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INFLUENCE OF VERTICAL IRREGULARITIES ON THE SIZE OF SOFT TISSUE CONVEXITY, NASOLABIAL AND LABIOMENTAL ANGLE

ВЛИЈАНИЕ НА ВЕРТИКАЛНИ НЕРЕГУЛАРНОСТИ ВРЗ ГОЛЕМИНАТА НА КОНВЕКСНОСТА НА МЕКОТО ТКИВО, НАСОЛАБИЈАЛНИОТ И ЛАБИОМЕНТАЛНИОТ АГОЛ

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Abstract

Introduction: Modern orthodontics is a creation for the best possible balance between occlusal relations, dental and facial esthetics, result stability, and their maintenance as well as teeth restoration. The configuration and expression of the face primarily depend on the skeletal build, the position and fit of facial bones, soft tissues covering, as well as the size of the nose, lips and chin. The soft tissues of the face are determined by three interactive factors: - Skeletal base which, in the middle and the lower third of the face, is represented by the jaws, - Dental support structures, represented by the teeth, - Soft-tissue mask, which is determined both by the underlying hard tissues and by the soft tissues themselves (nose, chin, lip thickness and their respective tonus). **Aim.** The aim of our study is to determine the size of the vertical skeletal dimensions of the face, N'Prn'Pg', NLA and LiB'Pg' angle in three experimental groups and determine the statistically significant differences between those groups. **Material and methods:** Depending on the vertical incisal rate characteristics - overbite, the respondents were divided into three groups: the first group consisted of respondents with open bite, meaning the overbite is smaller or equal to -1mm, the second group consisted of respondents with deep bite, meaning the overbite is over +4mm, and the third group consisted of respondents with normal overlap, meaning the overbite is more than +1mm, but lower or equal to +4mm. **Results:** The results show that the vertical incisal step has an effect on the convexity of the soft tissues, as well as the nasolabial and labiomental angle. **Conclusion:** The soft tissue convexity N'PrnPg' is bigger in the deep bite group (both male and female), while the labiomental angle LiB'Pg' is increased in the open bite group and decreased in the deep bite group. **Key words:** overbite, soft tissue convexity, nasolabial angle, labiomental angle, cephalometry.

Апстракт

Вовед: Современата ортодонција е креација за најдобра можна рамнотежа помеѓу окулзални односи, дентална и фацијална естетика, стабилност на резултатите и нивното одржување, како и реставрација на забите. Конфигурацијата и изразот на лицето претежно зависат од скелетната градба, позицијата и вградбата на фацијалните коски, меките ткива кои го покриваат, како и големината на носот, усните и брадата. Меките ткива на лицето се одредени од три интерактивни фактори: • Скелетна база која, во средниот и долниот дел на лицето, е претставена со вилиците, • Дентални поддржни структури, претставени со забите, • Мекоткивна маска, која е одредена и од основните тврди ткива и од самите меки ткива (нос, брада, дебелина на усните и нивниот респективен тонус). **Целта** на нашето истражување е да се определи големината на вертикалните скелетни димензии на лицето, N'Prn'Pg', NLA и LiB'Pg' агол во три експериментални групи и да определи статистички значајни разлики помеѓу тие групи. **Материјал и методи:** Во зависност од вертикалните инцизални карактеристики - преклоп, испитаниците беа поделени во три групи: првата група која се состои од испитаници со отворен преклоп, што значи дека преклопот е помал или еднаков на -1mm, втората група која се состои од испитаници со длабок преклоп, што значи дека преклопот е повеќе од +4mm, и третата група која се состои од испитаници со нормален преклоп, што значи дека преклопот е повеќе од +1mm, но помал или еднаков на +4mm. **Резултати:** Резултатите покажуваат дека вертикалниот инцизален чекор има ефект врз конвексноста на меките ткива, како и врз насолабијалниот и лабиоменталниот агол. **Заклучок:** Конвексноста на меките ткива N'PrnPg' е поголема во групата со длабок преклоп (кај мажите и жените), додека лабиоменталниот агол LiB'Pg' е зголемен во групата со отворен преклоп и намален во групата со длабок преклоп. **Клучни зборови:** преклоп, конвексност на меките ткива, насолабијален агол, лабиоментален агол, цефалометрија.

Introduction

Examining the factors that influence facial harmony and disharmony, it is proven that facial components are inherited regardless of one another, and not as a complex that leads to different facial configuration creations. The facial configuration and facial expression depend primarily on the constitutional build of the skeleton, facial

bones position and alignment, the upper and lower jaw position, bite type, soft-tissue components covering the facial base, as well as nose, lip, and chin size.

Modern orthodontics' goal represents the best possible balance between occlusal relations, dental and facial esthetics, result stability and their maintenance as well as teeth restoration[1]. The regular or irregular vertical development of the facial skeleton is connected to multiple skeletal groups: nasomaxillary complex, alveolar processes and mandible. There is a connection between the structure of the front part of the maxilla and mandible, and the lower part of the face, so in the case of an open or deep bite, the dentoalveolar development can be insufficient to compensate for the oversized or undersized detachment of the jaw system[2].

Zuzhelova[3] proves that the nasolabial structures, by virtue of their morphology and position, are directly involved in the formation of the external appearance of the face as a whole. Nasal structures, lips and chin are potential factors in the formation of facial appearance[4].

Angle points to the importance of facial harmony by emphasizing the role of soft tissues in shaping the facial region. She considers that the lips are an important factor in determining and evaluating the criteria for facial aesthetics[2].

Zuzhelova[5] examined the linear and angular dimensions of the nasolabial structures in individuals with normal occlusion, class II/1 and class III. According to her findings, the growth of the nose and the upper lip takes place simultaneously, they accompany each other and participate in the formation of a soft profile. The shape of the nasal structures is closely correlated with the general convexity of the face.

Lo and Hunter[6] found a high correlation between NLA and retroclination of the upper incisors. Each retraction of the upper incisors leads to an increase in NLA by 1.63º.

Coonor and Moshiri's[7] findings on the size of the NLA between black and white populations indicated marked significance. Perceptible differences appeared between the sexes in the white race. The NLA in female subjects was 107.34º, and 101.34º in males, which indicates that there is a more blunt relationship between the nose and the upper lip.

De Freitas et al.[8] analyzed the NLA in subjects at rest and when smiling. The difference between one angle and the other was statistically significant with a difference of 5.74º. Variations of NLA at rest and while smiling were significant in normal samples and are used as a diagnostic tool in treatment planning for sagittal and vertical dentofacial skeletal deformities.

Orthodontic treatment is directly influenced by the soft tissues, namely the pressure of the lips, cheeks and tongue on the teeth, the periodontal support system, the muscles and the connective tissue components of the TMJ, and the contours of the soft tissues of the face.

The aim of our study is to determine the size of the vertical skeletal dimensions of the face, N'Prn'Pg', NLA and LiB'Pg' angle in three experimental groups, and to determine statistically significant differences between those groups.

Material and method

For the realization of the set goal, examinations were conducted on 90 individuals from both sexes, aged 13-15, randomly chosen from the Clinic of Orthodontics at PHO – Dental Clinical Centre "St. Pantelejmon" in Skopje.

The selection of the respondents taking part in realizing the set goal was based on the following criteria: individuals that had not previously undergone orthodontic treatment, with no great craniofacial disorders, and with complete dentition.

In relation to the characteristics of the vertical incisal rate, the respondents were divided into three groups, and were classified as follows:

- The first group consisted of respondents with open bite, where the vertical incisal rate is lower or equal to -1mm.
- The second group consisted of respondents with deep bite, where the vertical incisal rate is over +4mm, and
- The third group consisted of respondents with normal incisal overlap, where the vertical incisal rate is more than +1mm, but lower or equal to +4mm. This group was also the control group.

Every group consisted of 30 respondents, 15 female and 15 male that came in the period from 2016 to 2022.

In the respondents from the research groups, standardized clinical and diagnostic procedures were conducted with X-ray cranial imaging in a standardized way in norma lateralis.

The soft tissue roentgen cephalometric points used in this investigation are:

- N' – the deepest part of the soft tissue outline in front of Nasion,
- Prn (Pronasale) – tip of the nose,
- C or Cm (Columella) – the most anterior point on the tip of the nose,
- Sn (Subnasale) – the junction of the nasal septum and the upper lip in the mid-sagittal plane,
- Ls (Labrale superius) – the most anterior point on outline of the upper lip (vermillion border),

- Li (Labrale inferius) – the most anterior point on outline of the lower lip (vermillion border),
- Sm (Supramentale) B' – the deepest midline point on outline of the inferior labial sulcus (soft tissue B-point),
- Pg' (Pogonion) – the most anterior point on outline of the soft tissue chin,
- Gn' (Gnation) – the lowest point on outline of the soft tissue chin.

We measured the following soft tissue angular variables: (Figure1)

Soft tissue convexity – angle **N'Prn'Pg'**,

Nasolabial angle – **NLA** or C Sn Ls,

Labiomental angle or contour of the mandibular sulcus – **Li B' Pg'** or Md S C or Li Sm Pg'.

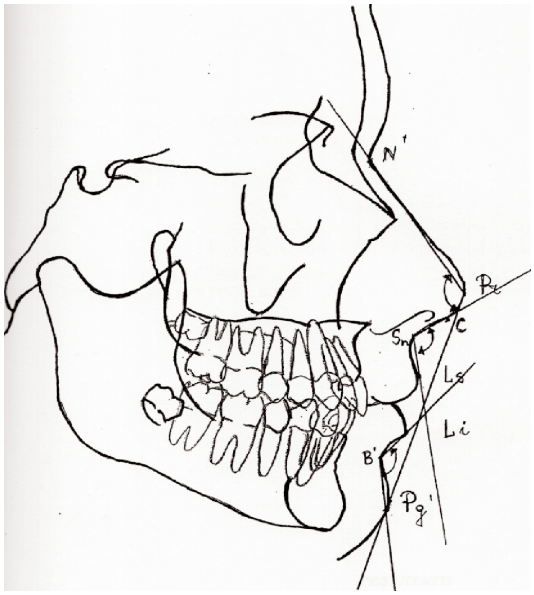


Figure 1. *Soft tissue angular variables*

The statistical data analysis was conducted in the SPSS 17,0 program for Windows.

- ✓ Shapiro – Wilk's W test was used for data testing,
- ✓ Descriptive statistics was used for data depiction,
- ✓ One Way Anova was used for comparing the analyzed parameters between the three analyzed groups, and Tukey – test was used for inter-group differences,
- ✓ The Student "t" test was used for comparison of the analyzed parameters in relation to gender,
- ✓ The levels of probability for achieving a null hypothesis, concordant with international standards for bio-medical sciences were 0.05 and 0.01.

Results

The average size of the soft tissue angle convexity (N'PrnPg') significantly differs between the three analyzed groups (F=18.7 p<0.001). This statistical significance is due to a significantly smaller average N'PrnPg' angle in the group of subjects with a deep bite compared to the other two groups, open bite (123.1±4.7º vs 127.43±3.8º), and normal bite (123.1±4.7º vs 129.9±4.4º). (Table 1, Graphic 1)

The results of the research show that the size of the soft tissue convexity angle does not significantly depend on the gender of the respondents for any of the analyzed groups: for open bite (t=1.09 p=0.28), for deep bite (t=0.341 p= 0.74), and for normal bite (t=0.28 p=0.78).

