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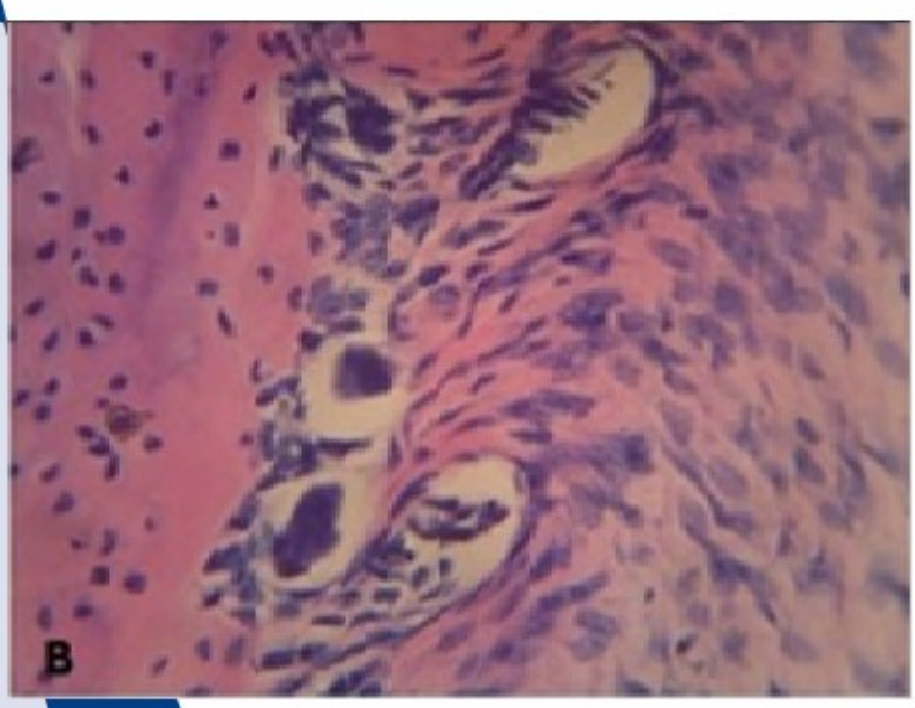

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Aims and Scope

Cumhuriyet Dental Journal (CDJ) is an international journal dedicated to the latest advancement of dentistry. The aim of this journal is to provide a platform for scientists and academicians all over the world to promote, share, and discuss various new issues and developments in different areas of dentistry.

CDJ publishes original research papers, reviews, and case reports within clinical dentistry, on all basic science aspects of structure, chemistry, developmental biology, physiology and pathology of relevant tissues, as well as on microbiology, biomaterials and the behavioral sciences as they relate to dentistry.

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The Potential of Bisphosphonate Risedronate Hydrogel in Preventing Relapse Movement

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Research Article

History

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ABSTRACT

Objectives: To analyze the effect of risedronate hydrogel on enzyme alkaline phosphatase (ALP) and osteoclast/osteoblast ratio during tooth relapse movement

Materials and methods: The research design is experimental with time series. The lower incisors of 75 guinea pigs are distally moved using open coil spring. The guinea pigs were divided into three groups: without risedronate (group A; n = 25); given 250 µmol/L of risedronate hydrogel (group B; n = 25), and given 500 µmol/L of risedronate hydrogel (group C; n = 25). Risedronate were applied intrasulcularly in the mesial part of the gingival sulcus every 3 days. After 14 days of stabilization, the open coil spring was removed (bisphosphonate administration was continued). The relapsed teeth and ALP levels on days 0, 3, 7, 14, and 21 were measured. The osteoclast/osteoblast ratio was measured by hematoxylin and eosin staining. ANOVA test was used to determine the difference in the three groups and their interactions with concentration and time.

Results: There was a significant difference in osteoclast/osteoblast ratio on day 3 and 14 the ratio was higher in group A than in groups B and C on day 3, and the ratio was higher in group C than in groups A and B on day 14. ALP levels were significantly different on day 14 and 21.

