (7.731 ± 1.151) and depression scores (9.115 ± 1.451) of the controls. Studies conducted by Hampf et al[12], Rojo MJ et al[13], Vallejo

MJ et al[14] and Sandhu et al[15] have concluded that significantly higher stress, anxiety and depression levels were observed in the OLP subjects when compared to the controls. In contrast to this, studies conducted by Allen et al[16] and Mc Cartan BE[17] found no statistically significant difference.

Stress alters the sympathetic and parasympathetic regulation of the autonomic nervous system, with alterations in hypothalamic control of the endocrine response which is controlled by the pituitary gland. Autonomic activation and hormone elevation plays a pivotal role in regulating immune surveillance mechanism and cytokine production that control inflammatory process.

We can elucidate that in lichen planus disease; there is a high activity of T cells, Langerhans cells, lymphocytes, and cyto-toxicities against epithelial cells. Therefore, any dysfunction in the HPA axis and increase blood & salivary cortisol cause diseases affecting the immune system like lichen planus.

Researchers have investigated numerous studies to determine the association between cortisol and stress and stress has been proposed as one of the causative and aggravating factors for the development of OLP lesions. In our study, serum samples were collected from OLP patients and healthy controls to estimate cortisol.

The mean serum cortisol analysis between test group and control group revealed a highly significant difference. Similar results were found by Prolo P et al[18] and Ivanoski K et al[19]. Prolo P et al found a significant alteration in the CD4/CD8 ratios. They suggest that altered CD4/CD8 ratios could be an effect of alterations in the serum cortisol levels. In our study, CD4/CD8 ratios were not considered but this could be the factor linking the altered serum cortisol levels with oral lichen planus.

Ivanoski K et al found higher levels of cortisol in patients with erosive OLP, but there was no difference in the values for the patients with reticular OLP compared to controls. In our study, the patients with OLP were not distributed into distinct groups according to clinical form of the lesions. This difference may have contributed to the contrasting results, suggesting that the psychological profile of the patient can play a more important role in the erosive-atrophic forms of the disease.

Very highly significant difference was shown in the mean serum cortisol level of OLP patients in the study conducted by Shetty S et al[20] which also coincided well with the present study.

Our results were contradictory with that of Seoane J et al[21] where they found no significant difference in the plasma cortisol levels between OLP patients & controls.

They concluded that cortisol did not have any influence on the neuro-endocrine system.

Several psychometric inventories have been administered to assess the psychological profile and also to determine the psychogenic casuality of OLP. Hospital anxiety and depression (HAD) scale which was used in the present study was developed by Snaith and Zigmond. This screening tool which comprises of quick and simple questionnaire consisted of 14 questions of which 7 reflected anxiety and 7 depression.[22]

Choudary S[23], Shetty S et al[20], Sandhu SV et al[15] also used HAD scale in their study to assess the anxiety and depression in OLP patients.

Ivanoski K et al[19] Studied the personality profiles of OLP patients using psychological Minnesota Multiphase Personality Inventory (MMPI) -202 test and they came to a conclusion that stress contribute to the initiation and the clinical expression of OLP.

Shah B et al[24] measured the psychosocial factors by the Depression Anxiety and Stress Scale (DASS). Significantly higher depression (83.4 ± 15.4%), anxiety (80.5 ± 11.3%), and stress (94.2 ± 6.2%) scores were observed in OLP patients and their results showed a positive correlation between psychological factors and salivary cortisol levels in OLP patients.

Hence in the present study there is a clear evidence of the psychological factors in the etiopathogenesis of this disease. The elevation in the serum cortisol levels and increased anxiety, depression scores among the study groups when compared to the control group is a clear indication of the stress factor in the etiology. As we have excluded systemic diseases like diabetes, hypertension, renal dysfunction, liver disorders and other oral mucosal diseases which may contribute to the initiation or progression of OLP, the increase in the serum cortisol levels are related to the stress which might be the possible causative agent resulting in the development of lesions in OLP.

CONCLUSION

After obtaining the data, the results were subjected to statistical analysis and the following conclusions were drawn from our study.

1. Serum cortisol levels were increased in patients with oral lichen planus with highly statistically significant difference when compared with controls.
2. The anxiety scores of OLP patients were high with a highly statistically significant difference when compared with that of the controls.

3. The depression scores of OLP patients were also high with a statistically significant difference when compared with the controls.

We would like to conclude that psychological factors play a role in the pathogenesis of OLP. Serum cortisol estimation could be a useful indicator in stressful conditions like in OLP disease.

Our results suggest that if a person is having high anxiety and depression scores and elevated levels of serum cortisol, he/she is at higher risk of developing oral lichen planus. Serum cortisol could be a useful indicator for screening the anxiety and stress from the multifaceted pathogenesis of OLP. A proper understanding of the pathogenesis of the disease becomes important for providing the right treatment. Stress management and counseling should be a part of management protocol of OLP which will help in reducing the cortisol levels.