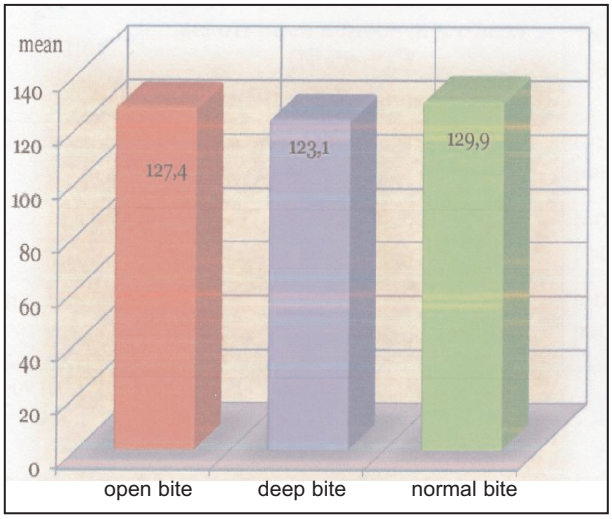
In the open deep bite groups, male subjects had a non-significantly smaller mean N'PrnPg' angle compared to female subjects (126.67±2.8º vs 128.2±4.6º, and 122.8±4.9º vs 123.4 ±4.8°), while in the control group, the average size of this angle is insignificantly higher in

Table 1. Soft tissue angle convexity (N'PrnPg') between groups with open, deep, and normal bite

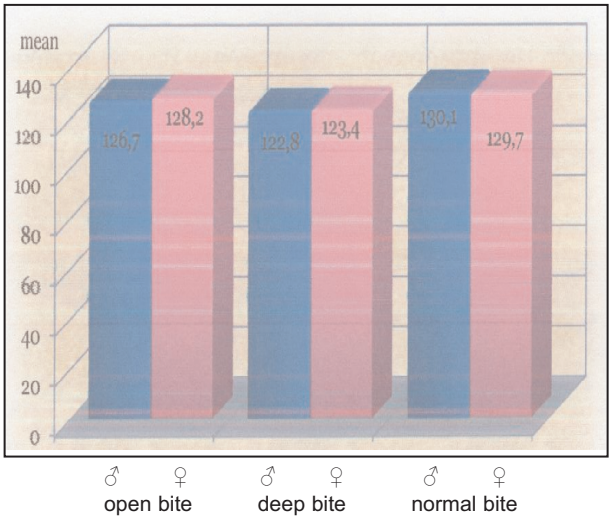
Group	Soft tissue angle convexity (N'PrnPg')		
	mean ±SD	min - max	median
OPEN BITE	127.43±3.8	121-137	127.5
DEEP BITE	123.1±4.7	110-132	123
NORMAL BITE	129.9±4.4	124-140	129.5
F – analysis of Variance	F=18.7 p<0,001 post hoc open bite vs deep bite p<0,01 open bite vs normal bite p<0,01 deep bite vs normal bite p<0,01		

Table 2. Differences between male and female subjects for soft tissue angle convexity (N'PrnPg') in groups with open, deep and normal bite

Group	Gender	Soft tissue angle convexity (N'PrnPg')			Student's t-test
		mean ±SD	min - max	median	
OPEN BITE	male	126.67±2.8	121-131	127	t=1.09
	female	128.2±4.6	121-137	129	p=0.28 ns
DEEP BITE	male	122.8±4.9	110-129	123	t=0.341
	female	123.4±4.8	112-132	123	p=0.74 ns
NORMAL BITE	male	130.13±4.7	124-137	130	t=0.28
	female	129.67±4.3	124-140	129	p=0.78 ns



Graphic 1. *Graphic image of mean values for N'PrnPg' angle in three groups*



Graphic 2. *Graphic image differences between male and female subjects for N'PrnPg' angle in three groups*

the group with male respondents (130.13±4.7º vs 129.67±4.3º). (Table 2, Graphic 2)

The average size of the nasolabial angle (NLA) in the group with an open bite is measured at 103.4±10.4º, at 108.03±10.8º in the group with a deep bite, while in the group with a normal bite the average size of the NLA is measured at 102.57±8.9º.

The average size of the nasolabial angle (NLA) in the group with an open bite is measured at 103.4±10.4º, at 108.03±10.8º in the group with a deep bite, while in the group with a normal bite the average size of the NLA is measured as 102.57±8.9º. The deep bite is characterized by a slightly higher average nasolabial angle compared to the open and normal bite. (Table 3, Graphic 3)

The average size of the nasolabial angle in the group of male subjects with an open bite is measured at 109.93±6.2º, while in the group of female subjects with an open bite is measured at 96.87±9.6º.

The difference of 13.06º was statistically confirmed as significant (t=4.42 p=0.00013). We can conclude that the size of the NLA in the open bite condition significantly depends on gender.

In the group with deep and normal bite, the male subjects presented a non-significantly lower average NLA than the female subjects (106.2±11.4º vs 109.87±10.1º, and 100.53±10.3º vs 104.6±7.1º), consequently. (Table 4, Graphic 4)

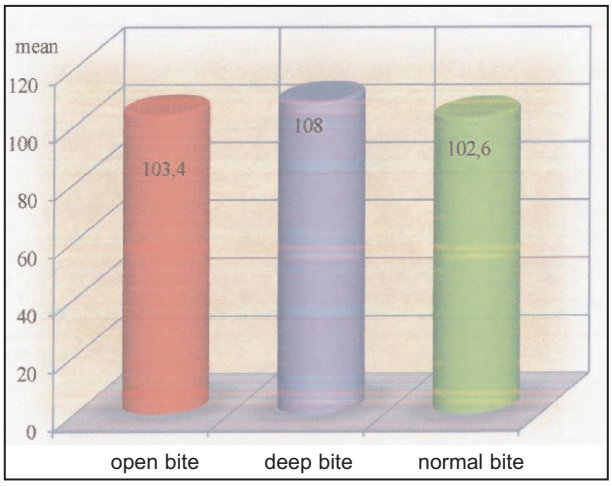
Subjects with open, deep and normal bites have significantly different average sizes of the labiomental angle LiB'Pg' (F=94.07 p<0.001). Post hoc analysis showed that the differences in all paired comparisons were statistically significant, that is, LiB'Pg' had a sig-

Table 3. Nasolabial angle (NLA) between groups with open, deep and normal bite

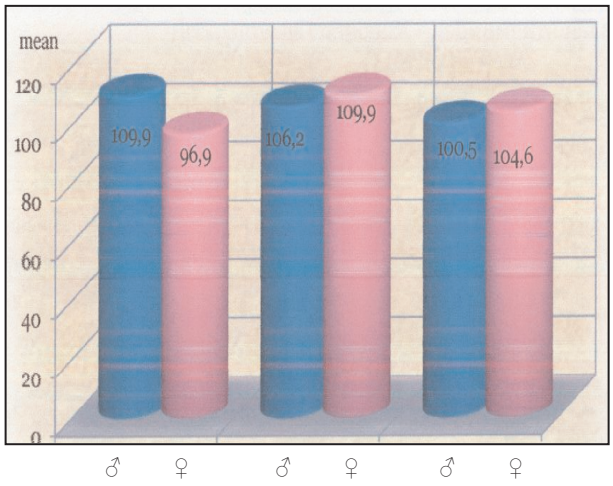
Group	Nasolabial angle (NLA)		
	mean ±SD	min - max	median
OPEN BITE	103.4±10.4	85-120	106
DEEP BITE	108.03±10.8	89-133	108
NORMAL BITE	102.57±8.9	77-119	102.5
F – analysis of Variance	F=2.58 p<0,08 ns		

Table 4. Differences between male and female subjects for nasolabial angle (NLA) in groups with open, deep, and normal bite

Group	Gender	Nasolabial angle (NLA)			Student's t-test (**p,0,01)
		mean ±SD	min - max	median	
OPEN BITE	male	109.93±6.2	100-120	108	t=4.42
	female	96.87±9.6	85-111	91	p=0,00013
DEEP BITE	male	106.2±11.4	89-125	106	t=0.93
	female	109.87±10.1	91-133	109	p=0,36 ns
NORMAL BITE	male	100.53±10.3	77-118	102	t=1.26
	female	104.6±7.1	95-119	104	p=0,22 ns



Graphic 3. *Graphic image of mean values for NLA angle in three groups*



Graphic 4. *Graphic image differences between male and female subjects for NLA angle in three groups*

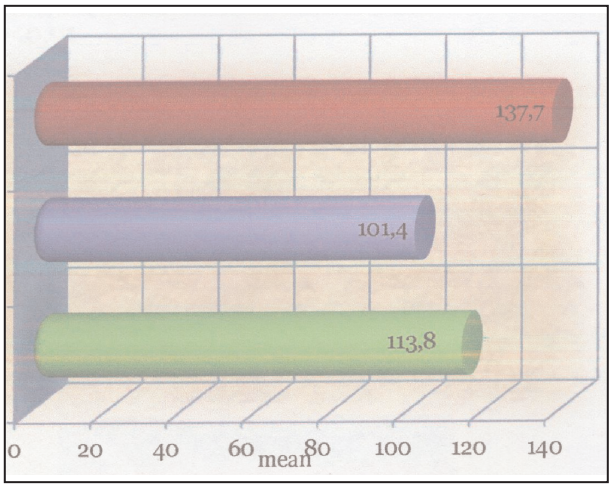
nificantly smaller average size in the group with deep bite versus open bite (101.37±11.2º vs 137.7±7.8º), and versus the normal bite (101.37±11.2º vs 113.83±11.8º), as well as significantly smaller average size in the group with normal bite versus open bite (113.83±11.8º vs 137.7±7.8º). (Table 5, Graphic 5)

Table 5. Labiomental angle (LiB'Pg') between groups with open, deep and normal bite

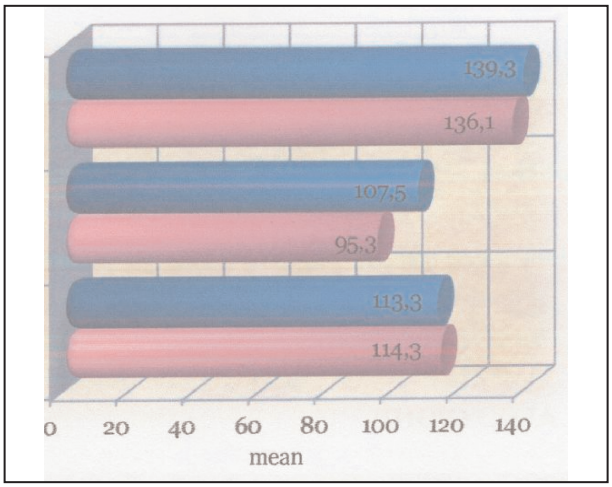
Group	Labiomental angle (LiB'Pg')		
	mean ±SD	min - max	median
OPEN BITE	137.7±7.8	125-154	136.5
DEEP BITE	101.37±11.2	72-119	102
NORMAL BITE	113.83±11.8	98-140	115.5
F – analysis of Variance	F=94.07 p<0,001 post hoc open bite vs deep bite p=0,0001** open bite vs normal bite p=0,0001** deep bite vs normal bite p=0,0001**		

Table 6. Differences between male and female subjects for labiomental angle (LiB'Pg') in groups with open, deep, and normal bite

Group	Gender	Labiomental angle (LiB'Pg')			Student's t-test
		mean ±SD	min - max	median	
OPEN BITE	male	139.27±8.1	128-154	137	t=1.104
	female	136.13±7.5	125-149	136	p=0,28 ns
DEEP BITE	male	107.47±8.7	91-119	109	t=3.5
	female	95.27±10.3	72-112	92	p=0,0016**
NORMAL BITE	male	113.33±12.7	98-140	111	t=0.23
	female	114.33±11.1	99-132	113	p=0,82 ns



Bar Graphic 5. *Graphic image of mean values for LiB'Pg' angle in three groups*



Bar Graphic 6. *Graphic image of differences between male and female subjects for LiB'Pg' angle in three groups*

The influence of gender on the size of the labiomental angle was confirmed as significant only in the deep bite group (t=3,5 p=0,0016). In this group, male subjects present a significantly higher average LiB'Pg' angle compared to female subjects (139.27±8.1º vs 136.13±7.5º).

In the open and normal bite group, the differences in the average size of the labiomental angle between male

and female subjects are insufficient to be confirmed as significant (p>0.05). (Table 6, Graphic 6)

Discussion

The soft tissue convexity is the angle formed by the points N'Prn'Pg'. This angle presents the convexity of the face. The average size of the soft tissue angle convexity significantly differs between the three analyzed groups (F=18.7 p<0.001). This statistical significance is due to a significantly smaller average N'Prn'Pg' angle in the group of subjects with deep bite compared to the other two groups, open bite (123.1±4.7º vs 127.43±3.8º), and normal bite (123.1±4.7º vs 129.9±4.4º).

The obtained values indicate that the subjects with irregularity II/2 have a convex face, but the convexity is more pronounced in subjects with irregularity II/1. Our findings coincide with the findings of Nanda et al.[10], and they do not coincide with the findings of Zuzhelova[3] in which the respondents from the open bite group, aged 10-16 years, had a mean value of 136,75±4,70º for the soft tissue convexity. This angle increases during growth, although insignificantly, which coincides with the findings of Posen, who points out that this angle increases by 8.65º from 2 to 18 years of life. Subtenly and Chaconas[9] indicate that the soft tissue convexity angle decreases during growth. The results of the research showed that the size of the angle of soft tissue convexity does not significantly depend on the gender of the respondents for any of the analyzed groups. In the open and deep bite groups, male subjects had a non-significantly smaller mean N'Prn'Pg' angle compared to female subjects (126,67±2,8º vs 128,2±4,6º, and 122,8±4,9º vs 123,4±4,8º), while in the control group, the average size of this angle is insignificantly higher in the male respondents group (130,13±4,7º vs 129,67±4,3º).