Conclusions: The intrasulcular application of bisphosphonate risedronate affected the osteoclast/osteoblast ratio and increased ALP levels.

Keywords: Alkaline Phosphatase, Orthodontics, Osteoclasts, Risedronic Acid, Tooth Movement.

Ortodontik Nüks Hareketi Esnasında Bisfosfanat Risedronat Hidrojel'in Alkalin Fosfataz ve Osteoklastlar Üzerine Etkisi

Süreç

Geliş: 10/12/2021
Kabul: 12/01/2022

ÖZ

Amaç: Dişin relaps hareketi sırasında risedronat hidrojelin enzim alkalin fosfataz (ALP) ve osteoklast/osteoblast oranı üzerindeki etkisini analiz etmek.

Gereç ve Yöntem: Araştırma tasarımı zaman serileri ile deneyseldir. 75 kobayın alt kesici dişleri, açık helezon yay kullanılarak distale doğru hareket ettirilir. Kobaylar, risedronat uygulanmayan (grup A; n = 25); 250 µmol/L risedronat hidrojel uygulanan (grup B; n = 25) ve 500 µmol/L risedronat hidrojel uygulanan (grup C; n = 25) olmak üzere 3 gruba ayrıldı. Risedronat gingival sulkusun mezial kısmına 3 günde bir intrasulküler olarak uygulandı. 14 günlük stabilizasyondan sonra, açık helezon yay çıkarıldı (bifosfonat uygulamasına devam edildi). 0, 3, 7, 14 ve 21. günlerde nüks eden dişler ve ALP seviyeleri ölçüldü. Osteoklast/osteoblast oranı hematoksilen ve eozin boyama ile ölçüldü. Üç grup arasındaki farkı ve bunların konsantrasyon ve zamanla etkileşimlerini belirlemek için ANOVA testi kullanıldı.

Bulgular: Osteoklast/osteoblast oranında 3. günde ve 14. günde anlamlı bir fark vardı: 3. günde grup A'da grup B ve C'den daha yüksekti ve 14. günde grup C'de grup A ve B'ye göre daha yüksekti. ALP seviyeleri 14. günde ve 21. günde önemli ölçüde farklıydı.

Sonuçlar: Bifosfonat risedronat intrasulkuler uygulaması osteoklast/osteoblast oranını etkilemiş ve ALP düzeylerini yükseltmiştir.

Anahtar Kelimeler: Alkalen Fosfataz, Ortodonti, Osteoklastlar, Risedronik Asit, Diş Hareketi.

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Introduction

Orthodontic treatment aims to achieve occlusal balance and correction of stable teeth, but there remains an important problem in orthodontic treatment, that is, relapse.[1] Research conducted by Vaida *et al.*[2] shows that, from 771 samples of patients who returned to control after 6 months of post-orthodontic treatment with the use of a retainer, 72 (10.13%) patients experienced relapses. There were 41 (5.77%) patients who experienced relapses 12 months after using the retainer and 19 (2.67%) patients who experienced relapses 24 months after using the retainer.

Relapse is a condition in which the teeth alignment is returned to pre-orthodontic treatment. Relapse can be due to patient noncompliance with the retainer and occlusion of incomplete treatment results. The tooth began to relapse into its original position as soon as the orthodontic appliance was removed. Orthodontic relapse and orthodontic tooth movement undergo the same process, namely, an increase in osteoclast differentiation in the stress area and a decrease in the stress area;[3] therefore, post-orthodontic relapse involves tooth movement within the alveolar bone and a bone modeling process that requires osteoblast homeostasis in the stretch area and osteoclasts homeostasis in stress area.[4]

Bisphosphonates have been reported to inhibit bone resorptive function by osteoclasts and reduce relapse. Simvastatin can prevent relapse by inhibiting osteoclast bone resorption activity and stimulating bone formation. Bone morphogenetic protein has also been used to inhibit relapse, and the results have shown that it can promote bone and cementum formation. The results of the study of Zhao *et al.*[5] using osteoprotegerin (OPG) showed significant inhibition of relapse and decreased number of osteoclasts. These data suggest that relapse can be inhibited by manipulating alveolar bone remodeling.

