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IDENTIFICATION OF OSTEOPOROSIS IN DAILY DENTAL PRACTICE AND ITS IMPORTANCE

ИДЕНТИФИКАЦИЈА НА ОСТЕОПОРОЗАТА ВО СЕКОЈДНЕВНАТА ПРАКСА НА СТОМАТОЛОГИЈАТА И НЕЈЗИНАТА ВАЖНОСТ

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Abstract

Osteoporosis is progressive metabolic bone disease, which is characterized with decreased bone mass, microarchitecture weakness which further is accompanied with increased bone fragility and increase of risk of bone fracture. Osteoporosis is a health condition which is furtively developed in asymptomatic forms. Since most of the cases are diagnosed only when a bone breaks, the disease is a high risk for population's health, followed with high cost of healing and rehabilitation. In this context, science broadens its research dimensions, including other diagnostic methods, except the standard one, such as the DXA test which is more affordable and accessible for the population. In this manner, the disease can be diagnosed on time and patients can start their treatment in appropriate time before the fracture happens, which, in most of the cases, is life endangering. Panoramic radiography is a diagnostic method, which is routinely used in the dental practice. Since it is cost-effective and taking into consideration the frequency of its application, there is a necessity for research and defining the radio morphometric parameters which identify bone quality. Scientists used some of the radio morphometric parameters for this purpose, but most of the studies showed the great importance of defining some of them: MCI-Mandibular Cortical Index, PMI-Panoramic Mandibular Index, MI-Mental Index and M/M report of Panoramic Radiography by documenting their connectivity and early defining of bone quality and connectivity with body BMD (Bone mineral Density). **Key words:** osteoporosis, panoramic radiography, mandibular cortical index, panoramic mandibular index, mental index.

Апстракт

Остеопорозата е прогресивна метаболна болест на коските, која се карактеризира со намалена коскена маса, слабеење на коските кое дополнително е придружено со зголемена кршливост на истите и зголемен ризик од фрактура. Остеопорозата е здравствена состојба која се развива тајно во асимптоматска форма. Бидејќи во повеќето случаи се дијагностицира само кога доаѓа до фрактури на коските, болеста претставува голем ризик за населението, каде спаѓаат и високите трошоци за заздравување и рехабилитација. Во овој контекст, науката ги проширува своите истражувачки димензии, вклучително и други дијагностички методи, покрај стандардните, како што се DXA тестовите кои се подостапни за населението, за да може болеста навремено да се дијагностицира и пациентите да започнат со лекување пред да настанат скршеници кои во многу случаи го загрозуваат животот. Панорамска радиографија е дијагностичка метода која рутински се користи во стоматолошката пракса. Поради исплатливоста и зачестеноста на нејзината примена, воочена е потребата од истражување и дефинирање на идентификационите параметри со кои се идентификува квалитетот на коските. Научниците користат некои од радиоморфометриските параметри за оваа цел, но бројни студии ја истакнуваат големата важност за дефинирање на три од нив: MCI - кортикален мандибуларен индекс, PMI - панорамски мандибуларен индекс, МИ - ментален индекс, како најсигурни показатели за евалуација на квалитетот на коските во панорамската радиографија што ја документира нивната поврзаност и рано одредување на квалитетот на коските со телесна BMD. Потребни се дополнителни научни истражувања за да се стандардизираат податоците и индикаторите со висока чувствителност и специфичност за идентификација на знаците на остеопороза во стоматолошката пракса. **Клучни зборови:** остеопороза, панорамска радиографија, мандибуларен кортикален индекс, ментален индекс.

Introduction

Osteoporosis is progressive metabolic bone disease, which is characterized with decreased bone mass, microarchitecture weakness which further is accompanied with increased bone fragility and increase of risk of bone fracture[1, 2, 3].

This disease develops in silent progressive forms and quite often is not detected until the bones are broken spontaneously without immense trauma. So, rightfully the disease is called silent epidemic. Women over 50 (fifties) develop osteoporosis 50 (fifty) times more than men[1,4,6].

Since most of the cases are diagnosed only when a bone is broken, the disease shows a high risk for popula-

tion's health, followed with high cost of healing and rehabilitation[1, 2].

Based on WHO, the criteria for defining osteoporosis is when BMD (Bone Mineral Density) shows T-score under -2.5 and shows diagnostics and intervention threshold.

One of the most valid techniques for BMD (Bone Mineral Density) measurement is DXA-test, (Dual-energy x-ray absorptiometry).

In most of the countries, including USA, DXA-test is not easily applicable for mass population because of the high cost. Therefore, the scientists are seeking other accessible and effective diagnostics methods for the population, whose purpose is detection of early osteoporosis indication[4, 5, 6].

Morphological jaws changes in patients with osteoporosis

Morphological changes can be seen in both jaws, but especially in the mandibula and this is not a coincidence because the mandibula consists of cortical bone which surrounds the trabecular part of the lower jaw.

The cortical part of the mandibula is more conditioned from general conditions of the bones in the body than the trabecular part or elevation of the alveolar ridge, which in continuity is submitted to absorptive processes of multifunctional nature. Consequently, the cortical bone of the mandibular is submitted to absorptive processes in patients with osteoporosis. So, there is a significant relation between the mandibular cortical bone, quality, quantity and body BMD[6, 7, 25].

Researchers report that the mandibular cortex of buccal in the region distally from mental foramen has a closer correlation with the density of the body bones than the lingual part[8].

Patients in dental practice are subjected to panoramic radiography on routine basis. This routine examination, which is cheaper also, serves for identifying patients with osteoporosis by using the definite radio morphometric parameters[11, 27].

Radio morphometric indicators - their value in osteoporosis detection

A research found that the correlation between osteoporosis and oral health started in 1960. Kribbs et al concluded that women suffering from osteoporosis have three times higher chance for toothlessness. Tauchi et al, in 2005 concluded that Japanese women, who were identified by the dentists by using the data from the cortical part of the mandibular, were diagnosed with osteoporosis or osteopenia. Clementi in 1994 presented MCI index as measurement index of mandibular cortex density[9, 10, 27].

Scientists used some of the radio morphometric parameters for this purpose. In many studies they have highlighted the great importance of identifying some of them for which the studies are supplementary and more detailed: MCI - Mandibular Cortical Index, PMI-Panoramic Mandibular Index, MI - Mental Index, which serves for surveying signs of osteoporosis and bone quality in Panoramic Radiography and enables the identification of patients with osteoporosis and referring them further to start the treatment, and preventing the sore consequences which the disease carries.

MCI - Mandibular Cortical Index (MCI) or the Clement index refers to the appearance of the inferior cortex of the mandibula, distally from the mental foramen on both sides of the mandibular and, according to Clementi and the associates, was divided in three subgroups (C1-C3) based on the findings of the appearance in the lower boundary of the mandibular cortex.

C1 - Endosteum margins of the cortex is clearly uniform on both sides of the jaw.

C2 - Endosteum margins show semilunar defects (lacunar resorption or visual, it looks like they create endosteum cortical residue in one or both sides of the lower jaw).

C3 - Cortical layer of the lower jaw forms sore endosteum layers and is clearly very porous.

Many studies reported that women with medium erode cortex and those with emphasized erode of the cortex have higher possibilities to develop osteoporosis. Clement et al found the changes in mandibular cortex, observed in Panoramic Radiography, and have significant relation with BMD of the lower jaw. Researches made by Cakur and associates gave similar data. MCI Index validity is limited and liaisons a lot also with ability of the examiner [18, 31, 32, 33].

Horner and Dalvin in their long researches found a significant correlation between MCI and BMD of mandibular[25, 26, 27, 28].

High value index and researched in details is MI (Mental Index) or MCW (Mandibular Cortical Width) to which is referred the width of lower boundary of mandibular under two mental foramen according to the Lagerton methods[25].

Important study in this direction is a three year study called Osteodent, in this project are involved five European countries, their objective was to find trustful radiologic indicator which will serve to identify osteoporosis.

The study offered many detailed data by putting MCI index in an inferior position in report with MI index. In this case the researchers suggested that only the patients

with rate of MI < 3mm must be referred for DXA test and additional examination

These results were in the same line with the founding of Dalvin and Honer.

MI - MENTAL INDEX, is the average of width of boundary of lower mandibular under the mental foramen, in both sides of the lower jaw, according to Langerton method.

Boundary of MI index is MI < 3 mm.

PMI - PANORAMIC MANDIBULAR INDEX, presented by Benson was developed based on the work by Wical and Swoope, which after the long research came to the conclusion that no matter the constant absorptive multifactorial processes regarding the mental foramen, the part under foramen remains relatively constant. PMI, describes the proportion of the width of the cortex from the distance of mental foramen until the edge of lower mandibular cortex-MI/h, a technique prescribed by Benson.

Boundary of PMI index is PMI < 0.3mm.

M/M report, which is counted by separating total length of height of mandibular from the distance from the center of mental foramen until the edge of lower mandibular.

MI, PMI, M/M indicators are measured on both sides of the lower jaw by calculating the average[25, 26, 27, 28].

Highlights of Conclusions

The use of Panoramic Radiogrpahy in purpose to detect earlier the osteoporosis would bring great benefits in diagnostics economic costs, prevention and treatment of osteoporosis as a disease with immense consequences in human health.

Since Panoramic Radiography quite often is used in dental practice and is repetitive diagnostics method, with screening and same exposing parameters it makes it very suitable and for matching purposes.

Many researches founded a very valuable connectivity between the eroded cortex MCI C-2 and C-3 and dilution cortex of mandibula, MI<3mm and PMI<0.3 mm detected in Panoramic Radiography and suggested these indicators as very valuable for identification of low BMD of the body, especially in the women after the menopause.

Furthermore many challenging researches should be needed so we could have clear recommendation that if the dentist in primary care could use these data for referral of patients for additional examination in regards to osteoporosis and could we arrive to prevent the fractures of the bones to this disease with immense impact on the population health.

The use of radiological automatic digital software program is an imperative of time which mitigate a lot the precision of measurement by reducing in maximum the possible mistake of made measurement with other manual methods.

At the same time, before the prosthetics rehabilitation it is very important to evaluate the density of jaw bones, to define the referral point and radio morphometric measurements.

We clearly need to take into consideration the final diagnosis for osteoporosis and in the safe way to be done through the safe diagnostics methods DEXA - examination and signs in oral radiography can be used only as primary screening.

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HYPODONTIA: CLINICAL MANAGEMENT AND TREATMENT OPTIONS - CASE REPORT

ХИПОДОНЦИЈА: КЛИНИЧКИ МЕНАЏМЕНТ И ТЕРАПЕВТСКИ МОЖНОСТИ -ПРИКАЗ НА СЛУЧАЈ

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Abstract

Hypodontia is a condition used to describe the developmental absence of one or more teeth in primary or in permanent dentition, excluding the third molars. The tooth most commonly found to be missing is the third molar. It can be stated that a tooth is congenitally missing when it is clinically and radiographically (orthopantomogram) missing in the dental arch. Hypodontia can occur with or without syndrome. This developmental dental anomaly is the most common one and can be a challenge to manage clinically. The aetiology of hypodontia varies, so genetic, epigenetic and environmental may be contributory factors. Dental anomalies reported in literature associated with hypodontia include the following: microdontia, canine impaction, transposition, rotation of teeth, taurodontism and hypoplastic alveolar bone. Clinical management of hypodontia requires careful multidisciplinary planning. Congenital, bilateral absence of teeth is a very rare case in patients without syndrome. Orthodontic treatment of hypodontia depends on the area where the tooth is missing. Unerupted tooth might cause aesthetic and/or functional problems especially if it is situated in the maxillary anterior region. This article presents cases of hypodontia in early adolescent (agenesis of lateral incisor) and in adult period (bilateral absence of lateral incisors). **Key words:** hypodontia, aetiology, dental anomalies, orthopantomogram, orthodontic treatment.

