Clinical Cancer Investigation Journal-ISSN: 2278-0513

Examination of salivary cortisol levels in TMD patients sensitive to stress

Reza Korshidi khiavi[1], Vahid Baybourdi[2], Logman Ebrahimi[3], Xaniar Mohammadi Khaneqah[4], Mohammad hossein Asadi[5], Mojtaba Sheikhian[6], Mehran Rahbar[7], Ali Sharifi[8], Mehdi Dehghan[9]

1 Oromaxillofacial surgery department of Tabriz medical science university

/Dr_khorshidi@yahoo.com

2 Oromaxillofacial surgery Postgraduate student of Tabriz medical science university

/baybourdi@yahoo.com

3 Oromaxillofacial surgery student of Tabriz University Of Medical Sciences,

Iran/dr.ebrahimi65@yahoo.com

4 Oral and maxillofacial surgery resident at Tabriz University Of Medical Sciences,

Iran/ Xaniar.mkh@gmail.com

5 Postgraduate student of Tabriz University Of Medical Sciences, Iran/

mhasadi103@gmail.com

6 Postgraduate student of Oral and Maxillofacial Surgery, Department of Oral and

Maxillofacial surgery, Faculty of Dentistry, Tabriz university of medical sciences,

Tabriz, Iran/ Mojtaba9921@gmail.com

7 Postgraduate student of Oral and Maxillofacial Surgery, Department of Oral and

Maxillofacial surgery, Faculty of Dentistry, Tabriz university of medical sciences,

Tabriz, Iran/ mehranrahbar1374@gmail.com

8 Postgraduate student of Oral and Maxillofacial Surgery, Department of Oral and

Maxillofacial surgery, Faculty of Dentistry, Tabriz university of medical sciences,

Tabriz, Iran/ sharifiali357@gmail.com

9 Postgraduate student of Oral and Maxillofacial Surgery, Department of Oral and

Maxillofacial surgery, Faculty of Dentistry, Tabriz university of medical sciences,

Tabriz, Iran/ dehghanmahdi1997@yahoo.com

Abstract

After changing the cortisol level in the blood, the level of this hormone also changes in the saliva. The salivary level represents the free cortisol of the blood with active biological cortisol.
Cortisol, which is also known as stress hormone, is a determining index in stressful situations. In some stressful diseases, the level of cortisol increases. The biological and mental factors are effective for Temporomandibular (TMD) patients who are sensitive to the low level of cortisol. In this study, the salivary cortisol level of patients with TMD disorders and that of healthy people were compared with each other. This study is a kind of case-control observational study which was done in two groups of patients with TMD disorders referred to the surgery ward of the dental faculty of Tabriz University. The mean salivary cortisol level in healthy people was 8.89 ng/ml, while in patients with TMD was 29 ng/ml. The increase in cortisol can raise the risk of TMD.

Keywords: *cortisol, stress, TMD, Tabriz*

Introduction

Cortisol is a 21-carbon glucocorticoid (GC) that is constructed by the adrenal cortex and has high effects on metabolisms such as glycosides, proteins, and lipids [1]; Cortisol, termed a stress hormone, is considered a determinant index in stressful situations; and hypothalamus-pituitary-adrenal (HPA) axis is activated in response to the stress such that increase in the stress level can be the effect on the performance on this axis in