Bisphosphonates are synthetic analogs of pyrophosphate that are powerful inhibitors of bone resorption and are usually used as drugs for the prevention and therapy of osteoporosis and osteopenia, as well as for the treatment of tumors. The use of bisphosphonates can cause side effects in dental care, such as interfering with bone healing, inhibiting tooth movement, and causing osteonecrosis of the jaw[6] or bisphosphonate-related necrosis of the jaw (BRONJ). BRONJ is a condition in which the bone necrotizes; it does not heal for 8 weeks in the oral cavity due to bisphosphonate exposure. This can be due to the duration, dose, and route of intravenous and oral administration of bisphosphonates, which have a systemic effect. Also, the risk of BRONJ is increased with invasive dental procedures or exposure to high doses of bisphosphonates via the intravenous route. Invasive dental procedures such as tooth extraction will cause thrombus formation (blood clot) and create granulation tissue, and mineralization of the bone occurs. Bisphosphonates that have been bound to the bone will be slowly resorbed while the bone in the area that is removed still contains bacteria and cannot be resorbed. As a result, wound healing will take longer, increasing the risk of bacterial invasion that will cause chronic osteomyelitis.[6-8] Relapse occurs when the orthodontic treatment has been complete, the teeth are well arranged and oral hygiene is good, and does not require invasive action such as extraction, therefore, it is very unlikely that BRONJ will occur.

Bisphosphonates can prevent bone resorption by inhibiting osteoclast differentiation and activity, as well as breaking the attachment of mature osteoclasts to the bone, triggering apoptosis so that it can inhibit bone resorption[9]. Bisphosphonates are of two types: nitrogenous and nonnitrogenous.[10] One of the nitrogenous bisphosphonates that are often used is the risedronate type, which is known to have an effect through binding to hydroxyapatite in bone tissue, inhibiting osteoclastic activity, and inducing osteoclast apoptosis. Risedronate also induces apoptosis of macrophages at relatively low concentrations when compared to other bisphosphonates such as alendronate and pamidronate *in vitro.*[11] Several authors reported that bisphosphonates also influence osteoblast proliferation and differentiation, partly via the macrophage-activated protein kinase pathway and through different enzyme regulations.[12]

Osteoblasts are bone-forming cells responsible for the mineralization of the bone matrix by secreting type I collagen and releasing calcium, magnesium, and phosphate ions.[13] Increased activity of osteoblasts during bone formation will be accompanied by increased secretion of the enzyme alkaline phosphatase (ALP).[14] ALP has been widely recognized as a biochemical marker of osteoblast activity.[15] ALP is synthesized and secreted by osteoblasts during the bone formation process. ALP expression can reflect the biochemical changes that occur in the supporting tissue after orthodontic force[16], and in several studies, elevated ALP levels have been detected during orthodontic movement at weeks 1–3.[17]

One of the most up-to-date drug carrier materials that have biocompatible and biodegradable properties is hydrogel.[18] Hydrogel can be used to control drug release so that the drug can optimally work in topical applications.[19]. The active substance of the bisphosphonate risedronate carried by the gelatin hydrogel carrier medium and applied intrasulcular is expected to provide a local effect to prevent the occurrence of tooth relapse after orthodontic movement. This study was conducted to obtain an overview of the effect of the active substance bisphosphonate risedronate carried by the gelatin hydrogel carrier and applied intrasulcularly to the gingival crevicular fluid (GCF) ALP, as well as the ratio of the number of osteoclasts and osteoblasts during the movement of tooth relapse so that it is expected to have the potential to inhibit relapse. This study aims to determine and analyze the effect of bisphosphonate risedronate hydrogel on ALP and osteoclast/osteoblast ratio during tooth relapse movement.