Апстракт

Хиподонцијата е состојба која се користи при опишување на развоен недостаток на еден или повеќе заби во млечна или постојана дентиција, со исклучок на третите молари. Заб за кој е познато дека најчесто недостасува е третиот молар. Вроден недостаток на некој заб се смета онаа состојба кога и со клинички и со рендгенолошки преглед (ортопантомограм) одреден заб недостасува во денталниот лак. Хиподонцијата може да се јави во склоп на синдром или без појава на синдром. Оваа развојна дентална аномалија е многу честа појава и претставува предизвик во клиничкото менаџирање на истата. Етиологијата варира и како причинители за нејзина појава се наведуваат генетски, епигенетски и надворешни фактори. Во литературата може да забележиме дека хиподонцијата, како појава, се поврзува со одредени дентални аномалии, како што се: микродонција, импакција на канини, транспозиција, ротација на забите, тауродонтизам и хипопластична алвеоларна коска. Клиничкото менаџирање на хиподонцијата бара мултидисциплинарен и внимателен пристап. Вроден, обостран недостаток на забите е многу редок случај кај пациенти без синдром. Ортодонскиот третман на хиподонцијата зависи од регијата каде што недостасуваат забите. Вродениот недостаток на заби во максиларната фронтална регија доведува како до естетски така и до функционален проблем. Овој приказ покажува случаи на хиподонција во ран адолесцентен период (недостаток на латерален инцизив), и кај возрасен пациент (обостран недостаток на латерални инцизиви). **Клучни зборови:** хиподоција, етиологија, дентални аномалии, ортопантомограм, ортодонтски третман.

Introduction

Hypodontia is developmental absence of one or more teeth and it is the most common dental anomaly in humans, often representing a major clinical problem1. Congenitally missing teeth are classified according to the number of missing teeth, except the third molars. The term hypodontia is used to define agenesis of one to six teeth excluding the third molars. Oligodontia is absence of more than six teeth (excluding the third molars), also known as severe hypodontia, and anodontia is the complete absence of teeth[2, 3]. The incidence of hypodontia in permanent dentition varies from 2.6% to 11.3% in the overall population, while the incidence in primary dentition is rare, ranging from 0.08% to 1.55%. Hypodontia in primary dentition generally appears in the anterior region and often associates with missing the same permanent tooth[4]. Tooth agenesis affects the maxilla and the mandible with similar prevalence[5].

Most cases of hypodontia have a polygenetic inheritance pattern. Genetic studies suggest both, genetic and environmental aetiology toward this anomaly[6]. Various experimental studies show that the genes control the number and region of missing teeth. Mutation of genes,

such as MSX1 and PAX9, have been implicated with hypodontia in few studies[7-10]. Environmental factors, such as trauma in the dental region (fractures), surgical procedures on the jaws, chemotherapy and radiation therapy (depending of the age of the patient and the dose), may also contribute toward hypodontia[11]. Somatic diseases such as syphilis, scarlet fever and rickets are also associated with hypodontia, as well as nutritional disturbances during pregnancy or infancy. Hypodontia can occur as an isolated dental anomaly (associated with lesser craniofacial or dental anomalies) or as part of a syndrome (Ectodermal dysplasia, Down syndrome). It has been reported that non-syndromic hypodontia occurs in connection with other dental anomalies such as microdontia, canine impaction, taurodontism, transposition, rotation of teeth and hypoplastic alveolar bone. Microdontia (reduction in tooth size), as one of the most common dental anomalies, is associated with hypodontia of a maxillary lateral incisor on one side and a peg-shaped lateral incisor on the other side[12]. There is also relationship between palatal impacted canines, transposition of the maxillary canine and first premolar in cases of maxillary lateral incisor agenesis[13]. Other researchers have found that if there is a unilateral maxillary lateral incisor or premolar agenesis, it is more likely that the corresponding teeth on the other side will be rotated[14].

The absence of teeth may introduce several signs and symptoms such as reduction of chewing ability, malocclusions, difficulty pronouncing words, compromised aesthetics, periodontal damage and alveolar bone deficiency. These complications cause functional (posterior absence of teeth), as well as aesthetic limitation (anterior absence of teeth). Furthermore, hypodontia may extremely affect the patient's behavioural pattern, self-esteem and social life[15-16].

The complexity of hypodontia treatment varies widely, therefore managing hypodontia is a big challenge and needs multidisciplinary specialist approach[17-18]. There are not usually any noticeable changes on the skeletal pattern in the mild types of hypodontia, but it may be possible to see changes in cases of severe hypodontia. Unfortunately, there is no established formal procedure to manage patients with hypodontia. Treatment is individual and might range from single restorations to surgery and multiple restorations. Various options and methods have been suggested, such as: closing the space orthodontically; redistributing or re-opening of space for prosthetic appliances (crowns, adhesive or conventional bridges, removable prosthesis) and dental implants[19].

In general, treatment options depend on the age of the patient, the severity of hypodontia, the amount of space available, the type of malocclusion, the degree of inherent crowding, oral health, patient's motivation and opinion, skeletal pattern, soft tissue profile, bone anatomy and position of vital structures, as well the economic status of the patient (finances)[15]. Cooperation between different specialties (general dental practitioners, orthodontists, paediatric dentists, prosthodontists, oral and maxillofacial surgeons), provides the best individual results for each patient[20].

Case report (1)

A 13 -year-old male with permanent dentition was brought to the Clinic of Orthodontics for orthodontic treatment. The patient's main complaint was aesthetic, he has a big space between the central incisors (Figure 1). The patient did not complaint of pain, there were no signs of infection and he had good oral hygiene. Intraoral clinic examination revealed hypodontia of the permanent lateral incisor on the right side of maxilla, ½ Angle Class III on right and left side, anterior crossbite and spacing in the frontal teeth in the maxilla. According to morphological analyses, narrow mandible and asymmetric maxillary dental arch due to the hypodontia was diagnosed. Furthermore, the patient had reduced motility of the tongue due to low frenal attachment (frenulum linguae) and there was high maxillary frenum attachment (Figure. 2). The panoramic radiograph confirmed congenitally

Figure 1. *Intraoral view (occlusion of the patient)*

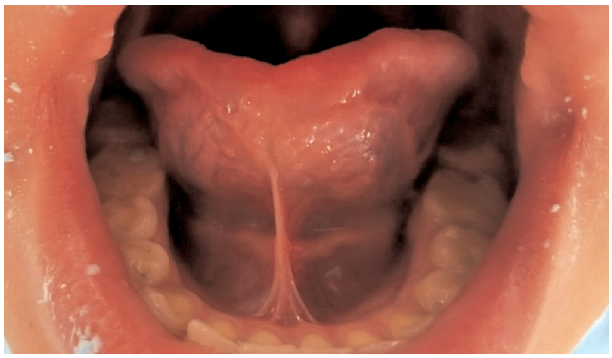

Figure 2. *Intraoral view (low frenal attachment)*

Figure 3. *Panoramic radiograph of the patient*

missing lateral incisor and presence of three third molars (Figure 3).

Therapy plan

Clinical management of this patient was necessary, and the orthodontic treatment included few steps. Frenectomy procedure would aid in tongue mobility, correct the tongue rest posture and establish a proper swallowing pattern. The oral surgeon performed the frenectomy, and the orthodontist started the therapy with fixed appliance (Figure. 4). Closure of the empty space (maxillary midline diastema) and re-opening of space for lateral incisor will be done by mesialization of the right central incisor. This patient is young and therefore, providing some type of final solution to replace the missing tooth in the long term should be a priority. There are two options for final restorative replacement of the missing tooth, a crown made over a dental implant or a prosthetic bridge. Temporary solution will be some prosthetic removable appliance. Also, the aim of treatment will be correction of occlusion, Angle Class 3 malocclusion and anterior crossbite bite of incisors achieved by fixed orthodontic appliance.

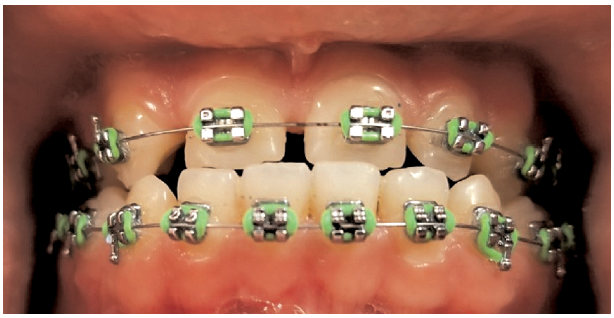

Figure 4. *Therapy with fixed orthodontic appliance*

Case report (2)

A 21-year-old female arrived at the Clinic of Orthodontics with main complaint of being "unhappy about her smile". Her family history was non-contributory with congenitally missing teeth. Extra oral examination revealed a facial asymmetry, whereas intra oral clinical examination revealed bilateral absence of lateral maxillary incisors, presence of maxillary primary canine, rotation and crossbite of permanent second premolar (Figure. 5 and Figure. 6 a, b). The molar relationship was ½ Angle Class II, there was anterior open bite and the overjet was 4 mm. Due to the presence of primary right maxillary canine, dental arch asymmetry was diagnosed. Panoramic radiograph confirms hypodontia of both later-

Figure 5. *Intraoral view (anterior posture of the tongue)*

Figure 6. *a) (rotated second premolar in right maxilla) b) (presence of primary canine)*

al incisors in the maxilla (Figure. 7). There is absence of third molars in the mandible. Furthermore, there was a poor oral habit (anterior posture of the tongue).

The aim of treatment of this clinical case include correction of the bad habit, levelling and coordinating the dental arches, correcting the centreline discrepancy, overjet and overbite, crossbite, achieving Angle Class 1 and retaining the corrected results.

Therapy plan

The stability of corrected relations after orthodontic treatment depends on regular tongue function. Therefore, based on clinical and radiographical examination, the correction of tongue posture with an individual myofunctional appliance was treatment priorit. Also, we recommended some oral myofunctional exercises. Appropriate use of this appliance and regular exercises (at least three times a day) give excellent results in correction of anterior tongue posture and facial asymmetry (Figure 8). The therapy will be continued with fixed orthodontic appliances that will correct the crossbite and rotation of the second premolar, the centreline, open bite, overjet and overbite. The final aim is to achieve "Happy smile", by remodelling canine into lateral incisors by laminates or dental composites.

