The effect of conscious sedation on salivary alpha-amylase levels during third molar surgery

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ABSTRACT

Aim: The aim of the present study was to investigate whether salivary alpha-amylase levels could be decreased by conscious sedation in the patients undergoing impacted third molar extraction.

Material and methods: A total of 18 male patients were recruited. All patients were administered the Modified Dental Anxiety Scale test. Patients were divided into a test group (procedures under sedation) and a control group (procedures under local anesthesia). Systolic blood pressure, diastolic blood pressure, oxygen saturation, and heart rate were monitored at different study time-points. Five samples of saliva were taken from each patient: the first time the patient came to the clinic, the patient sat in the chair for extraction, before local anesthesia, immediately after extraction, at 4 h after extraction.

Results: Although no statistically important difference was found for systolic blood pressure (p>0.05) between groups, postoperative diastolic blood pressure level of control group was statistically higher than the test group (p=0.030). Also, a statistically significant decrease was found in the oxygen saturation level in postoperative time compared to preoperative time (p<0.05).

Conclusion: Even though conscious sedation may be a solution for dental anxiety and phobia, our results indicated that sedation did not affect acute stress levels during oral surgery.

Key words: conscious sedation, dental anxiety, stress biomarkers, salivary alpha-amylase, tooth extraction

ҮШІНШІ АЗУ ТІСТІ АЛЫП ТАСТАҒАНДА САНАНЫҢ САҚТАЛУЫМЕН СЕДАЦИЯНЫҢ СІЛЕКЕЙ БЕЗДЕРІНІҢ АЛЬФА-АМИЛАЗА ДЕҢГЕЙІНЕ ӘСЕРІ

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ТҰЖЫРЫМДАМА

Мақсаты: Зерттеудің мақсаты ретинолярлық үшінші азу тісі алып тасталған пациенттерде есін сақтай отырып, седациядан кейін альфа-амилаза сілекей безінің азаюы мүмкін екендігін зерттеу болды.

Материалдар мен әдістер: Барлығы 18 ер адам іріктелді. Барлық пациенттер өзгертілген стоматологиялық процедураның қорқыныш шкаласы бойынша тексеруден өтті. Науқастар тәжірибелік топқа (седативті процедура) және бақылау тобына (жергілікті анестезиядағы процедура) бөлінді. Систолалық қан қысымы, диастолалық қан қысымы, оттегінің қанығуы, жүрек соғу жылдамдығы зерттеу уақытының әртүрлі нүктелерінде бақыланды. Әр пациенттен сілекейдің бес үлгісі алынды: пациент клиникаға келді, науқас алып тастау үшін орындыққа отырды, локальды анестезия алдында, шығарғаннан кейін, шығарылғаннан кейін 4 сағаттан кейін.

Нәтижелер: Топтар арасында систолалық қан қысымында статистикалық маңызды айырмашылық жоқ (p>0.05), бақылау тобындағы операциядан кейінгі диастолалық қысым деңгейі эксперименттік топқа қарағанда жоғары (p=0.030). Сонымен қатар, операциядан кейінгі уақытпен салыстырғанда оттегінің қанығу деңгейінің статистикалық тұрғыдан төмендегені анықталды (p<0.05).

Қорытынды: саналы седация стоматологиялық процедурадан қорқудың шешімі бола алатынына қарамастан, біздің нәтижелеріміз стоматологиялық операция кезінде өткір стресс деңгейіне әсер етпегенін көрсетті.

Негізгі сөздер: сақталған санамен седация, стоматологиялық процедуралардан қорқу, стресс биомаркерлері, сілекей безі альфа-амилаза, тіс жұлу

ВЛИЯНИЕ СЕДАЦИИ ПРИ СОХРАНЕННОМ СОЗНАНИИ НА УРОВЕНЬ АЛЬФА-АМИЛАЗЫ СЛЮННЫХ ЖЕЛЕЗ ВО ВРЕМЯ УДАЛЕНИЯ ТРЕТЬЕГО МОЛЯРА

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РЕЗЮМЕ

Цель: Целью настоящего исследования было изучить, может ли уровень альфа-амилазы слюнных желез снизиться после седации при сохраненном сознании у пациентов, подвергшихся удалению ретинированного третьего моляра.