Materials and Methods

Ethics committee approval

Research with experimental guinea pigs has received approval from the Research Ethics Commission of the Faculty of Veterinary Medicine, Gadjah Mada University (number 355/KKEP/FKH UGM/EC/2012).

Experimental animals

This study consisted of three groups: control (group A), those administered with risedronate at a concentration of 250 µmol/L (group B), and those administered with risedronate at a concentration of 500 µmol/L (group C). Control is the group that relapsed without receiving any treatment. Each group will be observed on days 0, 3, 7, 14, and 21; therefore, there are 15 groups with five guinea pigs each. Seventy-five male guinea pigs weighing 0.5–0.6 kg were fed and caged (Tomiwa, Japan) at room temperature. During the study, health and weight checks were carried out every day.[20]

Making hydrogel biphosphonate risedronate

The preparation is made using the active substance of the bisphosphonate risedronate, namely, risedronate sodium, which is made using gelatin hydrogel as a carrier so that the drug can have a topical effect. Gelatin (3%) was dissolved in distilled water and then homogenized with a magnetic stirrer for 3 hours at 37°C. Risedronate sodium was added; then, it was stirred for 2 hours, and NaOH was added until a neutral pH (7) was achieved. The mixture is added with a glutaraldehyde solution with a concentration of 25%, washed using glycine and milli-Q three times, and stored in a freezer at -300°C. Lyophilization was carried out afterward using a freeze dryer for 48 hours. The hydrogel will change from semisolid to solid. The hydrogel gelatin block matrix is then processed into microsphere preparations. When used, this preparation is mixed again using distilled water with a ratio of 1:20 (w/w). The final preparation is placed into the injection syringe and is ready to be applied.[21]

Treatment

The guinea pig was anesthetized with ketamine and xylazine by intramuscular injection in the thigh; then, a bonding cleat was placed on the lower incisors. A round stainless steel wire with a diameter of 0.016 and open coil spring with a length of 1.5 times the inter cleat distance (measured using a sliding caliper) were installed between the cleats. After the teeth moved and the open coil spring was no longer active, the open coil spring was replaced according to the new inter-clear distance until an inter-incisor distance of ±3 mm was obtained. A distance of ±3 mm was maintained for 14 days as a stabilization period. In the treatment group, bisphosphonate risedronate was administered in the form of a hydrogel dosage by intraligament injection every 3 days (Figure 1). After stabilization for 14 days, the wire and open coil were removed. The treatment group was still given topical bisphosphonate risedronate, and the relapse of the teeth on days 0, 3, 7, 14, and 21 was observed.

Alkaline phosphatase measurement

Sampling was carried out on days 0, 3, 7, 14, and 21. The area around the teeth was cleaned with cotton pellets to maintain the purity of the GCF so as not to be contaminated. Paper points are inserted approximately 1 mm into the gingival sulcus for 30 seconds with 90-second intervals to increase the volume of GCF taken per side (Figure 2). The Eppendorf tube was centrifuged for 5 minutes at a rate of 2000 g to elute the complete GCF components. Paper points were taken, and the supernatant solution was stored at -80°C until it was analyzed for a maximum of 1 week. ALP activity was determined using a spectrophotometer (model 6330 Jenway UK) at a wavelength of 405 nm.[22]