The average size of the nasolabial angle NLA in the group with an open bite is 103.4±10.4º, 108.03±10.8º in the group with a deep bite, while in the group with a normal bite, the average size of the NLA was measured as 102.57±8.9º. The average size of the nasolabial angle (NLA) in the group with an open bite was 103.4±10.4º, 108.03±10.8º in the group with a deep bite, while in the group with a normal bite the average size of the NLA was measured as 102.57±8.9º. The deep bite is characterized by a slightly higher average nasolabial angle compared to the open and normal bite. Compared with Zuzhelova's[5] results, Lo and Hunter6 found lower values of this angle. In subjects at the age of 13, its value was 106.80º, and in subjects at the age of 16, the NLA value was 105.76º. The differences in the value of this angle that we found among individual authors in individuals with a normal bite are the result of the subjects belonging to individual races, which is especially noticeable in the studies of Coonor and Mochiri[7]. De Freitas[8] has also performed tests on 40 white Brazilians with normal occlusion and facial harmony. NLA was analyzed in subjects at rest and while smiling. NLA at rest was 104.93º and 110.67º when smiling. The difference between one NLA and the other was statistically significant with a difference of 5.74º. Variations of NLA at rest and while smiling were significant in normal samples and were used as a diagnostic tool in treatment planning for sagittal dentofacial skeletal deformities.

The size of the nasolabial angle in the open bite condition significantly depends on the gender. In the group with deep and normal bite, the male subjects presented a non-significantly lower average NLA than the female subjects (106.2±11.4º vs 109.87±10.1º, and 100.53±10.3º vs 104.6±7.1º, consequently). Our studies are in agreement with the studies of Zuzhelova[3], Lo and Hunter[6], De Freitas[8], Coonor and Mochiri[7], Nandini et al.[11], however, only for the white population where the average value of NLA in female subjects is 107.34º, and 101.2º in male respondents, which indicates the fact that there is a more blunt relationship between the nose and the upper lip.

Subjects with open, deep and normal bites have significantly different average sizes of the labiomental angle LiB'Pg' (F=94.07 p<0.001). Post hoc analysis showed that differences in all pairwise comparisons were statistically significant. The influence of gender on the size of the labiomental angle was confirmed as significant only in the deep bite group (t=3,5 p=0,0016). In this group, male subjects present a significantly higher average LiB'Pg' angle compared to female subjects (139.27±8.1º vs 136.13±7.5º).

Liu Y[12], Jacobson et al.[13] examined the changes of hard and soft tissues in subjects with class III, and open bite after orthodontic-surgical treatment. After bilateral osteotomy of the ramus of the mandible in the 20 studied patients, there was a decrease in the SNB and LiB'Pg' angles (p<0.01), and an increase in the convexity of the face as well as the ANB angle.

Conclusions

The soft tissue convexity of the face or the **N'PrnPg'** angle is most pronounced in subjects with a deep bite compared to the other two studied groups.

The size of the N'PrnPg' angle does not significantly depend on the gender of the subjects for any of the analyzed groups.

The nasolabial angle NLA is characterized by a non-significantly higher value in the deep bite group.

The size of the **NLA** in the open bite condition is significantly gender dependent. Male subjects from the deep and normal bite group present a significantly lower NLA than female subjects.

The labiomental angle LiB'Pg' in the deep bite group has the smallest average size and the influence of gender on the size of this angle was confirmed as significant in the same group.

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DOUBLE MESIODENS: A CASE REPORT
ДВОЕН МЕЗИОДЕНС: ПРИКАЗ НА СЛУЧАЈ

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Abstract

Introduction: Mesiodens are the most common of all supernumerary teeth. Recently, the presentation of double mesiodens cases has increased, which may be due to the availability of sophisticated and accurate diagnostic methods. **Aim:** To present a rare case of double mesiodens in the anterior maxilla. **Material and method:** A 9-year-old male patient was diagnosed with double mesiodens in the anterior maxilla by CBCT. The patient is non-syndromic and has no other supernumerary teeth in the mixed dentition. **Results:** Using cone beam computed tomography (CBCT), we assessed the position, structure and shape of the supernumerary teeth and also made an appropriate plan for surgical extraction of them. **Conclusion:** This article shows the importance of early diagnosis and treatment of mesiodenses, in order to prevent or limit inflammatory, carious, periodontal and occlusal complications that can occur in supernumerary teeth conditions in jaws. **Key words:** Mesiodens, supernumerary teeth, CBCT, surgical extraction.

Апстракт

Вовед: Мезиодените се најчести меѓу сите прекубројни заби. Од неодамна, презентацијата на случаи со двоен мезиоденс се зголемени, што може да се должи на достапноста на софистицирани и прецизни дијагностички методи. **Цел на трудот:** Да се претстави редок случај на двоен мезиоденс во предната максила. **Материјал и метод:** На 9-годишен пациент од машки пол, со CBCT е дијагностициран двоен мезиоденс во предната максила. Пациентот е несиндромичен и нема други прекубројни заби во мешаната дентиција. **Резултати:** Користејќи компјутерска томографија со конусен зрак (CBCT), ја проценивме позицијата, структурата и обликот на прекубројните заби и воедно направивме соодветен план за хируршка екстракција на истите. **Заклучок:** Трудот ја покажува важноста на раната дијагноза и третман на мезиоденсите, со цел да се превенираат или ограничат воспалителни, кариозни, пародонтални и оклузални компликации кои можат да се јават при состојби на прекубројни заби во вилиците. **Клучни зборови:** мезиоденс, прекубројни заби, конусна компјутерска томографија, хируршка екстракција.

Introduction

Supernumerary tooth is a dental anomaly defined as an additional tooth beyond the normal number. It can occur in both the maxilla and mandible[1]. The most common type of supernumerary teeth is mesiodens which is an extra tooth located in the premaxilla with a reported prevalence of 0.15%-1.9%[2].

Many theories have been developed regarding the etiology of mesiodens; however, their origin is unknown to date. These include atavism, dichotomy, and hyperactivity of the dental lamina, with the last being the most logical and acceptable theory[3,4]. Additionally, mesiodens might be associated with multiple genetically inherited syndromes such as cleidocranial dysplasia, cleft lip and palate, Gardner's syndrome, and oral-facial-digital syndrome. It has also been reported that there is evidence that can be attributed to environmental factors as well as other factors such as heredity and family tendencies[5,6].

Mesiodens can give rise to numerous complications related to both the adjacent teeth and other vital structures. The effects on adjacent teeth may range from displacement, rotation, and interference with normal tooth eruption to even more severe complications such as root resorption or abnormal root formation[7].

Mesiodens may also affect adjacent vital structures, causing perforation of the nasopalatine canal or nasal floor, or the formation of cysts[8,9].

Supernumerary teeth are detected incidentally during radiographic examination since mesiodens rarely erupt within the permanent dentition (about 25%), so late diagnosis complications are very common[10]. Panoramic, max-

illary occlusal, and periapical radiographs are indicated to aid in the diagnosis of mesiodens. A panoramic radiograph serves as an aid for detection, and provides additional information on associated, missing congenital or supernumerary teeth. However, despite the great utility of panoramic radiography, it only provides two-dimensional information, making cone-beam computed tomography (CBCT) a useful diagnostic tool for identifying the precise location and shape of mesiodens without overlaps[11].

Case report

In 2022, a 9-year-old male patient was admitted in the Oral Surgery Department in the Faculty of Dentistry, Ss. Cyril and Methodius in Skopje, Macedonia. The reason for the consultation was prolonged eruption of tooth 11. He did not show any syndrome, systemic disease, or medication; He was a shy but cooperative patient who responded favorably to behavioral management techniques. In the intraoral clinical examination, the patient presented mixed dentition with multiple cavitated and non-cavitated, active carious lesions. In the soft tissue, there was an increase in volume in the hard palate between the upper central incisors (11 and 21) of hard consistency, painless, with years of evolution according to the mother's report. A radiographic examination, which was performed by using panoramic radiograph (Figure 1), and for better visualization and planning a cone-beam computed tomography (CBCT), was taken, confirming the presence of two supernumerary teeth in a vertical position in the upper arch. Also, there was not root resorption of the permanent roots of this region and no evidence of associated pathologies (Figure 2). The tuberculate mesiodens was located palatally 11, and conical mesiodens between 21 and 22. Vestibuloversion of teeth 2.1 and 2.2 was observed (Figure 3).

A comprehensive treatment plan was formulated, which included extraction of the mesiodens under local anaesthesia (Figure 4).

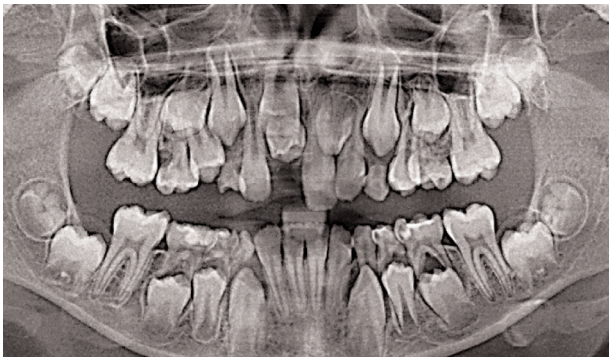

Figure 1. *Panoramic radiograph showing presence of mesiodens*

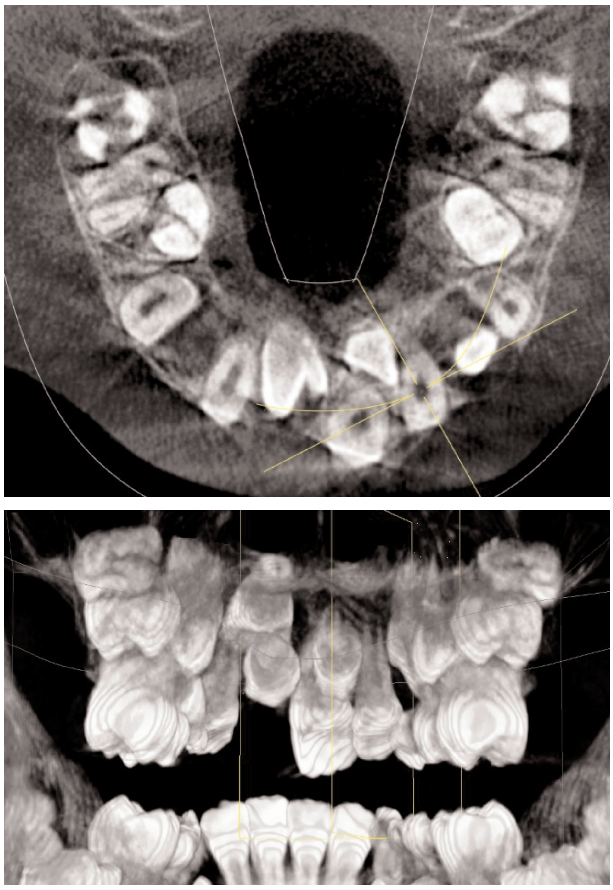

Figure 2. *CBCT images with the presence of tuberculate and conical mesiodens*

Figure 3. *Intraoral examination*

Figure 4. *The extracted mesiodens*

Discussion

The etiology of supernumerary teeth is not clearly understood, despite its regular presentation. Atavism (phylogenetic reversion) theory states that mesiodens represented a phylogenetic relic of extinct ancestors who exhibited three central incisors[12]. Dichotomy theory, in which a tooth bud is split into two separate teeth, usually occurs from complete gemination in the anterior maxilla region[12]. Palatal offshoots or hyperreactivity of active dental lamina are induced to develop into an extra tooth bud, which results in a supernumerary tooth developing into another extra supernumerary tooth[12]. Genetics are also thought to play a vital role in the development of mesiodens since such mesiodens have been diagnosed in siblings, twins, and sequential generations of a single family[12]. Autosomal dominant inheritance with sex-linked patterns with incomplete penetration has been proposed in the formation of such mesiodens. In twins, unilateral mesiodens may present as mirror images located in similar regions of the mouth in the same number[12].

Mesiodens teeth can be classified based on their occurrence in the permanent dentition (rudimentary mesiodens), which are usually smaller and abnormal in shape, or the primary dentition (supplementary mesiodens), which resemble natural teeth in both size and shape[13]. Based on the morphology (conical, tuberculate, or molariform), conical mesiodens usually occur alone. They are generally peg-shaped and usually located palatally between the maxillary central incisors, tending to displace the erupting permanent central incisors[13-15]. Conical mesiodens can often erupt into the oral cavity and have a completely formed root[16]. The crown can be inverted and pointing superiorly, in which case they are less likely to erupt into the oral cavity; inverted conical mesiodens have occasionally erupted into the nasal cavity[2]. Tuberculate mesiodens teeth are barrel-shaped, with several tubercles or cusps, and have incomplete or abnormal root formation. In contrast to conical mesiodens, tuberculate mesiodens teeth rarely erupt themselves but rather develop either unilaterally or bilaterally and delay the eruption of the permanent incisors[15]. Tuberculate mesiodens teeth develop later than conical mesiodens and usually occupy a more palatal position[15]. A third, much rarer type is the molariform mesiodens, which has a crown resembling a premolar tooth and a completely formed root.