Материалы и методы: Всего было отобрано 18 пациентов мужского пола. Все пациенты прошли тест модифицированной шкалы боязни стоматологической процедуры. Пациенты были разделены на экспериментальную группу (процедура под седацией) и контрольную группу (процедура под местной анестезией). Систолическое артериальное давление, диастолическое артериальное давление, насыщение кислородом и частота сердечных сокращений контролировались в разные моменты времени исследования. У каждого пациента было взято пять образцов слюны: пациент пришел в клинику, пациент сидел в кресле для удаления, перед местной анестезией, сразу после удаления, через 4 часа после удаления.

Результаты: Несмотря на то, что статистически значимого различия в отношении систолического артериального давления (p>0,05) между группами обнаружено не было, уровень послеоперационного диастолического артериального давления в контрольной группе был статистически выше, чем в экспериментальной группе (p=0.030). Кроме того, обнаружено статистически значимое снижение уровня насыщения кислородом в послеоперационное время по сравнению с предоперационным временем (p<0.05).

Заключение: Хотя сознательная седация может быть решением для боязни стоматологической процедуры, наши результаты показали, что она не повлияла на уровень острого стресса во время стоматологической операции.

Ключевые слова: седация при сохраненном сознании, боязнь стоматологической процедуры, биомаркеры стресса, альфа-амилаза слюнных желез, удаление зуба

Introduction

Dental treatments which are probably a reliable cause of stress, are often considered anxiety-producing and stressful events [1-3]. Dental anxiety has been registered with a prevalence of between 3% and 20% of the population [4]. The ability to perceive and cope with stress may vary according to genetics [5] gender and age [6]. Exogenous female hormones reveal estrogens to display an exacerbation effect in response to acute stress [7]. In oral and maxillofacial surgery, surgical extraction of impacted third molars is one of the most common surgical techniques performed in the oral cavity. Several factors such as complexity and duration of the surgery, the surgeon's technique, iatrogenic factors, can disturb patient comfort. These factors should be minimalized to increase satisfaction with the treatment, improve the quality of life and reduce the fear of surgical interventions [8]. Conscious intravenous sedation could be administered for the patients to provide anxiolysis, sedation, and analgesia for the patient.

Human saliva is a biological fluid with important diagnostic potential. As it can be collected non-invasively, it presents a viable alternative to blood, serum, or plasma [9-14]. Various proteins [15], hormones [16], antibodies [17], drugs [18], and cytokines [19] those were diffused from the blood are found in human saliva, so many compounds found in the blood are also transferred into saliva. Many of these arrays of proteins are useful for the detection and treatment of diseases [9]. As it suggests the composition of saliva can be influenced by systemic changes, specific biomarkers could help recognize certain pathologic conditions [16]. Recent studies have leaded how contains of saliva can aid in the diagnosis of cardiovascular disease, inflammation, hepatic damage, autoimmune disease, and insulin resistance [15, 20-23].

Salivary alpha-amylase (sAA) which reflect stress-related changes in the autonomic nervous system (ANS), has been proposed as a non-invasive stress biomarker which produced by the parotid, submandibular and sublingual glands [24]. Unlike most diagnostically important salivary substances, sAA that displays distinct diurnal secretion patterns is directly influenced by symphatic innervation of the salivary gland. Several studies have investigated that changes in the levels of sAA as an indicator of dental anxiety during the extraction [25-27]. There is lack of information about the effects of sedation on sAA levels at different time points during the operation of the impacted third molars.

Thus, the specific aims of the present study were to evaluate sAA responses to impacted third molar extractions at different time points in the patients under conscious sedation with local anesthesia and to examine the relationship between sAA, conscious sedation and dental anxiety.

Material and methods

A total of 20 male patients requiring impacted third molar extractions were initially considered for this study. Patients with sedation history were excluded. Women also were not included for this study because of their hormonal changes. The final study sample compromised 18 male subjects between 19 and 33 years of age. The saliva samples of the two patients were bloody, so they were excluded.

Complete anamnesis was collected and clinical examinations were done to determine infection, pu, swelling. Written informed consent forms were signed by all patients who agreed to participate in the study. The inclusion criteria for the study were the following: male patient with impacted third molar without relevant systemic pathology (ASA I as per the American Society of Anesthesiologists classification).

The study was approved by Local Ethic Committee (2018/24).