Figure 1. Bisphosphonate risedronate hydrogel is injected intraligamentary

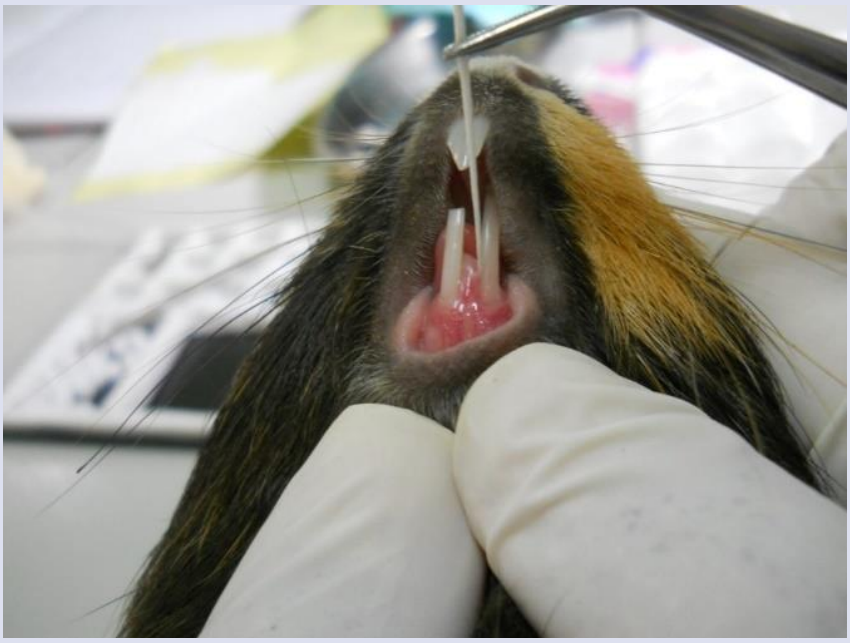

Figure 2. Gingival crevicular fluid withdrawal

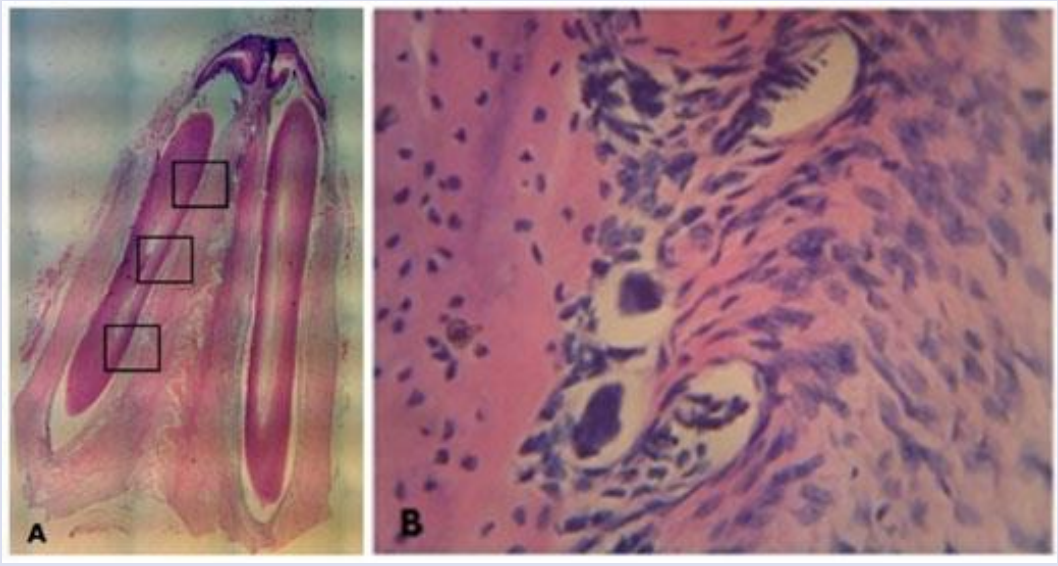

Figure 3. H&E: A. Staining three fields of view in one slide of the mesial side. B. Image of osteoclasts and osteoblasts in one field of view.