the long run and leads to the increase on the cortisol level in blood [3]. Saliva is an important factor in oral and dental health, which prevents dental caries [4]. After changing the cortisol level in the blood, the level of this hormone changes in the saliva, too. The salivary cortisol represents the free cortisol of the blood with active biological cortisol [5]. In recent years, the use of saliva has had a great deal of attraction due to its simple gathering of blood [6]. Of course, to ensure a high-value study, standard and irritational methods should be used [7]. Cortisol (hydrocortisone), named the stress hormone, is applied as the index for measuring and assessing the level of stress. The cortisol hormone plays the main role in internal metabolism and the mental defense mechanisms of a person. The level of the cortisol hormone increases in some stressful diseases. The salivary cortisol level is a trustful criterion for presenting the level of cortisol in the blood (serum). If it raises indirectly in the saliva, it represents its increase in the blood; so, in practical studies, its measurement is easier and more practical than the cortisol measurement of the blood. The salivary cortisol represents the stress position of the person better than the serum cortisol due to having the higher banded proteins [8]. The most important effects of cortisol in the body include a decrease in glucose used in the cells, acceleration in releasing amino acids and lipids from the cells in stressful and inflammatory situations, and inflammatory response inhibition in allergic reactions [4]. The secretion of cortisol induced by the 24-hour circulations is dependent on the hypotatlmose messages and adrenocorticotropic hormone (ACTH) secretion so that the highest level of this hormone secretion occurs in the morning and the lowest in the night. The factors controlling this 24- hour circulation have not been completely known [9]. This circulation is matured in the early fetal period, influenced by some physical or mental factors, and the regulation is possibly disturbed [10]. On the other side, the TMD joint disorder or TMD syndrome is the most common cause of pain after toothache in the face. The American Academy of Orofacial Pain (AAOP) has defined two groups for these kinds of disorders as follows:

1. Myogenous TMD is occasionally identified as secondary TMD to myofascial pain.
2. Atherogenic TMD which is occurred due to secondary joint disease.

The sexual concerns of TMD in women are more than in men (with a male-to-female ratio of 1-to-4). This disease usually occurs in 20-40 years old [11].

Some of the TMD symptoms (TMD disorder) are experienced between 65 and 85 percent of people in the US, and almost 12% have tolerated longer pains and disability, which are its chronic symptoms.

The existing research methods still cannot accurately distinguish a person with TMD from a non-affected person. The best method for assessing patients is history collection and physical examination. Most of the experiments used for examining the TMD are not approved due to the validation and standardization, and so far, an optimal method for the classification of these disorders has not been known. The identification tests such as ultrasonography of joint sounds, thermography (thermal), the devices for creating a groove in the jaw, and electrical thermography (electron tomography) do not offer more accurate assessing methods. One reliable and applied classification of patients with TMD, which is based on the behavioral, mental, and social factors consists of three subgroups of patients: (1) the patients who do not have practical efficacy, (2) the patients who tolerate personal pressures, and (3) the patients who have adaptional disorders. The TMD disorders are not the only ones that are related to behavioral, methal, and social factors, and patients with backache are also similar to TMD ones. Directional pains and dental pressures, which are such chronic pains in TMD disease, have the same importance. The mental and social assessment should cause the examiner to know which pain and inefficiency have reduced the quality of people's life. This assessment should introduce more investigations and possible treatments with the help of psychologists and psychiatrists to the patients. In addition, evaluating the intensity of pain and emotional situations as well as assessing the constraint level of the activity can reflect a range of existing disorders. An underlying method is necessary to evaluate mental patients because a dentist cannot act accurately to identify the mental issues of TMD patients. The research diagnostic criteria (RDC)/TMD system uses a relatively complete questionnaire for this classification, which has been designed using the scales already taken to evaluate the pain intensity, disability, depression, and other non-specific physical symptoms. The salivary cortisol level and its assessment efficiency have been emphasized in several studies. Vedhara et al. reported that the measurement of the salivary cortisol level relative to the cortisol measurement has higher benefits in the serum or plasma of people suffering from stress and anxiety, as salivary sampling is cheaper and non-invasive and done more convenient in children and babies [12]. A study of the psychological and endocrine differences of TMD patients compared with healthies reported that the salivary cortisol levels in these patients are not different from healthies [13]. In another study that, the salivary cortisol level in TMD patients examined after malocclusion treatment, the researchers concluded unlike successful TMD treatment, the salivary cortisol level has not been altered. Jhons et al. explored the salivary cortisol in TMD patients with mental stress. The results showed that there is a dual relationship between TMD and stress response. First that TMD can occur as a response to stress. The second is that the biological and mental factors are

more effective for TMD patients who are sensitive to stress and have low cortisol. According to this that the studies around the relationship between salivary cortisol and Temporomandibular Joint (TMJ) issues are spread, and regarding this, there is not an identified study in the country; we tried to compare the salivary cortisol level in patients with TMD with healthy people. If the salivary cortisol level in people affected by TMD is different from healthies, it can be effective for identifying the disease and determining the recovery course after treatment.

