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MANDIBULARNE ASIMETRIJE KOD PACIJENATA SA SKELETNIM KLASAMA I I II: KVANTITATIVNA ANALIZA I KOMPARACIJA

MANDIBULAR ASYMMETRIES IN PATIENTS WITH SKELETAL CLASSES I AND II: AN ANALYSIS AND COMPARISON

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Sažetak

Uvod: *Mandibularne asimetrije su česte kod ortodontskih pacijenata i utiču na estetiku lica i funkcije orofacialnog predela.*
Cilj *ovog istraživanja bio je da se analizira prevalencija i stepen mandibularnih asimetrija kod pacijenata sa skeletnim klasama I i II, koristeći ortopantomografske (OPG) snimke za procenu linearnih i angularnih parametara mandibule.*
Materijali i Metode: *Analizirano je 70 ortopantomografskih snimaka pacijenata starijih od 16 godina. Pacijenti su klasifikovani u grupe sa skeletnom klasom I i II na osnovu analize lateralnih kefalometrijskih snimaka. Linearna i angularna merenja mandibule kategorizovana kao blaga, umerena, izražena ili teška asimetrija.*
Rezultati: *Bez obzira što nisu pronađene značajne statističke razlike između pacijenata sa skeletnim klasama I i II u pogledu dužine ramusa, dužine korpusa mandibule ili asimetrije gonijalnog ugla postoji dominacija skretanja mandibule u levu stranu. Uzimajući u obzir razlike u dužini mandibularnog ramusa i korpusa, ukupno 19 učesnika (27,14%) – 10 u skeletnoj Klasi I i 9 u Klasi II – imalo je razlike manje od 2 mm za obe merene vrednosti. Preostalih 51 učesnik imalo je bar jednu merenu razliku veću od 2 mm, što ukazuje na to da mandibulofacijalna asimetrija jeste problem često prisutan u okviru analiziranih grupa.*
Zaključak: *Studija nije pokazala značajne razlike u mandibularnim asimetrijama između pacijenata sa skeletnim klasama I i II, naglašavajući značaj procene asimetrije kod svih ortodontskih pacijenata radi efikasnog planiranja tretmana.*

Ključne reči: *mandibularna asimetrija, dužina ramusa, dužina korpusa, gonijalni ugao, skretanje mandibule*

Abstract

Introduction: *Mandibular asymmetries are common in orthodontic patients and affect both aesthetics and function.*
The aim *of this study was to analyze the prevalence and degree of mandibular asymmetries in patients with skeletal Classes I and II, using orthopantomographic (OPG) images to assess linear and angular measurements of the mandible.*
Materials and Methods: *A total of 70 orthopantomographic images of patients over 16 years of age were analyzed. Patients were classified into skeletal Class I and II groups based on lateral cephalometric analysis. Linear and angular mandibular measurements were categorized as mild, moderate, pronounced, or severe asymmetry.*
Results: *Although no statistically significant differences were found between skeletal Class I and II patients in terms of ramus length, mandibular corpus length, or gonial angle asymmetry, there was a predominant deviation of the mandible to the left side. Considering differences in the length of the mandibular ramus and corpus, a total of 19 participants (27.14%)—10 in skeletal Class I and 9 in Class II—had differences of less than 2 mm for both measured values. The remaining 51 participants had at least one measured difference greater than 2 mm, indicating that mandibulofacial asymmetry is a common issue within the analyzed groups.*
Conclusion: *The study did not show significant differences in mandibular asymmetries between patients with skeletal Classes I and II, highlighting the importance of asymmetry assessment in all orthodontic patients for effective treatment planning.*

Key words: *mandibular asymmetry, ramus length, corpus length, gonial angle, mandibular deviation*

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Introduction

Orthodontic treatment transcends mere dental alignment—it serves as a powerful tool in sculpting facial harmony, a cornerstone of modern clinical aesthetics. Through strategic tooth movement, orthodontic therapy brings about nuanced yet significant changes in facial appearance. Variations in facial appearance are numerous and depend on genetic factors, sex, and evolutionary processes[1]. Differences in tooth position, occlusal relationship, skeletal growth patterns, and the thickness of facial soft tissues all shape an individual's facial appearance and identity.

A significant part of orthodontic diagnostics is dedicated to facial analysis. Numerous parameters are evaluated within this analysis, but the assessment often begins with the transverse dimension and the evaluation of symmetry. It is generally considered that facial beauty is directly linked to the degree of facial symmetry. However, perfect symmetry remains a theoretical concept, as minor morphological differences between the left and right sides are natural. Functional asymmetry, alongside morphological asymmetry, is widely recognized in clinical practice[2].

The face often shows mild asymmetry, known as relative, subclinical, or normal asymmetry, which typically goes unnoticed[2]; it may even contribute to a more natural appearance[3]. More pronounced asymmetries, however, are noticeable and can negatively impact facial aesthetics[4–7]. Anthropological and cephalometric studies have confirmed the presence of asymmetries as part of normal facial variation[8–10] and as a common occurrence at certain stages of development[11,12].

Asymmetries of the lower third of the face are far more common than those of the midface, primarily because the mandible is highly mobile, serves as the main skeletal support for the soft tissues of this region, and the mandible has a lengthier growth period than the maxilla[13,14]. Proffit noted that in 75% of patients with facial asymmetry, chin deviation is present, while midfacial asymmetry is observed in 36% of cases. Upper third facial asymmetry is noticeable in only 5% of these patients[14].

In the differential diagnosis of asymmetries, alongside clinical examination, radiographic imaging in various projections is carried out (orthopantomography (OPG), lateral cephalometric radiograph, posteroanterior (A)] radiograph). Modern radiographic techniques enhance diagnostic capabilities but also increase radiation exposure. Lateral cephalometric radiographs are insufficient for diagnosing asymmetries because they are not suitable for analyses in the transverse plane. Orthopantomograms, however, allow for bilateral visualization and accurate measurements, provided the patient is correctly positioned[15,16]. They offer insight into the condition of the teeth and bony structures of the maxilla and mandible, enabling comparisons of the shape and size of the ramus, corpus, and condyle[16].

The aim of this study was to analyze OPG of patients over the age of 16 without syndromes or deformities to determine the prevalence of mandibular asymmetries and the degree of mandibular deviation in patients at the Clinic of Dental Medicine in Niš. Due to the retrognathic position of the mandible and chin in patients with a Class II skeletal relationship, asymmetries may appear less noticeable compared to patients with a Class I or Class III skeletal relationship. This study was designed to compare the severity and prevalence of mandibular asymmetries between patients with Class I and Class II skeletal relationships. Linear and angular measurements on orthopantomographs allow for a more precise evaluation and a better understanding of these asymmetries in the examined population.

Materials and Methods

Ethical approval of the study was obtained from the Ethical Committee of the Clinic for Dental Medicine in Niš with reference No. 14/6-2023-2 EO. It was a retrospective cross-sectional study. This study reviewed over 300 patient records and OPG radiographs of patients with skeletal Class I and Class II malocclusions, aged 16 years and older, from the diagnostic database of the Department of Orthodontics at the Clinic for Dental Medicine in Niš. Skeletal classification was determined using patients' lateral cephalometric (Tl-Rö) radiographs prior to the start of orthodontic treatment, based on ANB angle values and Wits appraisal. Following the inclusion criteria, out of the 300 reviewed cases, 70 OPG radiographs (26 male, 44 female) were finally included in the study. These patients had no history of trauma, or orthodontic treatment recorded in their medical history. Patients with syndromes or craniofacial deformities were excluded from

the study. Only OPG radiographs without artifacts, with a complete display of the mandible, without distortion, and with good radiographic contrast were included.

OPG radiographs were obtained under standardized conditions using the same equipment Sirona Axeos CBCT Ceph (Sirona Dental System GmbH, Bensheim, Germany) and Sidexis 4 software, Galileos Viewer (Dentsply Sirona, USA). Radiographs meeting the inclusion criteria were manually traced on tracing paper made of lacquered polyester acetate (A4 size, 90 g/m²) using a 0.50 mm technical pencil. The tracing and measurement methodology was adOPGed from Gupta et al.[17]. All the measurements of the profile image were performed by the same examiner. The analysis of 20 profile images was repeated after two weeks in order to ensure reliability. Intra-class correlation coefficients were performed to assess the reliability of the measurements. The values of reliability coefficients were found to be greater than 0.91 for all the variables.

The following anatomical landmarks were traced: orbitale (Or), spina nasalis anterior (SNA), condylion (Co), gonion (Go) and menton (Me). The horizontal plane was determined by connecting the orbital points, while two vertical planes were drawn perpendicular to the bi-orbital horizontal plane—one passing through the SNA point and the other through the projection of the spina mentalis onto the lower border of the mandible (Me point). To assess mandibular deviation, the angle between the SNA plane and the line connecting the SNA and Me points was traced and measured (Figure 1).The linear measurements performed included the ramus length (Co–Go) and the mandibular corpus length (Go–Me), comparing the left and right sides[17].

The angular measurements included the gonial angle (intersection of the tangents to the ramus and the corpus of the mandible) and the mandibular deviation angle (SNA–Me), where the angle formed between the vertical SNA plane and the line connecting SNA and Me was measured and expressed in degrees. A deviation to the right side was recorded as a negative value, while a deviation to the left side was recorded as a positive value[18,19].

Asymmetry classification involves several measurements to evaluate the differences in facial structure. For linear asymmetry, the difference in the Co–Go length (left vs. right side) is classified as follows: a difference of 0–1.9 mm is considered mild, 2–2.9 mm is moderate, 3–4.9 mm is pronounced, and a difference of ≥ 5 mm is categorized as severe asymmetry. Similarly, the difference in the Go–Me length (left vs. right side) follows the same classification: 0–1.9 mm (mild), 2–2.9 mm (moderate), 3–4.9 mm (pronounced), and ≥ 5 mm (severe asymmetry).

For angular asymmetry, the classification is based on the difference in the left and right gonial angles: a difference of 0°–2.99° is mild, 3°–5° is moderate, 5°–10° is pronounced, and a difference greater than 10° is classified as severe. Finally, mandibular deviation is assessed according to the mandibular deviation angle values: 0° is considered no deviation, 0.1°–1.9° is mild, 2°–3.9° is moderate, and values greater than 4° are classified as pronounced.

Data were analyzed using IBM SPSS v27.0 software. The Kolmogorov–Smirnov test was used for assessing normality of distribution, followed by the Student's t-test, Mann–Whitney U test, and Chi-square test, with a significance level set at $p < 0.05$.

Results

The study included 70 panoramic radiographs (OPG) of patients (44 females and 26 males) with an average age of 20.44 ± 4.29 years. Participants were classified based on the skeletal sagittal relationship of the jaws: 35 subjects with skeletal Class I and 35 subjects with skeletal Class II.

In the analysis of linear and angular measurements, Student's t-test showed no statistically significant difference in the length of the mandibular ramus (Co−Go), corpus length (Go−Me), and gonial angle (Go Angle) between the left and right sides with respect to skeletal class ($p > 0.05$). No significant differences were found when linear measurements were compared according to sex, nor for differences in gonial angle values between male and female subjects ($p < 0.05$, Table 1).

Regarding the difference in mandibular ramus length between the left and right sides in the total sample, the majority of participants, 36 (51.43%), had no significant difference or a difference less than 1.9 mm, thus classified into the first group. Only 4 participants (5.71%) had a difference greater than 5 mm, with the maximum recorded difference being 6 mm (Graph 1).

Analyzing the difference in mandibular ramus length between the left and right sides

among participants with skeletal Class I, it was found that 17 participants (48.57%) had a difference less than 1.9 mm, while 3 participants (8.57%) had a difference greater than 5 mm. Among participants with skeletal Class II, 19 subjects (54.29%) were classified into the group with a difference less than 1.9 mm, and only 1 subject (2.86%) had a difference greater than 5 mm (Graph 1).

Regarding the difference in mandibular corpus length between the left and right sides in the total sample, the largest number of participants, 33 (47.14%), had a difference greater than 5 mm, thus classified into the group of severe asymmetries, with the maximum recorded difference reaching 18 mm; however, statistical analysis showed that the difference between sides was not significant (Graph 2).

Analyzing the difference in mandibular corpus length among participants with skeletal Class I, 18 participants (51.43%) had a corpus length difference greater than 5 mm, while 8 participants (22.86%) had a difference less than 1.9 mm. In the skeletal Class II group, 15 participants (42.86%) had a difference greater than 5 mm, and 6 participants (17.14%) had a difference less than 1.9 mm (Graph 2).

Considering differences in both mandibular ramus and corpus length, a total of 19 participants (27.14%), 10 in skeletal Class I and 9 in Class II, had differences less than 2 mm for both measured values. The remaining 51 participants had at least one measured difference greater than 2 mm, indicating more pronounced mandibulofacial asymmetry.

In the analysis of differences in left and right gonial angles within the total sample, participants were divided into four groups based on the magnitude of the difference. The majority of subjects, 51 (72.86%), belonged to the first and second groups, classified as having mild asymmetry, while 3 cases (4.29%) were recorded in the fourth group with differences greater than 10 degrees. One subject exhibited a difference of as much as 18 degrees between the left and right angles (Graph 3).

Statistical data on differences in ramus length (Co−Go), mandibular corpus length (Go−Me), and gonial angle size between the right and left sides showed that the mean values for the right side were slightly greater than those for the left, but without statistical significance (Table 2).

When comparing the values between the left and right sides for males and females, the following mean differences were obtained for male subjects: Co−Go 1.78 mm (± 1.31), Go−Me 4.59 mm (± 3.47), Go Angle 3.96° (± 2.59). For female subjects, the mean differences were: Co−Go 1.81 mm (± 1.40), Go−Me 4.89 mm (± 4.09), Go Angle 3.53° (± 3.68) (Table 2).

Analysis of the differences in the measured parameters between the left and right sides between patients with skeletal Class I and Class II did not show any statistically significant differences for Co−Go, Go−Me, or Go Angle (Table 2).

The distribution of mandibular deviation angles across the total sample showed that 24 participants (34.29%) exhibited mandibular deviation to the right, while 37 participants (52.86%) deviated to the left, and 9 participants (12.86%) showed no deviation (Graph 4). When looking at skeletal Class I participants, 13 (37.14%) had a rightward mandibular deviation, while 20 (57.14%) deviated to the left. In the skeletal Class II group, 11 participants (31.43%) displayed rightward deviation, and 17 (48.57%) showed leftward deviation (Graph 4).

Statistical analysis of the mandibular deviation angle (Chi-square test) showed no significant difference either between sexes in the distribution of skeletal classes ($\chi^2 = 0.110$, $p = 0.804$) or in the direction of mandibular deviation ($\chi^2 = 1.181$, $p = 0.307$).

Table 1. Mean values with SD of ramus length, corpus length, and gonial angles by side

	Side		Statistical significance (p)
	Right	Left	
Co−Go	61.72 ± 6.03	60.83 ± 5.82	0.374
Go−Me	95.37 ± 8.24	95.41 ± 8.32	0.980
Go Angle	125.15 ± 7.81	126.79 ± 7.90	0.220

Table 2. Mean values of differences between left and right side in ramus length, corpus length, and gonial angles by gender, and skeletal class

Parameter	Male (±SD)	Female (±SD)	p-value	Class I (±SD)	Class II (±SD)	p-value
Co–Go	1.78 ± 1.31	1.81 ± 1.40	0.931	1.83 ± 1.57	1.79 ± 1.14	0.896
Go–Me	4.59 ± 3.47	4.89 ± 4.09	0.763	4.49 ± 3.29	5.07 ± 4.36	0.528
Go Angle	3.96 ± 2.59	3.53 ± 3.68	0.579	3.83 ± 3.11	3.56 ± 3.09	0.715

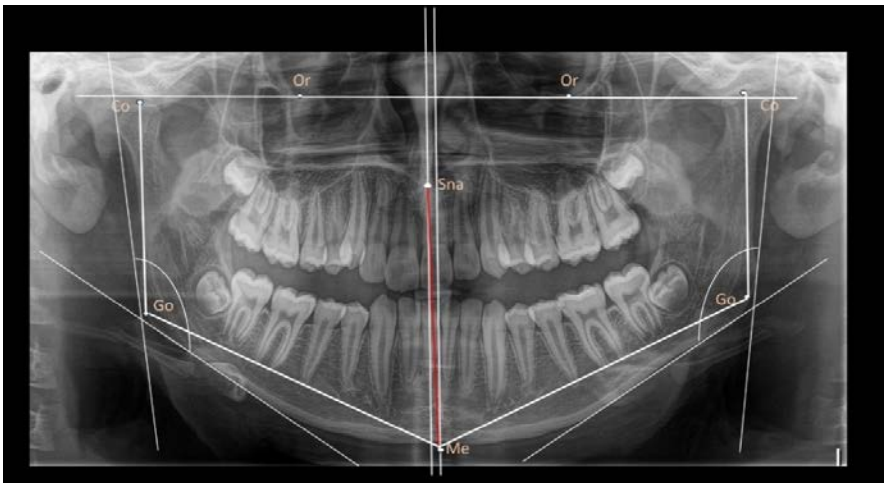
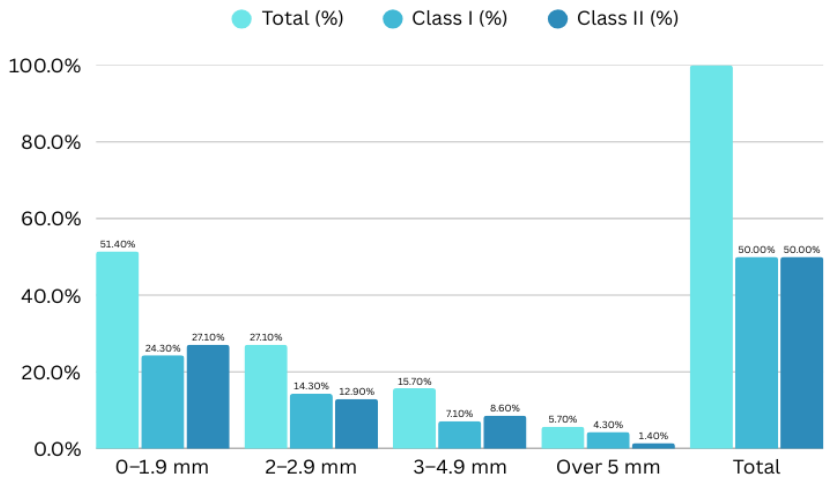
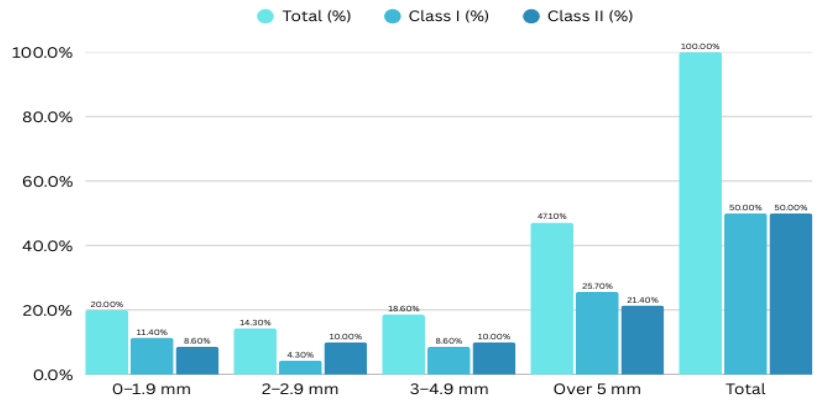


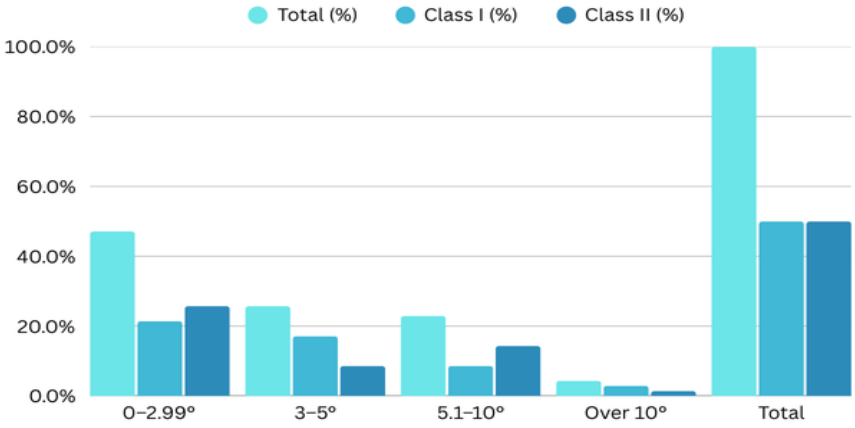
Figure 1. Example of an orthopantomogram with marked points, planes, and angles



Graph 1. Distribution of differences in the length of the mandibular ramus between the left and right sides according to the degree of asymmetry difference 0–1.9 (mild), difference 2–2.9 (moderate), difference 3–4.9 (pronounced), difference ≥ 5 (severe asymmetry)



Graph 2. Distribution of differences in the length of the mandibular corpus between the left and right sides according to the severity of the asymmetry difference 0–1.9 (mild), difference 2–2.9 (moderate), difference 3–4.9 (pronounced), difference ≥ 5 (severe asymmetry)



Graph 3. Distribution of differences in the gonial angle between the left and right sides according to the severity of the asymmetry difference 0°–2.99° (mild), difference 3°–5° (moderate), difference 5°–10° (pronounced), difference > 10° (severe)

Graph 4. Distribution of differences in the mandibular deviation angle according to the severity of the deviation deviation degree 0° (no deviation), 0.1°–1.9° (mild), 2°–3.9° (moderate), > 4° (pronounced)

Discussion

Facial symmetry is considered a crucial factor in determining facial attractiveness, as highlighted by numerous studies[14]. Given that asymmetries are more commonly observed in the lower third of the face than in the midface, many studies have focused on determining the prevalence of mandibular asymmetries in orthodontic patients. It is important to note that mandibular asymmetries in young patients are sometimes considered merely a phase of growth; therefore, most available literature focuses on adults[7,20]. Recently, there has been a growing interest in determining the degree and prevalence of mandibular asymmetries in relation to sagittal and vertical malocclusions, with patients with Class III malocclusion being the most extensively studied group[21,22].

Evangelista et al.[23], based on a systematic literature review, indicated that mandibular asymmetries are more common in Class III malocclusion compared to Class I and II. According to the literature included in their analysis, deviation of the chin to one side in Class I skeletal pattern ranges from 17.66% up to 55.6% of cases. In Class II skeletal pattern, chin deviation occurs in 10% to 25.5% of cases. The particular interest of researchers in asymmetries in Class III patients is due to the pronounced mandibular and chin prominence, which aesthetically emphasizes the asymmetry problem. In Class II malocclusion, the chin is positioned distally, making mandibular asymmetry less dominant. Within different malocclusions, especially sagittal ones, there are significant morphological variations of the mandibular base[21,24], which is one of the reasons why in our study we focused only on patients with Class I and II skeletal patterns.

Majeed et al.[25] conducted a study on 171 panoramic radiographs divided into Class I, II, and III skeletal groups, examining mandibular asymmetry at the level of the condyle and ramus. They concluded that although there are significant differences in condylar height among groups with different sagittal skeletal relationships, no statistically significant differences were found regarding mandibular asymmetry between the groups. Similar results were reported by Shireen et al.[24], who also did not find significant differences in ramus height asymmetry between patients with Class I and II skeletal patterns. These findings align with our results.

In contrast to these authors[26], Yu Wang et al. emphasized that there are significant differences in mandibular and gonial angle asymmetry between Class I and Class II skeletal patterns. They reported that asymmetry of the gonial angle is more frequent in patients with Class I skeletal pattern, which does not correspond with our findings regarding gonial angle asymmetry in Class I and II. However, it is important to consider that our research was conducted using 2D panoramic radiographs, while their study utilized 3D imaging.

Panoramic radiographs have limitations, such as image superimposition, varying magnifications, and distortions. Cone-beam computed tomography (CBCT) is a more advanced and accurate technology that can compensate for these limitations of 2D imaging, so the differences in obtained results may stem from the different methodologies. Additionally, mandibular asymmetry is inherently a three-dimensional issue, and reducing it to two dimensions carries inherent risks in interpreting linear and angular parameters.

Lower facial asymmetry is most commonly associated with chin deviation to the right or left side. According to Ting Dong et al.[27], both orthodontists and non-dental professionals clearly perceive these types of transverse deviations and consider them to significantly impair facial attractiveness.

Severt and Proffit[14] reported that in the North Carolina population, mandibular (chin) deviation is more often to the left than to the right, which is consistent with our results indicating a predominance of leftward chin deviation in both Class I and Class II skeletal patterns.

Another interesting finding of our study was the absence of predominantly present asymmetry on either side, as the measured average values with standard deviations were approximately equal. Other studies have reported that the right side tends to dominate over the left[7,28]. Based on our findings, it cannot be generalized that the right side dominates in the examined groups. Nevertheless, therefore the second part of the results is somewhat paradoxical, as it clearly shows that the majority of patients exhibited leftward chin deviation.

Our results are in line with studies suggesting that mandibular dimensional asymmetries are independent of gender[29,30].

Lu[31,32] and Kula[7] reported that mandibular linear asymmetries greater than 2–3 mm can affect facial appearance, whereas Skvarilová[28] considered a range of 4 to 5 mm as a normal asymmetry of facial dimensions. In our study, pronounced asymmetry was

defined as a 3–5 mm difference between the sides of the mandible, and severe asymmetry as greater than 5 mm.

Out of a total of 70 participants, 12 had pronounced ramus length (Co−Go) asymmetry, and 4 had severe asymmetry. Regarding the length of the mandibular corpus (Go−Me), 13 participants had pronounced asymmetry, while 33 had severe asymmetry. At the overall sample level, only 3 patients had an asymmetry greater than 5 mm in both ramus and corpus dimensions.

Only a few studies have examined angular asymmetries in the craniofacial complex. Some studies reported no statistically significant differences in gonial angle measurements between the sides[31,32]. The results of our study are contrary to these findings. It was determined that 18 patients had a gonial angle difference between 3 and 5 degrees, 16 had a difference between 5.1 and 10 degrees, and 3 patients had a difference greater than 10 degrees. This shows that more than half of the participants exhibited moderate, pronounced, or severe asymmetry when comparing left and right gonial angles.

A limitation of the present study is that it was conducted using two-dimensional radiographs, and no further classification of Class II patients into subgroups was performed.

Conclusion

There are no statistically significant differences between the left and right sides of the mandible in terms of ramus length (Co−Go), corpus length (Go−Me), and gonial angle (Go Angle) between patients with Class I and Class II skeletal patterns.

Statistical data on differences in ramus length (Co−Go), corpus length (Go−Me), and gonial angles (Go Angle) between the right and left sides showed that mean values for the right side were slightly higher than those for the left.

The majority of patients exhibited leftward mandibular deviation in both Class I and Class II skeletal patterns.

Considering differences in both mandibular ramus and corpus length, a total of 19 participants (27.14%), 10 in skeletal Class I and 9 in Class II, had differences less than 2 mm for both measured values. The remaining 51 participants had at least one measured difference greater than 2 mm, indicating more pronounced mandibulofacial asymmetry.