The recommended time for mesiodens removal is controversial[17]. Interceptive treatment has been advocated by some clinicians who believe that early removal before root formation of the permanent central incisor increases the chances of spontaneous eruption[18]. Others have advocated delayed treatment to lower the risk of iatrogenic surgical damage to the permanent central's apical development[19]. In a study of 170 permanent central incisors associated with impacted supernumerary teeth, increased root resorption was reported when the supernumerary was removed after complete closure of the central incisor's apex. Early removal of the supernumerary (ideally at 4–5 years and before 6–7 years) is recommended, due to reduced adjacent permanent incisor complications. It must be noted that surgical removal can cause complications such as root resorption, root dilacerations, arrested root development, loss of the lamina dura, and bone deformities[5].

Conclusions

Early diagnosis of the presence of mesiodentes is imperative. A CBCT is essential for properly evaluating its location in a three-dimensional view for its treatment planning. Before surgical removal of symptomatic mesiodens, a labial or palatal approach to mesiodens can be planned after radiographic evaluation by CBCT. Appropriate surgical and/or orthodontic traction is often indicated. Post surgical follow-up in frequent intervals is essential.

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USE OF PIEZO SURGERY DURING SINUS LIFT

УПОТРЕБА НА ПИЕЗОХИРУРГИЈА ПРИ СИНУС ЛИФТ ИНТЕРВЕНЦИЈА

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Abstract

Introduction: MInsufficient bone volume is a common clinical finding during rehabilitation procedures involving the posterior maxilla, and is a complicating factor in the placement of dental implants in this region. In case of greater resorption of the alveolar bone in the maxilla, an open method of raising the maxillary sinus, and creating conditions for placing implants in the posterior regions is used. **The aim** of this paper is to summarize the current knowledge about piezoelectricity/piezosurgery and its comparative analysis in terms of potency, efficacy, and safety in using during lateral sinus lift procedures. **Material and method:** To achieve the purpose, authors reviewed existing papers in the PubMed medical database, Web of Science, and Google Scholar database with access to full text documents, searching for the studies written in the last 10 years (50 analyzed articles). **Results:** The great variety of the analyzed articles emphasize the safety and advantages of using piezoelectric devices, with specific biologic effects on the bone, sustaining bone structure, and cell viability (vital bone) during osteotomies and bone harvesting. Piezosurgery is less invasive, mechanical and thermal injury of the vital structures is avoided, the intra and postoperative complications are decreased, the visibility of the operative field is ideal, and due to less vibrations and noise, the psychological stress and fear of the patient is reduced. **Conclusions:** Piezosurgery is a method of choice in the field of implantology and sinus augmentation procedures for precise, safe, and effective osteotomies sparing the adjacent vital structures. **Key words:** piezoelectricity, piezosurgery, lateral sinus lift, postoperative complications, sinus membrane.

Апстракт

Вовед: СНедоволниот волумен на резидуален алвеоларен гребен е вообичаен клинички наод за време на процедурите за рехабилитација кои ја вклучуваат задната максила и е комплицирачки фактор во поставувањето дентални импланти во оваа област. Во случај на поголема ресорпција на алвеоларната коска во максилата се користи отворен метод на подигање на максиларниот синус и создавање услови за поставување импланти во задните регии.
Целта на овој труд е да ги сумира тековните знаења за пиезоелектрицитетот/пиезохирургијата и компаративно да ги анализира во однос на моќта, ефикасноста и безбедноста при латерален синус лифт процедурите. **Материјал и метод:** За да се постигне поставената цел, авторите ги прегледаа постоечките трудови во медицинската база на податоци PubMed, Web of Science и Google Scholar базата со податоци со пристап до целосни документи, пребарувајќи ги студиите напишани во последните 10 години (50 анализирани статии). **Резултати:** Големата разновидност на анализираните статии ја нагласува безбедноста и предностите од користењето пиезоелектрични уреди, со специфични биолошки ефекти врз коските, одржување на структурата на коските и одржливоста на клетките (витална коска) за време на остеотомиите и при земањето автографтови. Пиезохирургијата е помалку инвазивна, се избегнуваат механички и термички повреди на виталните структури, се намалуваат интра и постоперативните компликации, видливоста на оперативното поле е идеална, а пониските вибрации и бучава го намалуваат психолошкиот стрес и стравот кај пациентот. **Заклучоци:** Пиезохирургијата е метод на избор во областа на имплантологијата и синус лифт процедурите за прецизни, безбедни и ефективни остеотомии со неповредување на соседните витални структури. **Клучни зборови:** пиезоелектрицитет, пиезохирургија, латерален синус лифт, постоперативни компликации, синусна мембрана.

Introduction

Dental implants are an effective method for rehabilitation of simple as well as complex cases of tooth loss. When patients lose their teeth in the posterior regions of the maxilla, there is bone resorption centripetally, as a result of physiological remodeling due to tooth loss, and also bone resorption in the direction from the sinus to the alveolar ridge. These two processes lead to a limited possibility of placing implants in the posterior maxilla, therefore, for this purpose, additional surgical procedures are needed to increase the dimensions of the alveolar ridge both vertically and horizontally. Insufficient bone volume is a fairly common clinical finding during rehabilitation procedures involving the posterior maxilla and is a complicating factor in the placement of dental implants in this region[1].

In order to increase the bone height of the maxillary ridge and to allow the placement of dental implants, the floor of the maxillary sinus is raised, and grafts are placed under the Schneiderian membrane[2].

The classic sinus lift procedure was first described in the seventies of the last century by Tatum, and consists of raising the maxillary sinus through the alveolar ridge dur-

ing bone preparation during the actual placement of the implants. This technique was modified by Summers in 1994, using concave osteotomes that fracture the maxillary floor allowing elevation of the maxillary sinus membrane.

This method, which is called the closed method, is less invasive, shorter and allows for greater bone density which contributes to better primary stability of the implant, and is most often used when the thickness of the alveolar ridge, i.e. bone, is 3 to 5 mm.

In case of greater resorption of the alveolar bone in the maxilla, an open method of raising the maxillary sinus, and creating conditions for placing implants in the posterior regions is used. With this method, the placement of the implants can be performed in the first phase or can be delayed after about 6 (six) months of raising the maxillary sinus by placing a bone graft in order to obtain sufficient height and thickness of the alveolar ridge. The technique is performed by opening a lateral bone window through which the bottom of the maxillary sinus is raised and a bone graft is placed, paying attention not to cause a perforation of the Schneiderian membrane (lateral window technique)[3], which is indicated in cases where the height on the residual ridge is less than 5mm. During the lateral approach, osteotomy is usually performed with rotating implant instruments and drills[2], during which the occurrence of postoperative complications such as pain, edema, limited opening of the mouth, hematoma is possible and common[4].

In order to minimize these clinical manifestations and optimize the surgical procedure, a piezosurgical approach can be used as an alternative in the sinus lift technique with a lateral approach.

Piezosurgery is based on an ultrasonic effect that is obtained as a result of the deformation (contraction and expansion) of certain materials (crystals and ceramics) under the influence of current, which results in oscillating movements[5,6]. In this way, selective cutting (removal) is ensured only in bone tissue, which is especially important in cases where soft tissue anatomical structures (nerves, blood vessels, sinus membrane, dura matter) are located near the operative field[5,7].

Piezoelectricity and piezoelectric bone surgery is contemporary, relevant, and original method of new oral surgery approach, and pre-implantation procedures in minimizing surgical trauma and postoperative discomfort. Piezoelectricity is the electric charge that accumulates in certain solid materials (such as crystals, certain ceramics, and biological matter such as bone, DNA, and various proteins) in response to applied mechanical stress. The word piezoelectricity means electricity resulting from pressure and latent heat. Piezoelectric bone surgery is a process that utilizes piezoelectric vibrations in the application of cutting bone tissue by adjusting the ultrasonic frequency of the device, making possible to cut hard tissue (cavitation phenomenon) while leaving soft tissue untouched by the process. The ultrasonic frequency is modulated from 10, 30, and 60 cycles/s (Hz) to 29 kHz. The low frequency enables cutting of mineralized structures, not soft tissue. The power can be adjusted from 2.8 to 16 W, with preset power settings for various types of bone density. The tip vibrates within a range of 60–200 μm which allows clean cutting with precise incisions.

Research across many fields of medicine now points towards the clinical advantages of minimum invasive piezosurgery. Piezosurgery has a wide application in implantology including sinus lift, provision of autologous bone grafts, bone crest splitting, removal of implants, etc.[8]. Bone removal that is performed using a piezotome is precise and safe without using high pressure while preventing excessive heat generation that would result in bone damage or osteonecrosis[9].

The aim of this paper is to summarize the current knowledge about piezoelectricity/piezosurgery and its comparative analysis in terms of potency, efficacy, and safety in using during lateral sinus lift procedures. Summarizing this information can be a step forward in choosing the most adequate sinus lift treatment in oral surgery practice.

Material and method

To accomplish our goal, we reviewed existing papers in the PubMed medical database as our main source as well as Web of Science, and Google Scholar search that covers wider variety of publications offering easier access to full-text documents, searching for the studies written in the last 10 years (50 analyzed articles). We used specific search query for every part of our research. For analyzing the potency and efficacy of piezosurgery in sinus lift procedures, compared with other classical techniques, we used this search query: “piezosurgery, comparative or compare with conventional surgery with burs”, with the only filter applied: “in the last 10 years”. For analyzing the safety of using piezosurgery in implantology practice we searched: “piezosuregry and safety”.

Results and Discussion

A piezosurgery unit consists of piezoelectric headpiece, control unit for vibrations frequency, cutting power and the amount of irrigation, holders for the headpiece, irrigation fluids, and foot switch which activates the headpiece tips. Various types of headpiece tips are available. Piezosurgery requires light headpiece pressure and continuous saline irrigation to avoid overheating of the bone, and to increase the visibility of the surgical

site. The frequency is usually set between 25 and 30 kHz, producing microvibrations of 60–210 mm amplitude, with power exceeding 5 W. The applied pressure and the speed of the tip in contact with bone influence the cutting power.

The piezoelectric devices have specific biologic effects on the bone, they sustain bone structure and cell viability (vital bone) during osteotomies and bone harvesting. In conventional oral surgery, high pressure from the applied burs and high temperatures, even for short time, may cause bone necrosis. In histomorphological studies, Preti at al.[10] reported that neo-osteogenesis was consistently more active in bony samples from implant sites prepared by piezosuregy with early predominance of anti-inflammatory cytokines BMP-4 and TGF-β2 proteins[11]. In some studies, authors report lower expression of pro-inflammatory cytokines after osteotomy with piezoelectric devices[11,12]. Various studies gave the evidence of improved wound healing and bone formation compared to conventional approaches. The soft tissue sparing capability with improved patient comfort and decreased blood loss gave high level of positioning piezosurgery in the modern world of surgery[13].

The piezoelectric device provides precise cutting of bone tissues without damaging the noble structures (vessels, nerves, and mucous membranes), less heating during osteotomies, and a more favorable postoperative period[14].

In order to increase the bone height of the maxillary ridge in clinical cases with insufficient bone quantity, and to allow the placement of dental implants, the floor of the maxillary sinus is raised (sinus lift procedure), and grafts are placed below the Schneiderian membrane increasing the bone height of the maxillary ridge (sinus augmentation procedures). One of the most used surgical techniques for this procedure is the lateral window technique.

In this technique, incisions should be made to allow adequate exposure of the surgical site in the region of posterior maxilla. After the lateral wall of the maxilla has been exposed, four linear ostectomies are performed to outline the window. The superior horizontal cut should be made at the level of the planned augmentation height, which should allow placement of implants at least 11 mm long. The lateral window approach involves the removal of outlined cortical bone from the lateral aspect of the maxilla without perforation of the sinus membrane using conventional round bur. Another method for exposing the sinus membrane is the use of a piezosurgery device.

Some postoperative complications are common after using lateral window technique in classical manner, such as pain, ecchymosis, limited mouth opening, and edema[15]. These complications are possibly due to high temperatures produced during osteotomy, which may induce marginal osteonecrosis and consequently compromise the bone repair processes[16].

As an alternative, using the piezoelectric device in the lateral window technique was proposed to optimize the surgical procedure and to minimize postoperative complications[17]. Piezosurgery has the advantages of greater precision, effective selective cutting of the bone tissue, protection of the soft tissue, less bleeding in the surgical field, and faster bone tissue regeneration[18].