Methodology

This study is a kind of case-control observational study which was done in two groups of patients with TMD disorders and healthy people.

The target population was all patients with TMD disorders referred to the surgery ward of the dental faculty at Tabriz University. To determine the sample size, the Power & sample size software was used. The number of samples was evaluated at 17 according to the $\alpha = 0.05$, power of 80%, and standard deviation of 0.5 (based on Jhons's study). To increase the study validation, 40 samples were considered in total for each of the groups.

The studied patients are selected randomly from those referring to the surgery ward of Tabriz dental faculty. The inclusion criteria include having content with participation in the patients' study with TMD as well as with oral or systemic disease (rheumatological diseases - disorders in the adrenal glands). Those who were not content with participation were excluded.

To measure the people's salivary cortisol to avoid from circadian effect, the sample was gathered in hours between 9-11 in the morning; and participants were asked to keep at least 2 hours between eating, drinking, and brushing their teeth. The first 1-minute salivary sample was discarded, and the 5-minute samples were gathered. The studied person was asked to bend his/her head forward while his/her eyes are open, keep his/her tongue and lips fixed and allow the saliva to flow through the lower lip into the sample collection container. The saliva was gathered in the plastic lab container and conveyed to the laboratory after sampling for a maximum of 2 hours.

The saliva collection was performed based on the spitting method [16]. The sample was conveyed to the laboratory, and the cortisol level was measured.

Results

Table 1. The frequency of women and men in patients suffering from TMD diseases and healthies.

			Group		Total
			Healthy	**Patient**	
Gender	**Woman**	Number	13	9	22
		Percent	50.0%	60.0%	53.7%
	Man	Number	13	6	19
		Percent	50.0%	40.0%	46.3%
Total		Number	26	15	41
		Percent	100.0%	100.0%	100.0%

According to table 1, Among 41 testing people, 26 were healthy, and 17 with TMD disorders. In the healthy group, 50% were women and 50% men, and in the patient one, 60% were women and 40% men.

Table 2. Comparison of the people's age in two healthy and patient groups.

	Number	Mean	StD.	The lowest	The highest	**Mann-Whitney U**	
						Z value	P value
Healthy	26	39.69	7.998	22.00	53.00	-4.611	.000
Patient	15	32.40	5.973	21.00	42.00		

As shown in Table 2, the mean age in the healthy group is 39, which alters from a minimum of 22 to a maximum of 53. The mean age in the patient group alters from a minimum of 21 to a maximum of 42.

Determining the salivary cortisol level in the patients with TMD

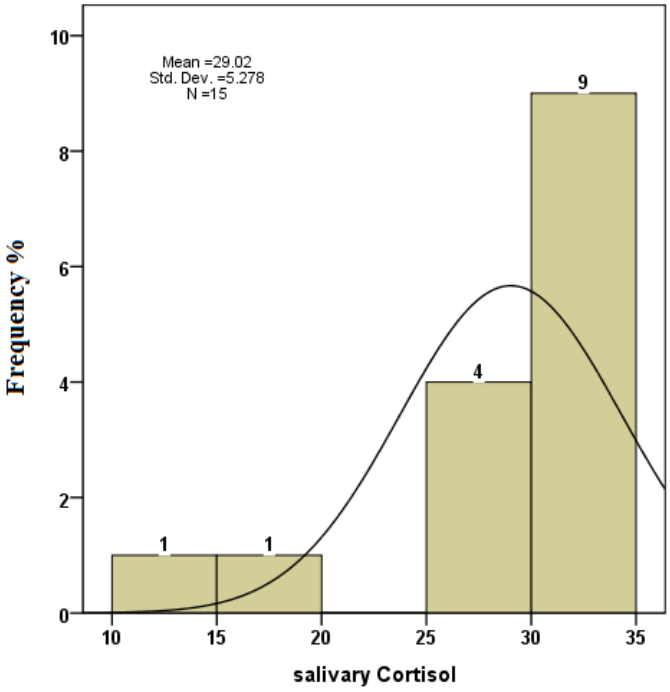

Figure 1. The distribution of the salivary cortisol level in the patient group

.