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Conflict of Interest: Nil

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POSTOPERATIVNI INTENZITET BOLA NAKON LEČENJA APIKALNOG PARODONTITISA

POSTOPERATIVE PAIN INTENSITY AFTER TREATMENT OF APICAL PERIODONITIS

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Sažetak

Uvod: *Tokom lečenja apikalnog periodontitisa, može doći do pogoršanja hroničnog stanja i pojave bola pri perkusiji, palpaciji ili čak otoka u predelu vrha korena zuba.*
Cilj *ovog istraživanja bio je da se utvrdi razlika u intenzitetu bola nakon endodontske terapije kod simptomatskog i asimptomatskog hroničnog apikalnog periodontitisa, između inicijalnog i ponovljenog tretmana.*
Materijal i metode: *Istraživanje je sprovedeno na 80 pacijenata podeljenih u dve glavne grupe: I grupu činili su pacijenti sa simptomatskim, a II grupu pacijenti sa asimptomatskim oblicima hroničnog apikalnog periodontitisa. Obe grupe su dalje podeljene na po dve podgrupe – pacijente koji su prvi put podvrgnuti endodontskoj terapiji i one koji su bili podvrgnuti reviziji (retretmanu). Svim ispitanicima je dodeljen upitnik u koji su unosili podatke o prisustvu i karakteristikama bola u određenim vremenskim intervalima: 6, 12, 24 i 48 sati, te 7 dana nakon inicijalne intervencije.*
Rezultati: *Pojava bola nakon endodontske terapije bila je česta, ali najčešće blagog do umerenog intenziteta. Bol se javljao već nakon 6 sati, a najizraženiji je bio posle 12 sati od intervencije. Bol pri perkusiji bio je intenzivniji od spontanog bola.*
Zaključak: *Nije zabeležena značajna razlika u učestalosti spontanog bola ili bola na perkusiju između zuba koji su bili simptomatski i asimptomatski pre početka terapije, iako je bol uvek bio izraženiji kod prethodno asimptomatskih zuba. Bol nakon revizionog tretmana bio je izraženiji u poređenju sa zubima koji su prvi put lečeni, u svim vremenskim tačkama. Intenzitet bola pri perkusiji bio je veći kod slučajeva retretmana, a statistička značajnost potvrđena je 12 sati nakon intervencije.*

Ključne reči: *apikalni periodontitis, postoperativni bol, endodontska terapija*

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Abstract

Introduction: *During the treatment of apical periodontitis, the problem can be the worsening of the chronic condition and the appearance of pain during percussion, palpation, or even the appearance of swelling in the area of the tip of the tooth.*
Aim *of the study was to determine the difference in the intensity of pain after endodontic therapy in symptomatic and asymptomatic chronic apical periodontitis, between initial and repeated treatment.*
Materials and methods: *The study was conducted on 80 patients, divided into two groups: I group comprised patients with symptomatic forms, and II group, patients with asymptomatic forms of chronic apical periodontitis. Both groups were divided into two subgroups consisting of patients who received endodontic therapy for the first time and patients who underwent retreatment. All patients were given a VAS questionnaire, in which they recorded pain and described its characteristics at specific time points: 6, 12, 24, 48 hours, and 7 days after the initial intervention.*
Results: *The occurrence of pain after endodontic therapy is quite common, but is usually mild or tolerable. Pain began as early as 6 hours and was most intense after 12 hours from the intervention. Percussion pain was stronger than spontaneous pain.*
Conclusion: *There was no difference in the occurrence of spontaneous pain or pain on percussion in teeth that were symptomatic or asymptomatic before the start of therapy, although pain was always more pronounced in previously asymptomatic teeth. The pain experienced after revision was always higher than in the group of teeth with newly initiated endodontic treatment at all time points. The intensity of percussion pain was also stronger in retreatment cases, but statistical significance was confirmed at the 12-hour time point after the intervention.*

Key words: *apical periodontitis, postoperative pain, endodontic treatment*

Introduction

Periapical lesions occur as a continuation of pathological changes of the dental pulp, and depending on the duration and intensity of the stimulus that caused them, they can be acute or chronic[1]. The prevalence of apical periodontitis increases if the teeth are untreated, but also if the performed endodontic therapy was inadequate. The frequency of apical periodontitis was significantly higher in teeth with inadequate fillings (72.2%) than in those with successful endodontic therapy (25.9%)[2].

Periapical lesions are mostly asymptomatic and are diagnosed mostly through control radiographs[3]. The suppurative form or the diffuse periapical process may have symptoms all the time, but also the existence of a permanent or occasional sinus tract. However, the clinical expression of chronic periodontitis is not static and it can be activated or exacerbated[4].

Endodontic therapy is the first choice for the healing of periapical tissues. After endodontic therapy, especially when it refers to teeth with a periapical lesion, it is necessary to monitor the patient's condition through control examinations.

Usually, in the first days after the completion of the instrumentation, a problem can be the exacerbation of the chronic condition and the appearance of pain on percussion, palpation, and even the appearance of swelling in the area of the apex of the tooth[5]. It is this appearance of pain that is the cause of mistrust that occurs in the patient. This is especially emphasized if, before the start of the treatment, the tooth did not cause pain or any discomfort, and the problems appeared after the start of the treatment.

Numerous studies have been conducted on the presence of postoperative pain and its aetiology and character. In his study, Alamassi et al. described the presence of 1.7% to 70% of postoperative pain[6]. This wide range of reported incidence is due to the different design of the studies performed, the preoperative condition of the teeth, the time of registration of pain, the index of pain measurement and the severity of pain included in the statistical analysis, as well as the procedure or technique of the treatment itself[7]. A higher incidence of postendodontic pain was determined in the treatment of necrotic teeth. According to a meta-analysis by Sathorn et al., the percentage of teeth where swelling is possible is 8.4%[8].

Aim: This paper aimed to analyze the occurrence of pain after initial endodontic therapy and retreatment between symptomatic and asymptomatic chronic apical periodontitis.

Materials and Methods

The examination was carried out in 80 patients at the private health care institution Private Dental prachce Vita Dent from Gevgelija, North Macedonia, who underwent endodontic therapy due to the existence of symptomatic or asymptomatic chronic apical periodontitis, with a lesion larger than 2 mm. Before the start of the treatment itself, the patients were informed about the protocol of the appropriate treatment, and according to the recommendations of the ethical committee, consent to participate in the trial was requested.

Patients over 18 years of age were included. Each patient had their card with data that had been recorded and was relevant to the trial. Before the start of the treatment, the tooth was recorded with a retroalveolar X-ray.

The patients were divided into two groups of forty participants each, based on their clinical presentation: the first group included patients with an asymptomatic form of chronic apical periodontitis, while the second group comprised patients who, in addition to radiographic changes, also exhibited symptoms such as percussion sensitivity, discomfort during mastication, and occasional exacerbation of periodontitis.

The two groups were divided into two subgroups, which differed according to whether that tooth was previously treated or not. In the first subgroup, endodontic therapy was performed on a tooth that was not previously endodontically treated, while in the other, retreatment was performed. All therapy, treatment, and testing were performed by a single therapist to exclude interpersonal variability in treatment.

The whole process of endodontic therapy was performed in the same way in terms of instrumentation, odontometry, type of endomotor, irrigation protocol, intersession application of medications, as well as the same type of definitive filling.

In the first visit, a complete treatment of the root canal and adequate irrigation was performed. An NSK endomotor was used for machining using the V-Taper Gold Rotary File (Fanta, Fanta Denta) machining instrument system. Irrigation according to the same protocol for each patient: NaOCL (sodium hypochlorite—Cerkamed), in a concentration

of 2% solution, followed by copious irrigation with saline solution, during processing, followed by the final irrigation with 17% EDTA solution (Cerkamed), and final irrigation with CHX 2% (Cerkamed) and Canal Clean (Cerkamed).

After the completion of that phase, medication was applied to all treated subjects, Solutio Chlumsky (Phytopharm - Phenolum 3 g, Camphora 6 g and Aethanolum 1 g) and the tooth was temporarily closed with phosphate cement.

In both groups and subgroups, each patient was given a questionnaire with a visual analogue scale (VAS), a psychometric response scale for subjective characteristics or attitudes that cannot be directly measured, where the patient noted whether there was pain or swelling[9]. Moreover, if pain or swelling was felt, the patient described its characteristics at specific time points: 6, 12, 24, 48 hours and seven days after the initial intervention when instrumentation and root canal treatment were completed.

Each patient made an appointment seven days after the intervention, when the tooth was filled with Dia Dent (Dia-Proseal), and the patient handed in the completed questionnaire.

Results

Table 1 shows the results obtained by comparing the intensity of spontaneous pain and pain on percussion, at the analyzed time points: 6, 12, 24, 48 hours and 7 days after endodontic treatment.

On average, the VAS score was higher for percussion pain compared to spontaneous pain at all time points: patients had significantly stronger percussion pain than spontaneous pain after 6 hours ($p = 0.000005$), after 12 hours ($p = 0.0000026$), after 24 hours ($p = 0.0005$) and after 48 hours ($p = 0.0018$), and non-significantly higher after 7 days after the treatment ($p = 0.27$). Z (Wilcoxon Matched-Pairs Signed-Rank Test) ***$p < 0.0001$ was used for comparison.

Table 2 shows the degree of spontaneous pain after therapy in symptomatic or asymptomatic cases. There was no difference in the occurrence of spontaneous pain in teeth that were symptomatic or asymptomatic before the beginning of the therapy; that is, in both types of periodontitis, the pain was equal. The tested difference in the distribution of patients with symptomatic and asymptomatic chronic apical periodontitis was statistically insignificant for the entire follow-up period ($p = 0.39$, $p = 0.7$, $p = 0.086$, $p = 0.36$ and $p = 1.0$, respectively, at the analyzed time points).

Table 1. Frequency distribution of spontaneous and percussive pain

Time after intervention	Type of pain	Pain				
		No pain n (%)	Mild n (%)	Moderate n (%)	Severe n (%)	Unendurable n (%)
6 hours	Spontaneous	56 (70)	17 (21.25)	2 (2.5)	2 (2.5)	3 (3.75)
	On percussion	47 (58.75)	23 (28.75)	2 (2.5)	4 (5)	4 (5)
12 hours	Spontaneous	50 (62.5)	22 (27.5)	3 (3.75)	2 (2.5)	3 (3.75)
	On percussion	45 (56.25)	24 (30)	2 (2.5)	5 (6.25)	4 (5)
24 hours	Spontaneous	58 (72.5)	15 (18.75)	1 (1.25)	4 (5)	2 (2.5)
	On percussion	54 (67.5)	15 (18.75)	4 (5)	4 (5)	3 (3.75)
48 hours	Spontaneous	67 (83.75)	9 (11.25)	3 (3.75)	1 (1.25)	
	On percussion	63 (78.75)	10 (12.5)	2 (2.5)	4 (5)	1 (1.25)
7 days	Spontaneous	75 (93.75)	5 (6.25)			
	On percussion	74 (95.5)	5 (6.25)	1 (1.25)		

Table 2. Spontaneous pain in symptomatic and asymptomatic chronic apical periodontitis

Time after intervention	Type of chronic apical periodontitis	Spontaneous pain					**P-value**
		No pain n (%)	Mild n (%)	Moderate n (%)	Severe n (%)	Unendurabl n (%)	
6 hours	Symptomatic	27 (67.5)	10 (25)	2 (5)	0	1 (2.5)	exact p = 0.39
	Asymptomatic	29 (72.5)	7 (17.5)	0	2 (5)	2 (5)	
12 hours	Symptomatic	24 (60)	12 (30)	2 (5)	0	2 (5)	exact p = 0.7
	Asymptomatic	26 (65)	10 (25)	1 (2.5)	2 (5)	1 (2.5)	
24 hours	Symptomatic	29 (72.5)	9 (22.5)	0	0	2 (5)	exact p = 0.086
	Asymptomatic	29 (72.5)	6 (15)	1 (2.5)	4 (10)	0	
48 hours	Symptomatic	34 (85)	5 (12.5)	0	1 (2.5)		exact p = 0.36
	Asymptomatic	33 (82.5)	4 (10)	3 (7.5)	0		
7 days	Symptomatic	37 (92.5)	3 (7.5)				$\chi^2 = 0.2$ p = 1.0
	Asymptomatic	38 (95)	2 (5)				

Exact (Fisher's Exact Test); χ^2 (Chi-square test)

Table 3 shows the degree of pain on percussion after therapy of symptomatic or asymptomatic cases. Patients with symptomatic and asymptomatic chronic apical periodontitis did not differ significantly in the frequency of pain on percussion, although pain was always more pronounced in previously asymptomatic teeth. The only significant difference was after 24 hours, when pain on percussion was stronger in asymptomatic cases.

In present study, the pain that occurs in teeth after treatment of previously untreated teeth or teeth where retreatment was performed after a previously unsuccessful outcome was followed. The obtained results showed that the pain experienced after the revisions was always higher than pain after the initial endodontic treatment of a group of teeth. Graphs 1 and 2 show the degrees of spontaneous and percussive pain and their decline.

The results of the statistical analysis presented a significantly stronger intensity of spontaneous pain in patients with retreatment compared to patients with first treatment during the first day after the intervention; in terms of pain intensity after 6, 12 and 24 hours after the endodontic intervention.

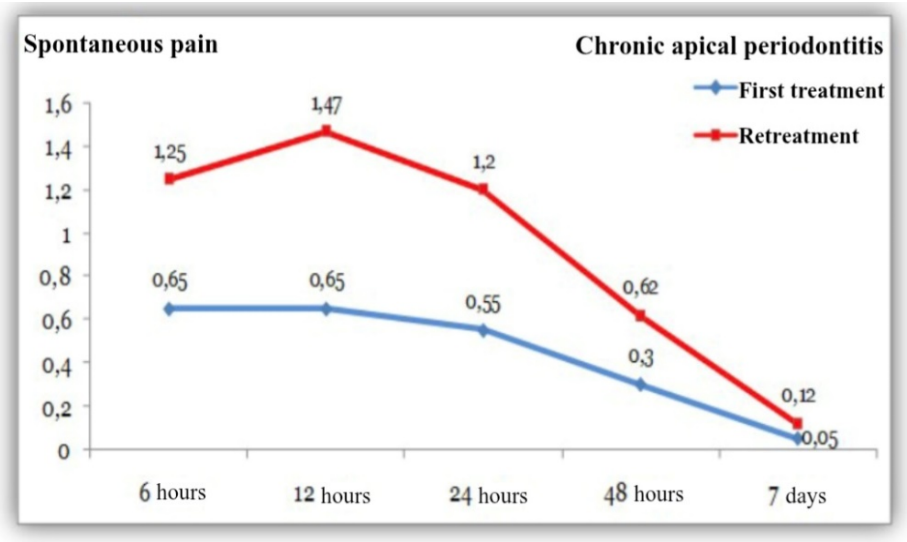
Patients in whom endodontic treatment was performed on a previously untreated tooth had pain on percussion less often than retreatment patients. Percussion pain intensity was stronger in the retreatment group compared to the first treatment group throughout the entire follow-up period of the patients, but statistical significance was confirmed only at the time point 12 hours after the intervention (p = 0.023).

Table 3. Distribution of pain on percussion in symptomatic and asymptomatic chronic apical periodontitis

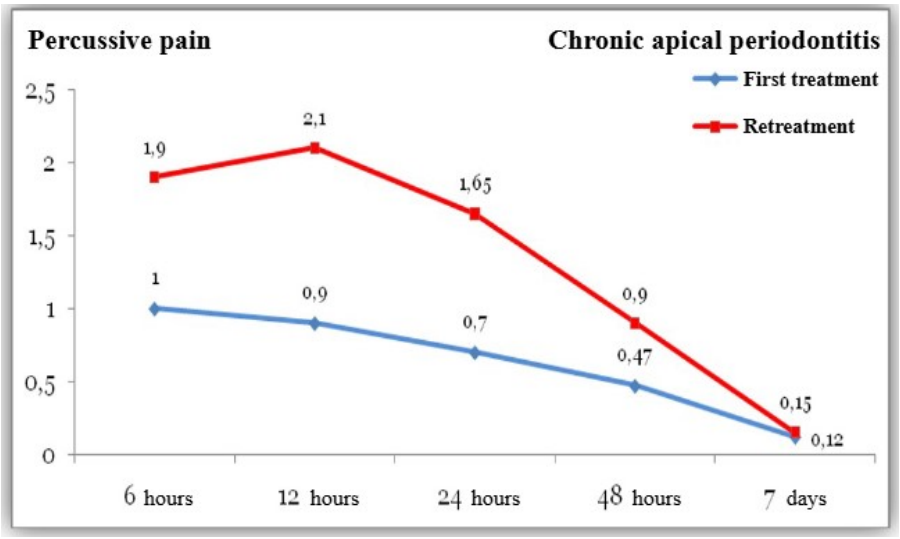
Time after intervention	Type of chronic apical periodontitis	Pain on percussion					**P-value**
		No pain n (%)	Mild n (%)	Moderate n (%)	Severe n (%)	Unendurable n (%)	
6 hours	Symptomatic	21 (52.5)	15 (37.5)	1 (2.5)	2 (5)	1 (2.5)	exact p = 0.43
	Asymptomatic	26 (65)	8 (20)	1 (2.5)	2 (5)	3 (7.5)	
12	Symptomatic	20 (50)	15 (37.5)	1 (2.5)	2 (5)	2 (5)	exact

hours	Asymptomatic	25 (62.5)	9 (22.5)	1 (2.5)	3 (7.5)	2 (5)	p = 0.71
24 hours	Symptomatic	25 (62.5)	13 (32.5)	0	0	2 (5)	exact ***p = 0.0001
	Asymptomatic	29 (72.5)	2 (5)	4 (10)	4 (10)	1 (2.5)	
48 hours	Symptomatic	30 (75)	8 (20)	0	1 (2.5)	1 (2.5)	exact p = 0.063
	Asymptomatic	33 (82.5)	2 (5)	2 (5)	3 (7.5)	0	
7 days	Symptomatic	36 (90)	3 (7.5)	1 (2.5)			exact p = 0.675
	Asymptomatic	38 (95)	2 (5)	0			

Exact (Fisher's Exact Test); χ^2 (Chi-square test) ***p < 0.0001



Graph 1. Occurrence of spontaneous pain after retreatment and initial endodontic therapy



Graph 2. Occurrence of percussive pain after retreatment and initial endodontic therapy

Discussion

Pain is a personal and subjective feeling and difficult to quantify and standardize[10,11]. It can be influenced by various factors, such as fear of dental procedures, anxiety, as well as many other physical and psychological factors that can affect the patient's perception of pain and reaction thresholds[12,13]. Most clinical studies use numerical, verbal, and visual analogue scales[14]. In this study, the widely accepted VAS scale was used. In addition to its simplicity, it is considered a reliable and reproducible measurement tool for clinical trials of pain[15]. Patients were informed about the purpose of the study and self-reported the level of pain. This phenomenon is called the Hawthorne effect, which means that when subjects are familiar with how to record their symptoms, interpretations and subjectivity of the pain response are minimized[16].

The occurrence of postoperative pain is not a rare occurrence in endodontics. It can last from a few hours to a few days after endodontic therapy, but it still largely depends on the diagnosis due to which endodontic therapy does[17]. According to studies by Kane et al., the reported incidence of post-obturation pain occurred in 18.75% of vital teeth and 13.15% of non-vital teeth (necrosis)[18].

The pain that occurs postoperatively in apical periodontitis may originate either from the extrusion of infected material into the periapical tissue or from a disturbance of the subtle balance between the bacteria present in the canal and the patient's immune response[19,20,21]. The balance can be disturbed at any stage of endodontic therapy, especially if a procedure is incorrect[22,23,24].

In our study, pain was observed early after the completion of root canal treatment, so after 6 hours of treatment, 30% of cases had spontaneous pain, and 41.25% of patients had percussive pain. After 12 hours, the highest intensity of spontaneous and percussive pain was observed. Furthermore, the pain gradually decreased, so after 7 days of endodontic treatment, only a few patients complained of both types of pain. At all time points, patients had significantly stronger percussion pain than spontaneous pain, except after 7 days of treatment, when that difference was insignificant. In terms of intensity and spontaneous and percussion pain, the patients mostly described it as mild at all time points. Our results were reduced compared to those of De-Figueiredo et al., in which, after 24 hours, pain was detected in 40% of the subjects and that in approximately 3% swelling occurred as a consequence of the therapy[17]. In our study, we did not have swelling, but the percentage of patients who presented with very severe pain was close.

One of our stated goals was to investigate whether the intensity and occurrence of pain depend on whether the teeth were symptomatic or asymptomatic before the start of the intervention. Symptomatic periodontitis has been shown to have a higher incidence of pain in the first 48 hours. Percussion pain was also more frequent and of greater intensity in symptomatic patients, but the difference was insignificant in all investigated periods, except after 24 hours.

Based on a similar conclusion, Abdel Hameed et al., showed a higher incidence of postoperative pain (15.9%) in previously symptomatic than in asymptomatic patients (7.1%)[20]. The finding of Sadaf et al. was similar, and led them to the same conclusion[25].

When asked whether we should expect painful symptoms if we perform endodontic treatment on teeth that have not been treated or on teeth where retreatment is indicated, it has been shown that retreatment causes clinical symptoms and pain much more often. This difference after 6 hours of treatment, after 48 hours and after 7 days was at the border of significance, but was significantly different after 12 and after 24 hours of treatment. It is interesting to note that the cases with very severe pain manifestations were detected in retreatments. Percussion pain intensity was stronger in the retreatment group compared to the first treatment group throughout the patients' follow-up period, but statistical significance was confirmed only at the 12-hour post-intervention time point. According to the results of Siqueira et al., there is no significant difference in terms of the incidence of postoperative pain between the initial treatments and the retreated ones, although they also showed mild pain in 10% of cases, moderate in 3.3%, and severe in 1.9%[26].

Conclusion

According to the results obtained from the examination and their analysis from this prospective study, the following conclusions can be drawn that in all time points, patients had significantly stronger pain on percussion than spontaneous pain, except after the seventh day of treatment which showed an insignificant difference. Symptomatic periodontitis had a higher incidence of

spontaneous pain and pain on percussion in the first 48 hours. The tested difference in terms of pain intensity was statistically insignificant for the entire follow-up period, except after 24 hours between percussive pain in symptomatic and asymptomatic cases. After retreatment, the appearance of clinical symptoms of spontaneous pain and percussion is much more frequent. It was significantly different for spontaneous pain after 12 and 24 hours of treatment, and for percussive pain at the time point of 12 hours after the intervention.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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KORELACIJA IZMEĐU RADIOLOŠKOG STADIJUMA I INTENZITETA BOLA KOD OSTEONEKROZE VILICE POVEZANE SA LEKOVIMA

CORELATION BETWEEN RADIOLOGICAL STAGE AND PAIN INTENSITY IN MEDICATION RELATED OSTEONECROSIS OF THE JAW

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Sažetak

Uvod: *Osteonekroza vilice se definiše kao avaskularna nekroza alveolarne spongiozne i kortikalne kosti maksile ili mandibule, najčešće kao rezultat terapijskih intervencija - bilo radioterapije ili farmakološkog tretmana. Osteonekroza vilice povezana sa lekovima (MRONJ) definiše se određenim kriterijumima i može se klasifikovati u četiri stepena. MRONJ se razvija kao posledica sistemskih efekata određenih lekova, prvenstveno bisfosfonata, koji inhibiraju remodeliranje kostiju suzbijanjem aktivnosti ćelija koje resorbuju kost - osteoklasta.*
Cilj studije *bio je da se uporede MSCT radiološke promene kod MRONJ-a izazvanog bisfosfonatima sa kliničkim znacima i simptomima kao što su prisustvo bola, infekcije i fistule kod pacijenata sa dijagnostikovanom MRONJ.*
Materijali i metode: *Podaci o pacijentima su prikupljeni iz medicinske dokumentacije i obuhvatali su trajanje terapije bisfosfonatima, stadijum MRONJ, nalaze MSCT radiografije i upitnik o prisustvu i intenzitetu bola, mereno pomoću numeričke skale za procenu bola.*
Rezultati: *Svi pacijenti su primali oralnu antiresorptivnu terapiju bisfosfonatima u periodu od 1 do 15 godina; 63,63% pacijenata je bilo na terapiji bisfosfonatima duže od tri godine, 27,27% manje od tri godine, 9,09% duže od 15 godina. Kod pacijenata sa razvijenim stadijumom II, prosečan intenzitet bola bio je 5,1±1,1; stadijum III je prijavio nivo bola 8, MRONJ u stadijumu I je imao blagi bol 2. Nije bilo prekida terapije ni kod jednog pacijenta uključenog u studiju.*
Zaključak: *Radiolozi igraju važnu ulogu u ranoj dijagnozi svih stadijuma MRONJ-a. Bol se može smatrati ranim znakom ovog patološkog stanja kosti i povezan je sa stadijumom MRONJ kod lezija izazvanih korišćenjem bisfosfonata.*

Ključne reči: *MSCT radiografija, MRONJ, bol*

Abstract

Introduction: *Osteonecrosis of the jaw is defined as avascular necrosis of the alveolar cancellous and cortical bone of the maxilla or mandible, most commonly as the result of a therapeutic intervention—either radiotherapy or pharmacological treatment. Certain criteria define medication-related osteonecrosis of the jaw (MRONJ) and can be staged in four degrees. MRONJ develops as a consequence of the systemic effects of certain medications, primarily bisphosphonates, that inhibit bone remodeling by suppressing the activity of bone-resorbing cells—osteoclasts.*
Aim. *The study aimed to compare the multislice computed tomography (MSCT) radiological changes in MRONJ caused by bisphosphonates stage to clinical signs and symptoms, such as the presence of pain, infection and fistula in patients with diagnosed MORNJ.*
Materials and Methods: *Patient data were collected from medical records and included duration of bisphosphonate therapy, stage of MRONJ, MSCT radiograph findings, and questionnaire about the presence and intensity of pain, measured using a numerical pain rating scale.*
Results: *All patients had been receiving oral antiresorptive bisphosphonate therapy for periods ranging from 1 to 15 years; 63.63% had been on bisphosphonate therapy for more than three years, 27.27% for less than three years, and 9.09% for more than 15 years. In patients who developed Stage II, the mean pain intensity was 5.1 ± 1.1; Stage III reported pain level 8, Stage II MRONJ experienced mild pain 2. There was no drug holiday in any patient involved in the study.*
Conclusion: *Radiologists play an important role in the early diagnosis of all stages of MRONJ. Pain could be considered as an early sign of this pathological condition of the bone, and it correlates with the stage of MRONJ in lesions caused by bisphosphonate intake.*

Key words: : *MSCT radiography MRONJ, pain*

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Introduction

Osteonecrosis represents the necrosis of bone tissue, resulting from impaired vascular perfusion and the loss of viability of bone marrow cells, with certain radiographic manifestations through structural and morphological alterations within the bone. The radiological presentation of osteonecrosis typically reveals a localized area of nonviable bone tissue characterized by necrosis, reparative processes, and resorption phenomena (osteolysis, osteosclerosis, or mixed patterns). In some cases, sequestra may be present, with a distinct line demarcating necrotic from viable bone. In advanced stages, cortical discontinuity and secondary infections may also be observed.

Radiological findings for MRONJ on Computed tomography (CT) include bone changes such as osteolysis/osteonecrosis—presents as an ill-defined zone of hypodensity with visible destruction of the edge of the cortex, osteosclerosis—presents as an increased density zone of the part of the bone where it occurs, periosteal reaction—abnormal bone formation on the surface of the bone itself, i.e. it presents as a thickening of the bone cortex, sequestrum—a fragment of dead bone that has separated from the surrounding bones, soft tissue inflammation—like swelling of the surrounding tissue around the bone.

Osteonecrosis of the jaw is defined as avascular necrosis of the alveolar cancellous and cortical bone of the maxilla or mandible, most commonly as the result of a therapeutic intervention—either radiotherapy or pharmacological treatment. Radiation-induced osteonecrosis of the jaw (RONJ) is the consequence of the therapeutic localized ionizing radiation, typically administered in the head and neck region, and occasionally in the treatment of breast malignancies[1,2]. RONJ represents ischemic necrosis caused primarily by vascular injury (endarteritis obliterans), causing the death of the osteocyte. Radiotherapy induces pronounced hypoxia within the jawbone, accompanied by ischemia and osseous fibrosis. The mandible is most frequently affected[2]. Medication-related osteonecrosis of the jaw (MRONJ) develops as a consequence of the systemic effects of certain medications, that primarily inhibit bone remodeling by suppressing the activity of bone-resorbing cells—osteoclasts. This inhibition disrupts normal bone turnover, leading to impaired remodeling, while vascularization is reduced but relatively preserved[3]. Necrosis develops due to the continuous exposure of the jawbones to daily microtrauma and the consequent remodeling inability, often accompanied by secondary infection[4]. Radiographically, MRONJ typically appears as diffuse osteosclerosis or a combination of osteosclerotic and osteolytic changes, sometimes followed by sequestrum formation[5]. Fibrosis is generally quite pronounced. The mandible is more commonly affected than the maxilla, with an approximate ratio of 2:1. MRONJ most frequently involves the alveolar ridge and, in advanced stages, extends to adjacent structures. A pronounced periosteal reaction is often observed. Soft-tissue changes range from mild to severe, including intraoral mucosal and extraoral cutaneous fistulas. Pain intensity may vary from mild to moderate, and less frequently, severe. It is emphasized that the intensity of pain does not necessarily follow the progression of the disease. MRONJ is the most common caused by antiresorptive drugs, such as bisphosphonates and denosumab[3–6].

This pathological condition may also be developed as a result of the action of antiangiogenic agents. These agents inhibit vascular endothelial growth factor (VEGF), preventing tissue neovascularization in oncological patients. In the jaw, this leads to a reduction in bone marrow microcirculation, resulting in ischemia and hypoxia of the bone, followed by avascular necrosis with secondary infection. In this case, radiography shows a combination of osteolytic and osteosclerotic changes, often accompanied by partial sequestration, cortical layer disruption, and soft tissue thickening. Compared with bisphosphonate-related osteonecrosis, these changes typically show less extension beyond the alveolar ridge and are generally less pronounced[4,5]. Other medications, such as antimetabolites and immunosuppressive agents (e.g., methotrexate or corticosteroids), may also induce osteonecrosis, although this occurs less frequently in the jawbones. Their isolated contribution to the development of jaw osteonecrosis is extremely rare and usually observed when administered concomitantly with drugs exerting similar effects. Osteonecrosis caused by these agents leads to immunosuppression, disturbances in bone remodeling and vascularization, but with less severe consequences for the jawbone. Radiographically, osteolysis predominates with significantly less pronounced osteosclerosis and minimal sequestration.