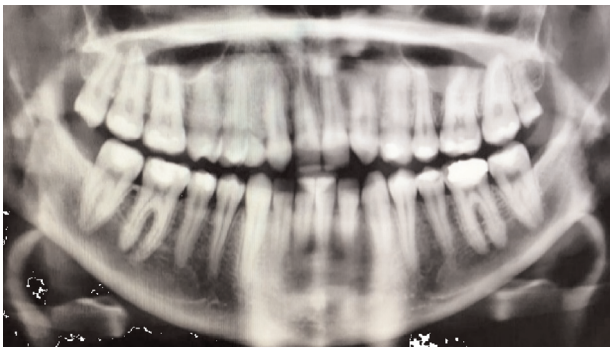

Figure 7. *Panoramic radiograph of the patient*

Figure 8. *Myofunctional individual orthodontic appliance*

Discussion

Diagnosis of dental anomalies is usually performed by paediatric dentists, as these professionals are the first to interact with children and adolescents[21]. The knowledge of odontogenesis is fundamental for understanding growth and developmental disorders affecting teeth. Hypodontia can be treated with different orthodontic modalities. The decision depends on various factors (patient's age, facial profile, severity of hypodontia, shape and size of the adjacent teeth, smile and gingival line)[22]. Presence of dental malocclusion, as well as poor oral habit, are very important for the final treatment plan. The orthodontic treatment in the first presented case (½ Angle Class III malocclusion) will be re-opening the space for lateral incisor after the frenectomy. The second presented patient (½ Angle Class II malocclusion), after correction of tongue posture, will be treated with orthodontic fixed appliances with camouflage treatment. The presented dental open bite and increased overjet is the result of incorrect rest tongue posture and lips posture[23-24]. The goal of orofacial myofunctional therapy is to correct oral rest posture of the tongue and lips which means, at rest, the lips should be closed without strain, the patient can breathe nasally, the tongue is resting against the mouth roof not touching the teeth.

These cases illustrate the need for a multidisciplinary team approach (orthodontic, dental practitioner, prosthetic and oral surgeon)[25]. Correction of myofunctional dysfunction is priority for any malocclusion and stability of corrected results depends on this. According to most authors, there is no age limit to perform myofunctional therapy and the results depend on the patient's cooperation. Age is an important factor in determining the type of treatment for hypodontia cases. Most authors agreed that priority in orthodontic treatment is correction of poor oral habits, myofunctional disorders and the stability of achieved results depends directly on these factors.

Conclusion

Hypodontia presents a complex problem to dentists worldwide. Clinical management of hypodontia requires careful multidisciplinary planning and has financial implications. A number of procedures can be performed to fullfill the patient's wishes considering their age. The primary motivating factor for individuals seeking orthodontic treatment is aesthetics, whereas the best time for orthodontic treatment with agenesis is early adolescence, since it is a period when most of remaining developing permanent teeth are erupting and notable facial growth has happened.

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ASSOCIATION BETWEEN CANDIDA SPECIES AND PERIODONTITIS

АСОЦИЈАЦИЈА ПОМЕЃУ КАНДИДИЈАЗНИ ВИДОВИ И ПАРОДОНТОПАТИЈА

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Abstract

The mycobiome from the oral cavity is not well characterized, particularly in relation to oral diseases such as periodontal disease. **Aim:** Analysis of the composition of the yeast microbiota present in the oral mucosa and subgingival sites of healthy individuals without periodontitis (HI), and patient with chronic periodontitis (CP), and assessment of the relationship between the severity of this condition and the Candida infection. **Material and methods:** Microbiological samples were obtained from 30 patients (25 and 62 years; 41.33±5.54), divided into 3 groups: 10 patients without CP (control), 10 with moderate CP, and 10 with severe CP. Oral swabs samples were collected from tongue and buccal mucosa with sterile cotton stick. The subgingival samples were obtained from gingival sulcus (HI) or deepest probing depths (patients with CP) by means of a sterile curette (S4L/4R SS). Swab cultures were immediately inoculated on CHROM agar and incubated at 37°C for 48 h. C.albicans and Non-albicans Candida, were identified by the morphology and pigmentation of the colonies. The results were processed by the method of descriptive statistics. **Results:** The percentage of yeast carriers in mucosa in the three groups was similar. Patients with chronic periodontitis showed significant differences in subgingival colonization compared to HI (45% severe, 30% moderate, versus 14,3% of HI). C. albicans was the most common species in the examined patients. **Conclusion:** Subgingival colonization by yeasts could be favored in chronic periodontal disease. **Key words:** Chronic periodontitis, C. albicans, Non-albicans Candida, periodontal pocket.

Апстракт

Микобиомот во усната празнина не е сосема дефиниран, особено во однос на оралните болести како што е пародонтопатија. **Цел:** Анализа на составот на габичниот микробиом присутен на оралната мукоза и субгингивалните регии, кај здрави лица без пародонтална болест (ЗП) и пациенти со хронична пародонтопатија (ХП), и одредување на поврзаноста на стадиумот на заболувањето со кандидната инфекција. **Материјал и метод:** Микробиолошките примероци беа земени од 30 пациенти (25 и 62 години; 41,33 ± 5,54), поделени во 3 групи: 10 испитаници без ХП (контрола), 10 со умерена форма на ХП и 10 со напредната ХП. Оралните брисеви беа земени од јазик и букална лигавица, со стерилно памучно стапче. Субгингивалните примероци беа земени од гингивалниот сулкус (ЗП) или од пародонталните џепови со најголема длабочина (пациенти со ХП) со помош на стерилна кирета (S4L/4R SS). Културите со брис беа инокулирани на подлога агар CHROM и инкубирани на 37 °C за време од 48 часа. Инокулатите од C.albicans и Non-albicans Candida беа идентификувани со морфологија и пигментација на колониите. Резултатите беа обработени со метод на дескриптивна статистика. **Резултати:** Процентот на мукозната габична инфекција кај сите три групи беше сличен. Кај испитаниците со ХП постојат значителни разлики во субгингивалната колонизација во однос на ЗП (45% напредната форма, 30% умерена, 14,3% ЗП). C.albicans беше најчестиот вид во однос на останатите специеси кај испитаниците. **Заклучок:** Субгингивалната колонизација на габи може да биде фаворизирана кај хроничната пародонтопатија. **Клучни зборови:** Хронична пародонтопатија, C. albicans, Non-albicans Candida пародонтален џеп.

Introduction

Periodontitis is a chronic inflammatory disease characterized by destruction of support connective tissue and alveolar bone loss with formation of a periodontal pocket[1]. Results of epidemiological studies have shown that chronic periodontitis (CP) has both a high prevalence and severity in the world and is the most common cause of tooth loss worldwide[2].

Periodontitis has a polymicrobial character; dental plaque with pathogens such as Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans and Tannerella forsythia initiating the disruption of tissue homeostasis[3, 4]. Besides periodontopathogens, dental

plaque contains other bacteria as well as fungi and viruses whose role is actively studied. The high compliance of C. albicans allows it to colonize indifferent media creating mixed biofilms with commensal as well as pathogenic bacteria in aerobic and anaerobic conditions, which makes C.albicans an active participant in the inflammatory-destructive process in periodontal diseases. Many researchers consider that yeast-like fungi, specifically Candida spp., are one of the important causes for development, progression, and complicated course of CP[5].

Candida species are commensal yeasts, around 40% of healthy people carry members of the genus Candida in saliva or oral mucosa[6]. Certain local and/or general predisposing factors can increase its invasion in mucosal tissues and cause opportunistic infections. It occurs usually in immunocompromised individuals with endocrinal disorders, blood diseases, and with long-term use of broad-spectrum antibiotic therapy.

C. albicans is the most prevalent yeast of oral microbiota. It constitutes 60% to 70% of total isolates of this genus, but other Candida species including Candida glabrata, Candida tropicalis, Candida parapsilosis, Candida krusei, Candida dubliniensis, Candida glabrata, are also found[7].

Candida species typically reside on the tongue, palate, buccal mucosa, saliva, but also in other oral sites such as pulp chamber, carious lesions and periodontal pockets. The periodontal pocket and gingival crevicular fluid are favorable media for C. albicans germination and hyphal tip growth.

Several studies have reported increased subgingival colonization by yeasts, particularly Candida albicans, in chronic periodontitis patients compared to periodontally healthy subjects[8,9,10]. Furthermore, it has been reported that the proportion of yeasts in periodontal pockets is similar to some bacterial periodontopathogens, suggesting a possible role for Candida spp. in the pathogenesis of the disease[11,12,13].

Aim of the study

The aim of the study was to analyze the composition of the yeast microbiota present in the oral mucosa and subgingival sites of healthy individuals without periodontitis (HI), and patient with chronic periodontitis (CP), and to assess the relationship between the severity of this condition and the Candida infection.

Material and method

Study Population and Clinical Examination

This prospective study randomly recruited 60 patients that attended a check-up or review appointment at the Faculty of Dentistry, Ss. Cyril and Methodius University in Skopje, and the University Dental Clinical Center "St. Pantelejmon" in Skopje, Republic of North Macedonia. Study sample consisted of 38 females (63,3%) and 22 males (36,6%) with a mean age of 48.2 years (age range between 30 and 62 years; 41.33±5.54). Individuals were notified of the nature of the study, by signing informed consent forms. All the subjects fulfilled the following general criteria; no history of systemic diseases, pregnancy, immunosuppression, antibiotic treatment, antimycotic and anti-inflammatory drugs in the 6 months prior to the study, previous periodontal treatment, use of orthodontic appliances, use of partial and/or total prosthesis and presence of local and/or systemic factors that predispose candidiasis.

Periodontal Examination

The assessed clinical variables were: plaque index (PI)[14], probing pocket depth (PPD), and clinical attachment loss (CAL). Probing pocket depth and attachment loss were measured using a standard periodontal probe, at six sites per tooth, i.e., distobuccal, buccal, mesiobuccal, distolingual, lingual, and mesiolingual, in all teeth, excluding third molars. A set of full-mouth standardized intraoral radiographs was obtained from each patient. The clinical diagnosis based on the classification of the American Academy of Periodontology (AAP)[15], was established according to clinical parameters and radiograph information. Patients were classified according to diagnosis and severity of Chronic periodontitis (CP) based on the probing pocket depth (PPD) and the CAL index (Clinical Attachment Loss), measured as a distance in mm from the cementoenamel junction to the bottom of the periodontal pocket, in 30% of the teeth; (American Academy of Periodontology 1999). Periodontitis is defined as the presence of clinical attachment loss in at least 2 nonadjacent teeth or the presence of buccal or oral clinical attachment loss ≥3 mm with pocketing >3 mm in at least 2 teeth[15]. Stages disease were defined according to severity of periodontal breakdown and the following criteria: Stage I, initial periodontitis where CAL at the site of greatest loss was 1 to 2 mm and maximum probing depth was 4 mm; Stage II, moderate periodontitis in which CAL at the site of greatest loss was 3 to 4 mm and maximum probing depth was 5 mm; Stage III, severe periodontitis with CAL at the site of greatest loss was ≥5 mm and probing depth was ≥6 mm. Based on these indexes, the patients were divided into 3 groups:

A. **Control group (CG)**: 20 periodontally healthy subjects;
B. **Moderate Chronic Periodontitis group (MCP)**: 20 patients with moderate chronic periodontitis;
C. **Severe Chronic Periodontitis group (SCP)**: 20 patients with severe chronic periodontitis (SCP).