Determining the salivary cortisol level in the healthy people

Based on the results of Figure 1, the mean salivary cortisol of people in the patient group is 29, which alters from a minimum of 14.02 ng/ml to a maximum of 33.1 ng/ml.

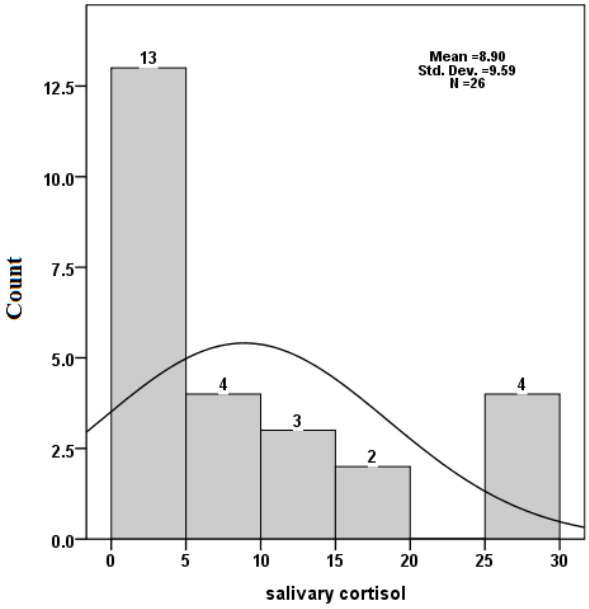

Figure 2. The distribution of the salivary cortisol level in the healthy group.

As seen in Figure 2, the mean salivary cortisol of people in the healthy group is 8.89, which alters from a minimum of 0.68 ng/ml to a maximum of 28.8 ng/ml.

Comparing the salivary cortisol level in people with TMD

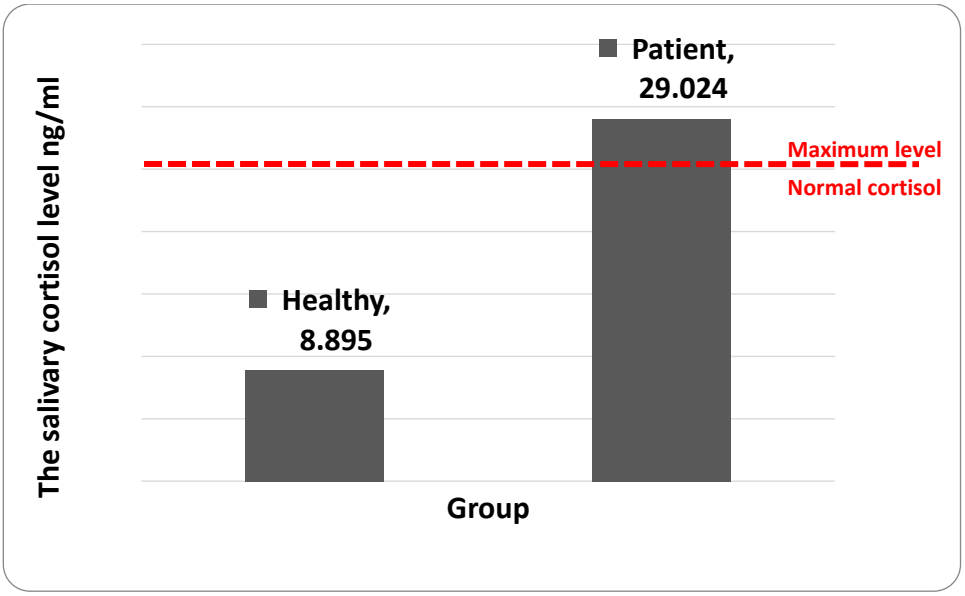

Figure 3. Comparing the salivary cortisol level of the healthy group with the patient one.