When the sinus lift surgery with lateral approach is performed with piezoelectric devices, patients experience less pain, less edema and greater mouth opening within 48 hours after the procedure[19]. Piezoelectric devices cause less inflammation after surgery, especially after 48 hours, when the inflammatory process reaches its peak. Less pain intensity and greater level of mouth opening seems to be associated with lower intensity of the inflammatory process after using piezosurgery approach in sinus lift procedures[19].

The performance of piezoelectric devices during sinus elevation was evaluated from various authors to determine the percentage of sinus membrane perforation, and the time required to perform the antrostomy and elevation of the membrane. Studies demonstrated that a piezoelectric device could be an attractive alternative for successful sinus augmentation with low rate of sinus membrane perforations[20].

The most common intraoperative complication during sinus lift surgical approach is perforation of the Schneiderian membrane, with reported perforation rates of 14% to 56% in the literature[21]. In most instances, perforation occurs either while using rotary instruments to make the window or when using hand instruments to gain initial access to begin the elevation of the membrane from the sinus walls. The membrane perforation rate in series of 100 consecutive cases using the piezoelectric technique has been reduced from the average reported rate of 30% with rotary instrumentation to 7%. Furthermore, all perforations with the piezoelectric technique occurred during the hand instrumentation phase and not with the piezoelectric inserts[21].

In the review article of Corinne et al., 377 articles were analyzed. Selected non-randomized and non-controlled prospective and retrospective studies were incorporated. Conventional rotary instruments were associated with a perforation rate of 24%, the piezoelectric devices with 8%, with statistically significant difference between both modalities ($p < 0.05$). The authors concluded that membrane perforations in maxillary sinus floor augmentations may be significantly reduced by using piezoelectrical devices[22].

Schneiderian membrane perforation is the most common complication (noted in the 25 percent of performed

sinus lifts). Some studies reported 56 percent of perforation accidents[23].

Reducing the risk of perforation can be achieved by ultra-careful evaluation of preoperative CT for the assessment of: the thickness of the sinus bone wall, the location of septa, and the membrane thickness; the incidence of perforation is higher when the thickness is less than 1.5 mm[24].

From the analyzed studies, the advantages of piezosurgery in lateral sinus lift procedures can be summarized: improved soft tissue protection, mechanical and thermal injury of the vital structures nerves, blood vessels, Schneiderian membrane are avoided; ideal visibility of the operative field by voiding the blood of the cutting area by cavitation and microvibration effects; reduced blood loss; piezosurgery can be performed with small amount of pressure, piezosurgery reduces the incidence of necrosis of osteotomized fragments and produces less vibrations and noise thereby reducing the psychological stress and fear of the patient (patient comfort).

Conclusions

Piezosurgery is a method of choice in the field of implantology and sinus augmentation procedures for precise, safe, and effective osteotomies sparing the adjacent vital structures. It facilitates the bone healing by increasing the bone morphogenic proteins and reduces the inflammatory process with less postoperative patient discomfort.

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LEVEL OF DENTAL ANXIETY AND STRESS IN PATIENTS WITH ORTHODONTIC APPLIANCES

НИВО НА ДЕНТАЛНА АНКСИОЗНОСТ И СТРЕС КАЈ ПАЦИЕНТИ СО ОРТОДОНТСКИ АПАРАТИ

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Abstract

Fear and anxiety of dentist and dental treatment are widespread problems that results in a significant barrier to the receipt of dental care. It can cause treatment difficulties for the practitioner as well as severe consequences for the patient. The level of stress can be evaluated directly or indirectly by psychometric tests. **Aim:** The aim of this study is to examine dental anxiety and stress in two groups of patients: children with orthodontic anomalies wearing removable orthodontic appliances, and children with caries on primary and permanent teeth. **Material and methods:** We examined two matched groups of patients: children with orthodontic anomalies (N = 31, mean age 10.3 ± 2.02) years and children with ordinary dental problems (N = 31, mean age 10.3 ± 2.4 years). Both genders were presented equally. As for psychometric instruments, we used 45 items Sarason's scale for assessing anxiety level, and 20 items simple Stress - test adapted for children for obtaining the level of stress. **Results:** The obtained results confirmed the presence of moderate anxiety in both groups as well as moderate stress level. For Sarason's test, the obtained scores for the group with dental problems are 20.63 ± 8.37 (from max 45); and for Stress test 7.63 ± 3.45 (from max 20); for the orthodontic group obtained scores are 18.66 ± 6.85 for Sarason's test, while for the Stress test were 7.76 ± 3.78. One way ANOVA confirmed significant.difference.in.values.of obtained scores related to age. Calculated Student t-test shows non-significant differences in obtained test results for both groups of examinees (t-test was > 0,05). **Conclusion:** This study confirmed that moderate anxiety and relatively normal stress level are present in both groups of patients (orthodontic and dental). The obtained results depend on age (one way ANOVA). **Key words:** dental anxiety, stress, orthodontics, assessment.

Апстракт

Стравот и анксиозноста од стоматолог и денталниот третман е широко распространет проблем кој резултира во значителна бариера за прифаќање на стоматолошката грижа. Може да предизвика потешкотии во третманот за докторот, како и тешки последици за пациентот. Нивото на стрес може да се евалуира директно или индиректно со психометриски тестови. **Цел:** Целта на оваа студија беше да се евалуира анксиозноста и чувството на стрес кај две групи пациенти, ортодонтски, односно деца кои носат мобилни ортодонтски протези, и педодонтски пациенти - деца со присуство на кариес на млечни и трајни заби. **Материјал и метод.** Примерокот содржеше две групи деца: деца со ортодонтски апарати (31 дете, средна возраст 10.3 ± 2.02 години) и деца со вообичаени дентални проблеми (31 дете, средна возраст 10.3 ± 2.4 години). Двата пола беа еднакво застапени. Беа употребени следниве психометрички тестови: Sarason's General Anxiety Scale - Сарасон скала за одредување на нивото на анксиозност и едноставни Стрес тестови адаптирани за деца за одредување на нивото на стрес. **Резултати.** Резултатите од Sarason тестот за анксиозност за ортодонтската група беа 18.66 ± 6.85, а за стрес тестот 7.76 ± 3.78. За групата деца со дентални проблеми резултатите беа 20.63 ± 8.37 и 7.63 ± 3.45, соодветно. Добиените вредности кореспондираат на ниво на средна анксиозност (од max 45) за Sarason тестот и ниско ниво на стрес (од max 20) од стрес тестот. ANOVA тестот покажа сигнификантна разлика во збирните вредности добиени со Sarason скалата за анксиозност по однос на возраста, во двете групи испитаници. Студентовиот t-тест покажа несигнификантна разлика во добиентите резултати од тестот за двете групи испитаници. **Заклучок:** Студијата потврди умерена анксиозност и релативно нормално ниво на стрес кај учениците под дентален и ортодонтски третман. Најдените збирни вредности за психометриските тестови се сигнификантно варијабилни во согласност со возраста. **Клучни зборови:** дентална анксиозност, стрес, ортодонција, проценка.

Introduction

Fear and anxiety of the dentist and dental treatment are widespread problems that results in a significant barrier to the receipt of dental care. It can cause treatment difficulties for the practitioner, as well as severe consequences for the patient. The level of stress can be evaluated directly or indirectly by psychometric tests.

As a physiological and psychological state characterized by cognitive, physiological and behavioural components, anxiety and its related conditions are one of the most prevalent psychological disorders in the general population[1].

In children, anxiety can be expressed by exclamations, choleric accesses, stupefaction or the urge of hanging on to something. Often, children do not admit

that their fear is excessive and they rarely relate their phobias.

Psychology and behavioural sciences have become increasingly important in dental education, clinical practice and research over the last twenty years. The incidence of dental anxiety and phobia ranges from 10% to 30%, depending on several factors such as nationality, socio-economic background and conditions, previous distressing experiences and type of intervention[2].

Dental anxiety is defined as a patient's response to stress that is specific to the dental situation. It is the most common psychological condition seen in dentistry and affects a significant percentage of the population. Because of this reason, it is well documented that dentists deal with anxious patients in their daily practice. Anxiety in patients influences both the psychology (e.g., avoidance of dental care) and the physiology (e.g., palpitations, nausea) of the dental experience, which leads to a variety of behaviours that impact dental care, such as delay and avoidance of dental treatment[3].

Dental anxiety was first studied by Shoben and Borland in 1954, who explained that this avoidance behaviour results from unfavourable attitudes toward dentists on the part of family members and a history of painful dental experiences. Dental anxiety not only leads to avoidance of dental care, but it may also affect individuals, generally by causing sleep disturbance, negative thoughts, and feelings of low self-esteem and confidence[4]. It was also described by Klingberg and Broberg as a state of apprehension that something dreadful is going to happen in relation to dental treatment or certain aspects of dental treatment[5].

As such, it has impact both on the patient and on patient management and treatment. Surveys indicate that a substantial proportion of the general population avoids making regular visits to the dentist because of their anxiety. That behaviour can be detrimental for them because untreated dental disease (e.g., periodontal disease, dental caries) leads to poorer oral health, reduced dental visits, and, consequently, poorer oral-health-related quality of life[5,6,7,8].

Dental anxiety is ranked fifth among commonly feared objects or situations. It is the most common psychological condition seen in clinical practice, and it affects a significant percentage of the population. There is a significant variability in the prevalence of dental anxiety reported in literature. Epidemiological studies suggest that between 3% and 20% of the population are anxious or have levels of fear about dental treatment[1,3,5].

The etiology of dental anxiety has been attributed to many factors, such as personality characteristics, traumatic or painful dental experiences in childhood, learned attitudes toward dental services that elicit fear from dentally anxious family members or peers, perception of body image, blood injury fears and pain reactivity[8].

According to Locker, several theories exist that attempt to explain the etiology of dental anxiety. Three main etiological hypotheses for explaining the cause of dental anxiety have been suggested, as follows: conditioning responses to aversive dental experiences, heightened pain sensitivity and/or fear of dental pain, and predisposing personality characteristics[9].

Other factors contributing to dental anxiety are gender (most of the studies report higher anxiety among females), age (young subjects tend to be more anxious than older individuals), personality, family members' fear, previous dental treatment experiences and type of intervention, subject's education level (patients with higher education level demonstrated lower dental anxiety), income level, and cultural background[10,11].

Anxiety in orthodontics

A significant number of patients were also identified as anxious about seeing an orthodontist. The prevalence of those anxious about orthodontic treatment was slightly lower than those anxious about dental treatment. Although the prevalence of dental anxiety is well-documented, less information is available about the prevalence of dental anxiety among orthodontically treated patients, most likely because of the lack of commonly reported evoking stimuli drill and needle associated with dental anxiety.

Orthodontic treatment remains associated with pain despite improvement in techniques or practitioners' technical abilities. Discomfort related to orthodontic treatment has been reported as one of the most negative aspect of treatment and is ranked fourth among major concerns and worries prior to orthodontic treatment.12 In dental literature, it is well documented that fear of pain is one of the possible etiologies of dental anxiety. Although pain is subjective, a certain discomfort is unavoidable during orthodontic treatment. Recent literature stated that some orthodontic procedures such as separator placement, arch wire placement and activations, application of orthopaedic forces, and debonding produce pain in patients. It has also been suggested that patients treated with fixed appliances, experience more pain than removable or functional appliances[1,10,12].

The aim of Prabhat et al., study was to examine the pain experienced by patient after the mini screw implant placement, and the dental anxiety that might influence the pain experience. The study showed a positive linear relationship between dental anxiety and patient pain experience following mini screw implants placement[6].

Pain experienced during orthodontic treatment can be a reason for discontinuing or delaying orthodontic visit

which not only prolongs treatment duration, but may also result in poor oral hygiene, compromised periodontal status, low self-esteem, and general well-being[10].

In their observational clinical study, Vaida et al., consider that the most important stress-generating sources, before, as well as, after the application of the orthodontic devices, are the patient's negative thoughts concerning the social integration, and also the family integration, the attitude of the entourage as in "what are my colleagues going to say when they they see me wearing it", the difficulties during speech or eating, the duration of the treatment (2-3 years average) also the need for check-ups, and activating sessions. They also concluded that the reduction of the anxiety level is mandatory at the beginning of the orthodontic treatment. Therefore, a basic set of child psychology knowledge should increase the competence and professionalism of the orthodontist[8].

Also, Trakyali et al. said that it would be useful to overcome the increased state of anxiety of the child in the orthodontic clinic by using educational and relaxation techniques[13].

In our country there is a study for dental anxiety from Sarakinova, Pop Jordanova et al., on 50 school children. They found high level of anxiety in children undergoing dental interventions, with higher results for the girls[14].

Aim

The aim of this paper is to evaluate the level of anxiety and stress in two groups of children with orthodontic anomalies, wearing removable appliances, and in children with ordinary dental problems, caries on primary and permanent teeth.

