ORIGINAL ARTICLE

Saliva cortisol levels and depression in individuals with temporomandibular disorder: preliminary study*

Níveis de cortisol salivar e depressão em indivíduos com disfunção temporomandibular: estudo preliminar

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DOI 10.5935/1806-0013.20140037

ABSTRACT

BACKGROUND AND OBJECTIVES: Temporomandibular disorders are common in general population and their etiology is also linked to psychological factors. Cortisol is a hormone the secretion of which may be increased during emotional changes. This study aimed at evaluating the presence of depression and saliva cortisol levels in patients with temporomandibular disorders.
METHODS: Participated in the research 48 students, being 36 females and 12 males, aged between 19 and 32 years. Participants were previously evaluated by means of the Research Diagnostic Criteria for Temporomandibular Disorders questionnaire and were classified in two groups: with temporomandibular disorders and without temporomandibular disorders. To establish the presence of depression the Symptom Checklist 90 – Revised test was applied. Saliva was collected between 9:00 a.m. and 9:25 a.m. and saliva cortisol levels were analyzed by spectrophotometry.
RESULTS: The Symptom Checklist 90 – Revised has suggested that 64% of patients with temporomandibular disorder were depressed as compared to 43% of individuals without temporomandibular disorder. Saliva cortisol level was 0.272µg/dL for the temporomandibular disorder group and of 0,395µg/dL for the group without temporomandibular disorder, with no statistical difference.
CONCLUSION: Within the limits of the study, it was possible to conclude that there is no association among saliva cortisol levels, depression and the presence of temporomandibular disorders.
Keywords: Hydrocortisone, Saliva, Temporomandibular joint.

RESUMO

JUSTIFICATIVA E OBJETIVOS: As disfunções temporomandibulares são comuns na população em geral e sua etiologia também se apresenta ligada a fatores psicológicos. O cortisol é um hormônio cuja secreção pode apresentar-se aumentada diante de alterações emocionais. O objetivo deste estudo foi avaliar a presença de depressão e os níveis salivares de cortisol em pacientes com disfunções temporomandibulares.
MÉTODOS: Participaram desta pesquisa 48 alunos, sendo 36 mulheres e 12 homens, com idades entre 19 e 32 anos. Os participantes foram previamente avaliados por meio do questionário *Research Diagnostic Criteria for Temporomandibular Disorders* e foram classificados em dois grupos: com disfunções temporomandibulares e sem disfunções temporomandibulares. Para determinar a presença de depressão foi utilizado o teste *Symptom Checklist 90 – Revised*. A coleta da saliva foi realizada entre as 9h00 e 9h25 da manhã e os niveis de cortisol salivar analisados mediante espectrofotometria.
RESULTADOS: A escala *Symptom Checklist 90 - Revised* sugeriu que 64% dos pacientes com disfunções temporomandibulares apresentaram-se deprimidos em comparação com 43% dos indivíduos do grupo sem disfunção temporomandibular. O nível de cortisol salivar foi de 0,272µg/dL para o grupo com disfunções temporomandibulares e de 0,395µg/dL para o grupo sem disfunção temporomandibular não havendo diferença estatística.
CONCLUSÃO: Dentro dos limites do estudo, pode-se concluir que não há associação entre os níveis de cortisol salivar, depressão e a presença de disfunções temporomandibulares.
Descritores: Articulação temporomandibular, Hidrocortisona, Saliva.

INTRODUCTION

Temporomandibular disorders (TMD) are characterized by alterations in jaw kinesiology, joint sounds and pain in stomatognatic system structures. TMD-induced pain is in general fluctuating and progressive[1], is present in approximately 10% of the population above 28 years of age and is most common among females[2]. TMD is known by its multifactorial etiology. Social, pathophysiological and psychological factors act alone or simul-

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Submitted in July 19, 2013.
Accepted for publication in July 28, 2014.
Conflict of interests: none.

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taneously to allow the establishment of such condition[3].

The hypothalamic-pituitary-adrenal axis (HPA) is the major respondent to stress and is critical for the maintenance of basal stress-induced homeostasis. Cortisol, final HPA axis product, is the major circulating glucocorticoid hormone and its release by the adrenal gland is stimulated by the hypophysis through the adrenocorticotropic hormone (ACTH). ACTH production is modulated by the hypothalamus through the secretion of corticotropin releasing hormone (CRH)[4].