Medication-related osteonecrosis of the jaw is defined by certain criteria: a current or previous history of antiresorptive or antiangiogenic drug use, exposed bone that can be probed through an intraoral or extraoral fistula in the orofacial region, persistence of the condition for at least 8 weeks, and no prior history of radiotherapy to the jaw, or metastases in jawbones[7].

The aim

The study aimed to compare the multislice computed tomography (MSCT) radiological changes in MRONJ caused by bisphosphonates stage due to clinical signs and the symptoms such as the presence of pain, infection and fistula in patients with diagnosed MRONJ.

Materials and Methods

The study was conducted at the Center for Radiology, University Clinical Center Niš, from January 2024 to December 2024. The research involved 11 patients who had been receiving antiresorptive medication. MRONJ diagnosis was based on clinical and radiographic findings and the criteria recommended in the American Association of Oral and Maxillofacial Surgeons position paper[7].

At-Risk Stage: Patients receive antiresorptive or antiangiogenic therapy but exhibit no clinical signs of necrotic bone or related symptoms. Stage 0: No clinical evidence of necrotic bone is present; however, patients may experience nonspecific symptoms or display subtle clinical and radiographic changes. Stage I: Exposed and necrotic bone, or a fistula through which bone can be probed, is present in asymptomatic patients with no signs of infection. Stage II: Along with exposed and necrotic bone or a probing fistula, there is clinical evidence of infection, and patients typically report pain or other symptoms. Stage III: Characterized by exposed and necrotic bone or a probing fistula, clinical signs of infection, and at least one of the following: necrotic bone extending beyond the alveolar region (e.g., into the maxillary sinus or mandibular border), extraoral fistula, pathologic fracture, oroantral or oronasal communication, or osteolysis reaching the sinus floor or mandibular border.

Patient data were collected from medical records and included information such as age, sex, lesion site, disease stage at admission, duration of bisphosphonate therapy, presence or absence of a drug holiday. All participants provided written informed consent before enrollment. They also completed a questionnaire assessing the presence and intensity of jaw pain, measured using a numerical pain rating scale. Clinical evaluations recorded the presence of intraoral or extraoral fistula, bone sequestra, infection, and soft tissue suppuration.

The patients received antibiotic therapy according to the protocol for MRONJ[6] and local hygienic treatment. The patients were further referred to radiological institutes for a more detailed MSCT analysis of changes in bone tissue. The patients were referred for exams in a GE Revolution EVO 128-Slice MSCT device located in the Center for Radiology, University Clinical Centre of Niš.

A correlation was established between the stage of MRONJ according to the clinical and radiological features of the disease and pain intensity.

Results

A total of 11 patients participated in the study; all of them were female, while there were no male participants. The mean age of the patients was 66.8 ± 5.1 years. All patients had been receiving oral antiresorptive bisphosphonate therapy for periods ranging from 1 to 15 years. Seven patients (63.63%) had been on bisphosphonate therapy for more than three years, three patients (27.27%) for less than three years, and one patient (9.09%) for more than 15 years (Figure 1).

The primary indication for bisphosphonate use was diagnosed osteoporosis in nine patients (81.8%), while two patients (18.2%) were oncology patients who received bisphosphonates for the prevention of metastatic bone fractures (Figure 2).

Stage I was diagnosed in one patient (9.09%), stage II in eight patients (72.7%), and stage III in two patients (18.1%). The reason for MRONJ development was a previous tooth extraction (Figure 3).

Pain intensity was defined as moderate (NRS 4–6) in six patients (54.5%), as mild pain (NRS = 2) in four patients (36.4%), and severe pain (NRS = 9) by one patient (9.09%) (Figure 4).

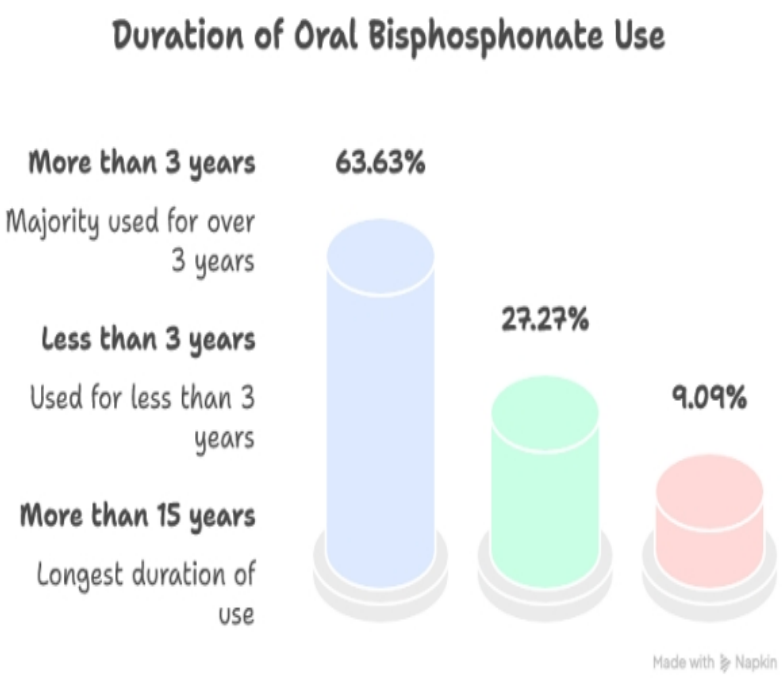


Figure 1. Duration of bisphosphonate intake

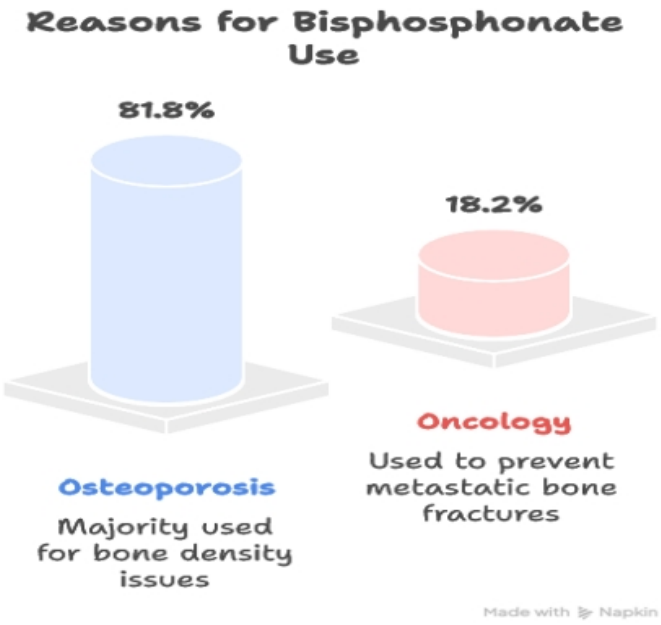


Figure 2. Bisphosphonate intake depends on disease

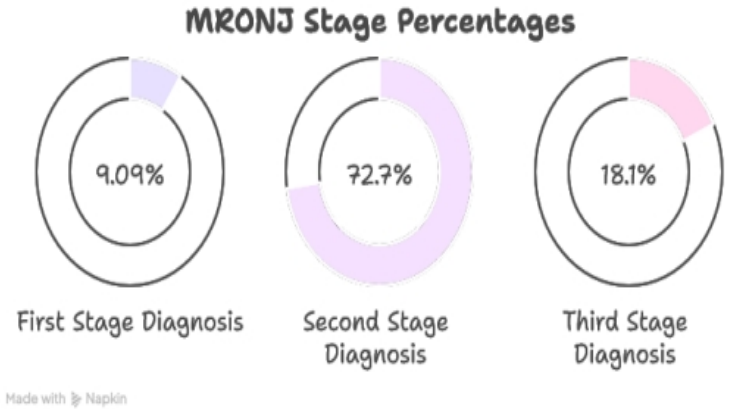


Figure 3. Patient representation by MRONJ stage

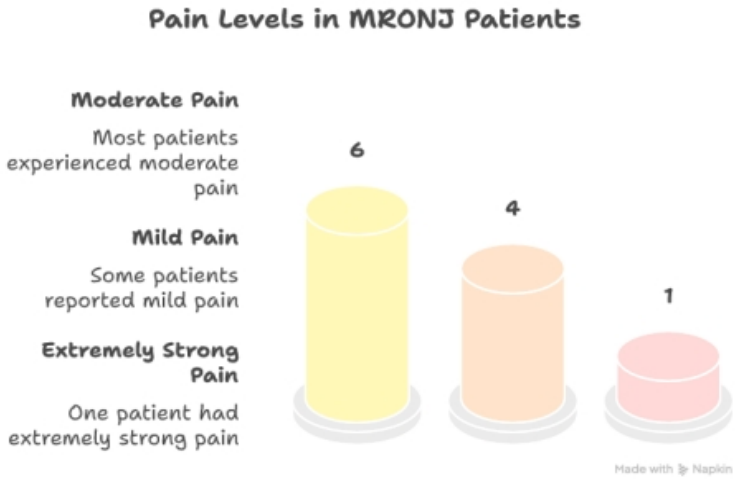
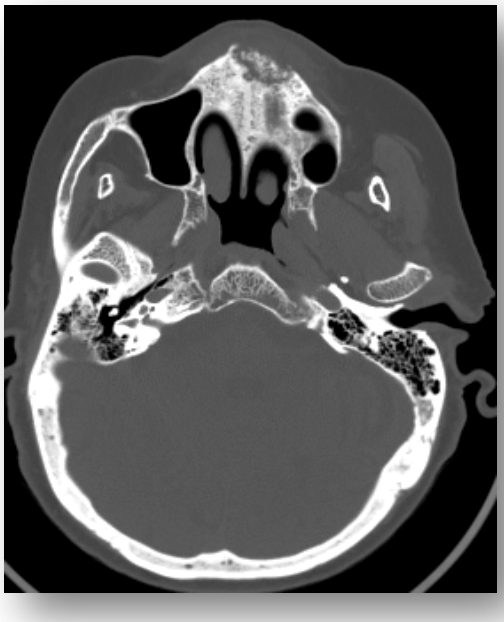


Figure 4. Intensity of pain in patients with different stages of MRONJ

Among patients in the largest subgroup with stage II—the mean pain intensity was 5.1 ± 1.1. Of the two patients with stage III, one reported extreme pain (NRS = 9)., While the other one reported pain on the border between moderate to severe pain (NRS = 7). In this group average pain was 8 (severe). In contrast, the patient diagnosed with stage I MRONJ experienced mild pain (NRS = 2).

The patient experiencing the most severe pain also presented with the most advanced stage of MRONJ, characterized by an intraoral fistula at the site of the previously extracted upper second molar. The lesion extended beyond the alveolar ridge and partially involved the maxillary sinus (Figures 5 and 6). The patient exhibited a poor response to analgesic therapy.

The other patient with stage III MRONJ. experianced moderate to severe pain, but destruction of bone was quite large, with bony sequestra inside (Figure 7,8,9,10). The patient also exhibited a poor response to analgesic therapy.



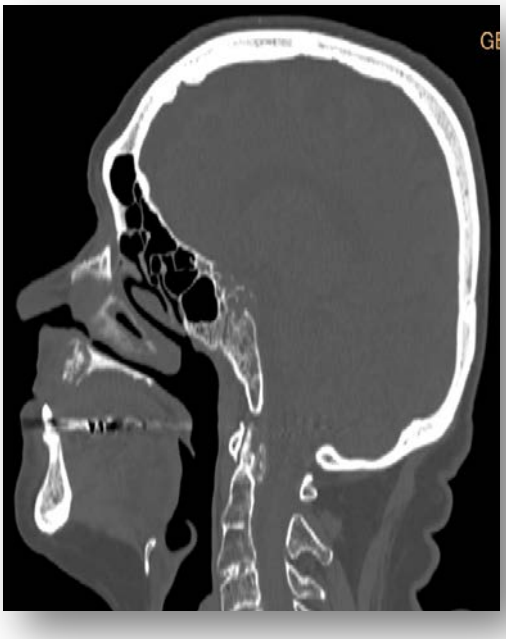


Figure 5. and 6. In this case MSCT findings for this patient revealed an ovoid, irregular hypodense area in the right half of the maxilla, accompanied by destruction of the outer contour of the mandibular cortex. Within this area, changes were observed along the root of the affected tooth, with a surrounding zone of osteosclerosis. The remaining portions of the maxilla demonstrated signs of osteoporosis

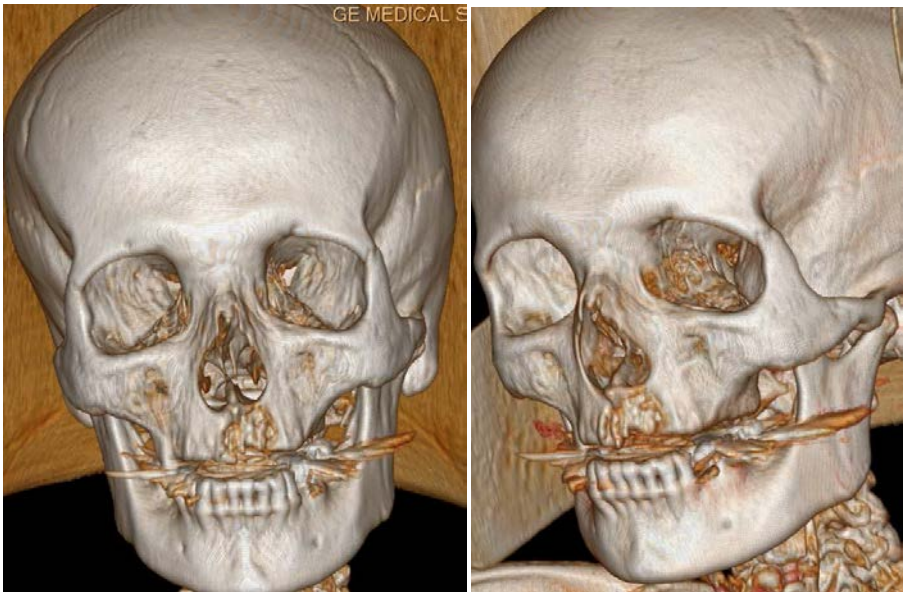


Figure 7. and ***Figure 8.***

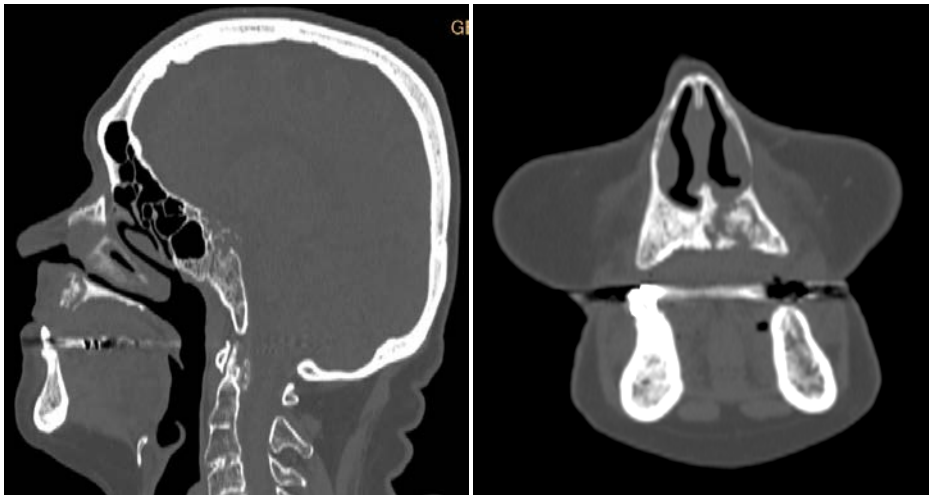


Figure 9. and ***Figure 10.***

Figures 7, 8, 9, 10. Stage III of MRONJ. Osteolytic irregular lesion with sequestrations on the left side of the maxilla

Discussion

Patients experiencing osteoporosis, osteopenia, and multiple forms of cancer are often prescribed agents that inhibit osteoclast resorption of the bone. A calendar year study demonstrated that 5.1 million patients aged over 55 years received prescriptions for IV bisphosphonates alone[7]. The development of MRONJ has been extensively investigated and is believed to be associated with impaired bone remodeling due to osteoclast inhibition, which may lead to bone sclerosis and reduced blood supply (ischemia). Research indicates that patients receiving these medications intravenously are at a significantly higher risk of developing this condition compared to those taking them orally. Genetic or individual predisposition plays an important role in the pathogenesis of MRONJ, as the condition does not occur uniformly among patients exposed to identical risk factors. The key factor in the pathogenesis of this condition is the oral biofilm and infection from the teeth[4,7].

The diagnosis of MRONJ is primarily based on clinical and radiographic criteria established by the American Association of Oral and Maxillofacial Surgeons (AAOMS)[7].

According to the AAOMS position paper, MRONJ can be diagnosed when the following criteria are met: 1) current or previous treatment with antiresorptive or antiangiogenic agents; 2) exposed bone, or bone that can be probed through an intraoral or extraoral fistula, persisting for more than eight weeks; and 3) no history of radiation therapy to the jaws or evident metastatic disease involving the jawbones. Based on the severity of clinical and radiological findings, MRONJ is classified into several stages, ranging from Stage 0—characterized by nonspecific symptoms and radiographic changes without bone exposure—to Stage 3, which involves extensive bone necrosis, pathologic fractures, extraoral fistulae, or involvement of the maxillary sinus or the inferior border of the mandible.

Radiologists play a crucial role throughout all stages of patient management—from the initial evaluation of lesions and monitoring of disease progression to the detection of potential complications, such as extension into adjacent structures[7]. Muttanahally et al.[5] suggest that there are no specific or distinctive radiographic patterns observed in any of the cases of MRONJ, regardless of the type of medication used. In this study, the pain as the predominant symptom of the stage of MRONJ depends on bone destruction and the presence of infection. The radiologists should possess a comprehensive understanding of the full range of imaging manifestations, recognizing that no single radiologic feature is pathognomonic for MRONJ in order to prevent the worsening of MRONJ, and to relieve the patient of pain. Imaging findings must always be interpreted in conjunction with the patient's clinical presentation and therapeutic history. In line with current radiologic standards, the diagnosis of MRONJ is primarily supported by advanced imaging modalities, including orthopantomography (OPT), cone-beam computed tomography (CBCT), and multislice computed tomography (MSCT). These techniques can demonstrate characteristic radiologic features such as areas of osteolysis, osteosclerosis, osteonecrosis, thickening of the lamina dura, widening of the periodontal ligament space, presence of bony sequestra, and pathological fractures. Radiologic imaging remains the cornerstone for confirming diagnosis, evaluating the extent of skeletal involvement, determining disease stage, and guiding the selection of appropriate therapeutic strategies. In cases where necrotic bone is not clinically exposed or when clinical findings are inconclusive, advanced imaging modalities—such as multislice computed tomography (MSCT), positron emission tomography (PET), and magnetic resonance imaging (MRI)—can greatly improve early detection and delineation of the affected bone structures[8,9].

Patients in Stage 0 should be regarded as potential precursors of MRONJ, where MSCT can assist in confirming the diagnosis, evaluating the extent of osseous involvement, and identifying possible complications. MSCT may also be valuable in detecting subtle bone alterations before MRONJ becomes clinically apparent[9,10]. Yanaguizawa et al.[11] in their MSCT study concluded that, in patients with Stage 0 (before the clinical manifestation of bone exposure), the computed tomography values of cancellous bone in affected areas were significantly higher than those in unaffected regions. Furthermore, compared with healthy controls, patients receiving bisphosphonate therapy—including those in Stage 0—demonstrated elevated CT values in cancellous bone, suggesting increased bone density relative to individuals not exposed to bisphosphonates. Additionally, thickening of the lamina dura and localized areas of sclerosis are considered potential early indicators that may be detectable before the disease becomes clinically evident. Even in the absence of distinct radiologic or clinical lesions, patients in Stage 0 may present with pain of varying intensity[12–14]. Pain often persists even after standard therapy (antibiotic treatment combined with local antiseptic measures) and demonstrates a certain degree of persistence, suggesting the presence of a neuralgiform component—that is, pain not solely attributable to inflammatory or infectious processes, but potentially possessing neuropathic characteristics. In this study, the patient, classified as Stage 1—where no distinct fistula is present—exhibited an intense, persistent, neuralgiform pain but mild intensity.

In patients receiving antiresorptive, antiangiogenic, or other medications associated with the development of MRONJ, the condition may occur spontaneously; however, the most common predisposing factor is tooth extraction or other invasive surgical procedures involving the jawbones. In this study, all patients developed MRONJ following tooth extraction.

Diagnostic and therapeutic strategies for MRONJ remain subjects of ongoing debate, as no universally accepted standard has yet been established. Currently, diagnosis relies on a combination of clinical, radiographic, and histopathological assessments. The most

common clinical manifestations include delayed healing of extraction sites, exposed necrotic bone, paresthesia, and pain. However, as noted by Kawahara et al., a substantial proportion of patients may remain asymptomatic, with the condition often identified incidentally during routine clinical or radiologic examinations[14]. In this study, the intensity of pain corresponded with the development of clinical signs and symptoms of the disease, equal to the MRONJ stage.

According to the literature, the staging of MRONJ is primarily determined by clinical symptoms and the duration of pain rather than by radiologic characteristics[15–18]. Notably, the early manifestations of different MRONJ stages may exhibit similar radiographic appearances. Duration of bisphosphonate intake affects the appearance of MRONJ. According to the Scottish Effectiveness Programe[4], bisphosphonate intake for longer than 5 years increases the possibility of MRONJ more times. In the present study, a clear correlation was observed between disease stage, clinical presentation, duration of medication intake and pain intensity. In the study by Haviv et al.[19], the stage of MRONJ, the type of pharmacotherapy, lesion size, and location were not correlated with the level of pain. Among patients diagnosed with MRONJ, a total of 67.5% experienced some pain, while 36.5% reported moderate to severe pain[19]. In contrast, the study by Polyakov et al. demonstrated a direct association between pain intensity and the stage of disease progression, with pain being analyzed both before and after treatment[20]. Patients who experienced a high level of pain had better responses to the surgical and conservative treatment and realizing of pain compared to those with moderate pain.

Conclusion

Radiologists play an important role in early diagnosis of all stages of MRONJ. Pain could be considered as early sign of this pathological condition of the bone, and it correlates with the stage of MRONJ in lesions caused by bisphosphonate intake.

CT characteristics of MRONJ can help in more accurate diagnosis and treatment planning, especially in differentiating active necrosis from other pathological conditions of the jaw. CT imaging plays an important role in the detection, classification and follow-up of MRONJ, as it provides detailed information on the degree of involvement of the bone and surrounding structures, which are not always clearly visible by clinical examination or classic X-ray. Future studies should include analyses of larger patient samples encompassing various medications as well as combination therapies.

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PREVALENCIJA KARCINOMA DONJE USNE U SEVERNOJ MAKEDONIJI: PETOGODIŠNJA RETROSPEKTIVNA STUDIJA

THE PREVALENCE OF LOWER LIP CARCINOMA IN NORTH MACEDONIA: A 5-YEAR RETROSPECTIVE STUDY

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Sažetak

Uvod: *Karcinom donje usne čini približno 5% svih malignih tumora u predelu glave i vrata. Najznačajniji faktori rizika za nastanak karcinoma donje usne su dugotrajno izlaganje sunčevoj svetlosti i pušenje duvana.*
Cilj *ove studije bio je da se analiziraju kliničke i patohistološke karakteristike karcinoma donje usne i ispita njihov uticaj na pojavu metastaza na vratu.*
Materijal i metode: *Ukupno je analizirano 120 pacijenata, od kojih je 76,6% bilo muškog, 23,3% ženskog pola. Najzastupljenija starosna grupa bila je između 60 i 80 godina, pri čemu je više od 90% pacijenata bilo starije od 50 godina. Većinu ispitanika činili su poljoprivrednici i radnici na otvorenom, bez značajnih razlika prema polu i starosnoj strukturi.*
Rezultati: *Tumori su najčešće dijagnostikovani u veličinama T1 i T2, odnosno u stadijumu II bolesti. Lokalni recidivi registrovani su kod 5,8% pacijenata, dok su regionalni recidivi zabeleženi kod 8,3%, najčešće u periodu između prve i druge godine nakon hirurškog lečenja.*
Zaključak: *Recidivi karcinoma donje usne su relativno retki, ali je neophodno redovno i učestalo praćenje pacijenata tokom prve dve godine nakon operacije. S obzirom na to da poljoprivrednici i radnici na otvorenom predstavljaju populaciju sa povećanim rizikom za razvoj ovog karcinoma, preporučuje se sprovođenje skrining pregleda tokom svake stomatološke ili lekarske kontrole radi ranog otkrivanja bolesti.*

Ključne reči: *karcinom donje usne, faktori rizika, retrospektivna studija, lečenje, recidiv*

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Abstract

Introduction: *Carcinoma of the lower lip constitutes approximately 5% of malignant tumors in the head and neck region. Timely treatment may lead to a favorable clinical outcome. Primary risk factors for its occurrence include excessive sun exposure and smoking.*
Aim: *The aim of this study was to analyze the clinical and pathological characteristics of lower lip carcinoma and their impact on the occurrence of neck metastases.*
Materials and Methods: *A total of 120 patients with diagnosed lower lip carcinoma, 92 (76.6%) male and 28 (23.3%) female, were included in the study. The majority of the patients were farmers and outdoor workers, regardless of gender and age. This study employed retrospective analysis for a period of five years. Hospital records of all patients treated for this condition were analyzed. Patient and tumor characteristics: gender, age, occupation, TNM classification, stage, cell differentiation, and occurrence of local and regional recurrences were examined.*
Results: *The most common age affected by lower lip carcinoma was between 60 and 80 years, with over 90% aged above 50. Tumors were most frequently diagnosed at T1, followed by T2 size and Grade II. Local recurrences were detected in 5.8% of patients, while regional recurrences were noted in 8.3% of patients, most commonly in the period between the first and second year post-surgery.*
Conclusion: *Recurrences of lower lip carcinoma are relatively rare, but frequent follow-ups in the first two years post-surgery are necessary. As farmers and outdoor workers represent a high-risk group for lower lip carcinoma development, screening during every dental and general medical visit is essential for early detection.*

Key words: *lower lip carcinoma, risk factors, retrospective study, treatment, recurrence*

Introduction

Lip carcinoma is a malignant neoplasm of the upper or lower lip or the commissure[1] and is coded under the International Classification of Diseases as C00. Some studies consider lip cancer to account for 25% of oral carcinomas[2]. However, lip carcinoma is distinct from other types of oral cancers, often associated with increased exposure to ultraviolet radiation from sunlight. Lower lip carcinoma constitutes less than 5% of malignant tumors in the head and neck region, excluding other nonmelanoma skin cancers[2]. Histologically, 90% of lower lip cancers originate from squamous cells, with the remaining 10% comprising basal cell carcinomas and adenocarcinomas.

Lower lip squamous cell carcinoma may exhibit a slow clinical progression with a favorable prognosis if treated promptly and appropriately. However, in some patients, it can be aggressive, with increased morbidity and mortality, often due to the subsequent appearance of metastases in the cervical lymph nodes[3]. Early identification and treatment of these patients improve the chances of complete recovery.

The commonly used classification of lip carcinoma is based on tumor size, lymph node involvement, and the presence or absence of distant metastases (TNM)[4]. Broder's grading system[5] is the primary system used in studies related to lower lip carcinoma to analyze the histological characteristics of tumor cells. According to this system, lower lip carcinoma is categorized by differentiation as well, moderately and poorly differentiated.

Globally, the incidence by gender is higher in men than in women[6,7], with most patients being over 50 years of age[8,9]. Risk factors for developing lower lip carcinoma can be defined as environmental, pathological, and endogenous factors. Environmental factors include UV exposure, more common among people living in rural areas and those involved in agriculture. Pathological risk factors include smoking (including pipe smoking), occupation, alcohol consumption, socioeconomic status, and viral infections (e.g., HPV). Endogenous factors include familial and genetic predisposition, immunosuppression, and immunodeficiency. Race and cultural characteristics can also be considered risk factors.

The standard treatment for lower lip carcinoma is surgical excision of the lesion, potentially followed by radiotherapy, depending on the stage of carcinoma, its aggressiveness and differentiation, and involvement of neural and vascular structures[10–17]. Postoperative (or adjuvant) radiotherapy is recommended for patients with close or positive excision margins when re-excision is not feasible[18–24].

Therapeutic outcomes in these studies include assessments of locoregional control, recurrence, metastasis, overall survival, cause-specific survival, and disease-free survival[25–30].

This study aimed to analyze the clinical and pathological characteristics of lower lip carcinoma and their impact on the occurrence of cervical metastases in patients who underwent surgical treatment at the University Clinic for Maxillofacial Surgery in Skopje from 2016 to 2021.