REFERENCES

1. Scully C et al. Update on Oral lichen planus: etiopathogenesis and management. Crit Rev Oral Biol Med. 1998;9:86-122.
2. Chainani-Wu N, Silverman S Jr, Lozada-Nur F, Mayer P, Watson JJ. Oral lichen planus: patient profile, disease progression and treatment responses. J Am Dent Assoc. 2001;132:901–9.
3. Sugerman PB, Savage NW. Oral lichen planus: Causes, diagnosis and management. Australian Dental Journal 2002;47:290-7.
4. Nancy WB, Eileen JB, Jefferson B, Laurie W. Assessing the characteristics of patients with oral lichen planus. JADA. 1996;127: 648-62.
5. Miller CS, Dembo JB, Fallace DA, Kaplan AL. Salivary cortisol response to dental treatmnent of varying stress. Oral Surg Oral Med Oral Pathol Oral RadiolEndod. 1995;79:436-41.
6. Sylvie B, Camille F, Marie-Christine B, Henri S, Yves Le C. Immunohistochemical study of oral lesions of Lichen planus: Diagnostic and pathophysiologic aspects. Oral Surg Oral Med Oral Pathol. 1990;70:462-5.
7. Singh OP, Kanwar AJ. Lichen Planus in India: an appraisal of 441 cases. Int J Dermatol. 1976;15:752-56.
8. Bhattacharya M, Kaur I, Kumar B. Lichen planus: a clinical epidemiological study. J Dermatol. 2000;27:576-82.
9. Brown RS, Bottmley WY, Puente E, Lavigne GJ. A retrospective evaluation of 193 patients with oral lichen planus. J Oral Pathol Med. 1993;83:21-25.
10. Gorouhi F, Davari P, Fazel N. Cutaneous and Mucosal Lichen Planus: A Comprehensive Review of Clinical Subtypes, Risk Factors, Diagnosis, and Prognosis. The Scientific World Journal 2014;1-22.
11. Silverman SJ, Grosky M, Lozada-Nur F, Gianotti K. A prospective study of findings and management in 214 patients with oral lichen planus. Oral Surg Oral Med Oral Pathol. 1991;72:665-70.
12. Hampf BGC, Malmstrom MJ, Aalberg VA, Hannula JA, Vikkula J. Psychiatric disturbance in patients with oral lichen planus. Oral Surg Oral Med Oral Pathol. 1987;63:429-32.
13. Rojo MJ,Bagan JV, Rojo-Moreno J, Donat JS, Milian MA, Jimenez Y. Psycologic factors and oral lichen planus. A psychometric evaluation of 100 cases. Oral Surg Oral Med Oral Pathol Oral RadiolEndod. 1998;86:687-91.
14. Vallejo MJ, Huerta G, Cerero R, Seoane JM. Anxiety and depression as risk factors for oral lichen planus. J Dermatology. 2002;205:226-8.
15. Sandhu SV, Sandhu JS, Bansal H, Dua V. Oral lichen planus and stress: An appraisal. Contemp Clin Dent. 2014;5:352-6.
16. Allen CM, Beck FM, Rossie KM, Kaul TJ. Relation of stress and anxiety to oral lichen planus. Oral Surg Oral Med Oral Pathol. 1986;61:44-46.
17. McCartan BE. Psycological factors associated with oral lichen planus. J Oral Pathol Med. 1995;24:273-5.
18. Prolo P et al. Psychoneuroimmunology in oral biology and medicine-the model of oral lichen planus. Annals of the New York Academy of Sciences. 2002;966:429-40.
19. Ivanoski K et al. Psychological profile in oral lichen planus. J Clin Periodontola. 2005;32:1034-40.
20. Shetty S, Thomas P, Chatra L, Shenai P, Rao P, Babu S. An association between serum cortisol levels in erosive and non-erosive oral lichen planus patients. Webmed central dentistry. 2010;1:1-15.
21. Seoane J, Romero MA, Varela-Centelles P, Diz-Dios P, Garcia-Pola MJ. Oral Lichen Planus: A Clinical and Morphometric Study of Oral Lesions in Relation to Clinical Presentation. Braz Dent J. 2004;15:9-12.
22. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale: An updated literature review. Journal of Psychosomatic Research 2002;52:69–77.
23. Choudhary S. Psychosocial stressors in oral lichen planus. Aust Dent J. 2004;49:192-5.
24. Shah B, Ashok L, Sujatha GP. Evaluation of salivary cortisol and psychological factors in patients with oral lichen planus. Indian J Dent Res. 2009;20:288-92.