Stress, depression and behavioral diseases are critical aspects observed in TMD patients, who frequently report stress and chronic or acute pain interfering with their daily activities[5]. It is possible that high cortisol levels in TMD patients represent a physiological response to chronic stress, being pain a potential stressor agent because it induces chronic increase of CRH or other central HPA axis mediators[4].

It has been suggested that depression is associated to TMD symptoms, especially when there is pain[6]. HPA axis hyperactivity during major depression is one of the most consistent psychiatric findings. A significant percentage of patients with major depression have increased plasma, urine and liquor cortisol concentrations; exaggerated cortisol response after stimulation with ACTH; and increase both of pituitary and adrenal glands, which may be considered a marker of excessive HPA axis activation[7].

It has been shown that saliva cortisol is a valid indicator for its serum concentrations[8].

Several studies have reported the presence of emotional alterations in individuals with TMD[9], which may change the HPA axis[5,10].

Since psychological symptoms, such as stress and depression, are common in TMD patients[5,10,11] and such symptoms increase cortisol secretion, our study aimed at evaluating saliva cortisol levels and depression in TMD patients.

METHODS

Students of the third year of the Dentistry School, Tuiuti University of Paraná, Curitiba, were invited to participate in the research. Sample was made up of 48 students, of whom 36 were females and 12 males, aged between 19 and 32 years. All were healthy, without systemic changes and not under any medication for emotional disorders.

Participants were previously evaluated through the validated questionnaire for TMD research and diagnosis, Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD), which enabled the establishment of TMD patterns and the classification of individuals as group without TMD and group with TMD. All participants were evaluated within the axis II by the Symptom Checklist 90 – Revised (SCL-90-R) to check negative affective dimensions, such as depression, commonly associated to pain experiences.

Saliva was collected from all participants in the same day, between 9:00 and 9:25 a.m. The Salivette kit (Salivette®, Sarstedt, Germany) was used according to manufacturer's instructions. After collection, the device was centrifuged at 1000xg for 2 minutes and saliva obtained from this process was frozen at -15º C until analysis.

Saliva analysis

Samples of both groups were thawn and centrifuged at 1500xg for 5 minutes in a CELM/COMBATE centrifuge (CELM - Cia. Equipadora de Laboratórios Modernos, São Paulo, Brazil) to separate saliva proteins precipitate from supernatant fluid. Then, saliva (supernatant fluid) was aspired and stored in duly identified 1.5 mL microtubes (Eppendorf do Brasil, São Paulo, Brazil). Saliva cortisol was evaluated by double spectrophotometry using specific kit for saliva cortisol (Salimetrics LLC, State College, Pennsylvania) according to manufacturer's instructions.

First, a standard curve was performed with known cortisol concentrations. Then, 25µL of each sample were aspired and transferred to a microplaque together with equal rates of working reagents supplied with the kit. After sample addition, color was analyzed by microplaque reading in spectrophotometer (Biotek Instruments Inc., Vermont, USA) at wavelength of 450nm. Results were expressed in µg/dL.

Statistical analysis

Data were tabulated and submitted to T test for comparison between groups, with the aid of the software Statistical Package for Social Science – SPSS 17.0 (IBM, Chicago, IL). Significance level to show differences between groups was $p<0.05$.

This study was approved by the Research Ethics Committee of the institution (CEP-UTP: 91/2003). All participants have signed the Free and Informed Consent Term (FICT).

RESULTS

From 48 participants, 25 had TMD with pain for at least 10 months, being three males and 22 females with mean age of 21.8 years. According to RDC/TMD, six individuals had muscle impairment, nine had joint impairment and 10 had muscle and joint impairment. The group without TMD was made up of 23 participants, being nine males and 14 females with mean age of 21.26 years.

SLC-90R scale has shown that 64% of participants with TMD had depression as compared to 43% of individuals without TMD. SLC-90-R scale scores for each group are shown in table 1.

Table 1. Comparison of age, presence of depression, saliva cortisol level and Symptom Checklist 90 – Revised value between groups with and without temporomandibular disorders

Variables	With TMD (n=25)	Without TMD (n=23)	p value
Age (years)	21.80 (2.98)	21.26 (1.54)	0.442
Depression (n)			
No	9 (36%)	13 (57%)	0.246
Yes	16 (64%)	10 (43%)	
Cortisol (µg/dL)	0.272 (0.20)	0.395 (0.33)	0.121
SCL–R90 (value)	0.97 (0.76)	0.71 (0.72)	0.240

Saliva cortisol level has varied from 0.1 to 1.0μg/dL for the TMD group and from 0.1 to 1.4μg/dL for the group without TMD. TMD group had lower means as compared to the group without TMD (Table 1). However, results have shown no difference between groups.