Clinical specimens

Following full-mouth periodontal examination, two oral samples were collected for the microbiological study, one from the tongue and buccal mucosa and one from the gingival sulcus/periodontal pocket. The samples of oral mucosa were collected before the subgingival plaque sample, from mucosa of both cheeks and from the third half of the dorsal side of the tongue using small sterile cotton swab.

For each patient with periodontitis (PD≥ 3 mm), three to five samples were collected from the deepest probing site, while for PH subjects, subgingival plaque samples were collected from the gingival sulcus (PD ≤ 3 mm), by means of a sterile Gracey curette (S4L/4R SS). Swab cultures were immediately inoculated on chromogenic medium- (CHROMagar Candida) and incubated at 37°C for 48 hours (Biobase Constant-Temperature Incubator, BJPX-H30II) in the biochemical laboratory at the Faculty of Dentistry Ss. Cyril and Methodius University in Skopje.

After the incubation period, the plates were observed for fungal growth, using morphology and color to identify C. albicans, based on the pigmentation of the developing colonies, which is due to different enzyme activities from Candida species. This medium shows different color colonies for C. albicans (medium-sized colonies with a smooth surface, dark green to metallic green-blue) and Non-albicans Candida species (bright color, which can range from light pink, light blue to light green) (Figure.1)[16].

Figure 1. *Macroscopic appearance of the Candida species on the CHROM agar culture medium: C. albicans (metallic green-blue) Non-albicans Candida (bright color).*

Statistical Analysis

Standard methods of descriptive statistics were used. The statistical analysis was performed with the statistical program SPSS 23.0 and STATISTICA 8.0.

Results

Gender distribution showed no differences between the studied groups of patients; however, differences were observed in relation to the mean age, which were lower in the control group ($p < 0.01$).

Analyzing the presence of the plaque in examined groups (Figure 1), it was observed that dental plaque was registered in 4/20 patients in CG (18%), in 10/20 in MCP (50,8%) and in 12/20 in SCP (61,5%). PI was significantly higher in SCP compared to CG as shown in Figure 2 ($p< 0.01$).

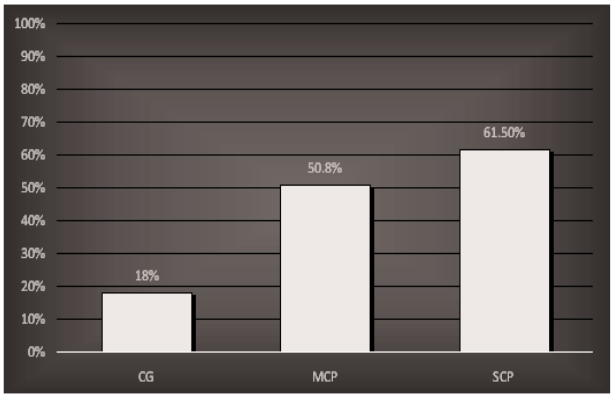

Figure 2. *The prevalence of dental plaque in examined groups: control group (CG), moderate chronic periodontitis group (MCP) and severe chronic periodontitis group (SCP).*

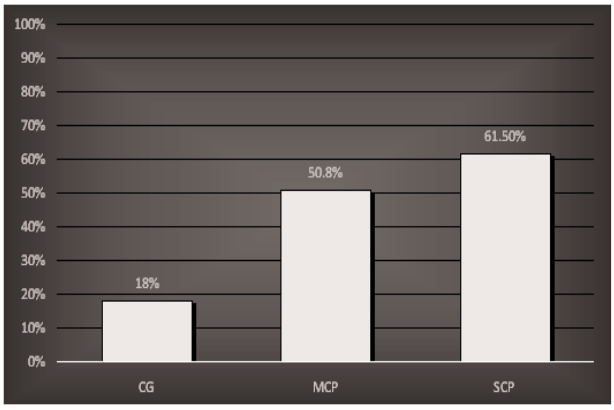

Figure 2. *Positive Candida colonization according to groups. CG-Control Group; MCP-Moderate Chronic Periodontitis group, SCP-Severe Chronic Periodontitis group.*

Considering all the individuals in each group, it was possible to observe that the most frequently colonized anatomic site was the oral mucosa, although no significant differences were found in the mucosa colonization

among the three groups ($\chi 2$, p = 0.060). Positive finding of Candida spp. at this site were found in 9/20 patients (45%) in CG, in 10/20 (49%) in MCP, and in 11/20 (52%) in SCP.

The subgingival findings of Candida spp. were positive in 3/20 (15%) at CG, in 6/20 (30%) at MCP and in 9/20 (45%) at SCP. Furthermore, a significant difference was observed in the number of total carriers in the SCP group with respect to the CG subjects (xi2; p= 0.014).

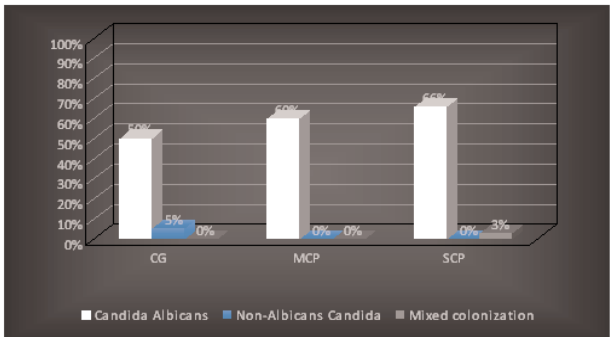

Figure 2. *Different fungal species according to the groups.*

CG-Control Group; MCP-Moderate Chronic Periodontitis group, SCP = Severe Chronic Periodontitis group.

In all studied groups, C. albicans was the most represented species. The highest percentage of C. albicans was isolated at SCP in 66% (13/20) with positive cultures, 60% (12/20) at MCP, and 50% (10/20) at CG. There were no statistical differences in the presence of C. albicans between groups (p>0.05). Non-albicans candida species were detected only at CG in 5%, they were not present in the other groups. Mixed colonization (C. albicans and Non-albicans Candida) was detected in 3% only at SCP group.

Discussion

Candida spp. colonizes the oral cavity, presenting the commensal or pathogenic properties that can be modified by direct or indirect interactions with different types of bacteria, depending on the localization of the microbial communities (e.g., supragingival plaque, subgingival plaque, and tongue coating).

Candida spp. is one of the fungi reported to be found in periodontal disease. The presence of its hyphae has been demonstrated in the connective tissue of periodontal patients in association with highly invasive anaerobic bacteria, such as Prevotella intermedia and Aggregatibacter actinomycetemcomitans[19]. These interactions, which are associated with their capacity to invade gingival connective tissue, may be important in microbial colonization that contributes to progression of oral diseases[20].

Yeasts and periodontal pathogens can interact physically, chemically, and metabolically to influence microbial survival, colonization, and biofilm formation. The pathogenic mechanism by which Candida species contribute to the progression of periodontal disease is attributed to the known virulent properties of these species, like adhesion, dimorphism, invasion, and biofilm formation, which facilitate colonization and proliferation in the oral mucosa and possibly in the periodontal pockets.

Anaerobic environment of the periodontal pocket can promote virulence of Candida spp. increasing the secretion of proteinases that damage tissues, modulate the immune response, and attract other periodontopathogens[18,21].

The subgingival biofilm, as the most complex microbial community, has been proven to be a reservoir of Candida spp. Biofilm formation is a major virulence factor in the pathogenicity of candida, and candida biofilms are difficult to eradicate especially because of their very high antifungal resistance[22].

A strong positive and significant correlation between Minimal Inhibitory Concentration MICs for subgingival isolates and full-mouth plaque score (FMPS) was also obtained, as a marker of oral hygiene for all antimycotics. This means that with a lower level of oral hygiene, which may provide conditions for maturity and higher complexity of biofilms, the MIC values increase. The susceptibility of C. albicans to antifungals correlates with oral hygiene and the severity of periodontal destruction[23].

In the present study (Figure1), dental plaque was detected in all studied groups, the expected lowest percentage (15%) was registered in the gingival sulcus in the control group, and the highest in the periodontal pockets in SCP (61.5%).

According to the obtained results from the present study, candida was present both in the oral mucosa and in the subgingival parts, in the studied subjects (Figure 2). The oral mucosa is still a place where candida develops in a higher percentage 45%, 49% and 52% in CG, MCP and SCP respectively, compared to the subgingival region (15%, 30% and 45%). The only exception is SCP, where an approximate percentage of candida (45%) was also registered in the subgingival region.

Several studies[25,26] have indicated a 35% prevalence of yeasts in oral mucosa in periodontally healthy subjects, which is somewhat lower than the 45% observed in this study. With respect to the subgingival sites of the CG, colonization of 15% suggest that, under normal conditions, yeast does not develop easily in the subgingival sites (Figure 2). The results from the present study are in accordance with previous studies (27,28,29) claiming

that not all mucosa carrier patients were also carriers in the subgingival sites, suggesting that the entrance of the yeasts to the subgingival areas is restricted. According to the study by Radunovic et al.[23], the prevalence of Candida spp. in subgingival areas in healthy subjects was up to 70%. Further, the cohorts of healthy subjects with periodontitis showed lower frequency of Candida spp. on the tongue, but the presence of subgingival Candida spp. varied from 14.3% to even 26.7%[30]. These studies initiate that subgingival areas may differ in incidence and/or species distribution of Candida from the oral mucosa, because of their differences. Subgingival biofilm is attached to a non-shedding hard surface, with different primary colonizers, pH and electrochemical potential and nutrients in the subgingival plaque differing from the tongue as well as the availability of oxygen, giving the subgingival area the potential to develop different biofilms from the tongue[31].

Most of the published studies about association of yeasts and periodontitis do not provide precise information relative to the severity of the disease. Several studies have indicated lower prevalence of yeasts in subgingival sites (17%), unlike 52,5% observed in the total sample of periodontitis patients in this study[8,11,13,17].

The percentage of yeast carriers in subgingival sites in periodontitis groups were similar. On the other hand, although no significant differences were found in the subgingival colonization among MCP (30%) and SCP (45%) (Figure 3), patients with SCP had a greater percentage of colonization than MCP and CG (15%).

Jabri et all.[32], reports that the prevalence of subjects with yeasts in the examined periodontal pockets has been ranging from 7.1- 9.6% to 15.6%. This suggests that subgingival colonization by candida species could be favored in chronic periodontal disease, and that they have a role to play in the infrastructure of periodontal microbiota[33]. The meta-analysis results demonstrated that Candida spp. detection rate and density were statistically significantly higher in CP patients than in subjects with clinically healthy periodontium. Whether this fact is the cause or consequence of periodontal disease, remains unclear[17].

As already mentioned, Candida colonization of the oral mucosa is not always associated with its presence in the subgingival regions, especially in patients who do not have periodontal pockets, but in already formed pockets with ulcerated and degenerated epithelium, there is probably a greater possibility of Candida entering the subgingival regions from the oral mucosa. It has been suggested also, that its presence in the subgingival area could be transient[34].

According to the obtained percentages for the subgingival presence of candida in the present study (CG-15%, MSC-30% and SC-45%), subgingival area as a reservoir of yeasts should be seriously considered. Candida spp. in subgingival areas is more resistant because it is always present within biofilms, and additionally these sites are inaccessible to conventional antifungal drugs[35]. In addition, refractory periodontitis, resistant to conventional therapy and requires systemic antibiotic therapy, may be associated with uncontrolled fungal growth in the periodontal pocket[36].