Variables and data measurement

Patients were divided into two groups: test group (procedures under sedation) and control group (procedures under local anesthesia). All patients were asked to fill MDAS form which consists of five questions: 'If you went to the dentist tomorrow, how would you feel?'; 'If you were sitting in the waiting room, waiting for treatment, how would you feel?'; 'If you were about to have a tooth drilled, how would you feel?'; 'If you were about to have your teeth scaled and polished, how would you feel?'; and 'If you were about to have a local anaesthetic injection in your gum, above an upper back tooth, how would you feel?'. The response alternatives ranged from 'not anxious' (score = 1) to extremely anxious (score = 5). The cut-off was set at ≥15 for dental anxiety and as ≥19 for being very dentally anxious, as described by Humphris et al. [28].

Systolic blood pressure (SBP), diastolic blood pressure (DBP), oxygen saturation (SO2), and heart rate (HR) were monitored at different time points: preoperative time (SBPa, DBPa, SO2a, HRa); intraoperative time - after local anesthesia (SBPb, DBPb, SO2b, HRb), intraoperative time - after extraction (SBPc, DBPc, SO2c, HRc), postoperative time (SBPd, DBPd, SO2d, HRd). The first specimen of saliva was taken at the first time patient came to clinic (t1). Saliva was allowed to flow in the floor of mouth, 1 ml was then collected using a Pasteur pipette. First day after examination, patient was given an appointment. The second time of the saliva was taken when the patient sat in the chair for extraction (t2). The other times of saliva samples were taken before local anesthesia (t3), immediately after extraction (t4) and 4h after extraction (t5). Due to the localization and position of the third molar, osteotomy was performed using a 20,000-rpm hand piece under irrigation for all patients. Some cases required tooth sectioning. 3-0 silk suture was used at the end of the surgery.

Ibuprofen (600 mg every 8 h for 7 days) and amoxicillin/clavunate (875 mg/125 mg every 8 h for 5 days) were prescribed. Detailed explanation of oral hygiene techniques and recommendations for the postoperative period were given to each patient.

Measurement of sAA activity

The sAA activity was measured by a colorimetric assay using 4,6-ethylidene-(G7)p-nitrophenyl-(G1)-D-maltoheptaoside in an automatic analyzer (Cobas Integra 800, Roche, Basel, Switzerland) after 1/400 dilution of saliva in distilled water.

Statistical analysis

IBM Statistical Package for Social Sciences (SPSS) version 22 (IBM Corp., Armonk, NY, USA) software program was run. The normal distribution of the parameters was evaluated by Shapiro Wilks test and it was found that the parameters did not show normal distribution. Descriptive statistical methods (mean, standard deviation) as well as quantitative data were compared; Mann-Whitney U test was used for the comparison of the parameters between the two groups and Wilcoxon sign test was used for the intra-group comparisons of the parameters. Spearman's Rho correlation analysis was used to evaluate the relationships between the parameters. Statistical significance was set as $p < 0.05$.

Results

A total of 18 patients fulfilled the study criteria; 2 patients were excluded because of their bloody saliva samples. A total of 18 impacted third molar extractions were performed. All patients (100%) were male; they ranged in age from 19 to 33 years. Only patients with a diagnosis of impacted third molars were selected for the study.

Each patient's SBP, DBP, SO2 and HR were recorded during surgical interventions (Table 1). Between groups, statistical analysis showed no correlation for SBP ($p>0.05$). There was a statistically significant difference between DBPd in control group and test group ($p<0.05$). DBPd of control group was found statistically higher than test group (p:0.030). HR did not show significant correlation in both groups ($p>0.05$). SO2d level compared to SO2a showed a statistically significant decrease (p3:0.046).

| Table 1 | Average (±SD) systolic blood pressure, diastolic blood pressure, heart rate, oxygen saturation levels at different study time-points |

	Test	Control	
	Mean±SD (median)	Mean±SD (median)	1p
SBPa	123,44±10,74 (120)	123±13,43 (125)	0,558
SBPb	121,78±13,54 (120)	130,11±16,8 (132)	0,268
SBPc	121,44±4,69 (122)	126,44±15,12 (130)	0,306
SBPd	117,44±7,78 (120)	127,67±17,33 (127)	0,059
DBPa	70,11±6,43 (70)	66±10,34 (64)	0,352
DBPb	65,78±11,09 (61)	68,67±9,7 (70)	0,330
DBPc	69±9,31 (65)	68,25±11,31 (66,5)	0,961
DBPd	63±4,82 (62)‡	71,56±8,89 (70)‡	0,030*
HRa	89±12,13 (92)	86,44±9,86 (89)	0,288
HRb	83,11±10,68 (80)	89,89±10,42 (87)	0,185
HRc	84±5,96 (83)	88,11±7,39 (88)	0,120
HRd	82,33±6,28 (80)	89,67±10,36 (88)	0,184
SO2a	99±0 (99)	99,44±0,53 (99)	0,028*
SO2b	99,11±0,33 (99)	99,22±0,44 (99)	0,539
SO2c	99±0 (99)	99,11±0,33 (99)	0,317
SO2d	99±0 (99)	99±0,5 (99)‡	1,000