DISCUSSION

Painful TMDs may change the HPA axis due to the presence of pain. Depression and anxiety symptoms may reflect a clinical manifestation of painful TMDs[12] affecting body alarm system as result of changes in HPA axis regulation[13], which would result in changes in cortisol hormone secretion. For this reason, saliva cortisol and depression levels were evaluated in individuals with TMD. The relationship between depression or anxiety symptoms and increased risk for the presence of pain in TMDs may be due to at least two reasons. First, depression and anxiety symptoms may trigger muscle hyperactivity followed by muscle abnormality and pain[14]. They may also start a joint inflammation process followed by biomechanical changes which may induce joint pain. Second, TMD may be related to an abnormal trigeminal system process caused by imbalances in common neurotransmitters, such as serotonin and catecholamines[15].

We decided for dosing saliva cortisol and not serum cortisol for being a noninvasive process which provides adrenal glucocorticoiod activity results as reliable as those from free plasma cortisol dosage[16-18]. Investigation was performed only in the morning, when the Circadian rhythm of glucocorticoid hormones secretion is higher[19]. As to collection time, this was based on a study[20] which mentions higher cortisol levels between 6:00 and 9:50 a.m.

Participants of the study were recruited by counseling and not by spontaneous search for treatment. No TMD subjects had high pain or depression values to cause a functional obstacle to their normal daily activities, factor which may justify low cortisol levels found in the TMD group.

On the other hand, cortisol hyposecretion may occur in pain disorders such as fibromyalgia which has many aspects similar to TMDs[21,22]. Authors[22] have observed decreased cortisol response in patients with fibromyalgia, even with normal ACTH response. There might be similarities between neuroendocrine factors responsible for low cortisol levels both in individuals with TMD and fibromyalgia, due to abnormalities involving serotonin, growth hormone, endogenous opioids and adrenocortical function[21].

Studies have reported increased cortisol levels for TMD patients. One of such studies[23] has evaluated the level of saliva cortisol between TMD patients and a control group after an experimental stress test and the filling of the Trier Social Stress Test (TSST) and has observed that after the stressing stimulation there has been significant increase of saliva cortisol levels in the TMD group, which has remained high even after a long period of time, as compared to the control group. Another study[20] has shown that patients with TMD related to muscle problems had higher cortisol levels, from 30 to 50%, as compared to the control group. Differences regarding present results may be due to the characteristics of each study.

Cortisol levels at 10-minute intervals during 24 hours were evaluated[20] and it was observed that they were higher both for TMD people and control group using oral contraceptives. It is believed that oral contraceptives act on cortisol binding levels to globulins. However, in our study, we have not considered the use of contraceptives during data collection, but female participants belong to an age group commonly using them. It is also known that cortisol regulation is extremely complex and is still not known in details, but acute stress may increase cortisol levels while chronic stress may lower them[24].

TMDs are frequently present in co-morbidity with depression. In our study, 64% of TMD patients had depression, result which is similar to other study[25] which has found 60% of depression in the TMD group. However, according to our results, depression does not seem to contribute for the increase of cortisol levels because although there has been more depression in the TMD group as compared to the group without TMD, there has been no correspondence for cortisol levels, result also found by other studies[20,23,26,27]. It has also to be considered that cortisol secretion pattern of TMD patients is different from the secretion pattern of patients with depression, which in general is more activated at the end of the day, at dawn[27].

For being a preliminary study, the sample was small, made up by convenience, and so TMDs were not considered in terms of muscle, joint or muscle/joint classification. However, there are studies evaluating the relationship between pain location and behavioral profile disorders, having observed that myogenic TMD patients in general report more psychological problems as compared to those with diagnosis of intracapsular problems or controls[28,29]. It would be important that future studies relate cortisol levels, depression and different TMD types.

Studies relating HPA axis, TMD and orofacial pain are not numerous. In addition, there is diversity of results. So, further studies are needed to conclude, in a clear and concise way, whether there is influence of glucocorticoid hormones on TMD.

CONCLUSION

Within the limits or this study, there has been no relationship between saliva cortisol, TMD and depression. The hypothesis that TMD patients would have higher cortisol concentrations due to higher stress and the suggestion that the high level of glucocorticoid hormones would justify the presence of depressive symptoms in these patients were not supported.

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