Usually, in clinical praxis, when candidiasis is suspected to be present, oral swabs are taken only from the oral mucosa, but not from the subgingival area. The mucosal colonization by C. albicans did not always ensure its presence in the periodontal pockets (confirmed by the lower percentage of candida in the subgingival parts vs mucosa)[37]. In contrast to this study, some cases were documented where C. albicans was isolated from periodontal pockets but not from the mucosa. This indicates that, in order to see the global picture of the yeast microbiota in the oral cavity, it is necessary to sample both the mucosa and the periodontal pockets[23,38].

With respect to the prevalence and yeast species profile, in mucous and subgingival sites, three different variants were identified at examined subjects: Candida albicans, Non-albicans Candida infection and mixed colonization (Figure 4). Candida albicans was the dominant yeast species found in both anatomical sites in all three groups. Although several yeast species were found, only C. albicans was present in all yeast-positive patients.

In the present study, ten periodontal healthy patients (50%) harbored C. albicans in the subgingival plaque. These results are high in comparison to other studies (8,36) which showed variable occurrence (16% to 36%) of C. albicans in the subgingival plaque of the healthy periodontium. Twelve patients (60%) with MCP presented yeasts in the subgingival biofilm, while thirteen patients (66%) in the SCP group were positive for these microorganisms. No statistical difference was observed between the examined groups ($P = 0.084$).

In the cases of patients without periodontitis (CG), only 5% of Non-albicans species were noted. The presence of Non-albicans species were not detected in MCH and SCH groups, except mixed colonization present only in SCP (3%). The results reported in this work, indicate that there are no significant differences in the characteristics of the yeast microbiota recovered from patients with CP when compared to patients without periodontitis. Also, the stages of the disease does not affect the type of candida. A possible explanation could be that the microenvironment hinders the co-existence of C. albicans with other yeast species, or where only C. albicans is capable of surviving given its wide range of virulence factors[39].

Urzúa's study[27] suggests that the degree of colonization is not related to the depth of the periodontal pocket in aggressive (AP) and chronic periodontitis (CP) groups, but with differences in the profile and in the diversity of species. The subjects with AP had C. albicans at all three depths, while C. dubliniensis, C. glabrata and C. albicans were noted in the CP patient population, probably related to co-existing of the periodontopathogens. In a study carried out by Popova et al.[40], no Candida species were observed in patients with chronic periodontitis, showing a negative correlation.

Certain studies report that detection rate of species such as C. glabrata, C. krusei, C. tropicalis and C. parapsilosis was similar in periodontal pocket samples and crevicular samples in CP patients and subjects with clinically healthy periodontium, respectively[41,42]. Colonization of periodontal pockets by these Non-albicans specie did not necessarily certify their activity in the pathogenesis of periodontitis. They can be transient members of the microbial consortium and can be evaluated as a potential reservoir for systemic distribution in case of favorable conditions[17].

Conclusions

Although the role of C. albicans in CP has not yet been established, this yeast is considered an important pathogen implicated in the pathogenesis of the tissue-destructive periodontal disease. However, further researches are needed to clarify the exact pathogenic mechanism of this opportunistic fungus in periodontal diseases.

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Declaration of Interest

We hereby state that no financial or material support was received for the work. No affiliation or organization will be affected by the material in the manuscript. We state that there is no conflict of interest.

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THE USE OF ND:YAG LASER IN ORAL SOFT-TISSUE SURGERY (CASE REPORTS)

УПОТРЕБАТА НА ND:YAG ЛАСЕРОТ ВО ОРАЛНА МЕКОТКИВНА ХИРУРГИЈА (ПРИКАЗ НА СЛУЧАИ)

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Abstract

Goal: To define the advantages and disadvantages of using the Nd:YAG laser in oral soft-tissue pathology (gingival enlargement, high frenulum attachment, operculectomy) treatment. **Materials and methods:** Case report of several different cases, where pain perceived by the patient, need of anesthesia, bleeding, duration of procedure, requirement of sutures, the occurrence of inflammation, scars formation were followed. For the procedures, Nd: YAG laser (1064 nm) was used with manufacturer's instructions for proper interventions. The aforementioned parameters were assessed with a numeric rating scale (NRS), with values of 0-5. **Results:** In the patients presented in this study, low levels of anxiety before intervention, reduced use of local anesthesia and significant hemostatic effect were detected. Also, the results showed minimum contraction of tissue without scarring, therefore application of sutures was not necessary. Reduction in post-operative pain was observed, with no inflammation. **Conclusion:** Lasers are effective and useful when it comes to soft-tissue surgery. They show clinical use with satisfying results if manufacturer's guidelines are strictly followed, and interventions are performed by experts and trained professionals. **Key words:** Nd: YAG; laser; soft-tissue surgery; gingivectomy; frenectomy; operculectomy.

Апстракт

Цел: Да се согледаат предностите и недостатоците при употребата на Nd:Yag ласерот во третманот на мекоткивната орална патологија (гингивални зголемувања, висок припој на френулум, оперкулектомија). **Материјал и метод:** Приказ на различни клинички случаи, во поглед на перцепирана болка од страна на пациентот, потреба од анесетезија, крварење при интервенција, времетраење на процедурата, потреба од сутури, појава на инфламација, формирање на лузни. За процедурите е користен Nd:YAG ласер (1064 nm) по упатствата на производителот за соодветните интервенции. Горенаведените параметри беа оценети со нумеричка скала за оценување (NRS), со вредности од 0-5. **Резултати:** Кај пациентите во оваа студија е забележно намалено ниво на страв пред интервенција, намалена употреба на локална анестезија и значително хемостатско дејство. Добивме минимална контракција на ткивото. Процедурите беа изведени без потреба од апликација на сутури. Кај пациентите нема постоперативни цикатрикси. Забележана е редукција во постоперативна болка, и не е забележана инфламација на ткивото во постоперативниот период. **Заклучок:** Употребата на ласерот има корисно и ефективно место во мекоткивната хирургија. Дава клинички задоволителни резултати доколку се почитуваат параметрите за употреба на произведувачот и доколку интервенциите се изведни од стручен и обучен кадар. **Клучни зборови:** Nd:YAG, ласер, мекоткивна хирургија, гингивектомија, френулектомија, оперкулектомија.

Introduction

Nd:YAG **(Neodymium: yittrum-aluminum-garnet)** The physical principles of the Nd: YAG laser are based upon Einstein's in the early 1900s. The first device was invented by Theodore Maiman in 1960. Only six years later, working prototypes of gas, liquid, solid, and semiconductor lasers had been constructed by several groups of investigators, spurred on by Maiman's achievement.

By the end of that decade, hundreds of materials had been found capable of laser action. The first prototype was made in 1961 by Snitzer E.

In 1990, the FDA is approving the Nd:YAG laser for usage in oral soft tissue surgery, thus making the laser an

optional approach in surgical treatments involving oral soft tissues. One of the first to successfully use the Nd:YAG Laser was White J.M.[1] doing soft tissue surgeries without using anesthesia and with minimal bleeding compared to conventional scalpel.

The Nd:YAG laser wavelength, which is produced for the specific active element, is characteristic and measured at 1064nm and the frequency measured in units of hertz (Hz) is the number of occurrences of a repeating event per unit of time.

The wavelength of the light is the primary determinant to the degree upon which the light will be absorbed in the target zone[2].

When the laser reaches biological tissue, the light can be reflected, scattered, absorbed, or transmitted to the surrounding tissues[3]. Nd:YAG laser penetrates up to 2-5 mm in depth, has high level potency of deep penetration compared to other lasers, with that said, the tissues/ structures under the surface are exposed to the laser energy. In the field of dentistry, Nd:YAG lasers work mostly in pulsed mode. Incision, excision, and removal of tissue is a result of photo ablative reaction defined by vaporization and superheating of the tissue fluids. The resulting hemostasis and protein denaturation form natural wound dressing and work towards lower infections, with no need for sutures and no scarring[4].

The work tip of the Nd:YAG laser offers flexible fiber delivery system with varying dimensions. For most applicable treatments, contact of the working fiber tip with the tissue is essential.

The use of Nd:YAG laser in soft tissue surgery

In the moment when the laser light is absorbed in the tissue, it is momentarily transformed into heat. The primary effect is photo – thermal, which results in structural changes: protein denaturation, vaporization – ablation of tissue, hemostasis, sterilization, carbonization.

The photo – thermal effect that is achieved by the laser lights tissue penetration and thermogenesis is useful, as it produces relatively thick layer of coagulation (0.3 – 0.8mm), which, in turn, guarantees hemostasis. This is beneficial as a therapy option, as it excludes post – operative infection, reduces post – operative inflammation, and provides a clear surgical field and better visualization during the intervention. This therapeutic modality is applicable in a wide range of indications: frenectomy, gingivectomy, gingivoplasty, de-epithelialization, periodontal flap, excision of granulated tissue, implant exposure, lesion ablation, incisional or excisional biopsy of benign or malignant lesions, coagulation of the donor side for the free gingival graft, crown – lengthening etc.

There is very few information available concerning tissue contraction and absent or low scarring that is strongly correlated with laser wavelength, and sensitive to the energy density or fluency (energy per unit area), as fluency is the most important parameter for laser therapy[5].

Delay in wound healing was registered by Romanos et Al.[6], but only in cases when 3W power and 20Hz pulsating tempo was used. Wound healing was similar or equal when comparing Nd:YAG laser and scalpel technique, with the following parameters used: 1.75 W and 20 Hz pulsating tempo. In relation to manufacturer's guidelines, in order to eliminate the need for using local anesthetic on the target place, initially the treatment should begin with the flexible fiber tip in non –contact position, 1W power and 10 pps (pulsating per second), for a period of 1-1.5 min. Following this, the power should be raised to 1.5 W for another period of 1-1.5 min, before starting the treatment. The soft tissue removal begins with 1.75 W power and 20 pps, while in contact mode. The value of 3 W and 30 pps should not be exceeded for this type of interventions.

A research presenting evidence that 90% of the patients were unable to go through the whole procedure without the administration of local anesthesia was published in 1999. Only 10 % of the patients included in this research didn't ask for additional anesthesia application[7]. Regarding these results, the use of local anesthesia became a routine for all patients, given that the laser pretreatment didn't secure the adequate analgesic effects.

The lasers are positively accepted by the patients as one of the available treatment options. Researches involving adults as well as pediatric patients, which required additional parental consent for undergoing laser surgery, showed that all the age groups involved had lower pre-operative stress level, compared to the scalpel technique. The treatment was accepted and chosen more frequently among other therapy approaches.

Goal

To define the advantages and disadvantages of using the Nd:YAG laser in oral soft-tissue pathology (gingival enlargement, high frenulum attachment, operculectomy) treatment.