Materials and Methods

A retrospective study was conducted for the period 2016–2021. All patients diagnosed with lower lip carcinoma were identified and analyzed in the database of the University Clinic for Maxillofacial Surgery in Skopje. For this purpose, electronic patient records were reviewed in the Hospital Information System, which integrates outpatient visits, hospital records, and all surgical interventions. The search used the International Classification of Diseases (ICD), 10th edition, code C00.4 for lower lip carcinoma. The database was also searched for codes C00, which denotes lip carcinoma in general, and C00.9, to avoid excluding any patients within the scope of interest. Since the preliminary diagnosis code D10.0, indicating benign lip neoplasm, is often used before final pathological confirmation, a review was also conducted of patients under this code, to include those with confirmed squamous cell carcinoma of the lower lip who might not have been subsequently recoded correctly. Additionally, operative logs, outpatient logs, and pathology reports were reviewed for the specified period to double-check data and include patients not entered electronically for any reason.

All identified patients were then thoroughly analyzed by reviewing their complete medical history, including the initial examination, type of surgical intervention, and follow-up visits.

The primary inclusion criteria for the study were as follows: patients must have a confirmed histopathological diagnosis of

squamous cell carcinoma of the lower lip, and have undergone surgical excision of the carcinoma, regardless of the technique used. Additionally, patients needed to have available basic demographic data (age and gender), and a postoperative follow-up, along with properly maintained medical records.

Patients were excluded from the study if they had previously received treatment for lower lip carcinoma outside the study period, had been treated in other institutions before being admitted to the Clinic in Skopje, had undergone neck dissection, or lacked postoperative follow-up and proper medical documentation.

The following data were analyzed in the selected patient group:

• **Age**—Expressed in years and categorized into 10-year age groups: 30–39, 40–49, 50–59, 60–69, 70–79, 80–89 and 90–99; Patients were further categorized into two age groups: under and over 50 years

• **Gender**—Expressed as male or female

• **Profession**—Categorized into three groups (farmer, worker, and other)

• **Tumor classification**—According to the TNM system

• **Definition of clinical stage**—By combining TNM classification parameters

• **Differentiation of tumor cells**—In histopathological analysis, graded from I to III, representing well, moderately, and poorly differentiated cells, respectively

• **Occurrence of local recurrence** (yes, no), as well as the time elapsed from surgery to recurrence in patients with detected local recurrence

• **Occurrence of regional recurrence** (clinically positive cervical lymph nodes).

The study was conducted in compliance with ethical principles and standards for conducting retrospective analyses, following the Ethical Code and the principles of the Declaration of Helsinki. Particular care was taken to protect personal data to ensure that patients could not be identified through the presentation and analysis of findings and results.

Data obtained during the research were statistically analyzed using the SPSS software package, version 22.0 for Windows (SPSS, Chicago, IL, USA). Qualitative variables were analyzed using ratio coefficients, proportions, and rates, presented as absolute and relative numbers. Quantitative variables were analyzed using measures of central tendency and dispersion. The Shapiro–Wilk W test was used to determine the normality of frequency distribution for the variables. Risk factors were quantified using the Odds Ratio (OR) and confidence intervals (CI). A difference test was used for comparing proportions. Pearson's chi-square test, Fisher's exact test, and the Fisher–Freeman–Halton test were used to determine associations between certain dichotomous variables. Spearman's rank correlation coefficient assessed the relationship between numerical variables with non-normal frequency distributions. Non-parametric tests, such as the Mann–Whitney U test for two independent samples and the Kruskal–Wallis H test for multiple independent samples, were used to test the significance of differences between two or more numerical variables with non-normal frequency distributions. All statistical analyses applied a significance level of $p < 0.05$.

Results

Over the five-year period covered by the study (2016–2021), a total of 120 patients of both sexes with squamous cell carcinoma of the lower lip were examined. According to the histopathological findings for each patient in the sample, the distribution was as follows:

• 115 cases (95.83%) of Carcinoma planocellulare Squamous cell carcinoma

• Three cases (2.5%) of Carcinoma planocellulare verrucous

• One case (0.83%) of Carcinoma planocellulare corneum

• One case (0.83%) of Carcinoma planocellulare invasivum

In the sample of 120 patients (100%), 92 (76.67%) were male and 28 (23.33%) were female patients, with a male-to-female ratio of 3.3:1. For $p < 0.05$, the percentage of male patients diagnosed with squamous cell carcinoma of the lower lip was significantly higher compared to female patients.

The average age of participants with squamous cell carcinoma of the lower lip across the entire sample was 67.15 ± 11.16 years, with a minimum/maximum age range of 34–87 years. Fifty percent of these patients were over 67 years of age, with a median interquartile range of 68 (59–75), and 25% were over 75 years. For $p < 0.05$, a significant age difference was observed between genders, with males diagnosed with squamous cell

carcinoma of the lower lip being significantly older than females. Within the sample of patients with squamous cell carcinoma of the lower lip, there were no patients under 30 years of age, and in the 30–40 age group, only one male patient (0.83%) was recorded. The highest proportion of patients was in the 70–79 age group, with 39 cases (32.5%), followed by the 60–69 age group, represented by 35 cases (29.17%). The lowest proportion of squamous cell carcinoma cases during the study period was in the 40–49 age group, with 9 cases (7.5%), followed by the 80–89 age group with 15 cases (12.5%) (Table 1).

Additional analysis of patients with squamous cell carcinoma of the lower lip by age ≤ 50/> 50 years showed that 108 patients (90%) were over 50, while only 12 (10%) were aged ≤ 50. Within the sample from 2016 to 2021, the distribution by age ≤ 50/> 50 showed that 81 male cases (88.04%) were over 50 years. Among female cases, 27 (96.43%) were over 50, with only one case (3.57%) aged ≤ 50, involving a 43-year-old female patient.

The majority of patients in the sample were farmers, totaling 73 (60.83%). Of the male patients, 58 (63.04%) were farmers, while 15 (53.33%) of the female patients had the same occupation. For $p < 0.05$, the percentage of male farmers was significantly higher than that of female farmers. The second most common occupation was general worker, with 34 patients (28.33%) in the total sample. Among male patients, this occupation was recorded for 28 individuals (30.43%), and among female patients, for six individuals (21.43%). For $p < 0.05$, the percentage of male workers was significantly higher compared to female workers. Other occupations were noted in 13 (10.83%) of the total patients, including 6 (6.52%) males and seven (25%) females. In the entire sample, for $p < 0.05$, a significant association was observed between gender and occupation among patients diagnosed with squamous cell carcinoma of the lower lip, as indicated by Pearson's chi-square test (Table 2).

According to the TNM classification for the primary tumor (T), the largest proportion of cases—68 (56.67%)—had a primary tumor classified as T1 (≤ 2 cm in the largest diameter), followed by 39 cases (32.5%) classified as T2 (> 2 cm but ≤ 4 cm in the largest diameter). Eleven cases (9.17%), were classified as T3 (> 4 cm in the largest diameter).

Among the total sample, four cases (3.54%) were identified with clinically positive regional lymph nodes classified as N1 (metastasis in a single unilateral lymph node, ≤ 3 cm), three cases (2.65%) with N2 (metastasis in a single or bilateral lymph node, > 3 cm but ≤ 6 cm), and two cases (1.77%) with N3 (metastasis in a lymph node > 6 cm).

No cases in the sample of patients with squamous cell carcinoma of the lower lip were diagnosed with distant metastasis M1 based on TNM classification.

It was found that the largest proportion of patients with squamous cell carcinoma of the lower lip (2016–2021), 63 (52.5%), had a TNM classification of T1NXMX (tumor ≤ 2 cm in its largest diameter, with regional lymph nodes and distant metastasis unable to be assessed). The second most common classification, found in 18 patients (15%), was T2NXMX (tumor > 2 cm but ≤ 4 cm in its largest diameter, with regional lymph nodes and distant metastasis unable to be assessed). The third most common TNM classification of squamous cell carcinoma of the lower lip was T2N0M0 (tumor > 2 cm but ≤ 4 cm in its largest diameter, without metastasis to regional lymph nodes or distant metastasis), with 15 patients (12.5%) in the sample. Full results of TNM classification by groups are presented in Table 3.

The analysis indicated that the majority of the sample with squamous cell carcinoma of the lower lip were categorized as G2 (moderately differentiated tumor cells), totaling 99 cases (82.5%). Only two patients (1.67%) had G1 differentiation (well-differentiated tumor cells), one from each gender. No cases were identified in the sample with G3 or G4 tumor cell differentiation.

Analysis showed that the majority of patients with squamous cell carcinoma of the lower lip (2016–2021) were classified as Stage I (localized tumor not spread to lymph nodes or other tissues), totaling 54 cases (45%). Stage II (larger tumor not spread) included 25 patients (20.83%). Eleven patients (9.17%) were designated as Stage III (a larger tumor likely spread to lymph nodes or other tissues).

Of the total sample, 97 patients (93.27%) were without local recurrence, with only seven cases (5.83%) experiencing a local recurrence. Regional recurrence was recorded in 10 patients (8.33%) with squamous cell carcinoma of the lower lip. Among those with regional recurrence, three cases (2.5%) experienced it within less than one year post-intervention, and seven cases (5.83%) between one and two year post-intervention.

Table 1. Distribution of patients with carcinoma of the lower lip by age groups and association calculated by Pearson chi-square test

Parameter		Men	Women	Total	p
Age groups					
30 - 39	**N** **%**	1 1,09%	0 0%	1 0,83%	X^2=5,829; df=5; p=0,2122
40 – 49	**N** **%**	8 8,70%	1 3,57%	9 7,50%	
50 – 59	**N** **%**	17 18,48%	4 14,29%	21 17,50%	
60 - 69	**N** **%**	30 32,61%	5 17,86%	35 29,17%	
70 - 79	**N** **%**	26 28,26%	13 46,43%	39 32,50%	
80 - 89	**N** **%**	10 10,87%	5 17,86%	15 12,50%	
≤50	**N** **%**	11 11,96%	1 3,57%	12 10%	X^2=1,677; df=1; p=0,1953
>50	**N** **%**	81 88,04%	27 96,43%	108 90%	
Total	**N** **%**	92 76,67%	28 23,33%	120 100%	
X^2=Pearson Chi-square test;					

Table 2. Differences among patients with lower lip carcinoma according to profession and gender

Profession		Men	Women	Total	Difference test	Pearson Chi-square test
Farmer	**N**	58	15	73	p=0,0001*	X^2=7,697; df=2; p=0,0213*
	%	63,04%	53,57%	60,83%		
General worker	**N**	28	6	34	p=0,0001*	
	%	30,43%	21,43%	28,33%		
Other	**N**	6	7	13	p=0,7768	
	%	6,52%	25%	10,83%		
Total	**N**	92	28	120	p=0,0001*	
	%	76,67%	23,33%	100%		
*significant at p< 0,05						

Table 3. Distribution of pathological parameters according to TNM classification

TNM groups		Gender			Difference test
		Men	Women	Total	
T1 NX MX	**N**	46	17	63	p=0,3224
	%	50%	60,71%	52,50%	
T2	**N**	2	0	2	-
	%	2,17%	0%	1,67%	
T1 N0 M0	**N**	4	1	5	p=0,8571
	%	4,35%	3,57%	4,17%	
T2 NX MX	**N**	14	4	18	p=0,9044
	%	15,22%	14,29%	15%	
T3	**N**	3	0	3	-
	%	3,26%	0%	2,50%	
T3 N1 MX	**N**	0	1	1	-
	%	0%	3,57%	0,83%	
T3 N2 MX	**N**	1	0	1	-
	%	1,09%	0%	0,83%	
T3 NX MX	**N**	1	0	1	-
	%	1,09%	0%	0,83%	
T2 N0 M0	**N**	11	4	15	p=0,7452
	%	11,96%	14,29%	12,50%	
T2 N0 MX	**N**	1	0	1	-
	%	1,09%	0%	0,83%	
T2 N1 MX	**N**	1	0	1	-
	%	1,09%	0%	0,83%	
T3 N1 M0	**N**	2	0	2	-
	%	2,17%	0%	1,67%	
T3 N2 M0	**N**	2	0	2	-
	%	2,17%	0%	1,67%	
T3 N0 M0	**N**	1	0	1	-
	%	1,09%	0%	0,83%	
T2 N3 MX	**N**	1	0	1	-
	%	1,09%	0%	0,83%	
T2 N3 M0	**N**	1	0	1	-
	%	1,09%	0%	0,83%	
TX	**N**	1	1	2	p=0,3717
	%	1,09%	3,57%	1,67%	
Total	**N**	92	28	120	-
	%	76,67%	23,33%	100%	

Discussion

Cumulative exposure to UV radiation, primarily from the sun, is considered the main risk factor for the development of squamous cell carcinoma of the lower lip[9]. With increasing age, cumulative UV exposure also increases proportionally, which accounts for the higher prevalence of lower lip carcinoma in older populations, particularly in individuals in their seventies and eighties[31,32]. For younger patients with lower lip carcinoma, other systemic factors, such as immunosuppression or immunodeficiency, should be ruled out[33]. In our analysis, the patient with carcinoma in the 30–40 age group did not exhibit immune system impairment. This patient probably had higher cumulative exposure to sunlight, but other molecular and cellular changes, which are beyond the scope of this study, should also be considered as potential contributors to the cellular mechanisms that allow uncontrolled cell division.

In the analysis conducted for this research, the highest proportion of patients was in the 70–79 age group, with 39 cases (32.5%), followed by the 60–69 age group with 35 cases (29.17%). Although age and gender differences in lower lip carcinoma groups were not markedly significant, a noticeably higher percentage of men aged 60–69 had lower lip carcinoma (32.61%) compared to women in the same age group (17.86%), which is consistent with data from the literature[10]. This discrepancy likely reflects the fact that male patients typically experience greater cumulative sun exposure due to occupations requiring outdoor work (e.g., agriculture, construction), as well as generally lower rates of protective measures against UV radiation. This rationale is further supported by the observation that the proportion of male patients with lower lip carcinoma under the age of 50 is slightly higher than that of female patients. Additionally, the accumulation of molecular changes resulting from exposure to risk factors, such as UV radiation, smoking, and other carcinogens, or as a consequence of the biological ageing process, which is associated with DNA damage accumulation, plays a significant role[11,12].

The findings from our study are fully consistent with those from available literature regarding the patients' profession[13,28,34,35]. It is well known that lower lip carcinoma is primarily associated with UVB radiation from sunlight, particularly affecting individuals with prolonged sun exposure, such as farmers and outdoor laborers. The highest proportion of lower lip carcinoma cases in our study was observed among farmers of both sexes, followed by laborers. The significant gender differences in patient proportions are largely attributed to men's generally greater cumulative sun exposure due to prolonged outdoor activity in agricultural and other work settings.

The relatively low rate of cervical lymph node metastasis aligns with the literature[30,36–38]. An 8.33% metastasis rate is neither excessively high nor particularly low. Studies indicate a marked decline in survival rates when nodal involvement is detected during follow-up, thus making neck dissection for patients with clinically negative cervical nodes a controversial issue. The "wait and watch" approach is advocated by some authors, given the low incidence of regional metastasis in lower lip carcinoma. However, when metastasis is detected, neck dissection combined with adjuvant radiotherapy is recommended.

The results obtained in our study align with findings in the literature, where recurrence most often occurs within the first two years following treatment[10,13,17,18,39–42]. Local recurrence, as expected, is observed within the first year post-surgery due to the proximity of tumor cells to resection margins and healthy tissue in the lower lip. In contrast, regional recurrences, represented by metastatic involvement of the cervical lymph nodes, are typically detected between the first and second year post-surgery, which is explained by the time required for malignant cells to disseminate through lymphatic circulation and establish growth within cervical lymph nodes[22,29,38,43–46].

A longer follow-up period for patients (preferably up to five years) is recommended to obtain a more objective picture of the time frame in which recurrences occur post-treatment.

A potential limitation of this study is the shorter follow-up period for patients treated at the Maxillofacial Surgery Clinic in Skopje during the later years of the study period. Nonetheless, all patients in the sample were followed for at least one postoperative year, with those treated in the early years of this study (2016, 2017, and 2018) having longer follow-up periods—six, five, and four years, respectively—compared to three, two, and one year for those treated in the subsequent years of the analysis. There are various weaknesses in many retrospective studies, noting that most studies lack two groups for direct comparison and often only describe the outcome of surgical therapy or radiation therapy as the sole treatment modality (Table 4).

Table 4. Data from retrospective studies about various survival rates and provided treatment for patients with squamos cell carcinoma of the lower lip.

Study	Year	n	OS	DFS	SS	LRC	Bt	Surg	Rad	S+R
de Visscher et al, 1999 (14)	1980-1994	256	+	+	-	-	-	+	+	-
Wilson et al, 2005 (15)	1980-2000	52	-	-	-	+	-	+	-	+
Beauvois et al, 1994 (16)	1972-1991	237	+	-	+	+	+	-	-	-
Tombolini et al, 1998 (17)	1970-1992	57	+	+	-	+	+	-	-	-
Cowen et al, 1990 (18)	1970-1985	299	-	-	-	+	+	-	-	-
Heller et al, 1979 (19)	1955-1969	171	+	-	+	+	-	+	-	-
Petrovich et al, 1979 (20)	1945-1975	250	+	-	-	+	-	-	+	-
Wu et al, 1985 (21)	1958-1974	74	+	-	-	-	-	+	+	-
Giuliani et al, 1989 (22)	1974-1986	121	+	+	-	+	-	+	-	-
Ngan et al, 2005 (23)	1996-2004	13	+	+	+	+	+	-	-	-
Aslay et al, 2005 (24)	1988-2003	41	+	+	-	+	+	-	-	-
Orecchia et al, 1991 (25)	1973-1988	47	+	+	-	+	+	-	-	-
Luna-Ortiz et al, 2004 (26)	1990-2000	113	+	-	-	-	-	+	+	-
Hemprich et al, 1989 (27)	15 years	352	+	-	-	-	-	-	+	-
Califano et al, 1994 (28)	1975-1987	105	+	-	+	-	-	+	-	-
Bilkay et al, 2003 (29)	1983-1999	118	+	-	+	+	-	+	-	-
Jaquet et al, 2005 (30)	1983-2001	24	+	-	+	+	-	+	-	-
van der Wal et al, 1996 (31)	1985-1992	14	-	-	-	+	-	+	-	-
Zitsch et al, 1995 (9)	1940-1987	1252	+	-	+	-	-	+	+	-
Beltrami et al, 1992 (32)		80	+	-	+	-	-	+	-	-
Gooris et al, 1998 (33)	1974-1994	85	-	+	-	+	+	-	+	+
Miltenyi et al, 1980 (34)		170	+	-	+	-	-	-	+	-
de Visscher et al, 1996 (35)	1980-1992	108	+	+	-	-	-	-	+	-
Boddie et al, 1977 (36)	1943-1974	1308	+	-	+	-	-	+	+	-
McCombe et al, 2000 (37)	1979-1988	323	-	-	-	+	-	+	+	-
Cerezo et al, 1993 (38)	1971-1976	117	-	-	-	+	-	+	+	+
Babington et al, 2003 (9)	1980-2000	130	+	+	-	+	-	+	+	+
Holmkvist et al, 1998 (39)	1986-1999	50	-	+	-	+	-	+	-	-
Cruse et al, 1987 (40)	1962-1982	117	+	-	+	-	-	+	-	-
Antoniades et al, 1995 (41)	1979-1989	906	+	-	-	-	-	+	+	+

Kutluhan et al, 2003 (42)	1994-2000	31	+	-	+	+	-	+	-	-
dos Santos et al, 1996 (43)	1980-1999	58	+	+	-	+	-	+	-	-
de Visscher et al, 1998 (44)	1979-1992	184	+	+	-	+	-	+	-	-
Rao et al, 1998 (45)	1987-1989	62	+	-	-	-	-	+	+	+
Blomgren et al, 1988 (46)	25 years	165	+	-	+	+	-	+	-	-

n- number of patients; OS- overall survical; DFS- disease free survival без болест; SS- specific survival; LRC- loco-regional control; Bt- brachitherapy; Surg- surgery; Rad- radiotherapy; S+R, surgery + radiotherapy

Conclusion

Farmers and outdoor workers over the age of 50 are at an increased risk of developing squamous cell carcinoma of the lower lip, and they should regularly undergo screening during visits to their general dentist and primary care physician, regardless of any other health issues they may be facing.

Patients who have undergone surgical intervention for squamous cell carcinoma of the lower lip should be monitored with regular and frequent follow-ups during the first two years, as local and regional recurrences are most likely to occur during this period. Timely monitoring can prevent local recurrence and the metastatic spread of the cancer, thereby increasing survival chances.

Conflict of Interest

All authors confirm that there is no conflict of interest of any form concerning the work presented in this article.

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PRIKAZ SLUČAJA
CASE REPORT
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PROCENA KVALITETA NOVOFORMIRANE ALVEOLARNE KOSTI POSLE PRIMENE „LEPLJIVE KOSTI“ – PRIKAZ SLUČAJA

QUALITY EVALUATION OF NEWLY FORMED BONE AFTER “STICKY BONE” SOCKET PRESERVATION: A CASE REPORT

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Sažetak

Uvod: *Resorpcija preostalog alveolarnog grebena nakon ekstrakcije zuba izraženija je u horizontalnom nego u vertikalnom pravcu. Proces je vremenski zavisan, a najintenzivniji je tokom prvih šest meseci i u prvoj godini nakon vađenja zuba. Za očuvanje zapremine alveolarne kosti koriste se različiti graft materijali, kao što su autografti, allografti, ksenografti i aloplastični materijali. A-PRF, kao autologni derivat krvi, poslednjih godina sve se češće primenjuje zbog svojih svojstava koja doprinose angiogenezi, epitelizaciji i hemostazi. Njegova jednostavna priprema, niska cena i odsustvo potrebe za antikoagulansima čine ga pogodnim za široku kliničku primenu.*
Cilj *ovog rada bio je da se ispita uticaj A-PRF-a kao adjuvansa na količinu i kvalitet novostvorene kosti u postupku očuvanja alveole nakon ekstrakcije zuba.*
Materijal i metode: *Očuvanje alveole (socket preservation) izvedeno je kombinacijom A-PRF-a i ksenografta u obliku tzv. „lepljive kosti” (sticky bone). Nakon intervencije evaluirani su klinički parametri, gustina kosti i histomorfometrijski pokazatelji kvaliteta novostvorene kosti.*
Rezultati: *Klinička merenja pokazala su smanjenje širine alveolarnog grebena za 1 mm, bez vertikalne resorpcije, četiri meseca nakon očuvanja alveole. Zabeležena je veća gustina novonastale kosti u poređenju sa gustinom kosti u periapikalnoj regiji, kao i odličan kvalitet kosti prema histomorfometrijskoj analizi.*

Ključne reči: *A-PRF, ksenograft, lepljiva kost, gustina kosti, histomorfometrija*

Abstract

Introduction: *Residual alveolar ridge bone resorption is more prominent in the horizontal, than the vertical direction. It is time-dependent, and most prominent in the first six months and the first year after tooth extraction. Several graft materials are used for keeping residual alveolar bone volume, like autografts, allografts, xenografts, alloplastic materials, etc. A-PRF as an autologous blood derivative, has been increasingly used in recent years because of its properties in angiogenesis, epithelialization and hemostasis. Simple production, low cost and non-use of anticoagulants are advantages for more mass use of it.*
Aim: *The aim was to investigate the impact of PRF as an adjuvant on bone quantity and quality in socket preservation.*
Materials and Methods: *Socket preservation with a combination of A-PRF with xenograft (sticky bone) was performed, and clinical parameters, bone density and histomorphometry were evaluated.*
Results: *Clinical measurements showed 1 mm horizontal and no vertical resorption four months after socket preservation, higher density of newly formed bone than bone density of periapical region and great bone quality based on histomorphometric analysis.*

Key words: *A-PRF, xenograft, sticky bone, bone density, histomorphometry*

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Introduction

Tooth extraction, for various etiological reasons, is the most commonly performed oral surgical procedure in everyday dental practice[1].

Following the extraction of the indicated tooth, the healing phases of the post-extraction wound begin, which have been studied extensively in numer of animal and human studies. The healing process of the post-extraction wound has been described in four phases in some studies and review papers, while the 2015 review by Araujo et al.[2] detailed the histological changes in three phases: the inflammatory phase, proliferative phase, and bone modelling and remodelling.

Bone resorption is more pronounced in the first six months after extraction, and continues at a rate of 0.5–1% per year throughout life[3,4].

In 2012, Lang et al., in a systematic review study, determined the following dimensional changes in the residual alveolar ridge after tooth extraction over six months: a 3.8 mm mean resorption in the horizontal (vestibulo-oral) projection; and a 1.24 mm mean value for vertical (coronal-apical) resorption[5].

In recent decades, with the development of technical and technological processes, the enormous rise and development of implantology, implant prosthetics and aesthetic dentistry have become inevitable, as has the ever-increasing need to preserve the so-called red-and-white aesthetics, and the need to preserve or create the biological foundation. In the last decade, in the field of implantology and implant prosthetics, long-term personal satisfaction or the so-called satisfaction rate has become increasingly important, and not just success and longevity, or the so-called success rate. From an aesthetic point of view, especially in the frontal region, the preservation of the so-called red-white aesthetics, which Furhauser et al. assesses through the Pink Esthetic Score (PES), is of key importance. This evaluates the condition of peri-implant soft tissues, while Belser et al. in 2009 introduced their simplified index for quantifying parameters for evaluating soft tissues and implant-prosthetic structure through the so-called White Esthetic Score (WES)[6,7].

In order to meet the aesthetic and functional needs of patients, the correct prosthetic placement of implants plays a key role. This has led to the need to develop two separate methods for preserving and creating the biological foundation, namely guided bone regeneration (GBR) and guided tissue regeneration (GTR). GBR methods, are divided into two separate methods: augmentation of the residual alveolar ridge (ARA), which involves increasing the volume of the ridge and is applied after a longer period of bone resorption, and preservation of the residual alveolar ridge (ARP), which involves the maximum possible preservation of the contours of the post-extraction alveolus immediately after tooth extraction[8]. Post-extraction socket grafting, or socket preservation (SP), as a segment of ARP, has become increasingly popular in recent decades due to its conceptual and technical attractiveness[9].

Several types of biomaterials have been used and investigated in a number of clinical studies, including autologous bone, or autografts (AG), allografts (AlG), xenografts (XG), alloplastic materials (AlP), autologous blood derivatives, and bioactive agents[10].

Characteristic of XG is their slow resorption and the presence in situ of 20% to 40% of the graft material during the first six months and presence up to 3 years, and in a longitudinal study, their presence has been proven even 18 months after application[11,12].

The history of autologous blood derivatives begins in the early 1970s with the innovation of fibrin glue until 2001, when Dr. Joseph Choukroun in France innovated PRF (Platelet Rich Fibrin) as the second generation of autologous blood derivatives, and further modification of production protocols. The PRF protocol is a physiological method based on the use of centrifugal force to fractionate the blood elements of platelet-enriched fibrin in specially designed tubes, lined with glass on the inside, unlike the complicated procedure of obtaining PRP[13]. The mechanism of action of PRF is through its structure and composition. It is a network of densely arranged fibrin fibers with a three and a tetramolecular structure in which a huge number of platelets and leukocytes are incorporated. By degranulating platelets from their dense α-granules, plasma proteins, pro- and anti-inflammatory cytokines (IL-1, IL-6, IL-4, IL-8), and growth factors (TGF, VEGF, PDGF, IGF) are released[14].

The properties of these components that make up the PRF coagulum are in inflammatory response and improvement, as well as the acceleration of bone and soft tissue

healing of the post-extraction wound, and th elimination of postoperative morbidity.

In order to improve the efficiency of different types of grafts, barrier membranes and biomaterials, as well as the combination of their osteogenic, osteoinductive and osteoconductive properties, there is often a need for mutual combination with the ultimate goal of improved results of the final outcome of GBR and GTR procedures.

Aim

The aim was to analyse the impact of PRF as an adjuvant on bone quantity and quality in socket preservation.

Materials and Methods

A 50-year-old male patient came to our clinic with pain, hyperemia and mild swelling on the left side of the lower jaw. Clinical examination revealed the presence of pain, local hyperemia and mild swelling in the area of tooth 36, which was tender to palpation and painful on vertical percussion. An ortho-pantomography was performed revealing an irreparable chronic periapical lesion (Figure 1). Extraction of the tooth was indicated with further socket preservation and subsequent implant-prosthetic rehabilitation. After the acute local infection subsided, oral surgical extraction and socket preservation with sticky bone as a xenograft mix (BioOss, Geistlich) in combination with A-PRF+ was carried out (Figure 2).

The A-PRF+ protocol involved venipuncture from the cubital vein into 2 specially designed 10 ccm A-PRF tubes, centrifuged in a centrifuge (BIOBASE) at 1300 rpm/8 minutes. The supernatant was collected with a sterile syringe, and 2 PRF membranes were prepared from the PRF coagulum in a PRF box. One membrane was chopped into small pieces and mixed with the xenograft and saturated to the desired consistency with the supernatant as sticky bone. Sticky bone was applied to the post-extraction alveolus, covered with the other PRF membrane, and a stabilizing X-suture was placed (Figure 3 and Figure 4).