Based on the results of Figure 3, the salivary cortisol level of the healthy group is 8.89 ng/ml, and of the patient group, 29.02 ng/ml; according to the Mann-Whitney test, there is a meaningful difference between the cortisol level of the two groups. So, the salivary cortisol level of patients with TMD has more significance than the healthiest.

Discussion

There are several reports associated with the relationship and intervention of mental factors with special diseases such as TMD, which have been expressed by different tests [16]. In this regard, also, there are various studies done on the relationship between anxiety and stress with diseases such as TMD [17]. But no study has explored the cortisol level and its effects on TMD disease.

As mentioned before, salivary cortisol is considered a representation of systemic cortisol [18]. So, this study has found a relationship with examining the salivary cortisol in TMD patients to be able to act better on medical programming around TMD disease.

According to this study, 60% of patients are women, and 40% are men. It can be said that women are more affected by TMD than men; related women have higher stress than men. This is the same result acquired from Ebrahimi et al.'s study [19].

The mean salivary cortisol level in healthy people is 8.89 ng/ml, while in people with TMD is about 29 ng/ml. Based on the results of the Mann-Whitney U test, this difference is meaningful. As a result, it can be said that salivary cortisol can be a creating factor in TMD. Because based on the different studies, the increase in salivary cortisol is related to various diseases in targeted people [20]. These diseases can be referred to as oral lichen planus [21].

Even though it can not be said accurately that the increase in cortisol does create TMD directly, it can assert that the increase of systemic cortisol can be a prone factor for TMD. This issue becomes important when we know that people with high salivary cortisol suffer from mental stress, which has been confirmed by different studies [22, 23].

Also, the majority of researchers know cortisol as a preventing factor for regenerating body tissues [51-55]. So, it can be explained that the increase in salivary cortisol detects the increase in systemic cortisol, creates a delay in regenerating traumas entering the TMJ, and subsequently increases the possibility that the people are affected by TMD.

As seen in this study that salivary cortisol has a direct relationship with TMF, but this issue requires more investigation to be approved as the main principle.

Unfortunately, there is no organized study around this issue; hoping that this research, in the future, opens doors for beginning broader studies around this problem and finds the main reasons for TMD.

Conclusion

Based on the acquired results of this study, it is concluded that the increase in cortisol can increase the risk of TMD.

Acknowledgments: None
Conflict of interest: None
Financial support: None
Ethics statement: None

References

1. de Weerth C, Zijl RH, Buitelaar JK. Development of cortisol circadian rhythm in infancy. *Early human development.* Aug 2003;73(1-2):39-52.