Materials and methods

During our research, we had the opportunity to work with Nd:YAG (Fotona XP series) laser and present some of our clinical cases, as well as our findings. All the soft-tissue related surgeries, that we are going to present in this paper, were performed in our University Dental

Clinical Centre St. Pantelejmon, Department of Oral Health and Periodontology. All the surgeries were performed by the same surgeon, and the level of pain, fear and other aforementioned parameters were assessed with a numeric rating scale (NRS), with values from 0 to 5, with 0 being the lowest value, and 5 being the highest[8]. The numerical values in our scale were 0 - no pain; 1 - mild pain; 2 - moderate pain (discomforting); 3 - severe pain; 4 - very severe pain (horrible); 5 – the worst pain (excruciating). The graphically presented values of pain in the tables 1-4, present the initial level, before additional anesthesia was administered. Six of our patient are the subject of discussion in this paper, all at the age between 8 and 68 years. We measured and recorded our findings for the related topics of interest: stress, pain, bleeding, tissue contraction/scarring, post-operative pain, post-operative inflammation.

Results

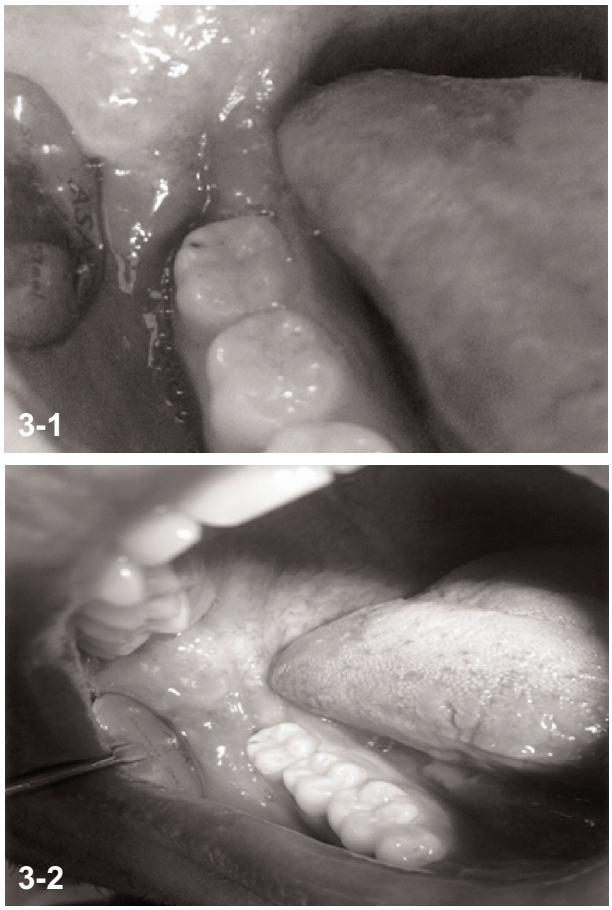
Clinical Case No.1 (Operculectomy)

Male Patient aged 25, presented with pain and difficulties when eating caused by pericoronitis (operculitis) on the lower right third molar. After discussing the patient's medical history, initial exam was performed. The patient was offered several options for treatment, whereas the approach with Nd:YAG laser was chosen. The settings used for this intervention were in the incision mode, power set at 3W and 20Hz frequency. Initial time was set for 60 sec with 20pps. The intervention started with application of topical anesthetic and incision in contact mode. (Picture 1, 2, 3-1, 3-2;)

Picture 1: *Showing initial situation*

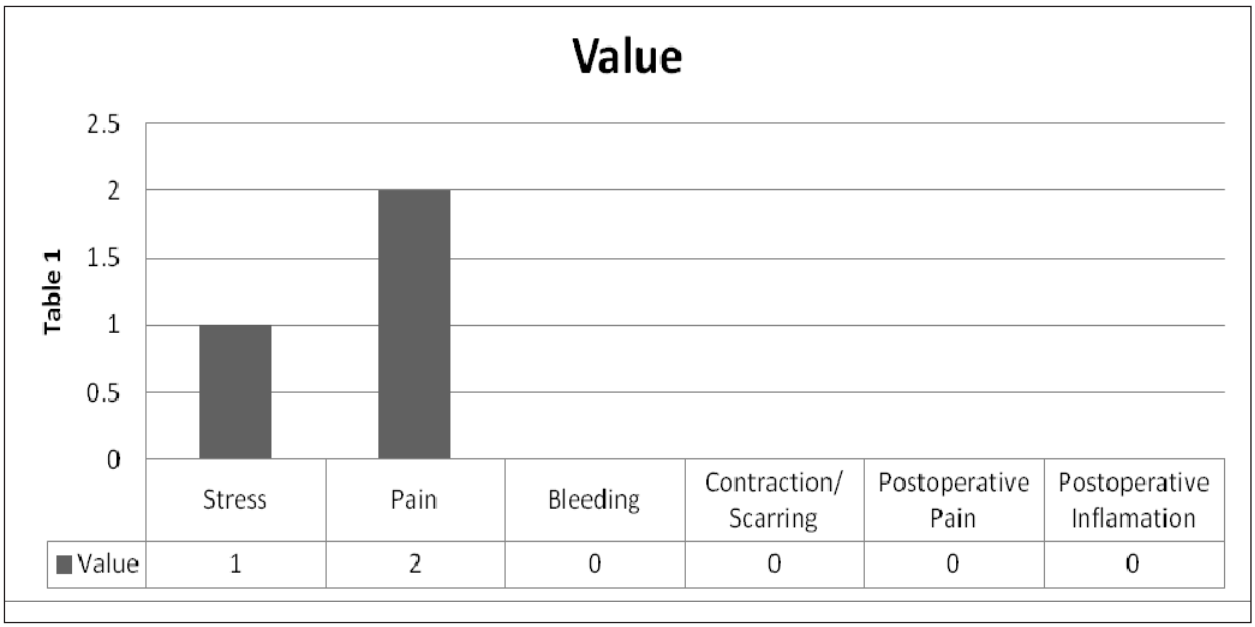
The patient was experiencing mild levels of stress and mild to moderate pain. In order to complete the intervention, mandibular nerve block anesthesia was administered. Bleeding was completely absent, due to coagulation, which provided a clean surgical field and better visualization. Sutures were not necessary due to the acquired hemostasis. The post-operative period was without any signs of pain or inflammation as well as no tissue contraction or scarring. (Table 1)

Picture 2: *Incision site immediately after surgery*



Picture 3. S-1/2: *One week later, incision site fully recovered*

Table 1: Numeric rating scale (0-5) presenting results in Case N° 1 (Operculectomy)



Clinical Case No.2 (Gingivoplasty)

Female patient, aged 15, underwent laser surgical removal of enlarged papillae. Medical history, initial intraoral and extraoral exam were performed at first visit. For the required procedure the settings were set at gingivoplasty mode, at 20Hz and 2W power. Pulsating

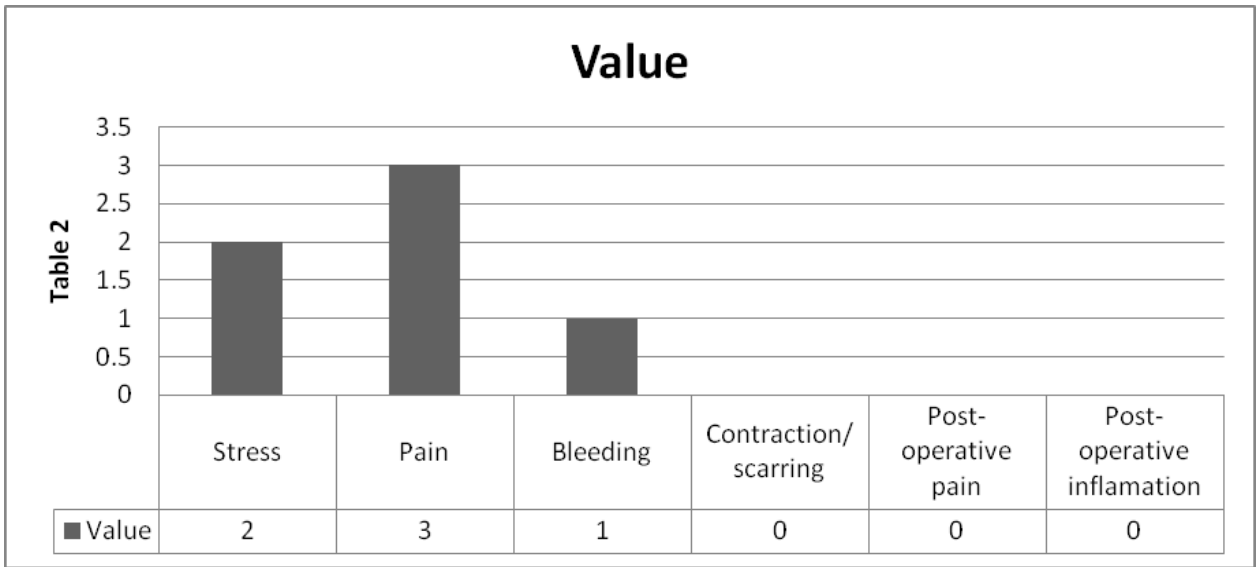
Picture 4: *Showing Initial Status*

Picture 6: *4 days after intervention*

Picture 5: *Status immediately after surgery*

Picture 7: *7 days after intervention*

Table 2: Numeric rating scale (0-5) presenting results in Case N° 2 (Gingivoplasty)

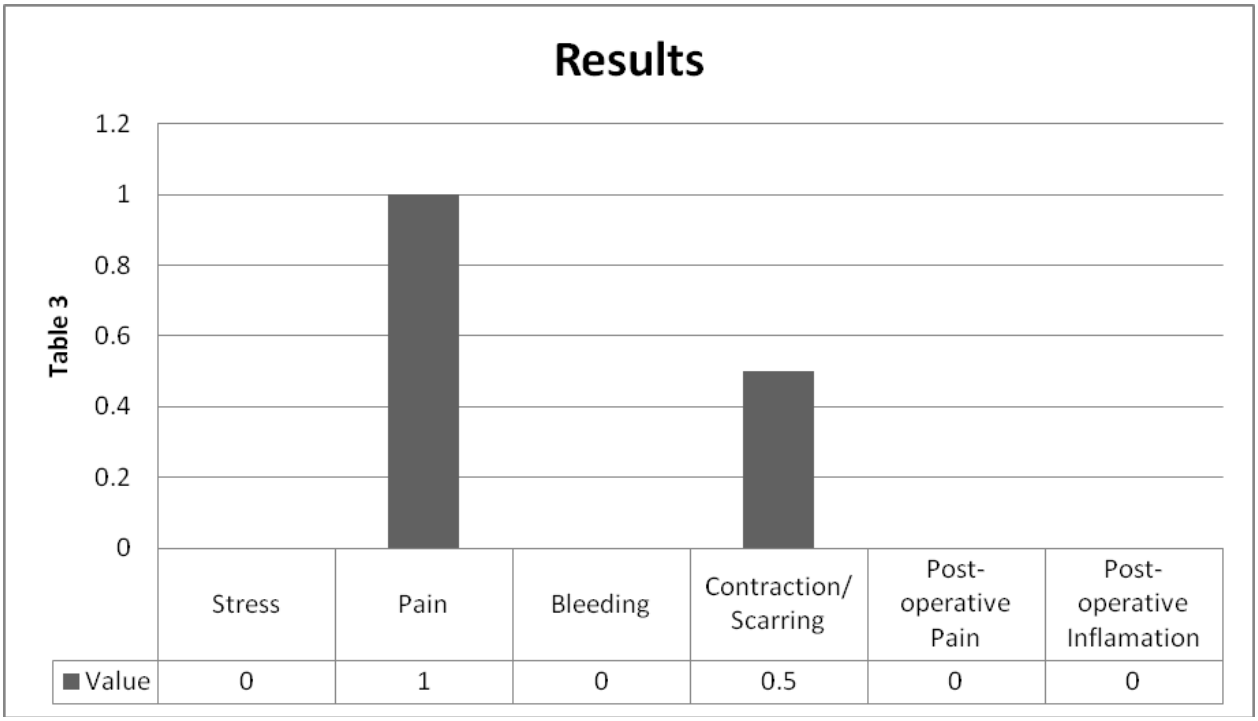


was set at 20 pps, for 60 seconds. Presenting the following results (Picture 4, 5, 6, 7). The patient was experiencing mild stress and moderate level of pain. The procedure was finished only with topical anesthesia. There was some mild bleeding that contributed to exacerbated visualization of the surgical field. Sutures were not necessary and zinc oxide eugenol based surgical packing was used. The post-operative period was without any signs of pain or inflammation as well as no tissue contraction or scarring. (Table 2)