Material and method

The evaluated sample was comprised of two groups of schoolers: a) children with orthodontic problems (anomalies in shape, position and function of dentofacial structures), wearing removable appliances (N=31, mean age 10.3 ± 2.02 years); and b) children with ordinary dental problems, caries on primary and permanent teeth (N=31, mean age 10.3 ± 2.4 years). Both genders were presented equally. Examinees were selected randomly.

The following psychometric tests were used: Sarason's General Anxiety Scale for assessing anxiety level and Stress test for children for obtaining the level of stress[15,16].

The Sarason's General Anxiety Scale for Children (GASC) is a 45-item yes/no scale for using with children from primary school. It measures chronic, generalised anxiety that is aroused in children by test situations. The items of the GASC are concerned with attitudes toward, and experiences in, test and test-like situations. The obtained score of 12 (yes answers) or below, ranks in the low anxiety range. A score of 12-20 ranks in the medium range. Any score above 20 signifies high anxiety. Scoring 15 or higher is a good indication that a child experiences considerable discomfort about the situation in which it is[15].

Stress-test is a simple yes/no 20-item questionnaire where the higher scores are related to higher stress level[16]. Tests were verbally administrated and were conceptualized as a single dimension measured by 45/20 items using yes/no response format.

The psychological tests in this study were applied prior to dental intervention. Children were usually accompanied by their mothers, who gave prior consent for the study.

For statistical calculations, the online package Statistics 8 was used.

Results

Two groups of examinees were included: a) 31 children with orthodontic problems, mean age 10.3 ± 2.02 years; and b) 31 children with simple dental problems, mean age 10.3 ± 2.4 years. Examinees were matched by age and gender.

Evaluated by Sarason's anxiety test, the obtained scores for the group with orthodontic problems were: 18.66 ± 6.85 using Sarason's anxiety tests, and 7.76±3.78 using Stress test. The obtained scores in the group with dental problems were: 20.63 ± 8.37 (from max 45); these

Table 1. Obtained results from the test in both groups

Orthodontic patients	Dental patients	Test
18.66 ± 6.85	20.63 ± 8.37	Sarason's anxiety test
7.76 ± 3.78	7.63 ± 3.45	Stress-test

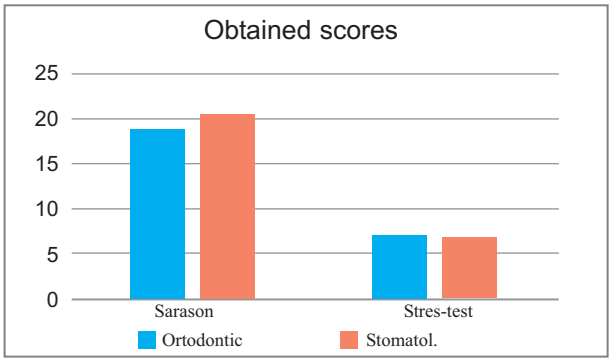

Figure 1. *Obtained scores for both psychometric test in orthodontic and dental patients*

Table 2. ANOVA-related-age and scores using stress-test in both groups

a)orthodontic group

Effect	Sum of Squares	Degr.of freedom	Mean Square	F-value	p-value
Intercept	2229.803	1	2229.803	400.6634	0.000000
Stress test	110.125	11	10.011	1.7989	0.129696
Error	100.175	18	5.565		

b)dental group

Effect	Sum of Squares	Degr.of freedom	Mean Square	F-value	p-value
Intercept	2229.803	1	2229.803	400.6634	0.000000
Stress test	110.125	11	10.011	1.7989	0.129696
Error	100.175	18	5.565		

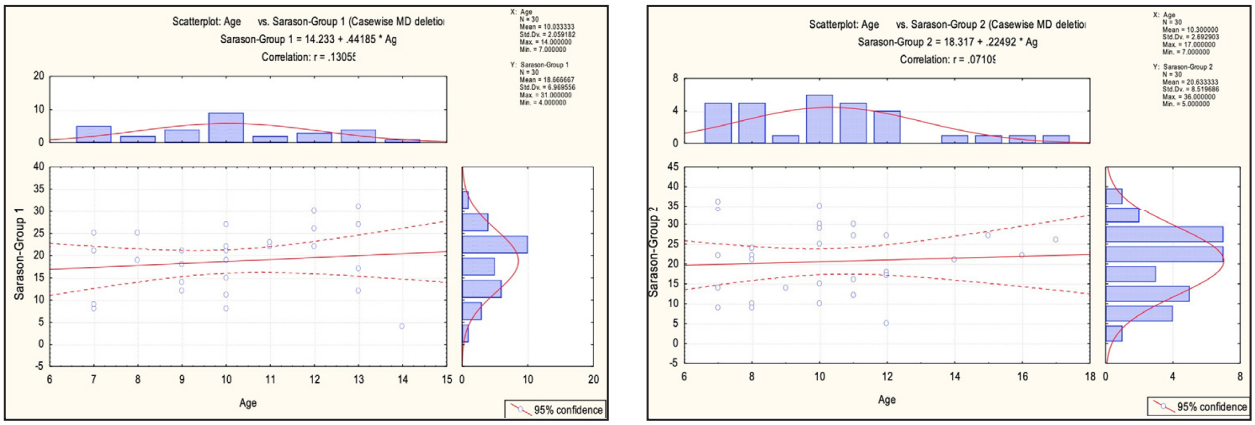

Figure 2. *Correlation between age and scores obtained with Sarason's anxiety test*

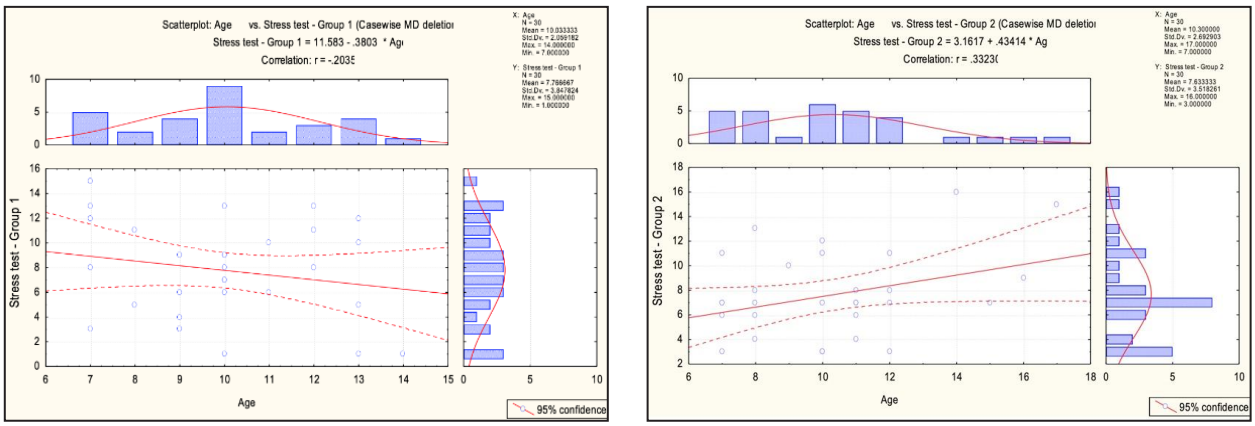

Figure 3. *Correlations between age and obtained scores with Stress-test in both groups of examinees*

results correspond to moderate anxiety level. Evaluated by Stress test 7.63±3.45 (from max 20), which correspond to small stress level. (Table 1, Figure 1).

Calculated one-way ANOVA showed a significant variance in scores obtained using Sarason's anxiety scale related to age in both groups of patients.

Calculated one-way ANOVA for the significance of age in stress test is presented in Table 2. In this calculation, results also confirmed the influence of the age on the variance of the obtained scores.

The correlation between age and scores evaluated by Sarason's anxiety test is shown in Figure 2. There was a small positive, not significant correlation between the two mentioned variables (r = 0.13; r = 0.7, respectively).

The correlation between scores obtained with Stress-test for both groups of patients is shown in Figure 3.

As it can be seen, the correlation between age and obtained scores using Stress-test is negative for orthodontic patients (r= - 0.20), but positive for dental patients (r=0.33).

Finally, we used Student's t-test for obtained scores in both groups for both psychometric tests (Figure 4 and 5).

The Student's t-test showed no significant differences in obtained scores for both tests in both groups of examinees (t-test > 0.05).

	T-test for Independent Samples (Copy of sarakinova-excel 97) Note: Variables were treated as independent samples										
Group 1 vs. Group 2	Mean Group 1	Mean Group 2	t-value	df	p	Valid N Group 1	Valid N Group 2	Std.Dev Group 1	Std.Dev Group 2	F-ratio Variances	p Variances
Sarason-Group 1 vs. Sarason-Gr	18.6666	20.6333	-0.9786	58	0.33183	30	30	6.96955	8.51968	1.49429	0.2852

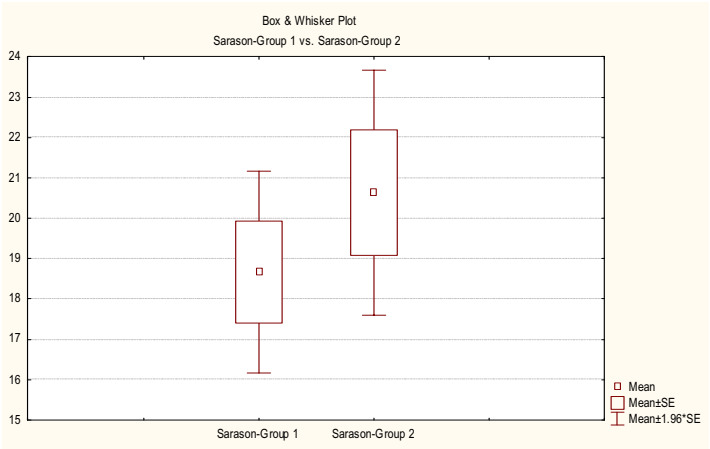

Figure 4. *T-test for scores obtained for Sarason's anxiety test in both groups*

	T-test for Independent Samples (Copy of sarakinova-excel 97) Note: Variables were treated as independent samples										
Group 1 vs. Group 2	Mean Group 1	Mean Group 2	t-value	df	p	Valid N Group 1	Valid N Group 2	Std.Dev. Group 1	Std.Dev. Group 2	F-ratio Variances	p Variances
Stress test - Group 1 vs. Stress test - Group 2	7.76666	7.63333	0.14006	58	0.88909	30	30	3.84782	3.51826	1.19611	0.63283

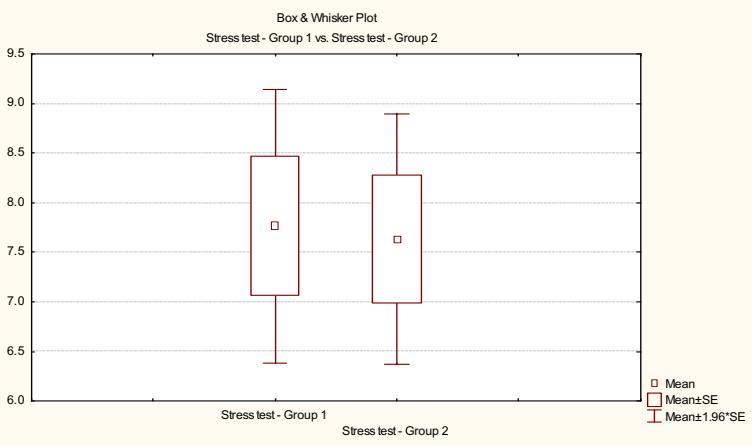

Figure 5. *T-test for scores obtained for Stress-test in both groups*

Discussion

Orthodontic science puts itself before other specialties of the dental medicine by the type of patients it refers to, children and adolescents. In most of the patients who have dento-alveolar abnormalities, the abnormality itself is a stress-generating factor. The stress level is different due to the degree in which it affects physiognomy and personal variables. To this primal stress factor, we add the anxiety and distress generated by the medical act itself, as to "what's going to happen to me". Children often confound the orthodontist to a pedodontist, the person who treats their cavities. Another major stress-generating factor is, at the beginning of the treatment, the patient's cognitions concerning the aspect of the orthodontic device, the difficulties of wearing it, and especially the social integration in the family and in society.

The results of our study revealed the presence of moderate anxiety and relatively low-stress level in evaluated school children in both groups (orthodontic and dental settings).

These results differ from the previous study by Pop Jordanova et al., from 2013 where obtained dental anxiety scores were more accentuated, and the same were higher for girls compared to boys[14]. We suppose that the level of anxiety/stress was not so high as a result of productive coping styles used by children in dental setting as well as the education in primary school for the need of dental health. Our results are quite similar to most of other studies in this context.