1Mann Whitney U Test   ‡Intergroups Wilcoxon sign test p<0.05 statistically significant   *p<0.05
SD: Standart Deviation, SBP: Systolic Blood Pressure , DBP: Diastolic Blood Pressure, HR: Heart Rate, SO2: Oxygen Saturation
Preoperative time (SBPa, DBPa, SO2a, HRa); Intraoperative time-after local anesthesia (SBPb, DBPb, SO2b, HRb), Intraoperative time-after extraction (SBPc, DBPc, SO2c, HRc), Postoperative time (SBPd, DBPd, SO2d, HRd)

Statistical analysis showed no significant comparison according to sAA levels in different study time points between groups ($p>0.05$) (Table 2). In test group t1 and t3 in comparison, decrease of sAA level in t3 were significantly higher than t1 (p:0.048). But when alpha-amylase level in t1 compared to t2, t4, t5, no statistically significant relationship was found between study time points (p1: 0.110, p2:0.208, p3:0.214; $p>0.05$). In addition, there was no statistically significant difference for sAA levels between t1 and t2, t3, t4, t5 in test group and there was no statistically significant correlation with sAA levels between t1 and t2, t3, t4, t5 in control group (p1:0.441, p2:0.139, p3:0.441, p4:0.314; $p>0.05$).

	Test	Control	1p
		Table2	Salivary Alpha-Amylase Levels in Groups During Study Time Points

Salivary Alpha-Amylase	Test Mean±SD	Control Mean±SD	1p
t1. The first time the patient came to clinic	851,22±723,25 (717)	589,78±330,5 (550)	0,566
t2. When the patient sat in the chair for extraction	829,33±706,45 (642)	547,78±228,98 (525)	0,508
t3. Before local anesthesia	541,78±431,2 (440) ‡	435,11±342,3 (355)	0,627
t4. Immediately after extraction	685,11±404,55 (440)	710,78±486,15 (467)	0,895
t5. 4 h after extraction	564,67±545,62 (304)	484,78±197,1 (487)	0,691

1Mann Whitney U Test   ‡ Intergroups Wilcoxon sign test
* Statistically significant at p<0.05

When the change in alpha amylase level between t1, t4 and t5 between two groups was examined; the alteration of sAA level between t1-t4 and t1-t5 was not found statistically significant (p>0.05).

Discussion

The specific aims of the present study were to determine the effect of conscious sedation on sAA levels and explain the relationship between sAA levels, dental anxiety and hemodynamic changes (blood pressure, heart rate, oxygen saturation) in patients undergoing impacted third molar extraction. The study results showed that there was no statistically significant difference between dental anxiety and sAA level in patients at different study time-points both under conscious sedation and local anesthesia.