After 4 months, implantation with an Ankylos implant was performed. Three months after implantation, the prosthetic super-structure was fabricated (Figure 4). After one year follow-up, clinically was detected a perfect condition of periimplant and peri-prosthetic soft tissues. Retroalveolar radiography was performed with significant bone condensation around the implant surface (Figure 5).

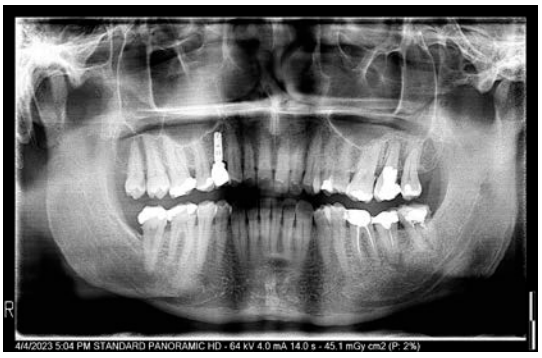

Figure 1. Orthopantomography

Figure 2. Sticky bone preparation

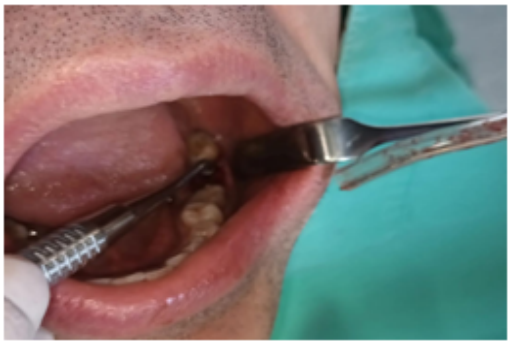

Figure 3. Application of sticky bone

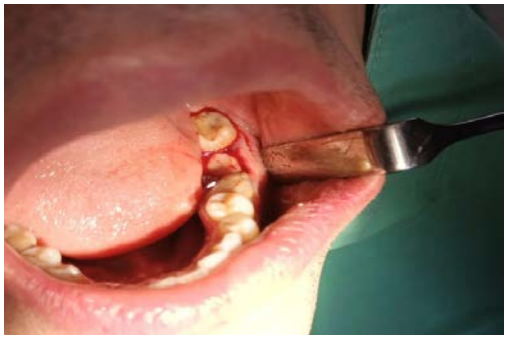

Figure 4. Covering with PRF membrane

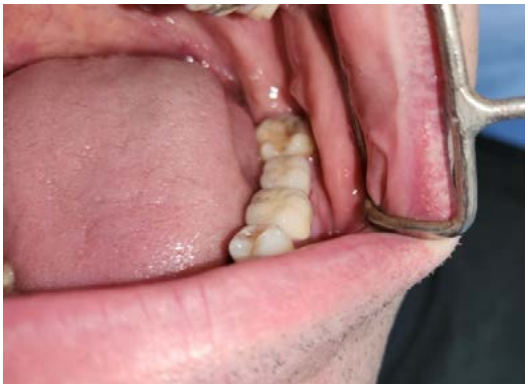

Figure 4. Superstructure over dental implant

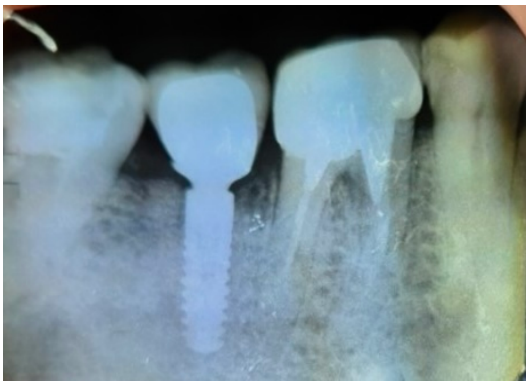

Figure 5. Retroalveolar roentgenography

Results

Immediately after the intervention, the clinical width of the residual alveolar ridge was evaluated. The measurement was performed with a bone measurement caliper in a vestibulo-oral direction. To evaluate the height of the residential alveolar ridge, a graduated periodontal probe was used to measure the distance from the cement-enamel limit of the adjacent tooth to two points: one on the buccodistal side and the other on the oral distal side, up to the top of the interdental septum. The mean distance between these two points was calculated. In addition, the height of the interdental papilla was measured and noted with a periodontal probe, from the cemento-enamel limit of the adjacent tooth to the highest point of the interdental papilla. The same clinical parameters were measured 4 months postoperatively (Table 1).

During preparation of the implant site, a bone biopsy was taken with a 2 mm trephine burr and sent for histomorphometric analysis (Figures 6 and 7). The following results were obtained:

- residual xenograft was not identified
- 70% of newly formed bone
- 20% woven bone
- 10% connective tissue
- 2–3 giant cells
- 5–6 osteoblasts
- 2 osteoclasts

Four months post-operatively, the quality of the newly formed bone was evaluated with the help of CBCT, 3D imagination technique, Owandy I-MAX 2/3D, and software support Quickvision 2/3D (Owandy radiology, Croissy-Beaubourg France) by notifying bone density expressed in Hounsfield units (Figures 8 and 9, Table 2).

Table 1. Clinical parameters of the measurements performed

	Immediate postoperative	4 months postoperative
Horizontal dimension	14 mm	13 mm
Vertical dimension	3 mm	3 mm
Papilla height	1 mm	1 mm

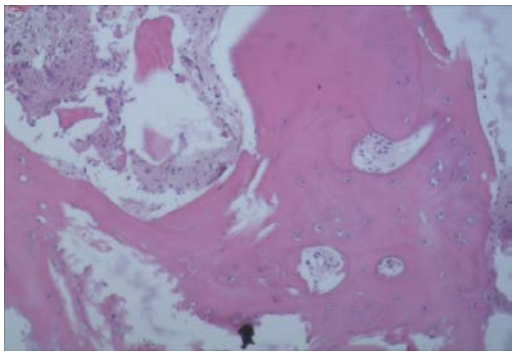

Figure 6. Histomorphometric analyses

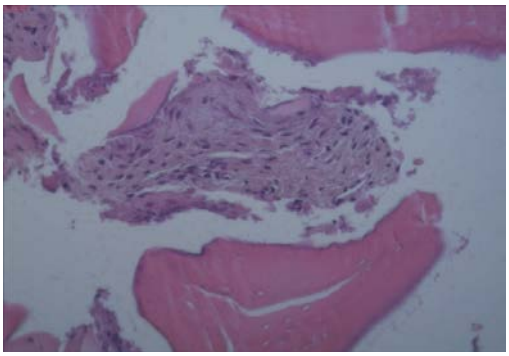

Figure 7. Histomorphometric analyses

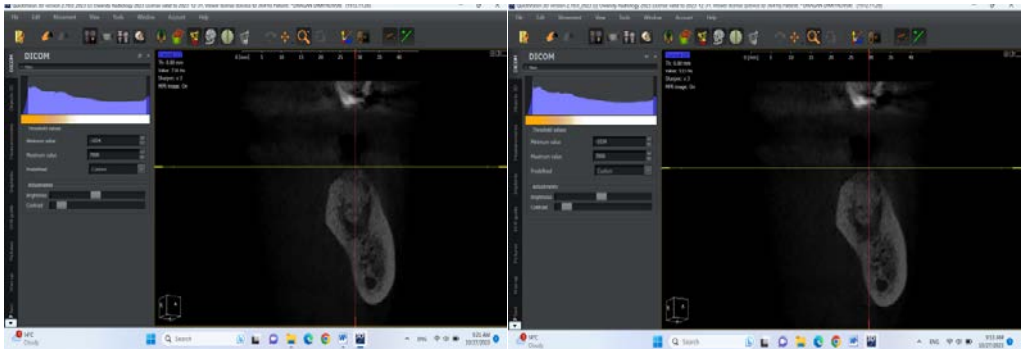

Figure 8. CBCT bone density-socket ***Figure*** 9. CBCT bone density- periapical

Table 2. Evaluation of the density of the newly formed bone

	CBCT 4 months postoperative
Post-extraction alveola	716 HU
Periapical region	533 HU

Discussion

Platelet-enriched fibrin, through its histomorphological characteristics, i.e., its three- and tetramolecular structure, in which 97% of platelets and more than 50% of leukocytes are captured and concentrated, plays a major role in the process of healing of the post-extraction wound, both in hard and soft tissues[15].

Growth factors released by platelet degranulation, from their dense α-granules, play a key role in neocollagenesis and neosteogenesis through their impact on fibroblast and osteoblast activity[16]. The presence of plasma proteins, growth factors, and cytokines in PRF plays a key role in the processes of hemostasis, angiogenesis, and epithelialization, thereby significantly affecting the healing processes of the post-extraction wound, thus finding application in oral and maxillofacial surgery[17].

In their study, Dohan et al.[18] describe PRF acting like a lymph node, which is able to stimulate defense mechanisms. It is even likely that the significant inflammatory regulation noted on surgical sites treated with PRF is the outcome of retro control effects from cytokines trapped in the fibrin network and released during the remodeling of this initial matrix. Cytokines play a significant role in the delicate balance of tissue homeostasis[18].

From the clinical measurements obtained, the improved effectiveness of the particulate graft in combination with PRF is notable, as in improving its properties in terms of preserving the volume of post-extraction alveoli, and smaller bone resorption in a horizontal and vertical direction.

The density of newly formed bone in 52 subjects with preserved post-extraction alveoli with different graft materials (DBBM, HA, collagen membrane, and non-grafted) four months postoperatively was evaluated using CBCT in a study by Cavdar et al. 2017. It concluded that the highest value of newly formed bone density was in the HA group, but that this was due to the presence of residual graft material that compromised the true value expressed in HU[19].

In an animal clinical study by Araujo and Lindhe[20] in 2011, a clinical and histomorphometric comparative analysis of preserved post-extraction alveoli with autograft and Bio-Oss was performed in experimental dogs. The analysis took place three months postoperatively, with bone biopsies being collected to evaluate the composition of the newly formed bone. The results indicated that the alveoli preserved with autograft (bone chips) showed a composition of 57.2 ± 8.6% mineralized bone, 38.3 ± 10.9% bone marrow and 1.9 ± 1.9% non-vital autograft particles. In contrast, the grafted alveoli treated with Bio-Oss exibited composition of 43.1% ± 10% mineralized bone, 16 ± 7.6% bone marrow, and 24.4 ± 3.7% residual xenograft. The xenograft material was surrounded by connective tissue and giant cells indicating a foreign body reaction that played a role in the resorption of residual graft particles. From a clinical perspective, the results show increased bone resorption of the alveoli augmented with autograft compared to those augmented with Bio-Oss[20].

In 2009, Nevins et al. examined the efficacy of PDGF-BB on Bio-Oss Collagen, and bone biopsies were taken after 4 and 6 months, with a large amount of new bone formation observed after four months (23.2 ± 3.2% new bone and 9.5 ± 9.1% residual graft material), and after six months (18.2 ± 2.1% new bone and 17.1 ± 7.0% residual graft) on histological analysis[21].

In 2021, a study conducted by Jose Ponte et al. used histomorphometric analysis to compare three different graft materials. The first examined group received only PRF, the second group used sticky bone, and the third group utilized a particulate graft covered with a collagen membrane. The results showed a significant difference in effectiveness with PRF achieving a success rate of (68.83%). In contrast, the sticky bone group had a success rate of 35.69%, while the group using the particulate graft and collagen membrane recorded only 16.28%)[22].

In 2016, Ahmed Halim Ayoub and Soulafa Mohamed Belal in a case report of a patient with an indication for the extraction of an irreparable root of tooth[23], and the need for further implant-prosthetic treatment, described socket preservation with sticky bone by using a combination of particulate allograft and PRF. Clinical and radiological examinations were performed after the intervention itself and a control CBCT before the implant therapeutic procedure. Results were obtained for minimized horizontal and vertical bone loss, as well as high-quality newly formed bone[23].

Large number of prognostic factors has been identified, which may be related to the success of GBR, like patient-related factors, level of hygiene, level of dental plaque, smoking habits etc[24].

Conclusion

The combination of A-PRF with a particular xenograft has superior properties in terms of the quality of the newly formed bone.

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CASE REPORT
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HORIZONTALNI PRELOM KORENA ZUBA: STUDIJA TROGODIŠNJEG PERIODA PRAĆENJA

HORIZONTAL FRACTURE OF THE TOOTH ROOT: 3-YEAR FOLLOW UP STUDY

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Sažetak

Uvod: *Traumatske povrede zuba predstavljaju značajan uzrok hitnih stomatoloških intervencija, jer pored samih zuba često zahvataju i okolna potporna tkiva, uključujući gingivu, alveolarnu kost i periodontalni ligament. Ove povrede mogu varirati od jednostavnih fraktura do kompleksnih oštećenja, a nastaju usled različitih uzroka, kao što su saobraćajne nesreće, sportske povrede, padovi ili fizički udarci. Horizontalne frakture korena najčešće se lokalizuju u srednjoj trećini korena, dok su frakture u koronarnoj i apikalnoj trećini znatno ređe. Dijagnoza se postavlja kliničkim pregledom i radiografski, a izbor terapije zavisi od položaja frakture, stepena zahvaćenosti korena, tačne dijagnoze, adekvatnog kliničkog pristupa i redovnog praćenja.*
Prikaz slučaja: *Predstavlja lečenje horizontalne frakture korena maksilarnog desnog centralnog sekutića uz primenu mineral trioksid agregata (MTA) i trogodišnjeg kliničkog i radiografskog praćenja.*
Zaključak: *Stalni zub sa frakturom korena može imati povoljnu prognozu, uz očuvanje estetskog izgleda i psihološkog integriteta pacijenta. Ključno je naglasiti značaj kontinuiranog kliničkog i radiografskog praćenja radi obezbeđivanja dugoročnog uspeha terapije, naročito kod zuba sa horizontalnim frakturama korena.*

Ključne reči: *trauma, horizontalna fraktura korena, MTA*

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Abstract

Introduction: *Traumatic dental injuries are a significant cause of emergency dental visits, impacting not only the teeth but also the surrounding supporting tissues, such as the gums, jawbone, and ligaments. These injuries can range from simple fractures to complex damage, and they can be caused by various factors, including accidents, sports injuries, falls, or physical trauma. Horizontal root fractures are most frequently located in the middle third of the root, with much less frequent occurrences in the coronal and apical thirds. Root fractures are diagnosed through clinical and radiographic examinations. Treatment depends on the position of the fracture, the extent of root involvement, correct diagnosis, clinical management, and radiographic follow-up.*
Case report *presents the treatment of a maxillary right central incisor with a horizontal root fracture, using MTA, along with a follow-up period of 3 years.*
Conclusion: *A permanent tooth with a root fracture that is endodontically treated may present a good prognosis, preserving the esthetic and psychological integrity of the patient. It is crucial to emphasize that continuous clinical and radiographic follow-up is necessary for ensuring the long-term success of the treatment, particularly for teeth with horizontal root fractures.*

Key words: *trauma, horizontal root fracture, MTA*

Introduction

Horizontal root fractures are relatively rare compared to other types of dental injuries, with an incidence of 0.5–7% in permanent teeth that have been injured[1]. Maxillary central incisors are most commonly affected by traumatic injuries, accounting for approximately 68% of cases, likely due to their position in the dental arch. The next most commonly affected teeth are the maxillary lateral incisors (27%), followed by mandibular incisors (5%)[2].

Root fractures are more commonly observed in male patients, possibly due to the higher incidence of trauma associated with activities such as automobile accidents, sports injuries, and physical altercations. These fractures are often seen in permanent, fully erupted teeth that have completed apex formation. The increased occurrence of root fractures in these teeth may be attributed to the support provided by the surrounding bone and periodontium.

Initial management typically involves repositioning and stabilizing the coronal fragment in its correct alignment, followed by ongoing monitoring to assess pulp health. Healing is successfully observed in approximately 83% of cases[3]. The management of horizontal root fractures depends on the location of the fracture, as well as the mobility and vitality of the tooth. Fractures located in the apical third of the root typically show no mobility and often do not require treatment. In contrast, fractures in the cervical third frequently necessitate extraction. If the coronal fragment is severely mobile, extraction may be the only viable treatment option. Root fractures in the middle third generally have a more favorable prognosis. When the coronal fragment is displaced, the first step in treatment is usually repositioning the fragments, followed by stabilization to allow the surrounding periodontal tissues to heal. However, in 5–25% of cases, horizontal root fractures may necessitate endodontic therapy if the pulp of the coronal segment shows signs of pathology, such as necrosis[4]. Andreasen et al. in their study found that necrosis of pulp after horizontal root fracture occurs in nearly 25% of cases[2,5].

Endodontic intervention is required for nonhealing fractures. Anderson and Hjorting Hanser[5] described four types of healing sequelae: 1) Healing with calcified tissue - there is close contact between fragments but the fracture line can be seen radiographically; 2) Healing with interproximal connective soft tissue - when viewed radiographically, the separation between the fragments is seen as narrow radiolucent line and the fractures edges appear narrow; 3) Healing with interproximal bone and connective tissue - the separation between fractured fragment as seen radiographically is through distinct bony bridge; and 4) Interproximal inflammatory tissue without healing - fracture line seems to widen when viewed radiographically[6].

Case report

A 21-year-old male patient presented to the Department of Pediatric and Preventive Dentistry at the University Dental Clinic “St. Pantelejmon”, Skopje, after experiencing trauma to the upper front region. Clinical examination revealed that the crown of the tooth was mobile. A complicated crown fracture of the right maxillary central incisor was observed, classified as grade II mobile according to Miller's classification of tooth mobility (Figure 1). Radiographic examination showed a horizontal root fracture in the middle third of the right maxillary central incisor, with no radiographic pathologies detected in the fracture line or the periapical area (Figure 2). Initial treatment involved repositioning, applying firm finger pressure to the coronal segments. An orthodontic stainless steel arch was then fitted, using rigid fixation with a 0.5 mm orthodontic wire sealed with a photopolymeric resin after careful assessment of lateral canine to lateral canine occlusal contacts (Figure 3). Anti-inflammatory drugs and antibiotics were prescribed for seven days. The treatment plan was explained to the patient, and his consent was obtained.

Root canal treatment was initiated in the maxillary right central incisor. Access opening was done using a round bur and a safe-end bur. Following pulp extirpation, working length was determined correctly using an electronic apex locator and radiograph. Working length was determined to the apex of the apical fragment (Figure 4). Both the coronal and apical fragments were cleaned and shaped. The canal was irrigated thoroughly using 3% sodium hypochlorite and 0.9% normal saline for the removal of remaining pulp tissue and debris. The calcium hydroxide paste was then placed as an intracanal medicament and a temporary pack with Cavit (3M™ Cavit™). On the second visit, after three weeks, the

temporary dressing was removed and the canal was irrigated using saline and 3% sodium hypochlorite and dried with paper points. The root canal was filled with mineral trioxide aggregate (MTA - BIO MTA®, (PPH CERKAMED Wojciech Pawlowski 37-450 Stalowa Wola, Poland) and it was obturated with gutta-percha using lateral condensation technique and restored with composite resin (Tetric Evo Ceram Bulk Fill, Ivoclar Vivadent, Schaan, Liechtenstein) (Figure 5). Immediate post-operative periapical radiographs were taken. Despite this therapeutic solution, correct oral hygiene was maintained thanks to professional hygiene and strong motivation of the patient. Moreover, the absence of the fracture line with the oral environment prevented any bacterial penetration. The splint was removed after 4 weeks. After the splint was removed, the mobility of the right maxillary incisor was within normal limits, and the patient reported no discomfort with his teeth and no pain during horizontal and vertical percussion tests. No sign of pathology was visible on the radiograms. Periodic clinical and radiographic follow-up evaluations were performed at 1, 3, 6, 12 months and after 3 years of the injury.

At 1, 3, 6 and 12-month recall, the clinical examination revealed no mobility or discomfort during percussion of the maxillary right central incisor. On radiographic examination, no pathological changes. After three years, there were no clinical symptoms, and the intraoral periapical radiograph revealed healing with interproximal bone and connective tissue, radiologically characterized by the clear separation of the two fragments (Figure 6).

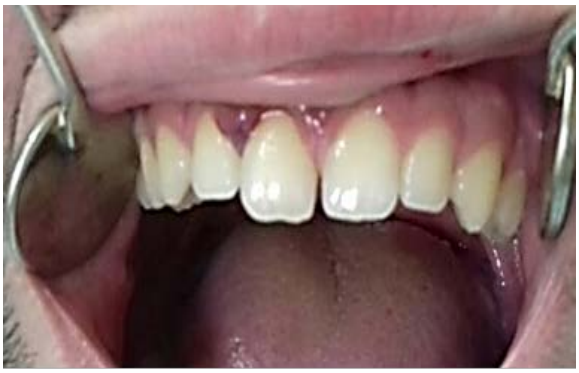

Figure 1. Preoperative intraoral view

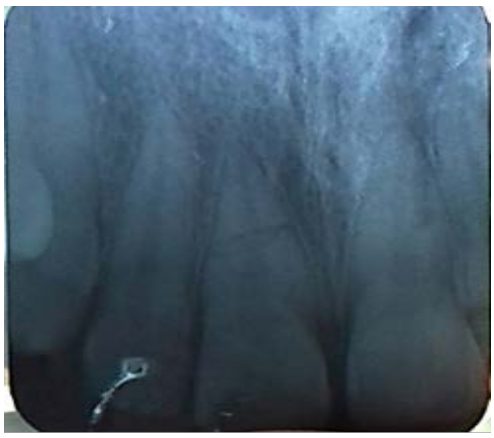

Figure 2. Preoperative radiographic view showing HRF at the junction of the middle and apical third of the tooth[11]

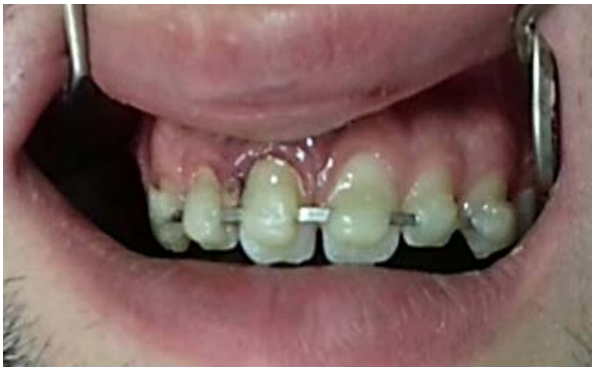

Figure 3. Stabilization with a composite wire splint

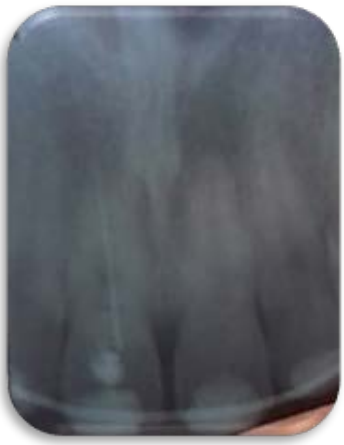

Figure 4. Working length measurement of teeth[11]

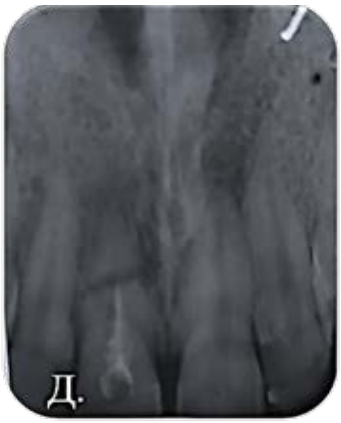

Figure 5. Post-obturation radiograph with MTA

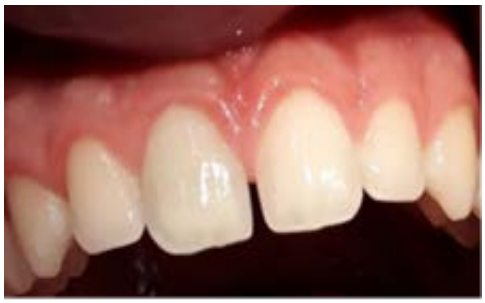

Figure 6. 3-year follow-up

Discussion

Preserving natural dentition and restoring its normal function is one of the goals of dentistry. Extraction of the tooth and its replacement with an osseointegrated implant should always be considered the last treatment option when all other means of retaining the natural tooth have been tried[7].

Root fractures typically result from an impact force applied to the crown of the tooth. Frontal forces cause compression to the labial and lingual/palatal sides of the root, splitting it into coronal and apical segments. This injury can damage the surrounding periodontal tissues, potentially causing displacement of the root fragments[8]. Accurate diagnosis of root fractures requires both thorough clinical and radiographic assessments. The clinician should assess the mobility of the coronal fragment and check the vitality of the pulp. Radiographs usually show a radiolucent line separating the coronal and apical fragments[9,10]. Ideally, two or three radiographs taken at different angles may be necessary to accurately assess the angle of the fracture.

Most root fractures occur in the middle third of the root, followed by fractures in the apical and coronal thirds. In permanent teeth with closed apices, mid-root fractures are most common, as the fully developed root is well-supported by the periodontal tissues. The healing process following such fractures depends largely on two conditions: whether the pulp is severed and whether bacteria invade the fracture site. If the pulp remains intact after trauma, a dentin callus typically forms between the fractured fragments, followed by cementum deposition on the peripheral edges of the fracture. This healing process can take several years. However, if the pulp is ruptured, revascularization of the coronal portion is required, which may occur through two potential mechanisms: either cell invasion from the apical pulp or cells from the periodontal ligament, leading to the union of the fragments via interposed connective tissue[11]. Root fractured teeth often possess a vital apical fragment[12,13];hence it was decided to perform the endodontic treatment of the coronal fragment leaving the apical fragment as such.

This report presents a case of a horizontal root fracture in the middle third of the root, and endodontic treatment using MTA. The 3-year follow-up shows the closure of the space between the fractured segments. This could be due to connective tissue formation, where PDL cells are the dominant contributors. Re-modelling via resorption at the edges of the fracture line is a common phenomenon, creating rounded corners. Cementum formation may have also occurred, which grows into the space, reuniting the two fragments to some extent. Regular follow-ups are necessary to ensure the success of the treatment[14,15].

Maintaining the position of fractured teeth in the dental arch is the main objective of treating such teeth. In recent times, there has been tremendous improvement in bonding agents and restorative resins, and also various new bioceramic materials used for endodontic fillings. Advantages of bioceramic materials include better biological properties, easier manipulation, radiopacity, dimensional stability, acceptable mechanical properties, and overall clinical performance. Bioceramic materials used in endodontics are calcium silicate-based materials[16].

One of the desirable properties of these materials, including the MTA, is the ability to form interfacial calcium-phosphate deposits between the materials and dentinal wall or bone, possibly resulting in direct and adherent bonding with hard tissues[17]. This property provides clinicians with various treatment options for managing fractured roots. MTA is a highly recommended material for teeth that have necrotic pulp and an open apex. Various studies have compared the apical closure using calcium hydroxide and MTA. Additionally, it has been observed that the success rate, as seen clinically and radiographically, is higher with MTA in terms of fracture resistance, hard tissue formation and inflammation. Therefore, MTA was selected for this case as it might improve treatment outcome[18]. When we consider the prognosis of permanent teeth with root fracture, this is related to the amount of dislocation, stage of root development at the time of injury and to some extent, it also depends upon whether the treatment was done.

MTA is the most biocompatible endodontic cement material, capable of promoting tissue regeneration[13]. Recently, MTA was used for root fracture repair. The use of MTA in intra-alveolar root fractures was described in some case reports. Eraden et al.[19] and Kusgoz et al.[20] reported the repair of horizontal root fracture sealing with MTA. During a follow-up period of 1 to 3 years, all teeth showed excellent clinical and radiographic healing. Yildirin and Gencoglu observed that the area of the MTA and fracture line was fully surrounded by new hard tissue formation. Healing with the interposition of connective tissue was found in the 10-year follow-up radiographic, although MTA was extruded between the fragments[21]. Kim et al. initially identified 22 teeth in 21 patients who

had horizontal intra-alveolar root fractures and who had received endodontic treatments with MTA. Seventeen teeth exhibited healing of the root fracture, and 2 teeth showed interposition of granulation tissue[22]. Furthermore, Taschieri et al. reported that 10 incomplete vertical root fracture repair surgical procedures were performed[23]. At 12-months follow-up, all cases remained successful. Hadrossek et al. also reported reimplantation with MTA repair VRFs teeth could be kept in situ after 2 years[24]. Those data show MTA was recommended to repair VRFs by preparing a groove along the entire vertical fracture, placing MTA in the groove, and covering it with a resolving membrane.

Treating such fractures can be challenging, particularly when dealing with an open apex at the fracture site. Mineral trioxide aggregate (MTA), a biocompatible material, has demonstrated excellent sealing properties, making it an ideal choice for managing cases with open apices[25].