Bhola[7] reported moderately high levels of anxiety with score of 60,75% in India. Because the time of the orthodontic treatment and the first probable visit coincided in many of the individuals, their anxiety was cumulative to both. They were anxious due to the various complex treatments, wires, and long durations of the orthodontic therapy.

In study by Khokhar, 46% of the participants had mild anxiety score whereas only 4% of the participants experienced severe anxiety[11].

In their study, Surabhi et al., found that 45% of the participants had mild anxiety, 32.5% of the participants had moderate level anxiety, 17% of the participants had high anxiety, whereas only 5.5% of the participants experienced severe anxiety or phobia[10].

Using the Sarason's anxiety test, a very small positive, but not significant correlation was obtained for age and scores, while using the Stress-test, the calculated correlations between age and scores were positive for dental, and negative for an orthodontic group of patients, but without statistical significance.

In 2007, Klingberg and Broberg published a review about prevalence of dental anxiety in children and adolescents. They found a decrease in prevalence with age in some studies they reviewed. They concluded that the decrease of dental anxiety with age may be due to normal psychological development[5].

The prevalence of dental anxiety in specific age groups has been studied by numerous authors, and there are a lot of controversies among those studies. According to Roy,1 a few studies have found no significant difference in dental anxiety level between different age groups, while recent literature reports an association between age and dental anxiety, with younger subjects being more dentally anxious than older individuals. He also added that, comparing results from studies using different dental anxiety measures as well as inconsistency in the use of cut points to define clinically significant anxiety lead to variation in the prevalence of anxiety.

The purpose of this study was to create an awareness of the problem by assessing the dental anxiety among orthodontic patients, so that anxious and fearful orthodontic patients can be facilitated accordingly.

Although studies[17,18] have assessed several aspects of anxiety related to dental treatment, no research in our country has investigated dental anxiety among patients receiving orthodontic treatment. This could be because dentists and orthodontists assume that their patients are not anxious because orthodontic treatment is not associated with dental drilling or injections for local anaesthesia, which are two of the most commonly cited stimuli associated with dental anxiety. However, pain is often cited as a cause of dental anxiety, and pain experienced during orthodontic treatment has been reported as the worst aspect of treatment by some patients and a primary reason for wanting to discontinue orthodontic care[1]. Some studies[19] reported moderate pain experienced by 62% of the patients and others[20] even 95%.

The data collected from this kind of studies will provide better understanding of the nature of anxiety in orthodontic patients as it relates to their treatment. This will hopefully benefit both orthodontists and patients by providing a more enjoyable treatment experience.

Conclusions

In conclusion, the study confirmed moderate anxiety level, and relatively normal stress level in school children undergoing orthodontic and dental interventions. The obtained scores for psychometric tests are significantly different according to age (one way ANOVA).

No significant differences were observed between mean values of scores in both groups of examinees, and for both psychometric tests. Using the Sarason's anxiety test, a very small positive, but not significant correlation was obtained for age and scores. Calculated correlations between age and scores, using the Stress-test, was positive for the dental, and

negative for the orthodontic group of patients, but without statistical significance.

Determining the prevalence of dental anxiety in orthodontics as well as the factors contributing to it will create an awareness of the problem and will help clinicians to identify patients who are anxious, and to facilitate appropriate treatment and management during orthodontic treatment.

In our country, we need further evaluation of dental anxiety in orthodontics and in other dental specialities on larger number of patients to obtain more concrete results.

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UDK: 616.316-008.831

ENZYMATIC ANTIOXIDANT CAPACITY AND SALIVARY OXIDATIVE STRESS REDOX MARKERS: VERIFICATION OF METHODS FOR FURTHER INVESTIGATION

ВЕРИФИКАЦИЈА НА МЕТОДИ ЗА ОДРЕДУВАЊЕ ЕНЗИМСКИ АНТИОКСИДАТИВЕН КАПАЦИТЕТ И НИВО НА САЛИВАРЕН ОКСИДАТИВЕН СТРЕС ПРЕКУ РЕДОКС МАРКЕРИ

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Abstract

Introduction: Saliva, as complex mixture of fluids, is an interesting alternative diagnostic tool which contains many immunoglobulins, enzymes, lactoferrin, lysosomes and histamines. Despite the role of oxidative stress in numerous systemic diseases, explaining the mechanisms which oxidative stress can contribute to pathology, makes the saliva screening methods specific and more sensitive in terms of evaluation of the biomarker level. **Material and methods:** This observational study included 20 participants (10 smokers and 10 non-smokers). Saliva samples were collected in the period between 9 and 12 hours in the morning, and centrifuged (15 minutes per 10000 g at 4oC). The supernatant was kept at -20oC until further analyses that included analysis of salivary enzymatic antioxidant capacity (activity of antioxidant enzymes superoxide dismutase- SOD, catalase-CAT and glutathione peroxidase-GPx) and the level of lipid peroxidation marker for oxidative stress – malondialdehyde (MDA). **Results:** Salivary levels of SOD were higher in smokers than non-smokers group and the average activity of GPx was with significant lower value in smokers group. There was noted positive finding in the imbalance of salivary enzymatic antioxidant activity due to the presence of free radicals in cigarette smoke group. The level of salivary redox biomarkers did not vary based on gender. **Conclusion:** According to our findings, the increased salivary levels of MDA in smokers as the result of process of peroxidation, which indicates oxidative stress, contributing to the increased levels of free radical–mediated oxidative damage of lipids, definitely supports the hypothesis that oxidative damage in smokers is due to their active exposure directly to saliva. **Keywords:** oxidative stress; saliva; malondialdehyde; superoxide dismutase; catalase.

Апстракт

Вовед: Плунката во чиј состав влегуваат значителен број компоненти, претставува ветувачки медиум и алтернативна дијагностичка алатка за детекција на голем број заболувања. И покрај улогата на оскидативниот стрес во голем број системски нарушувања, го прават овој метод поспецифичен и посензитивен за верификација на патолошки процеси. **Материјал и методи:** Во оваа опсервациска студија беа вклучени 20 испитаници (10 пушачи и 10 непушачи). Беше собрана нестимулирана плунка, во периодот од 9 до 12 часот наутро, и истата беше центрифугирана (15 минути на 10 000g, при 4 oC). Супернатантот беше чуван на -20 °C до понатамошните анализи кои вклучуваа анализа на ензимскиот антиоксидативен капацитет на плунката (активност на антиоксидативните ензими супероксид дизмутаза-SOD, каталаза и глутатион пероксидаза- GPx) и на степенот на липидна пероксидација – преку маркерот за нивото на оксидативен стрес – малондиалдехид (MDA). **Резултати:** Пушачите имаа значајно повисоко ниво на SOD активност во плунката во споредба со непушачите, додека пак просечната активност на GPx беше пониска кај пушачите. Забележана е позитивна корелација во нарушениот баланс помеѓу активностите на антиоксидативните капацитети на ензимите во плунката поради присуството на слободни радикали во цигарите. Имајќи ја предвид просечната возраст и половата дистрибуција како коваријанта при анализата на податоците за саливарен редокс, многу малку или речиси не се разликуваа. **Заклучок:** Индицирајќи ја состојбата на оскидативен стрес, забележано е зголемено ниво на MDA кај пушачите, процес посредуван од слободни радикали преку формирање липидни пероксиди, чија улога дефинитивно ја потврдува хипотезата за оксидативниот дисбаланс кај пушачите, кој се должи на директната исложеност на плунката и оралната празнина со цигарите. **Клучни зборови:** оксидативен стрес; плунка; малондиалдехид; супероксид дисмутаза; каталаза.

Introduction

According to the Global Cancer Observatory (GLOBOCAN), which is an online database providing global cancer statistics, 2019-2020 is considered the period when COVID-19 outbreak was declared a pandemic. Hence, on a global level, a total of 377.713 new cases of oral cell carcinoma were registered worldwide [1,3,5-16]. The geographical distribution of this type of carcinoma is of variable parameters, epidemiologically distributed: Asia - 248.360, Europe - 65.279, North America - 27.469, Latin America and the Caribbean - 17.888, Africa - 14.286, Oceania - 4.431[3-5, 8-11]. Early detection and screening of premalignant and malignant diseases in oropharyngeal region can have a significant influence on the patients' mortality and morbidity. Smoking, as a stress factor, impacts the absorption of harmful components in the human body such as: nitric oxide, carbon monoxide, nicotine, cadmium, methanol and polycyclic carbohydrate compounds[1,3,5,6,9,10]. These components or their metabolic compounds most commonly activate the biological macromolecules that further influence the level of salivary oxidative stress and generate free radicals that are responsible for tissue damage. Saliva is the first defense barrier that comes in contact with foreign bodies or gasses (such as cigarettes, for e.g.). The activity of salivary antioxidants in smokers can be disturbed in terms of cumulative stress caused by the decline of immune cells and metabolic processes in the gingival fluid. Saliva, as a medium, and its chemical composition are the most suitable constituent components that play a big role in the determination of the individual antioxidant capacity and status in the oropharyngeal cavity of smokers[1-6,10,11,14-16]. Damages to the oral mucosa include the initial stage of formation and colonization of reactive processes that take place at the level of cellular and extracellular matrix[9,13,14,17-21]. Significant values of increased salivary antioxidative stress have been detected in oral carcinoma compared to patients with other benign epithelial lesions[2-5,10,17,19]. Diagnosis of malignancy through saliva, evaluation of the level of salivary and serum biomarkers, and determining the redox status have seen enormous progress by confirming or rejecting most of its constituent parameters, especially when it comes to oral squamous cell carcinoma. The aim of this study was to determinate the methods for SOD, CAT and CPx activity following MDA concentrations in smokers and non-smokers group, representing the antioxidative status and oxidative stress levels which will be an important part from the perspective of using saliva for further research.

Material and method

Subjects and experimental design

This observational study included 10 smokers (group P, with a smoking history not less than 10 years, from 5 to 10 cigarettes per day) and 10 non-smokers (group K as a control group), who were selected by a simple, non-randomized method. In general, subjects were healthy and received no therapy for systemic diseases in the last 3 months. All of them were informed about the objectives of the study, that is, about the analyses of their saliva; they were guaranteed anonymity, and they filled out a written informed consent. Subjects were required not to consume food or water for at least 4 hours prior to collecting saliva samples. Smokers were forbidden to smoke for at least 2 hours prior to taking saliva samples. Unstimulated saliva was collected; each subject was asked to spit saliva in a 15 ml sterile vial. The procedure was performed in a standing position in the period between 9 and 12 hours in the morning. The saliva was centrifuged to remove squamous cells and different cellular fragments (15 minutes at 10000 g at 4^{O}C, Universal 320 centrifuge, Hettich Lab Technology, Germany). The supernatant was kept at -20^{O}C until further analyses that included analysis of salivary enzymatic antioxidant capacity (activity of antioxidant enzymes superoxide dismutase, catalase and glutathione peroxidase), and the level of lipid peroxidation marker for oxidative stress – malondialdehyde. All biochemical analyses were conducted at the Institute of Biology, Faculty of Natural Sciences and Mathematics - Skopje.

Determination of superoxide dismutase (SOD) activity

The activity of superoxide dismutase was determined by the kinetic method described by Marklund and Marklund (1974). It is based on the ability of superoxide dismutase to inhibit pyrogallol autooxidation in an alkaline environment. The reaction mixture contained 50 mM Tris-HCl, pH 8.65, 1 mM diethylenetriaminepentaacetic acid (DETAPAC) and a saliva sample. The reaction was started by adding pyrogallol (final concentration of 0.2 mM), and the absorption was measured kinetically at a wavelength of 420 nm (25^{O}C) for 3 minutes (Model 680 Microplate Reader, Bio-Rad Laboratories, USA). One unit of activity (U) is defined as the amount of the enzyme (from the sample) necessary to perform 50% of inhibition of pyrogallol oxidation.

Determination of catalase (CAT) activity

The catalase activity was measured by the method of Claiborne (1985). The reaction mixture contained 50 mM of potassium phosphate buffer (pH 7.0), 19 mM H_2O_2, and a saliva sample. The reaction was initiated by adding H_2O_2, and the absorption changes were measured at a wavelength of 240 nm for 30 seconds (every 5 seconds) at 25^{O}C. In such conditions, molar absorption coef-

ficient for H_2O_2 was 43.6 M^{-1} cm^{-1}. One unit of activity corresponds to the amount of the enzyme that performs conversion of 1 µmol H_2O_2 in 1 minute.