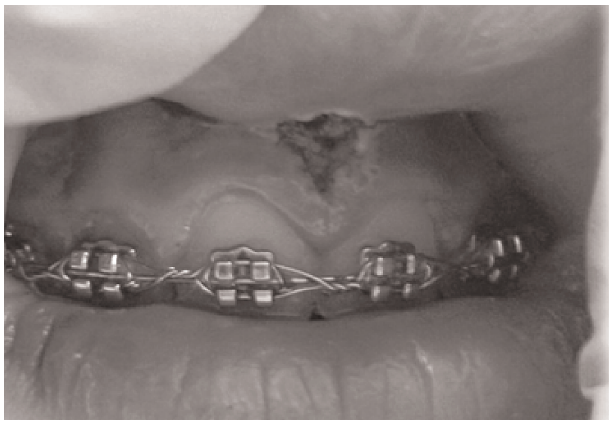
Clinical Case No.3 (Frenectomy)

Female patient, aged 9, after initial exam and diagnosis underwent laser surgery for frenulum removal.

Table 3: Numeric rating scale (0-5) presenting results in Case N° 2 (Gingivoplasty)

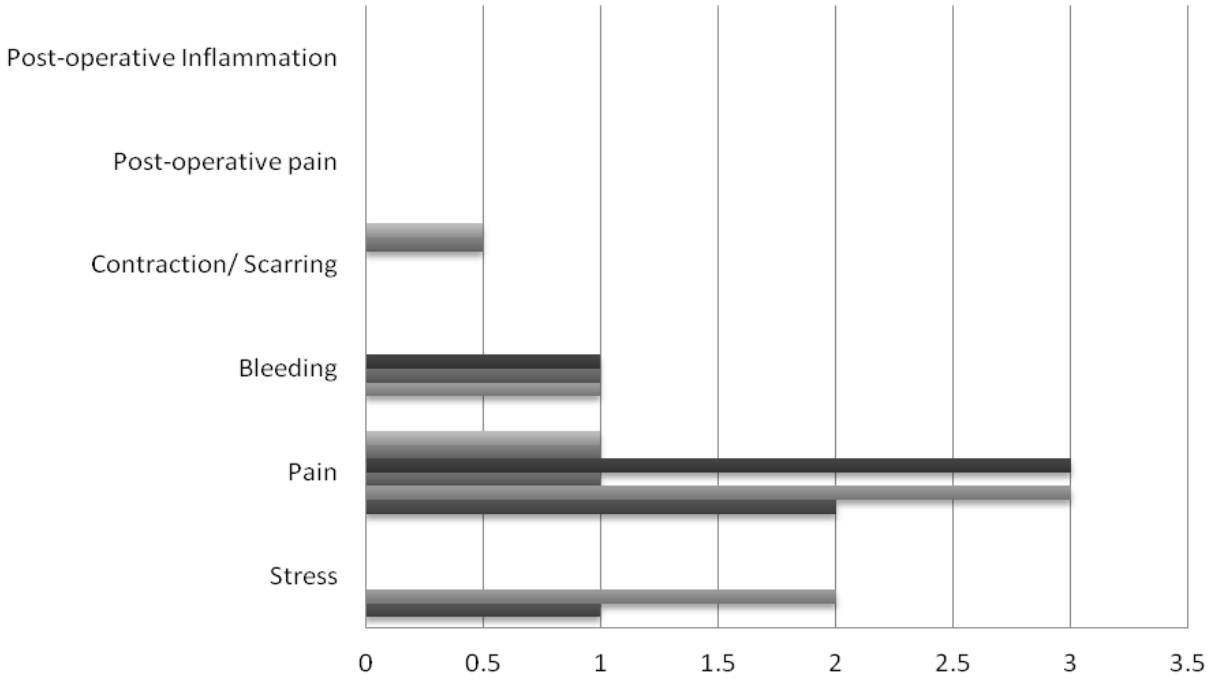


Picture 8: *Showing Initial Status*



Picture 9: *Status immediately after surgery*

Table 4: Numeric rating scale (0-5) presenting results in Case N° 2 (Gingivoplasty)



	Stress	Pain	Bleeding	Contraction/ Scarring	Post-operative pain	Post-operative Inflammation
Frenectomy 2	0	1	0	0.5	0	0
Frenectomy 1	0	1	0	0.5	0	0
Papilectomy 3	0	3	1	0	0	0
Papilectomy 2	0	1	1	0	0	0
Papilectomy 1	2	3	1	0	0	0
Operculectomy	1	2	0	0	0	0

Picture 10: *Status 7 days after the surgery*

Prior to the intervention, the necessary parental consent was obtained. Initially, the procedure started with application of topical anesthesia, the level of pain indicated that additional plexus block anesthesia was required. After administration of the anesthesia, the procedure was completed successfully. The settings used for this procedure were: 3W power, frequency of 20Hz and 20pps for an extended time of 60 sec at each turn (Picture 8, 9, 10). Sutures were not necessary and no surgical packing was used. There was moderate contraction that contributed to some scarring. The post-operative period was without any signs of pain or inflammation. (Table 3)

Aside from above mentioned, clinically described cases, the remaining 3 cases that were included in our review were another two cases of papillectomy and one frenectomy case. The following table is a graphic chart showing accumulated findings of all these cases, which, combined together, will contribute to the discussion regarding the advantages and disadvantages of using the Nd:YAG laser in soft-tissue surgery. (Table 4)

Discussion

Based on the considered scientific literature as well as the clinical results received from the patients in the study, the Nd:YAG laser has certain advantages that make it superior to the conventional scalpel technique in the field of soft tissue surgery. The removal of pigmented oral soft tissues, protein coagulation resulting in hemostasis and natural wound dressing, which brings out the preventive nature against bacterial opportunistic infection as well as bactericidal effect of the laser, that contributes to that prevention as well. This specific feature is something that is achievable only by this approach.

Another useful feature of this kind of procedure is the eliminated need for sutures. A study by M. Calisir and B. Ege[9] shows similar results, stating that after the operation, 77.5% of the patients (n=31) preferred laser frenectomy, while 22.5% (n=9) stated that conventional surgery was more preferable. The reasons for preferring the Nd:YAG laser method were mainly lack of sutures (31.4%) and less pain (29.4%). In addition, no bleeding during the operation was among the primary reasons of preference compared to the other methods. Also, the interventions take significantly less time, and without the part of suturing, patients are more comfortable, not having to take additional care of the stitches and without the financial cost for another visit to remove them.

The procedures are well accepted by all patients, young and adults. In a study by Yadav R.K[10], laser-group patients recorded significantly lower VAS score and used less analgesics than the scalpel group, indicating that laser-group patients experienced less pain during the procedure and post-operative time.

All the above-mentioned cases proved the beneficial outcome of the Nd:YAG laser regarding reduction of post-operative pain and inflammation as well as minimum or absent tissue contraction, with little or no scarring compared to the scalpel technique. In a study by Akpınar A.[11], similar results were presented stating that according to the female VAS scores of pain, chewing and speaking were statistically higher in the conventional group than those of the laser group on the operation day and first and third postoperative days. Male pain scores were statistically higher in the conventional group than those in the laser group on operation day. Male scores for discomfort while speaking were significantly higher in the conventional group than those in the laser group on the operation day and first postoperative day. In the conventional group, VAS scores for all parameters were significantly higher than laser group VAS scores on the operation day and first and third postoperative days.

As presented in a study by Romanos G.E[12], according to their findings, no clinically detected scar tissue formation could be established after the surgical incisions with the low-energy laser. With energy parameters of 1.75 W and 20 pulses per sec, the Nd:YAG laser presented a normal (not delayed) wound healing, compared to the control sites with the usual scalpel. This may have great advantages in the field of plastic and reconstructive surgery. Nd:YAG laser irradiation (wavelength of 1064 nm, 0.3 W, 10 pps, 30 mJ, 10.34J/cm2, irradiation time 60s) may contribute to regeneration of bone tissues due to enhanced osteoblast cell migration, as reported by Tsuka Y et al.[13].

On the other hand, some of our findings prove that the Nd: YAG laser analgesia is not effective with children, as they all experienced up to moderate levels of pain and, as mentioned before, the use of plexus block anesthesia was necessary in order to complete the procedure. Similar findings were reported by Mehmet M. Taskan et al.[14], as

they described, in 2 hour/8 hours/ 1, 2, 3, 4, and 5 days, Er:YAG laser and conventional surgery groups caused lower pain levels compared to the Nd:YAG laser ($p<0.05$). The disinfectant effects are a certain advantage, findings by Kadlecová M. et al.[15] stated that the Nd:YAG laser's (1.06 μm, 1,32μm, and 1.44 μm) disinfection effect is visible for all the three radiation wavelengths.

Some of the disadvantages of this laser, which we proved to be more difficult, are to remove some of the fibrous tissue, when certain procedures were made. The lasers are expensive and their servicing is additional cost that has to be considered as it affects the patient's cost of the surgical procedure.

Conclusion

The use of Nd:YAG laser was proven useful and effective in soft tissue surgery. It shows clinically satisfactory results, as long as manufacturer's guidelines are followed and properly trained medical personnel perform the interventions.

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Declaration of Interest

We hereby state that no financial or material support was received for the performed work. No affiliation or organization will be affected by the material in the manuscript. We state that there is no conflict of interest.

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THE ASSOCIATION BETWEEEN ESTROGEN AND PERIODONTAL DISEASE IN ADULT WOMEN

ОДНОСОТ ПОМЕЃУ ЕСТРОГЕНОТ И ПАРОДОНТОПАТИЈАТА КАЈ ВОЗРАСНИ ЖЕНИ

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Abstract

Literature supports the fact that estrogen plays an important role in skeletal maintenance and remodeling. Estrogen, acting through estrogen receptors in the cells of the periodontal ligament, has a regulatory interaction on bone dynamics through a complex set of basic multicellular units (BMUs). Deficiency of estrogen results in an increased number of BMUs and enhanced bone turnover. The impact of the changes in estrogen deficiency on bone dynamics is primarily mediated through osteoclasts, with greater interdiction of estrogen's actions on trabecular bone than on cortical bone. The purpose of this manuscript is to review literature for evidence to support the association between estrogen and periodontal disease in adult women, as well as bone mineral density, and to help clarify the mechanism of action. Key words: Estrogen, periodontal disease, bone, adult women, receptors.