Conclusion

Maintaining the position of fractured teeth in the dental arch is the main objective of treating such teeth. A permanent tooth with a root fracture that is endodontically treated may present a good prognosis, preserving the esthetic and psychological integrity of the patient. However, it is crucial to emphasize that continuous clinical and radiographic follow-up is necessary for ensuring the long-term success of the treatment, particularly for teeth with horizontal root fractures. These monitoring efforts are essential to detect any potential complications early and to verify that the tooth remains functional and stable over time. From this report, it is concluded that in dental trauma of teeth with root fracture, different healing processes occur in teeth in close proximity to each other; and that the long-term follow-up is recommended, so that any necessary procedures may be performed to maintain the teeth in the oral cavity.

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Conflict of Interest: Nil

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PRIKAZ SLUČAJA
CASE REPPORT
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ZBRINJAVANJE IZOLOVANOG PRELOMA ZIGOMATIČNOG LUKA KINOVIM PRISTUPOM: PRIKAZ SLUČAJA

MANAGEMENT OF ISOLATED ZYGOMATIC ARCH FRACTURE USING KEEN'S APPROACH: A CASE REPORT

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Sažetak

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Uvod: *Frakture zigomatične kosti spadaju među najčešće prelome u predelu srednjeg dela lica. Izolovane frakture zigomatičnog luka čine oko 10% svih fraktura zigomatične kosti.*
Materijal i metode: *U ovom radu prikazan je slučaj izolovane frakture zigomatičnog luka koja je tretirana primenom Keen-ovog pristupa.*
Rezultati: *Submentoverteksna radiografija pokazala je uspešnu repoziciju koštanih fragmenata u njihov anatomski položaj.*
Zaključak: *Keen-ov pristup predstavlja pouzdanu metodu u lečenju izolovanih fraktura zigomatičnog luka, jer omogućava adekvatnu repoziciju bez stvaranja vidljivih ožiljaka, čime se postiže i zadovoljavajući estetski rezultat.*

Ključne reči: *izolovana fraktura zigomatičnog luka, Keen-ov pristup, estetska procedura*

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Abstract

Introduction: *Zygomatic bone fractures are more prevalent among other associated midface fractures. Isolated fractures of the zygomatic arch comprise 10% of all zygomatic bone fractures.*
Matherials and methods: *This report presents a case of isolated zygomatic arch fracture which was treated through Keen's approach.*
Results: *The submentovertex radiograph revealed a successful reduction of the fractured fragments into its anatomical position.*
Conclusion: *Keen's approach is comparatively reliable method in the management of isolated zygomatic arch fracture without any scarring.*

Key words: *isolated zygomatic arch fracture, Keen's approach, cosmetic procedure*

Introduction

The zygomatic bone is formed by the lateral surface of the midface, inferior and the lateral orbital rims and the malar prominence, which constitutes its bony projection and facial width[1]. Zygomatic arch fractures comprise 10−15% of all facial fractures, and trauma being the most common etiological factor[1,2]. Patients with isolated zygomatic arch fractures present with a restriction in the mouth opening and painful lateral excursion of the mandible. Clinically, presents as a depression over the zygomatic arch. Management of isolated zygomatic arch fracture includes Gilles' temporal approach, Keen's vestibular approach, hooks elevation technique, intranasal transantral approach, sigmoid notch technique and modified lateral coronoid technique[3]. The present case report describes a fracture of an isolated zygomatic arch, which was surgically operated through Keen's approach under general anesthesia.

Case Presentation

A 25-year-old female reported to the Department of Oral Surgery with a complaint of pain and inability to close her mouth. The event history revealed that she had a fall from the bike 2 hours before the time of presentation. On inspection, abrasions on the right side of the face, arms and legs were elicited. Depression over the right zygomatic arch was evident, which signifies a zygomatic arch fracture. On palpation, tenderness was elicited over the right malar region and zygomatic arch. Submentovertex revealed a medially displaced fracture of the zygomatic arch (Figure 1).

According to Knight and North 1961, the present case was classified as group II arch fracture. Based on the clinical and radiographic interpretation, the present case was diagnosed as a right isolated zygomatic arch fracture, which was surgically planned for open reduction through Keen's approach. The authors certify that they have obtained written informed patient consent for images (the images enclosed in the current case report refers to authors: Dr. Balamurugan Rajendran and Dr. Karthik Kattur Premkumar) and other clinical information to be reported/published in the journal with an understanding that names and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

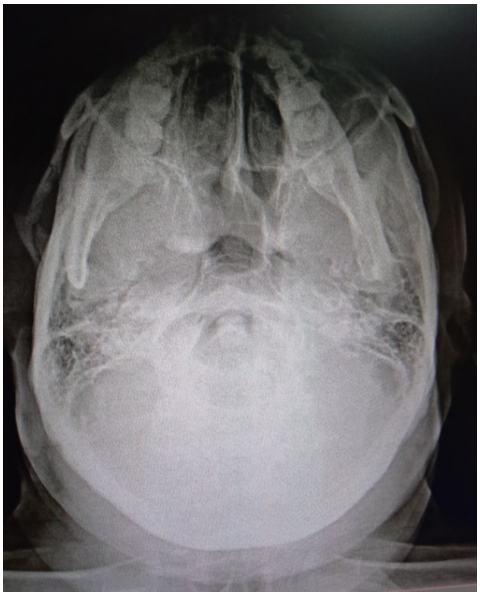

***Figure 1*:** Submentovertex radiograph showing isolated fracture of the zygomatic arch on the right side

Surgical procedure

General anesthesia was administered through nasal endotracheal intubation. Standard painting and draping were done to ensure a sterile surgical procedure. Markings were placed for Keen's approach. A surgical incision measuring 1cm in length was placed in the right upper buccal sulcus behind the zygomatic buttress. Further dissection was carried out to contact the infratemporal surface of the zygomatic bone (Figure 2). The elevator was then inserted in position, and gentle force was applied to reduce the medially displaced zygomatic arch. Once the fracture was reduced, a click sound was heard, which indicates that the fracture segments are snapped back to its anatomical position. The reduction of the fracture was confirmed by palpating over the zygomatic arch. The surgical site was irrigated with povidone iodine and approximated with 4-0 Vicryl sutures.

Postoperative outcome

The postoperative outcome was uneventful. The patient was subjected to a submentovertex radiograph, which revealed successful approximation of the fracture fragments in their anatomical position without any discontinuity in the zygomatic arch (Figure 3).

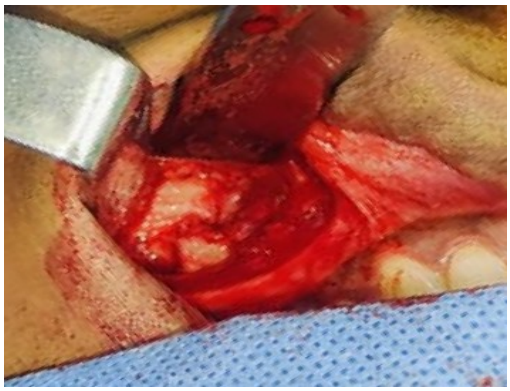

Figure 2. Maxillary vestibular incision was initiated, and further dissection was performed to contact the infratemporal surface of the zygomatic bone

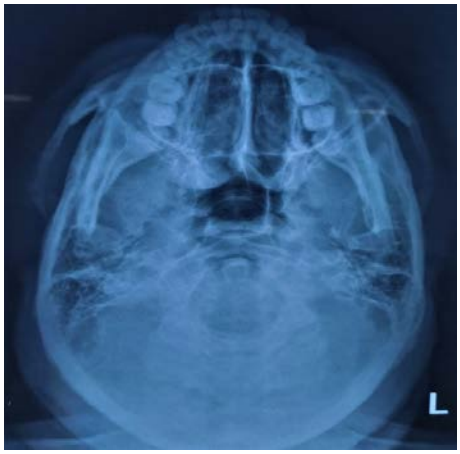

Figure 3. Submentovertex radiograph showing adequate reduction of the fracture segments in its anatomical position on the right side

Discussion

Zygomatic arch is often injured with trauma as the structure of the bone is long and thin, projecting outwards from the facial bones. Zygomatic arch fracture may be a single component when it is associated with other fractures of the midface. Isolated zygomatic arch fractures cause both cosmetic and functional disturbances when not intervened at the early stages[4]. In the present case, the authors have advocated the use of Keen's approach in the reduction of zygomatic arch fracture and postoperatively, a successful reduction was

achieved with good cosmetic results. The Gillies temporal approach is the most commonly employed method in combination with Keen's approach in the management of zygomatic arch fractures. The chances of damage to the middle temporal veins and the risk of hemorrhage may be a predominant drawback associated with the Gilles temporal approach[5].

Numerous alternative surgical treatment options for zygomatic arch fractures have been discussed in the English literature[1-3,6,10]. Bezuhly M et al.[6] performed Gillies' temporal approach combined with percutaneous fixation using Kirschner wire in the management of isolated zygomatic arch fracture. The author emphasized that although this technique restored the facial contour, there were certain disadvantages, including malar asymmetry and decreased sensation of the infraorbital nerve. However, Cohn JE et al.[1] claimed to have improvement in the zygomatic deformity, trismus and paresthesia of the infraorbital nerve with the use of the above technique.

Sorghabi W et al.[2] described a new technique in the management of zygomatic arch fracture using a percutaneous approach under local anesthesia. This technique was performed by placing a stab incision parallel to the skin tension line. Curved hemostatic forceps were then inserted through subcutaneous tissue and masseter muscle, reaching the deepest point of the fracture site. A curved dental elevator was then placed inside the pocket below the level of the fracture and meticulously reduced by pulling the elevator in a lateral motion. Further, the instrument was oriented along the entire length of the zygomatic arch to ensure adequate reduction and proper positioning of the fracture segments in its anatomical site. This technique offered a maximum mouth opening of 40 mm with no facial asymmetry. However, a visible scar was encountered at the incised site post-surgery.

Hayashi K et al.[3] utilized a modified towel clip method to reduce the zygomatic arch fracture and found that the authors have achieved an adequate reduction of the zygomatic arch with the favorable mouth opening of about 45 mm without any visible postoperative scars. The modified towel clip method is simple and minimally invasive technique, however, the events of encountering the associated nerves and blood vessels must be considered while performing such method of operation. Inclusion of C-Arm helps in acquiring adequate reduction of the zygomatic arch fracture intraoperatively. This method is of prime importance because C-Arm aids in better visualization and immediate monitoring of the reduced fracture, thereby eliminating the need for postoperative radiographs and imaging modalities[7,8].

Endoscopic guided reduction of arch fractures provides excellent visibility of the operating site, but the insertion of endoscopically assisted tools either through intraoral or extraoral approach may result in numerous postoperative complications such as damage to the neurovascular structures, infections and scar formation[3,9]. Krishnan B et al.[10] used dental forceps as an armamentarium in reducing the fracture of the zygomatic arch through Keen's approach. The author states that the use of dental forceps has brought a successful reduction of the fracture. However, a long delay during the reduction may lead to partial consolidation of the fracture fragments, causing difficulty in reducing the fracture through the intraoral method.

The employment of Keen's approach for the management of zygomatic arch fractures offers various advantages:

1. Keen's approach is advocated intraorally; hence, the use of extraoral intervention is eliminated.
2. The maxillary buccal sulcus incision is relatively simple and technically easier.
3. Intraoperatively, the technique involves minimal dissection and controlled bleeding.
4. The amount of force required to reduce the fracture is less and requires simple closure of the mucosa.
5. Highly cosmetic, as the scar line is not visible and lies within the maxillary vestibule.

Conclusion

The present case report illustrates the importance of Keen's approach in the surgical management of isolated zygomatic arch fracture. The Keen's approach using a maxillary vestibular incision is found to be a superior technique in providing adequate accessibility with definitive reduction and good cosmetic support.

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Conflict of Interest: Nil

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PREOPERATIVNA PRIPREMA PACIJENATA SA PRIMARNOM IMUNSKOM TROMBOCITOPENIJOM ZA IZVOĐENJE ORALNOHIRURŠKIH ZAHVATA

PREPARATION OF PATIENTS WITH PRIMARY IMMUNE THROMBOCYTOPENIA FOR ORAL SURGICAL INTERVENTIONS

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Sažetak

Uvod: *Primarna imunološka trombocitopenija (ITP) predstavlja stečeno autoimuno oboljenje koje se karakteriše izolovanim smanjenjem broja trombocita ispod 100×10⁹/L, bez prisustva drugih uzroka trombocitopenije. Smanjenje broja trombocita kod pacijenata sa ITP posledica je istovremenog ubrzanog razaranja trombocita i poremećene njihove produkcije. Dijagnoza se postavlja isključivanjem drugih mogućih uzroka trombocitopenije. Kod odraslih pacijenata najčešće se javlja hronični oblik bolesti, koji se karakteriše periodima remisije i relapsa.*
Cilj *ovog rada bio je da se istaknu principi oralno-hirurškog lečenja pacijenata obolelih od primarne imunološke trombocitopenije.*
Materijal i metode: *Analizirana je dostupna literatura kako bi se identifikovale osnovne karakteristike ITP-a, sa posebnim osvrtom na specifičnosti i principe stomatološkog i oralno-hirurškog tretmana ovih pacijenata.*
Zaključak: *Ne postoje jasno definisane smernice za pripremu pacijenata sa ITP-om za hirurške intervencije. Preporučuju se individualan terapijski protokoli koji uključuju primenu visokih doza kortikosteroida, imunoglobulina, kao i odgovarajuće postoperativne antikoagulantne mere. U poslednje vreme sve veću primenu nalaze i agonisti receptora za trombopoetin, sa ohrabrujućim terapijskim rezultatima. Primena svih sistemskih i lokalnih terapijskih mera pre, tokom i nakon oralno-hirurškog zahvata je od ključnog značaja. Takođe, bliska saradnja između oralnog hirurga i hematologa smatra se imperativom za uspešan ishod terapije.*

Ključne reči: *primarna imunološka trombocitopenija, lečenje, oralno-hirurške procedure*

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Abstract

Introduction: *Primary immune thrombocytopenia (ITP) is an acquired autoimmune disorder characterised by an isolated decrease in the platelet count below 100×10, in the absence of other identifiable causes of thrombocytopenia. The decrease in platelet numbers in patients with ITP results from both accelerated platelet destruction and impaired platelet production. The diagnosis is established by excluding other causes of thrombocytopenia. In adult patients, the chronic form is most often encountered, characterised by periods of remission and relapse of the disease.*
Aim: *This informative paperwork aims to highlight the principles of oral surgical treatment of patients with ITP.*
Material and Methods: *The available literature was analysed to identify the basic characteristics of ITP, with special reference to its specificity and principles of dental and oral surgical treatment of patients with ITP.*
Conclusion: *There are no guidelines for preparing patients for surgical interventions. Personalised therapeutic protocols with high doses of corticosteroids, immunoglobulins, along with postoperative anticoagulant protocols, are recommended. In recent years, thrombopoietin receptor agonists have also been increasingly used with success. The application of all therapeutic measures, both systemic and local, is necessary before, during, and after the oral surgical procedure. Numerous new medications enable the appropriate preparation of ITP patients for oral surgical interventions. In addition, close collaboration between oral surgeons and haematologists is considered imperative.*

Key words: *primary immune thrombocytopenia, treatment, oral surgical procedures*

Introduction

Primary immune thrombocytopenia (ITP) is an acquired autoimmune disorder characterised by an isolated decrease in the platelet count below 100×10^9, in the absence of other identifiable causes of thrombocytopenia. The incidence is approximately 2–10 cases per 100,000 adults annually[1]. ITP is more common in women of reproductive age, although its peak incidence occurs in individuals over 60 years old, affecting both sexes equally.

While the exact aetiology remains unknown, as with all autoimmune diseases, recent advances have clarified aspects of the disease pathogenesis. The decrease in platelet numbers in patients with ITP results from both accelerated platelet destruction and impaired platelet production. The key event is the loss of immune tolerance to platelet autoantigens, which triggers the consequent activation of T and B cells[2].

The primary mechanism in the pathogenesis of ITP involves autoantibody-mediated platelet destruction. Platelets marked with anti-glycoprotein autoantigens are destroyed by tissue macrophages by Fc-gamma receptor activation[3]. Additionally, these autoantibodies contribute to platelet clearance through complement-dependent cytotoxicity and the induction of apoptosis[4,5]. Thrombopoiesis is reduced or normal in most patients with ITP, and the absolute count of immature platelets is often decreased[6].

Given that there are no reliable diagnostic tests to diagnose ITP with certainty, the diagnosis is made by excluding other causes of thrombocytopenia. After taking an anamnesis and an objective examination of the patient, a complete blood count and a peripheral blood smear are performed. Additional tests include the determination of the number of reticulocytes and the levels of immunoglobulin, as well as serological tests for hepatitis B and C, HIV, and Helicobacter pylori. Bone marrow examination, tests for antinuclear and antiphospholipid antibodies are often required to rule out secondary thrombocytopenia.

Regarding the duration of the disease, ITP can be:

- Newly diagnosed—lasting up to 3 months from the time of diagnosis,
- Persistent—lasting 3–12 months from the time of diagnosis,
- Chronic—lasting longer than 12 months.

In adult patients, the chronic form is mostly encountered, which is characterised by remissions and relapses of the disease.

The clinical picture typically begins gradually, with the appearance of spontaneous bleeding on the skin and mucous membrane in the form of petechiae, ecchymosis, hematoma, frequent episodes of epistaxis and menorrhagia. Bleeding into the central nervous system is the most severe complication, although it is rare, occurring only in 1.5–1.8% of adult patients with ITP[7]. Risk factors that increase the likelihood of bleeding include advanced age, reduced platelet count, comorbidities, and the use of anticoagulant or antiplatelet medications[8].

Therapeutic Possibilities in the Treatment of ITP

The main goal of treating patients with ITP is to prevent the occurrence of bleeding, as well as to maintain the platelet number at a safe level. The latest guidelines recommend that treatment be initiated when the platelet count is 30x10 or less, and/or when the haemorrhagic syndrome is present[9]. First-line therapy consists of corticosteroids (Methylprednisolone 1mg/kg of body weight divided into 2–3 daily doses for up to a month, after which the dose is reduced, or Dexamethasone 40 mg for 4 days up to 3 cycles). Initially, therapeutic response is achieved in about 60–80% of patients, and after discontinuing therapy, 20–40% of patients maintain a favourable therapeutic response[10]. The drawback of corticosteroids is their limited use at high doses and numerous side effects (psychological disorders, elevated blood glucose levels, infections). Intravenous immunoglobulins (IVIg) are also used in the initial therapy. They can significantly raise the platelet count in more than 80% of newly diagnosed ITP patients. Disadvantages include a relatively high price and a short-term effect of 2–3 weeks[11]. They are used in severe forms of the haemorrhagic syndrome, at doses of 1g/kg body weight for 1–2 days or 0.4g/kg body weight for 5 days with a similar effect[12].

In recent years, the combination of Rituximab and high doses of Dexasone has been tested, but with no improvement in therapeutic response[13]. Therefore, it is still not recommended in the initial therapy of newly diagnosed patients.

Although there is a high percentage of therapeutic response to initial therapy in newly diagnosed patients, the vast majority will experience a relapse, and 60–70% will progress to persistent or chronic ITP[14]. Therapy for these patients includes the use of thrombopoietin receptor agonists (TPO-RAs), Rituximab and Fostamatinib, and splenectomy.

Thrombopoietin receptor agonists have dramatically changed the modality of ITP therapy, given that they have shown that therapy is possible without the use of immuno-suppressants. These include Eltrombopag, Romiplostim and Avatrombopag, and the first two are approved in Serbia. The overall therapeutic response in previously treated patients with chronic ITP is 70% to 90%, and 50–60% of these patients can maintain the response with prolonged treatment[15]. It is important to note that there are no serious side effects.

Rituximab reduces the production of antiplatelet antibodies. The initial therapeutic response is achieved in 60–70% of patients, and long-term in about 21%[16,17]. However, long-term treatment with Rituximab can lead to severe side effects.

Fostamatinib achieved the initial response in 43% of patients, and maintenance therapy achieved a prolonged response in 44% of patients[18]. The most common side effects include diarrhoea, nausea, hypertension, and mild or moderate transaminase elevation in up to 30% of patients.

Even though splenectomy is less frequently used today, it gives the possibility of achieving long-term remissions in 60–70% of patients[19]. In patients who have not achieved remission, the disease has a milder course and therapy is more effective[20]. Extensive diagnostic and therapeutic preparation, complications both during and after the intervention, as well as the availability of new medications, are the main reasons why splenectomy is now less commonly performed.

Many immunosuppressive or immuno-modulatory medications are used in the treatment of ITP, such as Azathioprine, Ciclosporin A, Danazol, Mycophenolate mofetil, and Vinca alkaloids. However, due to the appearance of new medications, their use has become increasingly rare[21].

Preparation of ITP patients for oral surgical interventions

The therapeutic approach to preparing patients with ITP for surgical interventions must be individualized. Factors to consider include the patient's age, existing comorbidities, whether the ITP is chronic or not, previous treatments and the patient's response to them.

According to clinical guidelines, patients undergoing surgical procedures should have a platelet count of at least 50,000×10. For minor oral surgical interventions, a minimum of 75,000×10 is recommended, whereas for procedures with a high risk of bleeding, such as major oral surgeries, neurosurgical, or cardiac surgical interventions, a platelet count of at least 100,000×10 is required[22].

There are no guidelines for preparing patients for surgical interventions. Personalised therapeutic protocols with high doses of corticosteroids, immunoglobulins, along with postoperative anticoagulant protocols are recommended[23].

Corticosteroids (mainly Methyl-prednisolone) are administered at a dose of 1–2 mg/kg body weight and are generally efficient. However, a drawback is their tendency to increase blood glucose levels, which can delay wound healing.

Intravenous immunoglobulins are given at a dose of 0.4g/kg body weight for 5 days or 1g/kg body weight for 2 days. In general, they are effective, but platelet counts may begin to decline again just a few days after the treatment[24]. In addition, they are relatively expensive.

The administration of platelet transfusions can be complicated and unreliable, although it is sometimes used with good results[25].

Recently, thrombopoietin receptor agonists have been increasingly used with success. Eltrombopag, in particular, has shown greater effectiveness in achieving adequate platelet counts compared to IVIg (79% and 61%, respectively)[26]. Patients undergoing dental procedures while receiving Eltrombopag therapy did not experience significant bleeding complications[27].

Romiplostim has also proven to be highly effective in preparing these patients for surgical interventions[28]. Thrombopoietin receptor agonists have not shown a significantly increased risk of thrombotic events[29].

Platelet count should be assessed preoperatively, both before and after the administration of concentrated platelets. The use of local haemostatic measures—commonly applied in other bleeding disorders—is strongly recommended.

These include gelatine- or collagen-based products, oxidized regenerated cellulose, and, if necessary, their combination with antifibrinolytics. Depending on the type and complexity of the procedure, haemostatic sutures should be used. For patients with ITP who are currently on corticosteroid therapy or have been within the past two years, it is advisable to increase the corticosteroid dose prior to the surgical intervention

Conclusion

The need for oral surgical interventions in patients with ITP is common. To avoid serious complications in these patients, adequate preoperative preparation is essential. This involves the application of all necessary therapeutic measures, both systemic and local, before, during, and after the oral surgical procedure. Regular postoperative monitoring of the patient is also crucial.

A wide range of new medications now enables appropriate preparation of ITP patients for oral surgical interventions. Furthermore, close collaboration between oral surgeons and haematologists is imperative. Equally important is the implementation of preventive measures aimed at reducing the need for oral surgical procedures.

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SAVREMENA DOSTIGNUĆA U MIKROBIOLOŠKOJ DIJAGNOSTICI TESTOVIMA PRIMENLJIVIM U STOMATOLOŠKOJ STOLICI

RECENT ADVANCES IN MICROBIOLOGICAL DIAGNOSTIC CHAIRSIDE TESTS: AN INFORMATIVE REVIEW

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Sažetak

Uvod: *Napredak u dijagnostičkim procedurama za periodontalne bolesti od suštinskog je značaja za tačno prepoznavanje, praćenje i efikasno planiranje terapije. Razvoj novih dijagnostičkih setova mogao bi unaprediti mogućnost identifikacije aktivnih oboljenja, predviđanja buduće progresije bolesti i procene odgovora na periodontalnu terapiju, čime bi se omogućilo personalizovano i efikasnije lečenje.*
Cilj *ovog rada bio je da se kliničarima pruži pregled koristi koje setovi za dijagnostiku na stolici (chairside kits) donose u svakodnevnoj kliničkoj praksi.*
Materijal i metode: *Informacije korišćene u ovom radu prikupljene su iz relevantnih izvora znanja, internet baza podataka, pretraživača i alata, te analizirane kao osnova za dokumentovano sagledavanje dostupnih dokaza i mogućnosti primene dijagnostičkih setova u parodontologiji.*
Rezultati: *Svaka pretraga treba da započne jasno formulisanim istraživačkim pitanjem. U cilju pronalaženja pouzdanih odgovora, predstavljeni su potencijalni izvori zasnovani na dokazima, poput PubMed/MEDLINE baze podataka, Cochrane Library i Google Scholar pretraživača. Rezultati su pokazali da su setovi za dijagnostiku na stolici efikasni u ranoj detekciji subgingivalne mikrobiote iz uzoraka dentalnog plaka.*
Zaključak: *Ova pregledna analiza obuhvata različite mikrobiološke dijagnostičke setove za primenu na stolici, uključujući i point-of-care sisteme, koji mogu značajno doprineti preciznijoj dijagnostici i planiranju terapije u periodontalnoj praksi.*

Ključne reči: *dijagnoza parodontopatije, mikrobiološki testovi, dijagnostički setovi na stolici, point-of-care testovi*

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Abstract

Introduction: *Advancements in diagnostic procedures for periodontal diseases are crucial for accurate detection, monitoring, and effective treatment planning. Developing novel diagnostic kits could enhance our ability to identify active disorders, predict future disease progression, and evaluate responses to periodontal therapy, leading to more personalized and efficient treatment strategies.*
Aim: *The aim was to provide for clinicians an overview of the benefits of chairside diagnostic kits in day-to-day clinical practice.*
Materials and Methods: *Information sources have been gathered, and discussed as a foundation for a documented vision on knowledge questions, online information sources, search engines, databases, and tools.*
Results: *Every search should start with a carefully phrased question. To help find a reliable answer, potential evidence-based online sources were presented, such as PubMed/MEDLINE, Cochrane Library and Google (Scholar). The results suggested that the chairside diagnostic kits were efficient in the early detection of subgingival microbiota from plaque samples.*
Conclusion: *This comprehensive compilation includes various chairside microbiological diagnostic kits, including point-of-care systems, which could be beneficial for periodontal diagnosis and treatment planning.*

Key words: *periodontal diagnosis, microbiological tests, chairside kits, point of care tests*

Introduction

Indeed, the interaction between pathogenic microbes and the host immune response plays a crucial role in the development of periodontal diseases. Researchers have delved into a holistic understanding of how the host's immune system responds to pathogenic bacteria in the oral cavity. Subsequently, this results in an inflammatory-mediated polymicrobial emergence and dysbiotic exacerbation model[1]. This dual focus on microbial etiology and host response enhances our comprehension of the mechanisms underlying periodontitis.

These revelations prompted a demand for diagnostic methods capable of accurately assessing disease activity in patients, marking a significant evolution in periodontal research and clinical approaches. Certainly, the accuracy of periodontal diagnosis is pivotal, influencing the success of subsequent therapy. To enhance this process and predict disease progression, incorporating newer diagnostic tests, including microbiologic, immunologic, systemic, and genetic factors, alongside traditional clinical and radiographic parameters, is crucial. The development of assays for identifying and assessing periodontal pathogens in patient samples reflects ongoing efforts to refine diagnostic approaches and tailor treatments effectively.

The focus on microbiological chairside kits in this consolidated review is well-founded. These kits offer clinicians valuable and timely information for early disease identification, enabling the formulation of precise treatment plans. This structured approach not only facilitates monitoring during periodontal therapy but also proves beneficial in the maintenance recall phase, enhancing overall patient care and outcomes.

Diagnostic Tests

For a periodontist, a diagnostic test determines whether the disease identified by clinical parameters is active or inactive. There are a few basic terminologies which need to be well defined for a detailed understanding of the topic. The ratio of sites with active disease that are acknowledged as positive by the diagnostic test is known as ‘sensitivity’. The ratio of sites without active disease that are rightly recognized by the diagnostic test is known as ‘specificity’. ‘Predictive value’ is the percentage of time a positive test correctly predicts disease. ‘Negative predictive value’ shows how often a negative test predicts health. There are basically four factual outcomes that can be achieved on comparison of test results of patients diagnosed with or without periodontitis[2,3].

Table 1 shows the variable outcome attained in the presence or absence of periodontal disease.

Chairside Diagnostic Tests

A few of the fundamental characteristics of chairside diagnostic kits have been illustrated in Figure 1.