Determination of glutathione peroxidase (GPx) activity

The activity of superoxide dismutase was determined by the modified method of Lawrence and Burk (1976). The reaction mixture contained 50 mM potassium phosphate buffer, pH 7.0, 1 mM sodium azide, 2 mM GSH, 0.2 mM NADPH, 1 U/ml GR, 1.5 mM cumene hydroperoxide and a saliva sample. The reaction was started by adding cumene hydroperoxide, and the absorption change originating from the NADPH oxidation was monitored at a wavelength of 340 nm for 3 minutes. The reaction took place at 25°C, in the presence of glutathione reductase and reduced glutathione. One unit of activity is defined as the amount of the enzyme (from the sample) that catalyzes oxidation of 1 µmol of NADPH for 1 minute.

Determination of malondialdehyde (MDA) concentration

The concentration of malondialdehyde in saliva was determined by the modified method of Yagi (1998). Solutions of 50% trichloroacetic acid (TCA), and 1.3% thiobarbituric acid (TBA) (dissolved in 0.3% NaOH) was added to the saliva sample. After 20 minutes of incubation at 90-95° in a water bath, samples were instantly chilled/cooled in ice and then centrifuged (10 min. per 4000 g). The supernatant absorption was measured at a wavelength of 535 nm. 1,1,3,3-tetraethoxypropane was used as a standard.

Statistical analysis

Data in the figures are presented as mean ± standard deviation (SD). Normal distribution of data was verified with Kolmogorov-Smirnov test. The statistical analysis for comparison of the means of the examined parameters between the groups was made with the Student's t-test for independent groups of samples. The correlation between the variables was analyzed with the Pearson's test. All analyses were made with the statistical package GraphPad Prism, version 8.0.0. (GraphPad Software, San Diego, CA, USA). Values of $p<0.05$ were considered to be statistically significant.

Results

Twenty patients, including 10 non-smokers (4 males and 6 females) and 10 smokers (6 males and 4 females) were included in this study. The statistical distribution according to gender in both groups (K-non-smokers and P-smokers) was almost equal. The mean age of participants in non-smokers was 48.4 years (aged 37-61) and 49.1 years (aged 40-59) for the second group (smokers). The age wasn't observed as covariant, then we respectfully and mathematically output to verify that there is no statistically significant difference between the groups.

Table 1. Distribution according to the patients' gender and mean age (**K** - nonsmokers, **P** - smokers).

Parameters/ Group	K	P
Number	10	10
Gender (m/f)	4/6	6/4
Mean age	48,4 ± 7,9 (37-61)	49,1 ± 6.3 (40-59)

The analysis showed that salivary levels of SOD were higher in the smoker's group than in the non-smokers group (p=0,0008) (Figure 1.). On the other hand, the average activity of GPx had a significantly lower value in smokers compared to non-smokers group (p=0,0001) (Figure 1). Similarly, the mean activity of catalase (CAT) in saliva among the participants in the smokers group was observed to be lower than in the non-smokers group, but there was no evidence of statistical significance between the two groups. Thus, there was positive finding in the imbalance of salivary enzymatic antioxidant activity, and due to the presence of free radicals in the smokers group, increased levels of salivary MDA are observed in smokers (p=0,0102) (Figure 1), and consequently induces oxidative stress.

The data obtained in this study show negative correlation between SOD and MDA (r = -0,4313, p=0,0567), CAT and MDA (r = - 0,5726, p=0,0083),), GPx and MDA (r = -0,4818, p=0,0315) (Figure 2). So, there is a marked increase of SOD, GPx and MDA salivary levels in group of participants that smoked cigarettes, contributing to increased levels of free radical–mediated oxidative damage of lipids, supporting the hypothesis that oxidative damage in smokers is due to their active exposure directly to saliva.

Fig 1. show the results evaluated for total antioxidant capacity of saliva and lipid peroxidation biomarkers for evaluating oxidative stress.

Figure 2 presents the statistical correlation between every mathematical parameter which represents the total

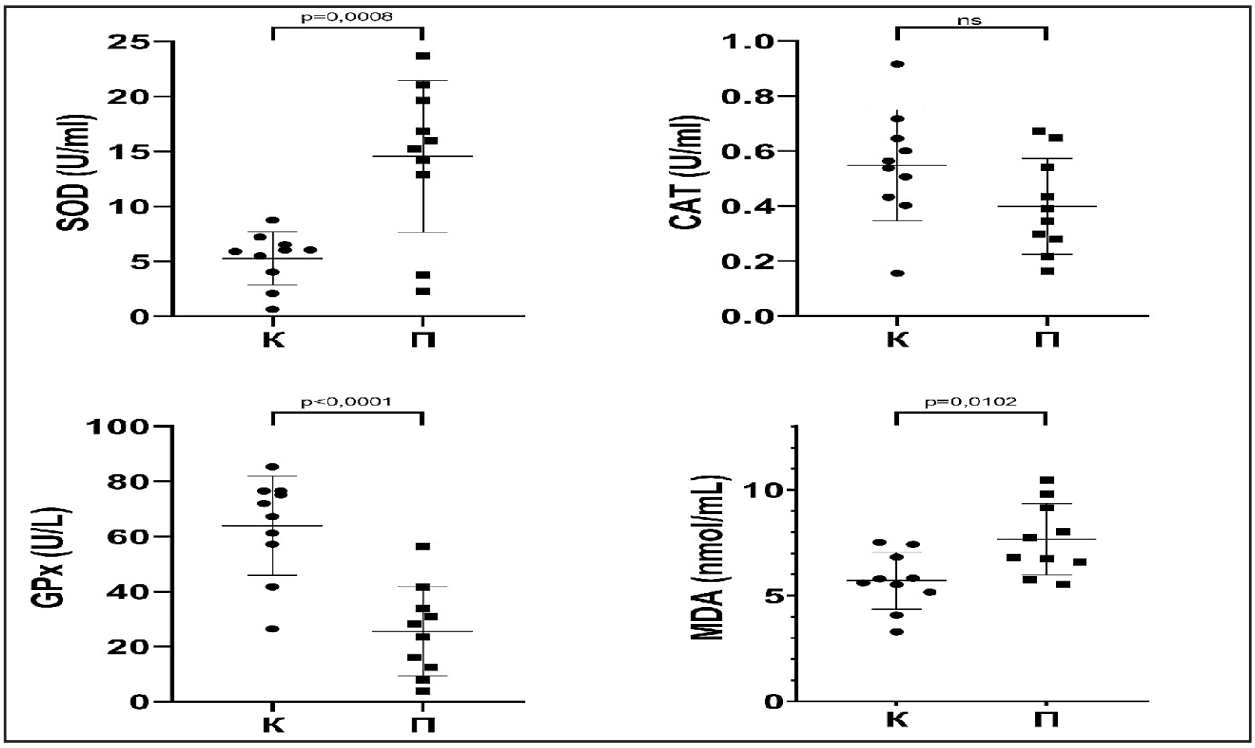

Figure 1. *Salivary total antioxidant capacity and oxidative stress in smokers and non-smokers. (mean ± SD; K – non-smokers, П – smokers; SOD, CAT, GPx, MDA).*

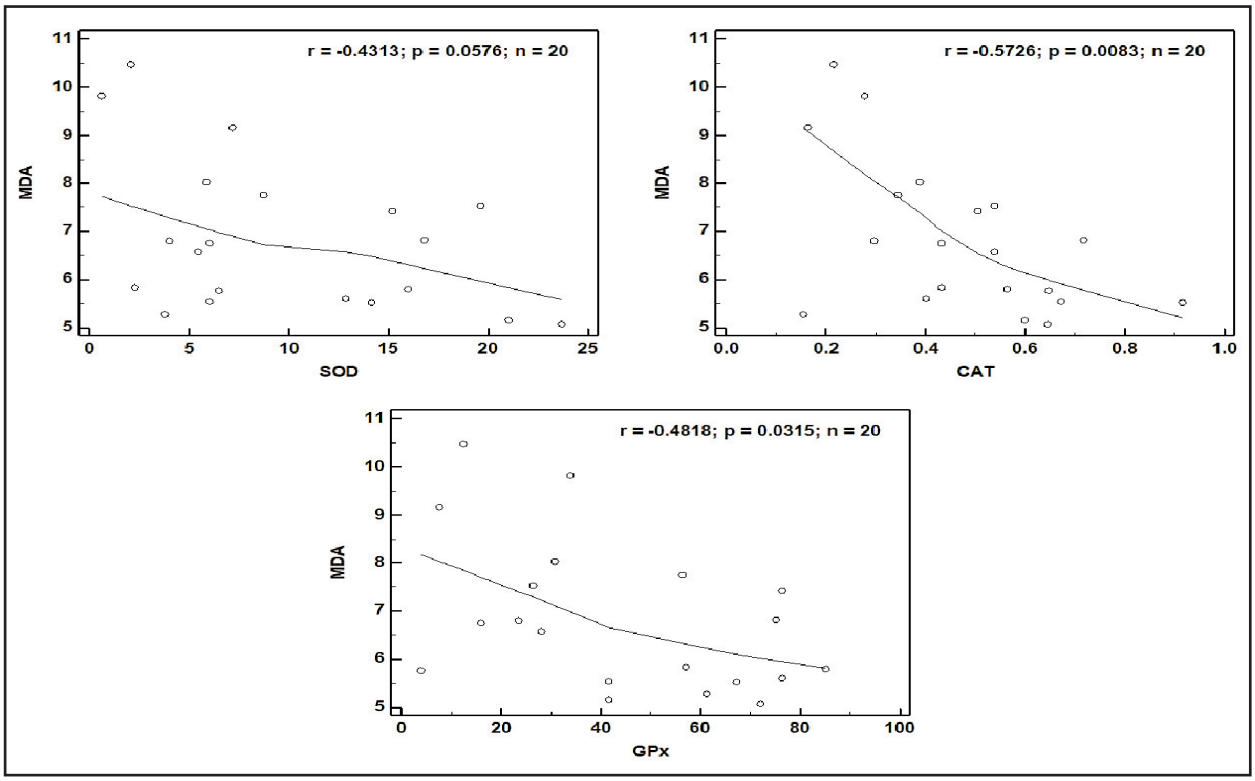

Figure 2. *Correlation between parameters that explains the oxidative stress level in smokers and non-smokers group. (mean ± SD; K – non-smokers, P – smokers; SOD, CAT, GPx, MDA)*

oxidative status, and lipid peroxidation biomarker for oxidative stress in both groups.

Discussion

Cigarette consumption is connected with many diseases including malignant neoplasms in the oral cavity or the mouth, causing and showing some imbalance between antioxidants in saliva[1-5, 18, 20]. We also know that tobacco contains more than 4500 toxic substances which can cause programmed cell death, related with necrosis and structural mitochondrial defects, especially in airway cells called A549[15-19]. The harmful effects of smoking results in production or clearance of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px), and malondialdehyde (MDA) as a lipid peroxidation marker[18, 20]. All these products of reactive oxygen species and its effects could be beneficial for monitoring and progression of some oral diseases, including primary oral squamous cell carcinoma. The primary objective of this study was to evaluate the total antioxidative capacity, and the salivary markers of oxidative stress in oral diseases in two health groups (smokers and non-smokers, participants without any disease or cardiovascular issue). Also, sample of saliva was taken with methods for unstimulated saliva because several studies show that the activity of antioxidant enzymes or total antioxidative capacity in unstimulated saliva is higher compared with others group.

In our study, we observed increased levels of SOD saliva in tobacco users compared with non-smokers, and significant decreased GPx activity in the same group. The reviewed literature indicates that smokers are more likely to suffer from progressive elevation in SOD[17-21]. The increased SOD levels in healthy smokers-participants, measured in the present study, showed us that the salivary MDA levels (as an indicator of the degree of lipid peroxidation in the saliva of smokers), at baseline, were significantly higher for the same group. Similarly, we observed negative correlation between SOD and MDA levels among participants, resulting in a pathway progress of cells with tissue destruction by oxidative stress. Our findings are in agreement with Balasubramaniam A and Arumugham MI[15], V Sosa[16], Maciejczyk M[17], Vo TTT[18], Forni C et al.[19] In this research, MDA levels were found to be increased with overproduction of oxidants, leading to oxidative imbalance, and decreased results for GPx, which can be attributed to the different ingredients in cigarettes. In another study, Dhama K et al.[20] explained that various interactive species outcomes with arterial and venous metabolic circulation stress. Research in these field should give us accurate results for identification of potent biological marker, objectively measured and evaluated for different kind of mouth disease, including oral squamous cell carcinoma.

Conclusions

Cigarette smoking is associated with increased lipid peroxidation, generating free radicals in the mouth that are responsible for imbalance and oxidative stress. Furthermore, our results suggest that the collection and analysis of saliva samples may be an alternative tool for further analysis of the role of antioxidants and oxidative stress in more specific mouth disorders, such as oral squamous cell carcinoma, understanding its relation and disturbance between free radicals produced, and the capability of the antioxidant system.

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