The surgical extraction of impacted third molars is known one of the most common surgeries performed in the oral and maxillofacial surgery field. The surgical difficulty of removal of the impacted third molars may cause a dental fear. From this starting point, sedation has been carried out by oral and maxillofacial surgeons [29]. The use of sedation in dental practice is commonly used to reduce anxiety so that collaboration with dentist for dental treatment may be achieved. Several dental-anxiety measures have been developed to help the dentist to manage anxious patients. Modified Dental Anxiety Scale (MDAS) has been developed by Humphris et al. for this reason [28]. Dental anxiety tests should be evaluated with various stress biomarkers such as cortisol, α-amylase, IgA, total protein for objective assessment. Nowadays saliva can be used as an easy, noninvasive method to analyze the levels of stress markers when compared with serum that is an invasive method [26]. Several studies investigated the concentrations of α-amylase, IgA, cortisol, total protein in saliva to determine dental anxiety [26,30,31]. sAA constitute proxy measures of the hypothalamic-pituitary-adrenal axis and the autonomic nervous system [32]. Chatterton et al. reported that there was a correlation between the sAA and blood levels of catecholamines [33]. Therefore, the measurement of sAA concentration can give a clue about the level of stress. Also it is known that sAA activity peaks in response to mild to moderate level challenge within 10 minutes of the operation [34]. In our sAA levels at different study time points did not differ statistically in the groups. In addition MDAS test results and amylase levels in comparison did not show statistically significant correlation. Unlike our results, Furlan et al observed higher sAA levels before dental prophylaxis compared to after the procedure [31]. Gutiérrez-Corrales et al. analyzed the relationship between inflammatory response and sAA concentration in patients undergoing impacted lower third molar surgery. They found that sAA level 2 h after operation was higher than the preoperative value [27]. Although, in our study the decrease in the level of sAA just before the local anesthesia was statistically significant compared to the first time point, postoperative sAA levels did not differ from preoperative time points. The difference between two studies may be the time points when sAA levels were measured. Nater and Rohleder [24], Allwood et al. [35], and Kang [36] evaluated the relationship between stress conditions and the sAA concentration. They reported that stress causes significant increase in sAA concentration when patients were faced to a stressful position compared to a rest condition. In our study we found that anxiety levels revealed by MDAS did not affect sAA level. Regardless of the anxiety sense, biological stress could affect sAA. Perhaps conscious sedation is not a procedure that reduces biological stress markers caused by autonomic nervous system, so our study results may have shown that conscious sedation does not affect sAA levels.

A surgical dental procedures can cause anxiety which can affect the patient's psychological condition and thus increasing SBP and DBP. These hemodynamic changes in medically compromised patients may induce adverse cardiac effects. Hence, previous studies estimated that it could be useful to perform surgery with patients under conscious sedation in those with high levels of dental anxiety, as the hemodynamic variables are controlled by adjusting the dosage of the sedative drugs [37]. In our study, only DBP levels showed positive correlation in sedation and control groups at preoperative and postoperative times. Even though there was no statistically significant correlation with SBP in both groups at postoperative times, control groups had higher DBP levels prior to test group. Unlike this result, preoperative DBP level in control group had statistically important increment prior to postoperative DBP level. Although test group did not have statistically significant change in SOb level, in control group decrease of SO2d level was found statistically significant prior to SO2a level. Several studies also analyzed the hemodynamic changes in patients undergoing third molar surgery with local anesthesia. They reported statistically significant differences of hemodynamic variables [37-40]. However the present study failed to show overall perfect correlations between the dental anxiety level and hemodynamic variables. Because patients did not show any abnormalities. This is justified by the sedation carried out in which the levels of consciousness and dental anxiety are controlled.

Our study was the first to evaluate the correlations between MDAS, sAA and hemodynamic changes during impacted third molar surgery under conscious sedation and local anesthesia. In this study, we evaluated the effects of anxiety on biologic surgical stress and psychological stress on SAA. Anxiety was not increasing the impacts of biological surgical stress on sAA. These results can create question marks to start future designed future studies.

The results of the present study should be viewed within the limitations of the data. First, the numbers of study time points should be increased. In the late healing period time, all measurements should be repeated. Second, the effects of general anesthesia, conscious sedation and local anesthesia on sAA levels and dental anxiety should be compared in the same study. Third different dental anxiety tests should be used to compare the results. Anxiety was recognized as different tests as cross. Also, using 19 limits, instead of 15 limits, according to MDAS, maybe give us different results.

We were informed about the patients' dental anxiety with the body language and verbal expressions of the patients and we monitored the anxiety with MDAS. These patients had not previously undergone conscious sedation. Therefore, we did not think that they would be able to abuse sedation. However, as a result of the study, we could not detect any systemic symptoms or monitorable anxiety symptoms except MDAS results and body language. In this case, even if we cannot monitor these fears, we believe that the answer to the question "Do we practice conscious sedation?" should be discussed.

Conclusion

In conclusion, conscious sedation is not a physiological stress reducing procedure. Based on the results of our study, no significant difference on sAA and dental anxiety levels were observed between the two anesthesia methods. Future researches should aim to explain the effects of general anesthesia, conscious sedation, local anesthesia on sAA and various stress markers in the same study and use different dental anxiety scales to confirm the study results. But future studies should compare the effects of general anesthesia and type of sedations on the alpha-amylase levels and other biomarkers that are not affected by the acute inflammatory process after extraction and explain the effects at early and late stages of the healing period.

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