2. Gorges R, Knappe G, Gerl H, Ventz M, Stahl F. Diagnosis of Cushing's syndrome: re-evaluation of midnight plasma cortisol vs urinary free cortisol and low-dose dexamethasone suppression test in a large patient group. *Journal of endocrinological investigation.* Apr 1999;22(4):241-249.
3. Husband AJ, Brandon MR, Lascelles AK. The effect of corticosteroids on absorption and endogenous production of immunoglobulins in calves. *The Australian Journal of experimental biology and medical science.* Oct 1973;51(5):707-710.
4. Lagerlof F. [Saliva: natural protection against caries]. *Revue belge de medecine dentaire.* 1998;53(1):337-348.
5. Golf SW, Bender S, Gruttner J. On the significance of magnesium in extreme physical stress. *Cardiovascular drugs and therapy / sponsored by the International Society of Cardiovascular Pharmacotherapy.* Sep 1998;12 Suppl 2:197-202.
6. Trifonova ST, Gantenbein M, Turner JD, Muller CP. The use of saliva for assessment of cortisol pulsatile secretion by deconvolution analysis. *Psychoneuroendocrinology.* Dec 13, 2012.
7. Vining RF, McGinley RA, Maksvytis JJ, Ho KY. Salivary cortisol: a better measure of adrenal cortical function than serum cortisol. *Annals of clinical biochemistry.* Nov 1983;20 (Pt 6):329-335.
8. Clements AD. Salivary cortisol measurement in developmental research: Where do we go from here? *Developmental Psychobiology.* Apr 4, 2012.
9. Tai YH, Decker RA, Marnane WG, Charney AN, Donowitz M. Effects of methylprednisolone on electrolyte transport by in vitro rat ileum. *The American journal of physiology.* May 1981;240(5): G365-370.
10. Barger AC, Berlin RD, Tulenko JF. Infusion of aldosterone, 9-alpha-fluorohydrocortisone, and antidiuretic hormone into the renal artery of normal and adrenalectomized, unanesthetized dogs: effect on electrolyte and water excretion. *Endocrinology.* Jun 1958;62(6):804-815.
11. Seligman DA, Pullinger AG. Dental attrition models predicting temporomandibular joint disease or masticatory muscle pain versus asymptomatic controls. *Journal of oral rehabilitation.* Nov 2006;33(11):789-799.
12. Vedhara K, Tuinstra J, Miles JN, Sanderman R, Ranchor AV. Psychosocial factors associated with indices of cortisol production in women with breast cancer and controls. *Psychoneuroendocrinology.* Apr 2006;31(3):299-311.
13. Ortega AO, Guimaraes AS, Ciamponi AL, Marie SK. Frequency of temporomandibular disorder signs in individuals with cerebral palsy. *Journal of oral rehabilitation.* Mar 2008;35(3):191-195.
14. Irving J, Wood GD, Hackett AF. Does temporomandibular disorder pain dysfunction syndrome affect dietary intake? *Dental update.* Nov 1999;26(9):405-407.
15. Ferrari R, Schrader H, Obelieniene D. Prevalence of temporomandibular disorders associated with whiplash injury in Lithuania. *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics.* Jun 1999;87(6):653-657.
16. Rollman A, Visscher CM, Gorter RC, Naeije M. Improvement in patients with a TMD-pain report. A 6-month follow-up study. *Journal of oral rehabilitation.* Jan 2013;40(1):5-14.
17. Yamaguchi T, Shioji I, Sugimoto A, Yamaoka M. Psychological stress increases bilirubin metabolites in human urine. *Biochemical and biophysical research communications.* Apr 26 2002;293(1):517-520.
18. Greenberg MS, Glick M. *Burket's oral medicine diagnosis and treatment 11th ed*2008.
19. Ebrahimi M, Dashti H, Mehrabkhani M, Arghavani M, Daneshvar-Mozafari A. Temporomandibular Disorders and Related Factors in a Group of Iranian Adolescents: A Cross-sectional Survey. *Journal of dental research, dental clinics, dental prospects.* Fall 2011;5(4):123-127.
20. van Holland BJ, Frings-Dresen MH, Sluiter JK. Measuring short-term and long-term physiological stress effects by cortisol reactivity in saliva and hair. *International archives of occupational and environmental health.* Nov 2012;85(8):849-852.
21. Girardi C, Luz C, Cherubini K, de Figueiredo MA, Nunes ML, Salum FG. Salivary cortisol and dehydroepiandrosterone (DHEA) levels, psychological factors in patients with oral lichen planus. *Archives of oral biology.* Sep 2011;56(9):864-868.
22. Tlili C, Myung NV, Shetty V, Mulchandani A. Label-free, chemiresistor immunosensor for stress biomarker cortisol in saliva. *Biosensors & bioelectronics.* Jul 15 2011;26(11):4382-4386.
23. Rydstedt LW, Cropley M, Devereux J. Long-term impact of role stress and cognitive rumination upon morning and evening saliva cortisol secretion. *Ergonomics.* May 2011;54(5):430-435.