Periodontal diagnostic procedures provide valuable details to the clinician regarding the nature of the existing periodontal disease, the involved site, and the severity of the disease. Bleeding on probing, probing pocket depth (PPD), clinical attachment loss (CAL), oral hygiene index, and radiographs are traditional landmark clinical measurements used for periodontal diagnosis, which are rather inadequate dimensions since they indicate former periodontal disease status instead of current disease activity. Various diagnostic tests are available for the detection of periodontal pathogens; amongst these, chairside tests offer rapid results compared to traditional laboratory processes[4].

Table 1. Variable outcome attained in presence or absence of periodontal disease

Outcome	Diagnosed with periodontal disease	Absence of periodontal disease
Characteristics of disease present	True positive	False negative
Characteristics of disease absent	False negative	True negative

Figure 1. Chairside diagnoshcs kits

1. ***Microbiological Test Kits***

The diagnosis of various forms of periodontal disease is supported by the microbiological tests that are directed towards the elimination of periodontopathogens. These provide guidelines for disease origination and help in the determination of periodontal sites that are at greater risk for active destruction.

The following are a few of the chairside test kits:

Omnigene[5]

The early 1980s marked an era focussed on microbial etiology as the basis of periodontal disease, and a demand for newer therapeutic methods to supplement conventional periodontal treatment. During this course, market analyst, Dr. Lynn Klotz at BioTechnica International, Inc. (BTl) identified a tool to provide enhanced microbiological information to dental clinicians, which could be used as a guide for diagnosis and treatment strategies for periodontal disease. It has been well documented that the predominant pathogen for periodontitis belongs to the anaerobic species, and its procurement from clinically diseased sites is difficult to cultivate or culture. Hence, a technical assay was explored which did not require viability of the species for the identification and quantification of the clinical samples. Since the understanding of periodontal disease confirmed its slow progressive process with the absence of mortality, an off-site assay kit was tested using recombinant DNA technology, which worked on the principles of genetic engineering. This information is directed towards the alternative of the DNA probe technique as the foundation for the test.

The DNA probe systems identify several known periodontopathogens. However, the development of species-specific DNA probe tests was labelled for eight periodontal pathogens, namely Porphyromonas gingivalis (Pg), Prevotella intermedia (Pi), Aggregatibacter actinomycetemcomitans (Aa), Fusobacterium nucleatum (Fn), Eikenella corrodens (Ec), Campylobacter rectus (Cr), Bacteroides forsythus (Bf) and Treponema denticola (Td).

The advantages stated are fewer efforts on the part of the clinician, wherein subgingival plaque samples can be collected and sent to OmniGene Diagnostics, a licenced clinical laboratory. Once the data is analysed, the information can be quickly transferred to the clinician via emails, phone or fax. Thereafter, it reduces the time required for commencement of appropriate treatment.

Al Yahfoufi Z and Hadchiti W assessed the prevalence and association of three putative periodontal pathogens, Aa, Pg and Pi, in a group of subjects diagnosed with minimal periodontal disease with no history of periodontal treatment. The methodology involved the procurement of subgingival plaque samples on a sterile paper point from the deepest pocket. Further, DNA probes (Omnigene) was utilized for specific identification and quantification of Aa, Pg, and Pi. The results showed 23% of samples presented with positive Aa comitans; 79% of plaque samples had Pg, and 82% of plaque

samples contained Pi. A significant association was observed between the presence of Aa comitans and Pg ($p = 0.016$). The authors concluded that a high frequency of the three periodontal pathogens (Aa, Pg, and Pi) was observed in the plaque samples[6].

Micro Probe Corporation

This company has created an in-office nucleic acid probe assay to semiquantitatively detect periodontal pathogens. Patient plaque samples are treated to lyse bacterial cells through heating with detergent. The extracted DNA is loaded into the initial well of a multiwell cassette, which is then inserted into a machine featuring a programmable robotic arm. The device provides a digital readout of the current bacterial load[7].

Evalusite

A chairside kit employs membrane-bound immunoassay for the detection of three popular and prevalent periodontal pathogens, namely, Aa, Pg and Pi. The identification of bacterial organization in subgingival plaque requires a distinct plan for microbiological sampling due to the large number of potential sample sites within periodontal patients. Approximately 5 minutes are needed to identify and separate the bacteria, following which the results can be visually translated. The plaque sample procured from the patients is prepared by the addition of a detergent, and then the mixture is spread through a filter into a reagent well of the assay test kit. Membrane-bound antibody in the well specific to Aa, Pg, and Pi reacts with the plaque sample. Antigen and antibody complexes formed on the membrane are detected by the addition of an enzyme-labelled second antibody together with a coloured enzyme substrate. Separate dots indicate the presence of 3 different species[8].

Perioscan

Another diagnostic test kit which provides detection of bacterial trypsin-like proteases in the dental plaque by using the BANA hydrolysis reaction. One of the contemporary replacements to bacterial cultures is the microbial-enzymatic BANA (N-benzoyl-DL-arginine-2-naphthylamide) test. This test is extremely susceptible, noticing lesser amounts of pathogens. However, within the subgingival biofilm, it recognizes the presence of three periodontal pathogens, which include Td, Pg and Tf. The peptide analog BANA can be hydrolysed by the peptidases of these three bacterial species. The collection of subgingival plaque specimens should be carried out cautiously using either a gracey curette or a paper point. The specimen should be procured from at least 4 teeth with maximum probing depth. A sterile piece of cotton or any other suitable cleanser is used to wipe the curette to prevent carry-over of plaque before taking another specimen. The contents of the test kit include reagent strips that are plastic cards. Separate reagent-containing matrices are affixed on the plastic cards. B-naphthylamide is implanted in the upper strip of the test and is one of the hydrolytic outcomes of the effect, which reacts with a reagent and creates a permanent blue colour. Two separate reagent matrices are attached to a plastic strip. The lower white reagent matrix is soaked with BANA onto which the subgingival plaque samples are smeared. Then saline solution is used to moisten the upper matrix, and the test is pleated so that the two matrices are impending in contact. It is then incubated for 5 minutes at 55 °Celsius. A chromogenic diazo reagent is present on the upper buff reagent matrix and reacts with one of the hydrolytic outcomes of the enzyme reaction, forming a blue colour. The concentration of bacterial species also propitiates the color[4]. The permanent blue colour appears in the upper buff matrix. The intensity of the colour indicates if the test is positive, negative or a weak reaction.

In 2018, Fenol A et al.[9] conducted a trial to compare and detect the presence of periodontal pathogens in chronic periodontitis patients after nonsurgical periodontal therapy with and without the use of diode laser disinfection using the BANA test. Subgingival plaque specimens were applied onto the test strip using a curette. The change from colourless to blue indicated the presence of periodontal pathogens. The authors observed a reduction of the key pathogens in both groups at the end of 2 weeks. Further, at the end of 2 months, the test group showed a more statistically significant reduction. Hence, the conclusion derived was that BANA-enzymatic kit was a simple chairside kit that could be reliable indicator of BANA positive species in dental plaque.

In another study in 2017, Turton MS et al.[10] tested the hypothesis if BANA diagnostic test for periodontal disease could be used as an indicator of the risk of adverse pregnancy outcomes in mothers attending antenatal clinics. Plaque was collected and wiped onto the BANA impregnated strip.

Significant differences were found between the pregnancy outcomes of BANA-negative and BANA-positive mothers. The sensitivity and negative predictive values were 87% and 91%, respectively. In detecting low birth weight, the sensitivity ranged from 75% to 78%. For identifying preterm delivery and preterm low birth weight delivery, the sensitivity and negative predictive values were 87% and 94%, respectively.The authors concluded that the BANA test signifies the need for periodontal therapy so as to reduce the risk of adverse pregnancy outcomes and could form part of the routine antenatal examination.

My Periopath

MyPerioPath is a point-of-care (POC) device manufactured by Oral DNA Labs for detecting periodontal disease-causing pathogens in saliva samples. This test utilizes the DNA polymerase chain reaction to identify the species and concentration of bacteria in the saliva samples[11].

Iai Pado Test Kit 4.5

The IAI Pado RNA probe test kit (Institut für Angewandte Immunologie, Zuchwil, Switzerland) is useful for the identification of the four widespread periodontal pathogens. This chairside assay test uses an oligonucleotide probe corresponding to sustained remnants of the 16S rRNA gene that encrypts the rRNA, which belongs to the subcategory of bacterial ribosomes. These tests have detection limits which are 103 for Aa and 104 for Pg, Tf and Td. Associated with the checkerboard technique, the identification frequencies attained with this assessment showed a minimal sensitivity of the Pado Test 4.5 technique[12].

In 2017, Pretzl B et al. evaluated the intra-test agreement of pooled samples from the deepest periodontal pocket of each quadrant with a commercially available test kit based on hybridization of 16S rRNA. Subgingival plaque samples collected on two sterile paper points were placed into two separate vials, which were immediately sent for detection by using IAI Pado-Test 4.5. Cohen's κ for detection and counts Tf and Td presented a perfect agreement. Pg showed a substantial agreement, whereas Aa demonstrated a good agreement. Test results of the commercial 16S rRNA test were perfectly reproducible regarding the detection of periodontopathogens[13].

Recent Advancements in Micro-biological Diagnosis

Point-of-Care Test (POCT)

Currently, in periodontal diagnosis, Point of Care Test platforms can be allotted into three groups: Lab-on-Chip (LOC), paper-based platforms, and chairside tests. POCT in periodontitis can help in early detection of the disease, monitoring disease progression, and evaluating the effectiveness of treatment. It can also improve patient outcomes by facilitating timely intervention and personalized treatment planning.

Lab-on-Chip (LOC) Platforms

Chairside Lab-on-a-chip (LOC) technology is poised to play a significant role in detecting biomarkers in saliva, which could enhance global periodontal health efforts. A technique for operating smaller quantities of solutions by contracting and assimilating compound lab actions into a tiny microchip is known as Microfluidic LOC[14]. Currently, immunoassays are the chief method used in the LOC program for diagnosing periodontal disease. Microfluidic LOC techniques have been advanced swiftly and employed extensively in several domains due to their incorporated elements, minute specimens, reagent volume, and quick response. A LOC platform was developed for measuring three salivary biomarkers (MMP-8, IL-1b, and C-reactive protein) to diagnose periodontal disease, utilizing a combination of a microfluidic chip and a fluorescence-based visual method[15].

Impedimetric Antimicrobial Peptide-Based Sensor

This biosensor detects the presence of bacteria using specific peptides. It combines miniaturized and integrated impedimetric transducers with antimicrobial peptides (AMPs) to monitor bacterial colonization with high sensitivity. The biosensor operates within a frequency range of 100 Hz to 1000 kHz with a 100 mV voltage excitation, using the Quadtech 7600 Plus LCR Meter. It is capable of detecting bacteria at concentrations of 101 colony-forming units (CFU) per milliliter in KCl solution and 102 CFU per milliliter in artificial saliva.

The AMPs, when coupled with 3D-IDEA biosensors, demonstrate rapid implementation, label-free detection, and

sensitivity in detecting the periodontitis-associated pathogenic strain S. sanguinis. The AMP-based sensor array can detect a wide spectrum of bacteria and serves as a tool to prevent the initial formation of biofilm, thereby reducing the risk of implant-related infections commonly found in periodontitis patients[16].

Paper-Based Platforms

Paper-based platform is one of the most cost-effective technology with the simple fabrication and is independent from external instruments.

Magnetic-Nanobead-Based Assay

A magnetic-nanobead-based assay, labeled with a gingipain-specific peptide, is utilized for diagnosing infections related to periodontitis caused by P. gingivalis, a common pathogenic bacterium. Gingipains are specific proteases released by the bacteria during inflammatory stages. The sensor is linked with gingipain biomarkers, which are immobilized on a gold biosensing platform through gold-thiol linkage, causing the gold layer's color to change to black. When the immobilized substrates are cleaved by gingipain, the magnet is attracted to the magnetic-nanobeads-peptide fragments, resulting in an observable golden surface color change. This biosensor offers rapid action and higher sensitivity and specificity[17].

Biotechnological advancements have spurred the development of lab-on-a-chip technology and biosensors for analyzing oral biomarkers. These innovations in oral biomarker discovery and validation aim to enhance precision oral medicine by improving diagnosis, prognosis, and patient stratification. Their application has the potential to enhance clinical outcomes for periodontitis and related chronic conditions, benefiting both dental and overall public health[18].

Conclusion

Numerous oral diseases involving carious lesions, endodontic lesions, several types of periodontal diseases, halitosis, and odontogenic infections have well-characterized infectious causes. In the selection of antimicrobial therapy and performing post-treatment periodontal risk assessments for patients with chronic periodontitis, microbiological testing may be predominantly supportive. The accomplishment of every therapy is reliant on the precision of the early analysis. From clinical investigation to further precise, innovative diagnostic procedures, there is a constant evolution in periodontal disease diagnosis. For early diagnosis and treatment, the accessibility of chairside diagnostic test kits will be beneficial. It likewise aids in enhancing patients' amenability for periodontal therapy concerns. Point-of-care testing in periodontitis involves using diagnostic tools or tests to assess the condition directly at the point of patient care, such as in a dental office. These tests are designed to provide quick and accurate information to aid in the diagnosis and management of periodontal disease.

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Abbreviations

Aa—Aggregatibacter actinomycetem-comitans, Pg—Porphyromonas gingivalis, Pi—Prevotella intermedia, Tf—Tannerella forsythus, Td—Treponema denticola, Fn—Fusobacterium nucleatum, Ec—Eikenella corrodens, Fn—Fusobacterium nucleatum, Cr—Campylobacter rectus, Bf—Bacteroides forsythus

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NOVITETI U MATERIJALIMA ZA PREKRIVANJE PULPE

NOVELTIES IN PULP CAPPING MATERIALS

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Sažetak

Uvod: *Terapijski pristupi koji naglašavaju očuvanje pulpe od suštinskog su značaja za održavanje vitalnosti zuba sa izloženom pulpom i dubokim kavitacijama. Iako se indirektne i direktne metode prekrivanja pulpe koriste već više od jednog veka, ove vitalne terapije pulpe (VPT) ne predstavljaju novinu. Vitalnost zubne pulpe značajno utiče na dugovečnost stalnih zuba. Budući da je dokazano da inflamirana pulpa ima sposobnost regeneracije, terapija vitalne pulpe u poslednjim godinama privlači sve veću pažnju. Koncept izložene pulpe, nekada smatran beznadežnim stanjem, doživeo je značajnu transformaciju – od percepcije „osuđenosti" ka mogućnosti izlečenja. Ova promena shvatanja potpomognuta je razvojem savremenih materijala za prekrivanje pulpe, čime je označen početak nove ere u terapiji očuvanja vitalne pulpe.*
Cilj: *Cilj ovog rada bio je da pruži pregled i diskusiju o savremenim materijalima koji se koriste za prekrivanje pulpe i zaštitu kompleksa dentin–pulpa.*
Zaključak: *Kada se patološke promene pulpe tačno dijagnostikuju, očuvanje zuba moguće je primenom adekvatne terapije i odgovarajućih dentalnih materijala. Efikasnost prekrivanja pulpe i vitalne terapije pulpe zavisi od stručnosti kliničara, pravilnog izbora materijala i adekvatne selekcije slučajeva. Napredak u očuvanju vitalnosti pulpe donosi značajne koristi i pacijentima i stomatolozima zahvaljujući boljem razumevanju bioloških procesa karijesa, tehnološkim inovacijama i savremenim restaurativnim materijalima.*

Ključne reči: *biokompatibilnost, dentinski most, prekrivanje pulpe, materijal za prekrivanje pulpe*

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Abstract

Introduction: *Therapeutic approaches that emphasize preserving pulp are essential for maintaining vital teeth with exposed pulp and deep cavities. However, indirect and direct pulp capping methods reportedly have been used for more than a century, so these vital pulp therapies (VPTs) are not new. The vitality of the dental pulp greatly influences the longevity of permanent teeth. Since it has been demonstrated that the inflamed pulp can heal, vital pulp therapy, or VPT, has received a lot of interest in recent years. The concept of an exposed pulp organ, once considered a dire situation, has undergone a remarkable transformation. It has transitioned from being perceived as 'doomed' to one of hope and healing. This shift in perception has been facilitated by the development of various pulp capping materials, marking a new era in vital pulp treatment.*
Aim: *This paper aimed to provide an overview and discussion of the various, more recent pulp capping materials utilized to protect the dentin-pulp complex.*
Conclusion: *When pulpal pathosis is accurately diagnosed, teeth can be preserved with appropriate treatment using suitable dental materials. Effective pulp capping and vital pulp therapy rely on the clinician's ability, material selection, and proper case selection. The advancement of pulp preservation has proven beneficial for patients and clinicians due to an increased understanding of technological developments, the biology of dental caries, and better restorative materials.*

Key words: *biocompatible, dentin bridge, pulp capping, pulp capping agent*

Introduction

The main challenge of today's restorative dentistry methodology is the induction of remineralization in hypomineralized carious dentine, hence protecting and preserving the vital pulp. Historically, pulp exposure and subsequent root canal therapy were common outcomes of deep caries management. It has been recommended to promote biologically-based treatment techniques for partial caries removal in order to prevent exposure to carious pulp. Complete or nonselective carious removal is currently regarded as overtreatment, according to recent consensus studies[1]. When it comes to managing the cariously exposed pulp, management approaches are also changing by preventing procedures like pulpectomy and instead emphasize the benefits of vital pulp therapy (VPT) methods, including pulp capping and partial and complete pulpotomy[2].

Pulp preservation methods and vital pulp treatment (VPT) are experiencing somewhat of a resurgence. As gold was applied to injured pulp as early as the 18th century, VPT is not a novel treatment approach; rather, it is an old one that incorporates a variety of methods with an emphasis on minimal intervention and preserving pulp tissue health[3,4].

Rebel claimed in 1922 that the "exposed pulp was a doomed organ," an idea that people still hold today. Even though pulp was deemed "doomed" in 1922, systematic, rigorous research on pulp healing and the reaction to direct pulp capping was not conducted until the 1940s and 1950s. This research not only highlighted the unpredictable nature of the results of direct pulp capping but also made significant contributions to understanding how the pulp reacts to the injury and subsequent repair[4,5]. These findings may have contributed to the scepticism around VPT as a substitute for more established treatments, like root canal therapy (RCT), in which success rates were reported at the time to be between 60% and 70% for direct pulp capping and 80% to 90% for RCT[5].

In the past, calcium hydroxide (CH) was the preferred material used as a GOLD standard for DPC[6]. When CH is first applied to exposed pulp, superficial necrosis develops as a result[7]. When there is firm necrosis, the pulp is prompted to protect and repair itself. Cellular differentiation, extracellular matrix secretion, and mineralization finally result in the production of a reparative dentin bridge. This irritates the pulp slightly. Tunnel defects were detected in 89% of the dentin bridge built below CH[8]. These tunnel defects in the heterogeneous dentin barrier not only fail to form a suitable and long-lasting barrier against pathogenic microorganisms, but they also fail to establish an efficient long-term seal. One of the limitations of CH is dissolution[9]. These days, newer materials that produce more consistent clinical results—calcium silicate materials, or CSMs—are replacing calcium hydroxide.

The introduction of bioactive hydraulic calcium silicate cements (HCSCs)[10,11], advances in our biological understanding of pulp reparative processes[12], and scientific and biological advancements in wound lavage and tissue handling[2,13] have all significantly altered our perspectives and revitalized the VPT field.

It's interesting to note that the term VPT was formerly only used to refer to direct pulp capping. However, the latest definitions of the term have simplified and expanded its meaning to encompass all "strategies aimed at maintaining the vitality of the pulp"[14]. This naturally includes direct pulp capping, pulpotomy procedures, one- and two-step selective caries removal techniques, and indirect pulp capping to prevent pulp exposure.

The ideal characteristics of the pulp capping material should include:

- Reparative dentin formation
- Maintaining the vitality of the tooth
- Release fluoride
- Bactericidal or bacteriostatic
- Adhere to dentin and restorative material
- Resist forces during restoration placement and its life in the oral cavity
- Sterile and radiopaque
- Provide a seal against bacteria[15]

Mineral Trioxide Aggregate

In the 1990s, MTA was first described in the literature as an experimental substance based on calcium silicate[16]. According to Tanomaru et al., MTA is a material that is commonly used to seal pulpal cavities and external root surface communications. MTA has the ability to keep pulp viable and has been shown to cause mineralization in exposed pulp.

MTA can be used in many other clinical applications, such as direct[17] and indirect pulp capping, root perforation repairs or in furcations[18], and apexification treatment It has been used recently as a preferable replacement

for Ca(OH)2. MTA is made up of bismuth oxide, a radiopacifier, and Portland cement, which is mostly made up of tri- and dicalcium silicate[19].

ProRoot MTA has been on the market for 20 years, during which time it has undergone thorough testing and been shown to be biocompatible. To address these issues, new MTA-based material types have been developed in response to the lengthy setting time and high cost. In addition to meeting the benefits of ProRoot MTA, the substitute materials need to be easier to get, less costly, and able to set faster. Alternatively, MTA Angelus was created, which has the benefit of having a final setting time that is lowered from 228–261 minutes specific for ProRoot MTA to 24–83 minutes[20]. Retro MTA is one of the recently introduced fast-setting calcium silicate cements that takes approximately 12 minutes to set completely[20]. The predominant calcium ion released from the material combines with phosphates in tissue fluid to generate hydroxyapatite, which is the basis for the biocompatibility and sealing ability of MTA[21].

MTA was first formulated in a gray color, but a distinct chemical structure was introduced in response to reports of tooth discolouration[22]. White MTA lacks the chemical component of iron, but discolouration is still noticeable and is one of the material's key drawbacks[23]. When calcium silicate and dicalcium silicate are combined with water, they react to form calcium hydroxide and calcium silicate hydrate. Despite MTA cement's many beneficial effects, there were certain drawbacks that kept clinicians from utilizing it regularly. The main drawbacks are that the powder contains heavy metals, has a long setting time (up to 284 min)[24], is difficult to handle, and discolours the remaining tooth structure[25].

Confirmatory evidence for MTA's higher efficacy as a DPC agent was found when it was compared with Ca(OH)2 in a randomized clinical trial[26].

Furthermore, MTA is less irritating to the pulp than Ca(OH)2, less toxic, and easier to use during pulp capping methods[27]. A histological investigation verified that the administration of MTA directly impacts the dental pulp's capacity for regeneration and is related to a rise in TGF-β1 production from pulp cells[28]. This component influences the quality of the induced hard barrier by directing the progenitor cells' migration to the material–pulp contact and stimulating their dif-ferentiation into odontoblastic cells secreting reparative dentin.

Therefore, it can be said that normal dentine did not regenerate. Additionally, pulp-capping material (RetroMTA) has limited bioactive potential, indicating that it cannot be used in regenerative dentistry. Furthermore, mineral trioxide aggregate (White-ProRoot®MTA, Dentsply Sirona, York, PA, USA) promotes the same desired cellular response. It exhibits positive metabolic activity in contrast to calcium hydroxide, leading to a decreased incidence of tunnel defects and a higher clinical success rate[29]. When compared to the Biodentine group, the MTA group exhibits a more regular, homogenous reparative dentin layer with consistent thickness in terms of dentin bridge creation, as determined by the micro-CT imaging technique.

For direct pulp capping, MTA is the preferred material[29]. The ability of the bioactive materials to seal the tooth structure, the bond strength between the pulp capping material, and restorative qualities are further essential components for successful pulp capping treatments.

Novel Mineral Trioxide Aggregate Restorative Cements

New generation MTA-based cements, such as Neo MTA Plus (Avalon Biomed Inc., Houston, TX, USA) and the iRoot (Innovative BioCeramix Inc., Vancouver, BC, Canada) product family, have recently been developed as a result of alterations in material features.

Because bismuth oxide is eliminated, Neo MTA Plus was created to be used in pulpotomies without the possibility of discolouration. Tantalum oxide, which has a radiopacity value of 3.76 ± 0.13 mm Al and has no effect on hydration, was utilized in place of the radiopacifying agent[30].

Neo MTA Plus was shown to have a final setting time that was up to 315 ± 5 minute[30]. Additionally, NeoMTA Plus showed greater apatite formation, higher crystallinity, and higher Ca/P in comparison to MTA Angelus. However, it also displayed a lower CO3/PO4 ratio, which may have led to increased bioactivity. Additional *in vivo* and *in vitro* research is needed to support such claims.

Resin-based MTA

TheraCal LC

A few modified resin-based MTAs were developed in order to address the original MTA's drawbacks. Most of these MTAs are designed to reduce the setting time via modifying the particle size or composition of the powder[31].

TheraCal LC is a substance based on calcium silicate resin that can be used in conjunction with restorative materials as a protective liner and as a pulp capping agent. This substance is classified as a fourth-generation calcium silicate material and is a light-curable MTA-cement.

According to Gandolfi et al., TheraCal LC has shown its ability to release calcium ions, which is essential for the material's ability to stimulate human dental pulp cells to proliferate and differentiate, as well as for the formation of new mineralized hard tissues[32]. The concentration of calcium ions generated by TheraCal LC fell within the range that can stimulate the dental pulp and odontoblasts.

TheraCal LC's clinical success rate in comparison to other materials over a shorter time span has been studied[33]. Over six months, the effects of TheraCal LC, Biodentine, and MTA on carious pulp exposure in ninety permanent important teeth were assessed. TheraCal, Biodentine, and MTA did not show a statistically significant difference in overall success rate when compared to one another. As a result, using TheraCal LC as a DPC material was advised.

Super MTA Paste

Super MTA Paste,a resin-based MTA material, has recently been introduced. Portland cement is combined with tributylborane (TBB) as a polymerization initiator in Super MTA Paste, a resin-modified MTA that doesn't need light curing.

In addition to its great biocompatibility, Super MTA Paste may promote the formation of a homogeneous dentin bridge by acting as a pulp capping material. TheraCal LC's therapeutic efficacy is comparable to that of Super MTA Paste's tissue reactivity in exposed pulp.

To substantiate its efficacy in both short- and long-term therapeutic outcomes, clinical trials are required.

Biodentine

A newly developed material by Septodont is called Biodentine (BD; Septodont, Saint-Maur-des-Fosses, France). It is a Portland cement made of calcium silicate. BD comes in capsule form and is made up of powder that includes calcium carbonate, iron oxide, zirconium oxide, tricalcium silicate, and dicalcium silicate.

The manufacturer claims that the setting should take nine to twelve minutes; however, it took forty-five minutes to set completely. One of the material's disadvantages is that, even with zirconium oxide present, radiopacity is much lower than MTA Angelus[34]. Additionally, radiopacity generally diminishes over time, making long-term radiographic examinations challenging.

By stimulating tertiary dentin formation and remineralization, BD's interactions with hard and soft tissues in both the direct and indirect capping procedures result in marginal sealing and protect the underlying pulp. Tricalcium silicate materials such as BD, may be better for IPC based on the release of hydroxide (OH^-) and calcium (Ca^{2+}) ions from the material. It's a biocompatible and bioactive substance.

Improvements in BD properties, such as mechanical properties, initial cohesiveness, and setting time, compared to MTA, have led to a wider variety of uses, such as endodontic repair and vital pulp therapy. It has been demonstrated that Biodentine is readily tolerated by the pulp tissue when it is in proximity (in situations of direct pulp capping), producing reparative dentine. Biodentine has a beneficial effect on vital pulp cells and promotes tertiary dentine formation[35].

Nowicka et al. found that placing MTA required more time and technically more difficulty than placing Biodentine in a study evaluating the pulpal response to various pulp capping materials (MTA and Biodentine). Additionally, they found that Biodentine exhibited similar efficacy in clinical settings, suggesting its potential as an alternative to MTA.

According to a recent study, which assessed the effectiveness of Biodentine in fifteen cases with follow-up periods ranging from 12 to 24 months, all 15 cases showed no symptoms during the follow-up period. This suggests that Biodentine should be used as a vital pulp therapy material[36].

Mtya1-ca

Calcium hydroxide-containing resinous direct pulp capping agent was created by Atsuko Niinuma. The mixture of liquid (67.5% triethyleneglycol dimethacrylate, 30.0% glyceryl methacrylate, 1.0% o-methacryloyl tyrosine amide, 1.0% dimethylaminoethylmethacrylate, and 0.5% camphorquinone) and powder (89.0% microfiller, 10.0% calcium hydroxide, and 1.0% benzoyl peroxide) was combined.

MTYA1-Ca was shown to have good physical properties, dentine bridge formation without the development of a necrotic layer and was histopathologically comparable to Dycal. Niinuma et al. believe that MTYA1-Ca, a recently produced material, has the potential to be used as an effective direct pulp capping material[37].

BioAggregate

When compared to MTA, BioAggregate, a bioinductive tricalcium cement, can induce mineralization with greater efficacy. The main components of this material include tantalum oxide, which is used as a radiopacifier, tricalcium silicate, dicalcium silicate, monobasic calcium phosphate, and amorphous silicon dioxide[38].

According to Kim et al., BioAggregate exhibits improved sealing performance and biocompatibility compared to MTA[38]. BioAggregate is significantly more effective than MTA at stimulating odontoblastic development and mineralization in pulp capping[39].