Апстракт

Литературата го поддржува фактот дека естрогенот игра важна улога во скелетното одржување и ремоделирање. Естрогенот, дејствувајќи преку естрогенските рецептори во клетките на пародонталниот лигамент, има регулаторна интеракција во динамиката на коските преку комплексен сет на основни мултицелуларни единици(БМУ). Недостаток на естроген резултира во зголемен број на БМУ и зголемен обрт на коските. Влијанието на промените во недостатокот на естроген првенствено се посредува преку остеокластите и тоа повеќе на трабекуларната отколку на кортикалната коска. Целта на овој труд е да се разгледаат литературните податоци за асоцијацијата помеѓу естрогенот и пародонталната болест кај возрасни жени, како и густината на коската и механизмот на дејствување. Клучни зборови: естроген, пародонтална болест, коска, возрасни жени, рецепотри.

Introduction

Periodontal disease is observed more frequently in postmenopausal women whose menopausal status has been altered either surgically or as a side effect of chemotherapy. Oral bone loss may also be an indicator of periodontal disease[1,2]. However, the specific nature of the relationship between estrogen levels and periodontal disease is still being investigated. It suggested that women who were post-antineoplastic therapy had a higher plaque index, increased gingival inflammation and bleeding upon probing compared to healthy controls. With regard to periodontal disease, the weighted prevalence of severe gingivitis was 20.3% higher compared to the healthy control group[1]. Most chemotherapeutic agents affect estrogen levels by causing the death of ovarian cells. This is a result of the cytostatic effect of chemotherapy agents. These drugs prevent cell division of cancer cells and prevent cellular mitosis. However, normal cells are also killed, especially sensitive reproductive cells in the ovaries. This is known as "chemotherapy induced ovarian failure" which, in turn, causes a large decrease in estrogen that affects changes in bone mineral density. These changes are mediated by estrogen receptor alpha (ERa) and estrogen receptor beta (ERb.) Estrogen receptors are found in all layers of the gingival epithelium, buccal mucosa and salivary glands. Estrogen receptors exist as two subtypes: estrogen receptor alpha (ERa) and (ERb)[3].

Some research articles have shown that ERa was completely undetected in oral tissues, whereas ERb was expressed in high levels in oral epithelium and salivary glands[4,5]. The differential expression of ERb in these tissues may account for the conflicting results in estrogen receptor expression in earlier studies. In this study, the results show that a tissue-specific subtype distribution is also observed in oral tissues with ERb but not ERa. ERa is usually expressed in classic target tissues, such as breast tissue. The identification of ERb in these tissues has significant clinical importance and suggests a direct role for estrogen in the physiology of the oral mucosa and salivary gland function[4]. Forty percent of these cells demonstrate ERb immunoreactivity.

In a study by Pan, Zhang et al.[4], both estrogen receptors, ERa and ERb, have been detected in periodontal ligament cells (PDLCs). And both receptors have been shown to stimulate the bone formation capacity of cultured PDLCs by increasing alkaline phosphatase (ALP) activity, osteocalcin distribution and formation of mineralized nodules[6,7]. These compounds are markers for bone formation.

ALP activity was much higher in the estrogen-treated periodontal ligament stem cells (PDLSCs) than in the control group[6]. Additionally, in the estrogen-treated groups, the ALP activity was stimulated in a dose-dependent manner. The higher expression of ERa and ERb in PDLSCs as compared to PDLCs indicates a potential involvement of ERa and ERb in the process of estrogeninduced osteogenic differentiation of PDLSCs[8].

Evidence suggests that insufficient estrogen levels are a major cause of osteopenia and postmenopausal osteoporosis. Metabolic diseases that may also affect the levels of estrogen include hyperparathyroidism, hypopituitarism, Cushing's disease, adrenal insufficiency, rheumatoid arthritis and malignant disease. Several studies suggest that osteoporosis is a risk factor for periodontal disease and tooth loss[2-5,7]. Cells of the periodontal ligament are capable of producing all of the structures of the attachment apparatus. They can differentiate into osteoblasts (bone formation), cementoblasts (cementum formation) and fibroblasts (collagen formation)[8-10]. These cells also modulate the production of osteoclasts, which induce the breakdown of bone[5,8]. Estrogen plays a regulatory role in maintaining the balance between osteoblast production and osteoclast production. This role of estrogen is vital to maintaining normal bone mass and bone density. Thus, a relationship between estrogen levels and periodontal disease is plausible.

During menopause, the onset of ovarian deficiency (resulting in a decrease in estrogen levels) affects bone mass density (BMD). Normal loss of BMD is 0.7 percent per year during menopause. This may be explained by the inhibition of the down-regulating effects of osteoclasts, resulting in increased bone breakdown unlike bone apposition[8,11]. Other effects include loss of keratin, thinning of gingival tissues, redness, soreness and decreased salivary gland function. Estrogen can also modulate the pathogenicity of periodontal pathogens, such as P. Gingivalis and P. Intermedia; and it is reasonable to expect that its reduction may imply more severe periodontitis.

A study by Bin Zhang, Ying Li, et al.[12], utilizing ovariectomized rats with induced periodontitis and a SHAM control, explored the effect of estrogen on the potential for osteogenic differentiation of periodontal ligament stem cells. The results showed there was a lower expression of estrogen receptors (ERa and ERb) in the ovariectomized group than the sham group. Treatment with 17beta estradiol significantly increased osteogenic differentiation of PDLSC in both groups in vitro. The results seem to indicate that estrogen plays an important role in maintaining osteogenic differentiation of periodontal stem cells, which act through ERa and ERb[3].

Evidence suggests that "estrogen deficiency leads to impaired osteogenic differentiation of periodontal stem cells in rats"[12,14-16].

Stossi et al.[4] demonstrated that both ERa and ERb transcriptionally up-regulated bone morphogenic protein-6 (BMP-6), a key factor in bone formation. This supports the findings of the present study by Feng Pan, Zhang, et al.[4] that both ERa and ERb may function in the osteogenic differentiation of periodontal stem cells. This difference may be explained by the fact that in the different types of cells, the varied expression patterns of ERa and ERb are under the control of specific mechanisms. Investigators have also considered the role of a variety of inflammatory cytokines and growth factors and the effect of estrogen on the gingival fibroblast. Cytokines, such as interleukins and interferons, are substances that are produced by specific cells of the immune system and have an immune modulating effect and are critical to the functioning of the immune system[14].

Estrogen may suppress osteoclastogenesis by modulating the synthesis of cytokines produced locally by human PDLCs. There is now convincing evidence that estrogen, acting through ERa, stimulates osteoclast apoptosis 16 and, conversely, suppresses osteoblast and osteocyte apoptosis. Therefore, estrogen deficiency is associated with an increase in the lifespan of osteoclasts, as well as a concomitant decrease in the osteoblastic lifespan[15].

During the postmenopausal process, women lose 30% to 50% of the trabecular bone and 25% to 35% of the cortical bone mass that was present during the peak bone mass years between ages 20 to 30 (normal bone loss averages 0.7% per year)[17]. Postmenopausal women with osteoporosis and concurrent periodontitis may show a loss of dentoalveolar bone height and decreased BMD of the alveolar crestal and subcrestal bone[17].

Clinical research by Atkinson et al.[18] demonstrated a reduction in bone mineral content between six and nine months after MTX treatment (methotrexate, cytostatic drug and, thus, lowers estrogen production). It is unknown whether the bone mass remains depressed indefinitely, slowly recovers to normal levels or recovers to osteopenic levels below the normal range. It is known that one course of methotrexate therapy will induce osteopenia and depress bone formation 14 days following treatment[18].

Friedlander et al.[19,20] also reported significant reduction (27%) in cancellous bone volume after one course of methotrexate. There is an important association between loss of bone mass and periodontal disease.(21) Kribbs showed there was a significant correlation between skeletal bone mass measurements and the number of remaining teeth[21].

Yoshihara et al. and Klemetti et al. showed that the BMD of the mandible is affected by the mineral status of the skeleton and by any disease that causes generalized bone loss[22]. Ward and Manson were able to find an association between the periodontal disease index and alveolar bone loss[23].

Groen et al. assessed the relationship between osteoporosis or low bone density and clinical attachment loss. Toothlessness and severe periodontal disease were found in 38 patients aged 43 to 73 who exhibited clinical and radiographic signs of advanced osteoporosis[24]. Most studies showed a correlation between reduced bone mineral density and increased severity of periodontal disease.

The findings from the Women's Health Initiative (W.H.I.) on 42,171 postmenopausal women showed the overall risk of tooth loss was 24% lower in current hormone replacement therapy (HRT) users when compared to nonusers. Furthermore, the results showed that estrogen may promote tooth retention by strengthening the periodontal attachment surrounding the teeth, without increasing oral bone height or decreasing oral bone porosity.

Tagutchi et al.[25] and Grossi[26] further showed that women who were not treated with estrogen replacement therapy (ERT) were twice as likely as their ERT counterparts and three-times more likely than premenopausal women to exhibit severe attachment loss. The individual percentages of women affected by severe attachment loss were 18.6%, 11.9% and 6.3% for non ERT, ERT and premenopausal women, respectively. Also, severe alveolar bone loss (ABL) was detected in 34%, 20.3% and 9.7% of the non-ERT, postmenopausal ERT, and premenopausal women, respectively. The authors, therefore, concluded that ERT appears to have a protective effect on the severity of periodontal disease and the periodontium[26]. The duration of estrogen use was significantly associated with the number of remaining teeth.

Discussion

At this time, a thorough review of all databases revealed there are few studies that provide evidence of the direct association between estrogen deficiency, and periodontal disease and between BMD and periodontal disease. Furthermore, there are no prospective observational studies to assess estrogen as a risk factor for periodontal disease that account for confounding factors such as age, socioeconomic status, nutrition, smoking and health status.

Clinicians have found that "HRT (hormone replacement therapy) can improve the clinical outcome of periodontal disease and may serve as an effective adjunct treatment for preserving periodontal bone mass"[4].

Despite these limitations, there is evidence to suggest an association between estrogen and periodontal disease, because estrogen receptors are found in the cells of the periodontal ligament, gingiva, salivary glands and jaw bone. Estrogen has an effect on these tissues and exerts its effect locally. These effects include maturation of gingival connective tissue, osteoblastic differentiation and mineralization. Estrogen deficiency will alter skeletal remodeling and, thus, affect bone mass density, and bone volume.

Conclusion

Estrogen, acting through ERa and ERb located in the cells of the periodontal ligament, may have a significant impact on the periodontium. Estrogen receptors have a regulatory effect on both the maturation of gingival epithelium and on the osteoblastic differentiation of periodontal ligament cells. ERb may play an important role in bone formation.

Estrogen deficiency may result in osteoporosis, which is considered to be a risk factor for periodontal disease, loss of BMD and tooth loss. Both disease processes share common risk factors, are inflammatory in nature, and are bone-resorptive entities.

Further research is necessary to establish better associations between periodontal disease, estrogen and bone mineral density, so that at-risk patients can be identified earlier to avoid the functional and esthetic sequellae of periodontal disease.

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