Tantalum oxide makes up the majority of BioAggregate's composition, with the absence of aluminium and a little amount of bismuth oxide and calcium phosphate[40]. Its lack of aluminum in its chemical composition may account for its less harmful effects on the inflammatory cell response[38].

According to recent research, the MTA greatly outperformed the BioAggregate in terms of thicker hard tissue formation. However, a thick and uniform hard tissue barrier formation was also seen in the BioAggregate group[38].

Castor Oil Bean Cement

The COB is believed to be a naturally occurring polyol made up of 81–96% triglyceride of ricinoleic acid and three hydroxyl radicals. RCP (Ricinus Communis Polyurethane) or COB was first developed biomaterial to regenerate and heal bone in the event of a localized bone injury. These benefits make the material a great option for pulp capping[41].

Emdogain (EMD)

An enamel matrix derivative called EMD is released from Hertwig's epithelial root sheath during the formation of porcine teeth. It is an essential regulator of enamel mineralization and plays a significant role in the development of periodontal tissue. EMD contains both BMP-expressing cells and BMP-like substances. EMD stimulates the growth of odontoblasts and the production of reparative dentin, just like BMP molecules do.

Recent research has revealed that EMD, which has components resembling TGF-β, inhibits immune cells' production of inflammatory cytokines.

Nakamura Y et al. reported that teeth treated with EMD produced more than twice as much hard tissue as teeth treated with calcium hydroxide. Al-Hezaimi K evaluated ProRoot White MTA, calcium hydroxide, and white Portland cement following the application of EMD to the exposed pulp. The quality of the reparative hard tissue response was higher when EMD was used in addition to MTA than when calcium hydroxide was used alone[42].

Calcium Aluminate-Based Materials (EndoBinder)

A novel calcium aluminate-based endodontic cement called EndoBinder (Binderware, So Carlos, SP, Brazil) was developed to maintain the beneficial properties and therapeutic applications of MTA while eliminating its drawbacks.

In contrast to MTA, EndoBinder lacks ferric oxide, which causes tooth discolouration, and magnesium and calcium oxides, which contribute to the material's undesirable expansion.

Due to reduced release of calcium hydroxide, EndoBinder demonstrated superior osteoblastic differential as compared to MTA, which is another characteristic that makes it a good bioactive material[43]. Based on the research data that is currently available, it could be a valuable addition to VPT operations. However, physicians may be hesitant to utilize it due to a lack of studies elucidating and substantiating its biological and physiochemical characteristics.

Calcium Enriched Mixture

Calcium-enriched mixture (CEM) cement was introduced as an endodontic filling material in dentistry. In contrast to Portland cement (PC) and mineral trioxide aggregate (MTA), the composition of cement powder is calcium oxide (CaO), sulfur trioxide (SO3), phosphorous pentoxide (P2O5), and silicon dioxide (SiO2)[44,45].

Three-dimensional seal, appropriate antibacterial characteristics, and biocompatibility are important for the effectiveness of VPT[46]. Comparable to MTA[44], CEM's sealing ability is enhanced by storing in phosphate-buffered saline solution[47]. According to Soheilipour et al., CEM has smaller particles than MTA; this could be the reason for its better sealing qualities[48]. It can stimulate the creation of hydroxyapatite in saline solution[45]. It may also stimulate the differentiation process in stem cells and cause cementogenesis, the induction of hard tissue[49].

CEM's antibacterial properties are comparable to those of CH[44]. According to a comparison of CEM and MTA's antifungal qualities on *Candida albicans*, they both cause the fungal cells to die completely after 24 hours[50].

The alkaline pH of ~11 of CEM is essential for this biomaterial's antibacterial characteristics. According to a number of animal studies[44], the induction of dentin bridge formation in CEM under various VPT treatments was superior to that in CH and comparable with that of MTA. Full pulpotomy treatment studies employing CEM, MTA, and CH have demonstrated that samples in the CEM group showed superior pulp vitality status, better quality/thickness of calcified bridge, and morphology of odontoblast cells in comparison to CH. Nonetheless, Tabarsi et al. found no significant differences when compared to MTA[51].

In comparison to the white/gray MTA groups, the CEM group had considerably lower levels of inflammation after 60 days. Partirokh et al. reported that the biomaterials' ability to induce osteogenesis was indicated by the dystrophic calcification[52].

Pre-Mixed Bioceramics

The iRoot products address the challenges faced during MTA handling and come in a variety of consistencies, which may provide the benefit of choosing the appropriate one for each clinical application. The novel premixed bioceramics are composed of "calcium silicates, zirconium oxide, tantalum oxide, calcium phosphate monobasic, and fillers".

Their mechanical and biological qualities are superior to other materials. Their outstanding handling properties make them ready-to-use materials. Because premixed bioceramics are hydrophilic, they require moisture from the surrounding tissues to solidify. These are categorized according to consistency

1. Syringe form
2. Putty form
3. Fast-set putty form.

There are three premixed bioceramics currently available to date:

• iRoot BP (Innovative Bioceramics, Vancouver, Canada)

• EndoSequence root repair (Brasseler USA, Savannah, GA)

• TotalFill (FKG Dentaire SA, Switzerland)

iRoot BP is a recently discovered calcium silicate-based bioactive ceramic that mainly consists of tri-calcium silicate, bi-calcium silicate, and calcium phosphate[53]. The use of iRoot BP Plus and Ca(OH)2 as pulpotomy materials in cases of complex crown fractures in permanent incisors and found that most dentin bridges with iRoot BP Plus had no tunnel defects and were able to produce reparative dentin within 6 weeks[54].

No inflammation or multinucleated giant cells were observed surrounding the material in the histological analysis. Results after three months revealed more than 75% of the bridge formation showing irregular tubules[53].

Microcomputed tomography study of tertiary dentin revealed that iRoot BP had no defects, while some ProRoot MTA samples exhibited small defects and a lack of continuity[55]. iRoot BP Plus can be used as a pulp capping material in vital pulp therapy as it has been shown to have good biocompatibility and can induce the formation of a reparative dentine bridge[56].

Another novel material developed for pulp capping is Endosequence Root Repair Material (ERRM; Brasseler USA, Savannah, GA). This bio-ceramic material has a high pH, is hydrophilic, radiopaque, and has no aluminium. According to Silva et al., the investigations revealed that ERRM had an identical antibacterial effect on *Enterococcus faecalis* as MTA[57]. Hirschman WR et al. tested four pulp capping materials for cytotoxicity on adult human skin fibroblasts. They concluded that, in terms of cell viability, ERRM outperformed MTA, Dycal, and Ultra-blend

Plus (a calcium hydroxide liner based on resin). When compared to CH, the antibacterial characteristics of endo sequence root repair material against the primary cariogenic bacteria, salivary *Streptococcus mutans* (SM) and *Lactobacilli*, were comparable to those of MTA[58]. The authors concluded that ERRM was a good substitute for other pulp capping materials. According to Damas et al., it contains calcium silicates, zirconium oxide, tantalum oxide, thickening agents, and proprietary fillers[59]. The cytotoxicity of Brasseler Endosequence Root Repair Putty (ERRP), Ultra-blend Plus (UBP)-(light curable Ca(OH)), Dycal, and MTA-Angelus was assessed by Hirschman et al. They discovered that ERRP and UBP have lower cytotoxicity.

Conclusion

Recent advancements in pulp capping materials have significantly enhanced the predictability and success rates of vital pulp therapy. Innovations such as bioactive materials, including calcium silicate-based cements, have demonstrated superior biocompatibility, promoting dental pulp healing and regeneration. Additionally, the development of modern resin-based materials and improved adhesion properties has facilitated better sealing capabilities, reducing the risk of contamination. Understanding the biology of caries, conviction about better restorative materials, and having clarity about technological advancements have led to the initiation of pulp preservation, which is beneficial to both the patient and the physician. When pulpal pathosis is accurately diagnosed, teeth can be preserved with appropriate treatment using suitable dental materials. Effective pulp capping and vital pulp therapy rely on the clinician's ability, material selection, and proper case selection.

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VARIATION IN THE COLOR OF THE LABIAL SURFACE OF THE UPPER CENTRAL INCISORS (Vol. 40, No. 90, p. 2884−2890, 2024)

Editorial Board of the journal Acta Stomatologica Naissi

Abstract

This erratum is issued because there was an oversight and the Acknowledgement was not inserted into the paper. First author, Nenad Stošić, noticed this mistake. Mistake most likely occured during the editing process. We are very grateful to him that he noticed this mistake and we are very sorry that this happened.

In the article *Variation in the Color Of The Labial Surface of the Upper Central Incisors* authored by: Nenad Stošić, Jelena Popović, Aleksandar Mitić, Antonije Stanković, Marija Nikolić, Radomir Barac, Kosta Todorović published in Volume 40, issue 2 (december), pages 2884−2890, Acknowledgement has been left out, and should be added.

The acknowledgement should be as stated:

Acknowledgement

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VARIJACIJA U BOJI LABIJALNE POVRŠINE GORNJIH CENTRALNIH SEKUTIĆA (Vol. 40, br. 90, str. 2884−2890, 2024)

Uređivački odbor časopisa Acta Stomatologica Naissi

Apstrakt

Izdajemo ovaj erratum zbog greške koja je nastala u procesu tehničkog uređivanja časopisa. Naime, greškom je izostao deo "Acknowledgement" iz rada. Grešku je primetio prvi autor rada, Nenad Stošić, na čemu smo mu jako zahvalni i ovom prilikom izražavamo žaljenje zbog propusta.

U radu *Varijacija u boji labijalne površine gornjih centralnih sekutića* autora: Nenada Stošića, Jelene Popović, Aleksandra Mitića, Antonija Stankovića, Marije Nikolić, Radomira Barca, Koste Todorovića objavljenog u časopisu *Acta Stomatologica Naissi*, Volumen 40, broj 2 (decembarski broj), strane 2884−2890, deo "Acknowledgement" je greškom izostavljen. Taj deo treba da glasi:

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Kada se radi o eksperimentima na humanom materijalu ili pacijentima, ukazati da li je primenjeni postupak u skladu sa etičkim standardima odgovornog komiteta za ljudske eksperimente ili sa Deklaracijom iz Helsinkija (1964, amandmani iz 1975 i 1983) Svetske medicinske asocijacije.

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Originalni radovi moraju da sadrže strukturni apstrakt od 250 reči, podeljenih na sledeća 4 paragrafa:

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Rezultati: opisuje primarno rezultate

Zaključak(ci): saopštenje autora o zaključcima proisteklim iz rezultata, i implicira njihovu kliničku primenljivost.

Strukturni apstrakti nisu potrebni kod uvodnika i pisma. Ispod apstrakta stoje ključne reci i to tri do pet. Ključne reči mogu biti uzete samo iz Medical Subjects Headings (MeSH).

Apstrakt treba da bude preveden i na engleski jezik (US style), sa naslovom, imenima autora, institucija i ključnim recima.

Za pisanje radova u formi prikaza slučaja, treba uraditi strukturirani apstrakt, na sledeći način:

Osnova problema: (opisati problem ili pojavu u nekoliko rečenica),

Metode rada: (opisati kako je obrađen i dijagnostikovan pacijent i koja bolest ili poremećaj je u pitanju),

Rezultati: (opisati rezultate rada i krajnji ishod),

Zaključak: (1-3 rečenice koja može da služi i kao opis celog postupka koji je rađen i napisan u radu).

TABELE I FIGURE

Svaka tabela sa jasnim naslovom na srpskom i engleskom treba da bude otkucana sa duplim proredom na odvojenom papiru. Obeležiti brojevima tabele jednu za drugom kako nailaze posle prvog navođenja u tekstu (obeležavaju se arapskim brojevima). Dati svakoj kolumni kratko ili skraćeno zaglavlje. Staviti objašnjenja u legendama svih nestandardnih skraćenica korišćenih u tabeli. Za jedinice i merenja vidi odeljak niže. Ne koristiti unutrašnje horizontalne i vertikalne linije. Staviti sve tabele na kraju vaseg fajla. Uvek odvojiti posebne kolumne upotrebom tabulatora, a ne upotrebom razmaknice, tabele moraju biti u tekst formatu.

Linijski prikazani dijagrami i ilustracije (fotografije, fotomikrografije itd.), trebaju biti osmišljene kao figure. Oni takođe treba da budu smešteni na odvojenom listu papira i numerisani jedan za drugim arapskim brojevima u saglasnosti sa prvim koji je citiran u tekstu. Figure treba da budu profesionalno nacrtane i fotografisane. Svaka figura treba da bude etiketirana pozadi ukazujući broj figure, prezime i prvo slovo imena autora, i vrh figure. Fotografije treba da se daju u dva primerka. Kolor fotografije ce se štampati samo u dogovoru sa urednikom ili ako autor sam snosi troškove. Fotomikrografije moraju imati obeleženu unutrasnju razmeru, i simbole, i strelice ili slova treba da su u kontrastu sa pozadinom. Na fotografijama pacijenata mora se sakriti identitet, osim ako se pacijenti u pismenoj formi slože sa objavljivanjem njihovih fotografija sa identitetom. Ukoliko ste pozajmili ili već publikovali negde fotografije priložite i pismenu dozvolu za reprodukovanje. Naslovi i detaljna objašnjenja fotografija treba da budu data u legendama. Ako su korišćeni simboli, strelice, brojevi ili slova za identifikaciju delova slike objasniti svaku jasno u legendi.

ZAHVALNOSTI

Priznanja i zahvalnosti prethode literaturi specificirajući generalnu podršku kao i odeljenje i ime šefa odeljenja, priznanja tehničkoj pomoći i konačno finansijskoj i materijalnoj pomoći. Navesti naziv i broj projekta, odnosno naziv programa u okviru koga je nastao članak i naziv institucije koja je finansirala projekat, u posebnoj napomeni pri dnu prve strane članka.

LITERATURA

Autori su odgovorni za tačnost literaturnih podataka. Reference treba da budu na posebnom listu i delu odmah iza teksta. Samo reference bitne za studiju mogu biti citirane. Kada je citiranje literature neophodno primeniti Vankuver stil. Na posebnom listu se navode citati referenci koji su označeni rednim brojevima po redosledu u kome se pojavljuju u tekstu i svaki citat odgovara brojevima koji sadrži navedenu referencu. Primeri tačnih oblika referenci :

RADOVI U ČASOPISIMA

1. Standardni članak u časopisu (lista svih autora, ali ako je broj veći od šest citirati tri i dodati et al): Glass DA, Mellonig JT, Towle HJ. Histologic evaluation of bone inductive proteins complexed with coralline hydroxyapatite in an extraskeletal site of the rat. J Periodontol 1989; 60:121-125.

2. Organizacija kao autor: Federation Dentaire Internationale. Technical Report No. 28. Guidelines for antibiotic prophylaxis of infective endocarditis for dental patients with cardiovascular disease. Int Dent J 1987;37:235.

3. Nije dat autor: Coffee drinking and cancer of the pancreas (editorial).BMJ 1981;283:628.

4. Volumen sa suplementom: Magni R, Rossoni G, Berti R, BN52021 protect guinea pig from heart anaohylaxis. Pharmacol Res Commun 1988; 20 Suppl 5:75-8.

Knjige ili druge monografije

5. Lični autor (i): Tullman JJ, Redding SW. Systemic Disease in Dental Treatment. St.Louis: The CV Mosby Company;1983:1-5.

6. Poglavlje u knjizi: Rees TD. Dental management of the medically compromised patient. In: McDonald RE, Hurt WC,Gilmore HW, Middleton RA, eds.Current Therapy in Dentistry, vol.7. St. Louis: The CV Mosby Company; 1980:3-7.

7. Disertacije i teze: Teerakapong A. Langerhans Cells in human periodontally healthy and diseased gingiva. (Thesis). Houston, TX: University of Texas; 1987.92 p.

Ostali publikovani materijal

8. Novinski članak: Shaffer RA.Advances in chemistry are starting to unlock mysteries of the brain. The Washington Post 1989 Ang 7; Sect. A:2 (col. 5).

Reference-elektronski citati

9. On line časopisi bez podataka o volumenu i strani. Berlin JA , Antman EM. Advantages and limitations of metaanalytic regressions of clinical trials data. Online J Curr Clin Trials (serial online). June 4;doc 134. Accessed July 20, 2000.

10. Online časopisi sa podacima o volumenu i strani. Fowler EB, Breault LG. Ridge augmentation with a folded acellular dermal matrix allograft: A case Report. J Contemp Dent Pract (serial online). 2001;2(3):31-40. Available from: Procter&Gamble Company, Cincinnat, OH. Accessed December 15, 2001.

11. World Wide Web.Centers for Disease Control and Prevention. Preventing emerging infectious diseases: Addressing the problem of antimicrobial resistance. Available at: http://www.cdc.gov/ncidod/emergplan/antiresist/. Accessed November 5, 2001.

JEDINICE MERE

Sva merenja treba da budu izražena u terminima Internacionalnog Sistema Jedinica (Si).

SKRAĆENICE I SIMBOLI

Ako se koriste nestandardne skraćenice potrebno je prilikom prvog korišćenja celog izraza u tekstu dati njegov puni naziv, a zatim u daljem tekstu koristiti skraćenicu. Nazivi simptoma, znakova i bolesti, kao i anatomski i histološki detalji ne mogu se skraćivati.

OFFPRINTS

Korespondirajući autori svih tipova radova izuzev pisama, novosti i pregleda knjiga primiće 1 broj časopisa oslobođena plaćanja.

SIMBOLI ZA OZNAČAVANJE (FUSNOTE)

Mogu se koristiti samo za identifikaciju zapošljenja autora, za objašnjenje simbola u tabelama i ilustracijama itd. Koristite sledeće fusnote: *,&, #,**, itd.

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Poslati 3 kopije rada i elektronsku verziju (CD-ROM, E-mail). Kopije rada i sav sadržaj treba spakovati u tvrdu kovertu kako bi se sprecilo oštećenje za vreme poštanskog saobraćaja. Radovi moraju biti potkrepljeni sa zatvorenim pismom potpisanim od svih autora. Ono mora da sadrži: a) izjavu da je rad pročitan i odobren od svih autora; b) informaciju o prethodnoj ili dupliciranoj publikaciji ili davanju rada na drugom mestu ili nekog njenog dela ranije; c) izjavu o finansijskim ili drugim vezama koje mogu dovesti do sukoba interesa; d) ime, adresu i broj telefona autora za korespondenciju koji je odgovoran za komunikaciju i korespondenciju; e) izjavu da su klinička i eksperimentalna istraživanja sprovedena u skladu sa institucijskim etičkim komitetom ili sa Helsinskom deklaracijom. Sem ovoga, pismo treba da sadrži i obaveštenje o vrsti rada i da li autori plaćaju ekstra cenu za kolor reprodukcije.

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Sekretari: Asist. Simona Stojanović, Mr. sci dr Miloš Tijanić

Klinika za Stomatologiju

Bul. Zorana Đinđića 52

18000 Niš, Srbija

E-mail: tarana.simona@gmail.com, tijanicm@yahoo.com

Predavanje materijala direktno uredniku ili bilo kom članu uređivačkog odbora otežaće i odužiće proces recenzije i prijema rada za štampanje.

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Skladištenje informacije: CD-ROM u Windows XP ili veći format. Software: radovi na disku treba da budu u Word-u za Windows. Etiketa: Napišite prvo ime autora na nalepnici CD-a, zajedno sa imenom i verzijom korišćenog word procesora. Oznaciti sve CD sadržajem figura, dijagrama itd, sa imenom prvog autora, imenom fajla, formatom i sabijenim šemama ako su korišćeni. Fajlovi: priložiti tekst i tabele svakog rada kao pojedinacni fajl, ali stavite sve figure, grafikone itd., u odvojenim fajlovima. Dozvoljeni grafički formati su EPS i TIF. Veličina figura treba da bude 8,5 cm ili 18,0 cm u rezoluciji od minimalno 300 dpi. Molimo Vas da pošaljete originalne fotografije, ne šaljite foto-kopije. Format: unosite svoj tekst besprekidno, samo umetnuti hard return na kraju paragrafa ili poglavlja, podnaslova, lista itd. Ne upotrebljavajte softwareski plan stranica. Molimo Vas da koristite Times New Roman 12 font za Word za Windows. Neku reč ili frazu u tekstu koju želite da izdvojite označite kroz rad u italic pismu. Boldirajte ono što se koristi uzastopno u tekstu za određene matematicke simbole, na primer, vektori. Molimo da proverite disk na virus i verifikujte da on sadrži ispravan fajl.

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Autori mogu predati svoje revidirane radove uključujući tabele i figure na CD-u sa PC ili Mac fajlom. Vratiti revidirane radove sa celokupnim materijalom na istu adresu sekretarijat.

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Acta Stomatologica Naissi is a scientific journal of the University of Niš, Faculty of Medicine and Clinic of Dental Medicine, which publishes articles relevant to the science and practice of Dentistry in general and related areas.

Please read carefully the following instructions to authors prior to manuscript preparation and submission. Papers which are not prepared according to the propositions and instructions will be returned to authors for corrections before forwarding them to reviewers. In case of unacceptable articles only illustrations will be returned.

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Acta Stomatologica Naissi publishes editorials, original scientific or clinical articles, review articles, preliminary reports, case reports, technical innovations, letters to the editor, articles from up-to-date literature, book reviews, reports and presentations from national and international congresses and symposiums which have not been previously submitted for publication elsewhere. All submitted articles will be reviewed by at least 2 reviewers, and when appropriate, by a statistical reviewer. Authors will be notified of acceptance, rejection, or need for revision within 6 weeks of submission. Articles are not paid for.

LANGUAGE

All submitted articles should be written in bilingual (Serbian and English) language. Abstracts should be written in Serbian and precise and grammatically correct English language, preferably US English. Avoid using Latin terms; however if necessary, put them in parentheses.

ETHICS

When reporting experiments on human subjects, indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) or with the Helsinki Declaration (1964, amended in 1975 and 1983) ofthe World Medical Association.

GENERAL INSTRUCTIONS

PREPARATION

Articles should be written on A4 white bond paper size (21x29.5cm) on one side of the paper only, and double-spaced (including illustration legends and references) providing 25 mm ample margins all around. Only one copy of the manuscript should contain the surname and the author's first name initial in the upper right corner. Manuscripts should be organized as follows: Title Page, Abstract and Key words, Introduction, Patients/Materials and Methods, Results, Discussion, Conclusions, Acknowledgments, References, Figure Legends, Tables, Figures. Title page is numbered as page 1, and all other pages should be numbered conse-quently.

TITLE PAGE

The title page should contain: a) the full title of the article (in upper case); b) first name, middle initial, and last name of each author without the academic degree; c) name of department and institutional affiliation for each author; d) running title of no more than 10 characters. At the bottom of the page, please indicate the name, academic degree and address (including E-mail, telephone and fax number) of the author responsible for correspondence.

It is recommendable to use the words appropriate for indexing and searching. If there are not such words in the title, then subtitle should be added.

If the article in the previous version has been orally exposed (under the same or similar title), such information should be separately noted at the bottom of the first page ofthe article.

Abstract and Key words

All original abstracts should be submitted with a structured abstract, consisting of no more than 250 words, and the following 4 paragraphs:

Background: Describes the problem being addressed.

Material and Methods: Describes how the study was performed.

Results: Describes the primary results.

Conclusion: Reports what authors have concluded from these results, and notes their clinical implications.

Key words: A maximum of 5 key words drawn from MeSH documentation. Abstract should be translated into English (US style), with the title, name(s) of author(s), institutional affiliation and key words.

To write papers in the form of a case report, a structured abstract should be done, as follows:

Basis of the problem: (describe the problem or occurrence in a few sentences),

Methods of work: (describe how the patient was treated and diagnosed and which disease or disorder is in question),

Results: (describe the results of the work and the final outcome),

Conclusion: (1-3 sentences that can also serve as a description of the whole procedure that was done and written in the paper).

To write papers in the form of a case report, a structured abstract should be done, as follows:

Basis of the problem: (describe the problem or occurrence in a few sentences),

Methods of work: (describe how the patient was treated and diagnosed and which disease or disorder is in question),

Results: (describe the results of the work and the final outcome),

Conclusion: (1-3 sentences that can also serve as a description of the whole procedure that was done and written in the paper).

TABLES AND FIGURES

Each table with a brief title (on Serbian and English) should be typed double-spaced on a separate sheet of paper. Number tables consecutively (with Arabic numbers) in the order of their first citation in the text. Give each column a short or abbreviated heading. Place explanations in legends of all nonstandard abbreviations which are used in table. For units and measurements see paragraph below. Do not use internal horizontal and vertical rules. Place all tables at the end of your file. Always separate the individual columns using tabulators, not using space bar, i.e. tables must be in text format. Line drawings diagrams and halftone illustrations (photographs, photomicrographs, etc.) should be designated as figures. They should be listed on separate sheet and numbered consecutively with Arabic numerals according to the order in which they have been first cited in the text. Figures should be professionally drawn (not simply typewritten) and photographed. Each figure should be labeled on its back indicated the number of the figure, last name and the first letter of the author, and the topside of the figure. Photographs should be supplied in two copies. Color photographs are published only in case if author himself bears expenses. Photomicrographs must have internal scale markers, and symbols, arrows or letters should contrast with the background. Photographs of patients must conceal their identity unless patients approve the publishing of the photograph in written form. If you borrow or use already published photographs please submit a written permission for reproduction. Permission is not required for the documents in the public domain. Figures will not be returned unless requested. Captions and detailed explanations of the figures should be given in the legends. If symbols, arrows, numbers, or letters are used to identify parts of the figure identity and explain each one clearly in the legend.

ACKNOWLEDGEMENTS

Acknowledgements are positioned before the reference list specifying general support by department chairman, acknowledgements of technical as well as financial and material support. Acknowledgement includes the title and number of the project, i.e. the title of the programme within which the article was composed and the title of the institution funding the project; it should be written as a separate notification at the bottom ofthe first page of the article.

REFERENCES

Authors are responsible for accuracy of literature data. References should be listed in a separate section immediately following the text. Only references important for the study should be cited. It is necessary to apply Vancouver style. Citations are numbered consecutively in the order in which they appear in the text and each citation corresponds to a numbered reference containing publication information about the source cited in the reference list at the end of the publication. Examples of references are given bellow:

Journals:

1. Standard journal reference. (Note: list all authors if six or less; when seven or more, list only first three and add et al): Glass DA, Mellonig JT, Towle HJ. Histologic evaluation of bone inductive proteins complexed with coralline hydroxyapatite in an extraskeletal site of the rat. J Periodontol 1989;60:121-125.

2. Corporate author: Federation Dentaire Internationale. Technical Report No.28. Guidelines for antibiotic prophylaxis of infective endocarditis for dental patients with cardiovascular disease. Int Dent J 1987;37:235.

3. No author given: Coffee drinking and cancer of the pancreas (editorial). BMJ 1981;283:628.

4. Volume with supplement: Magni R, Rossoni G, Berti R, BN52021 protect guinea pig from heart anaphylaxis. Pharmacol Res Commun 1988; 20 Suppl 5:75-8.

Books or other monographs:

5. Personal author(s): Tullman JJ, Redding SW. Systemic Disease in Dental Treatment. St. Louis: The CV Mosby Company; 1983:1-5.

6. Chapter in a book: Rees TD. Dental management of the medically compromised patient. In: McDonald RE, Hurt WC, Gilmore HW, Middleton RA, eds. Current Therapy in Dentistry, vol. 7. St. Louis: The CV Mosby Company; 1980:3-7.

7. Dissertations and thesis: Teerakapong A. Langerhans Cells in human periodontally healthy and diseased gingiva. (Thesis). Houston, TX: University of Texas; 1987.92 p.

Other published material:

8. Newspaper article: Shaffer RA.Advances in chemistry are starting to unlock mysteries ofthe brain. The Washington Post 1989Ang 7; Sect.A:2 (col. 5).

References - electronic quotations:

9. Online journals without volume and page information. Berlin JA, Antman EM. Advantages and limitations of metaanalytic regressions of clinical trials data. Online J Curr Clin Trials (serial online). June 4; doc 134. Accessed July 20, 2000.

10. Online journals with volume and page information. Fowler EB, Breault LG. Ridge augmentation with a folded acellular dermal matrix allograft: A case Report. J Contemp Dent Pract (serial online). 2001;2(3):31-40. Available from: Procter&Gamble Company, Cincinnat, OH. Accessed December 15, 2001.

11. World Wide Web.Centers for Disease Control and Prevention. Preventing emerging infectious diseases: Addressing the problem of antimicrobial resistance. Available at: http://www.cdc.gov/ncidod/emergplan/antiresist/. Accessed November 5, 2001.

UNITS OF MEASUREMENTS

All measurements should be reported in terms of the International System of Units (SI)

ABBREVIATIONS AND SYMBOLS

Avoid abbreviations in the text but whenever possible use standard abbreviations. However, if nonstandard abbreviations are used, the full term of which and abbreviation stands for should precede its first use in text. Names of symptoms, signs and diseases, as well as anatomic and histologic characteristics cannot be abbreviated.

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