Measurement of the osteoclast/osteoblast ratio

The guinea pig was decapitated, and the mandibular alveolar bone was dissected until all the mesial and distal sides of the right and left lower incisors and the root ends of the teeth were removed. Preparations and staining were carried out at the Histology Laboratory of the Faculty of Medicine using hematoxylin and eosin (H&E) staining. The number of osteoclasts and osteoblasts was measured at the Pathology Laboratory of the Faculty of Veterinary Medicine. The data were obtained by calculating the mean number of osteoclasts and osteoblasts from three fields of view that were randomly taken on the slices of the preparation. Observations were carried out by two observers, namely, researchers (TR) and veterinarians at the anatomical pathology from Faculty of Veterinary Medicine (YN). The results of the first observer's observations were clarified to the second observer. Osteoclasts are multinuclear cells containing 4–20 nuclei and are found in contact with bone surfaces and within the lacunae. Osteoblasts were found in cuboidal cell clusters along the cell margins of the new bone (Figure 3). Osteoblasts are flat and round, essentially one or mononuclear cell usually lined up on the bone surface. Osteoblasts are usually found on the surface of solid bones, while osteoclasts are usually present in basins because the bone area has been resorbed and the cells are large and multinuclear/multinucleated.

Statistics

The data obtained in this study were statistically analyzed by SPSS. The homogeneity and normality test was carried out followed by one-way ANOVA test to determine differences in ALP levels and osteoclast/osteoblast ratios on days 0, 3, 7, 14, and 21 in groups A (without risedronate), B (250 µmol/L), and C (500 µmol/L). To find out which group of days had the most influence, the least significant difference (LSD) test was used. There is a significant difference if $p<0.05$.

Results

Effect of bisphosphonate risedronate hydrogel on alkaline phosphatase levels

The results of measuring the levels of ALP on days 0, 3, 7, 14, and 21 in the group without risedronate bisphosphonate (A), group that was given bisphosphonate risedronate at a dose of 250 µmol/L (B), and group that was given bisphosphonate risedronate at a dose of 500 µmol/L (C). The results showed that there was a significant difference in the increase in ALP levels on days 14 and 21 (Figure 4).

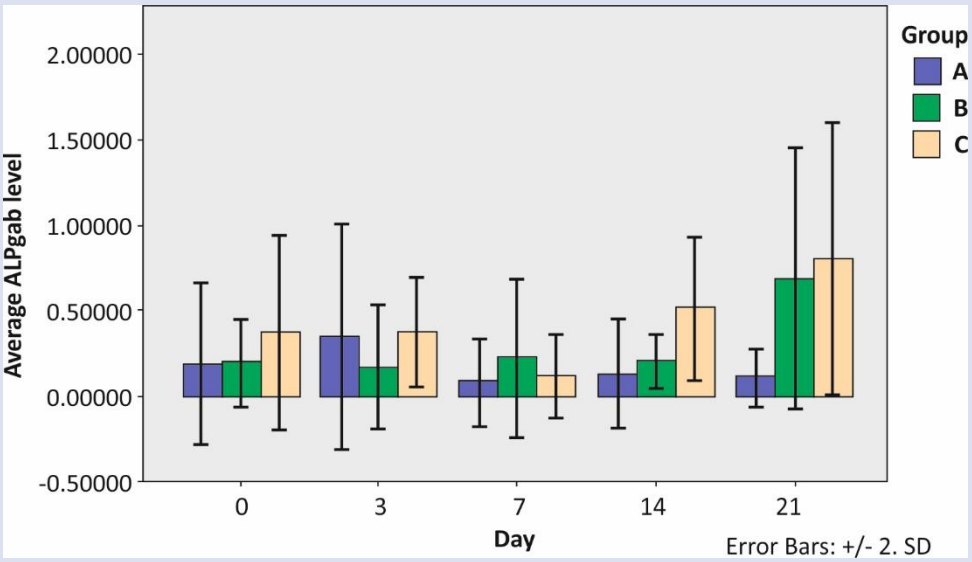

Figure 4. Effect of bisphosphonate risedronate hydrogel on ALP levels. There is a significant difference in the increase in ALP levels on days 14 and 21.

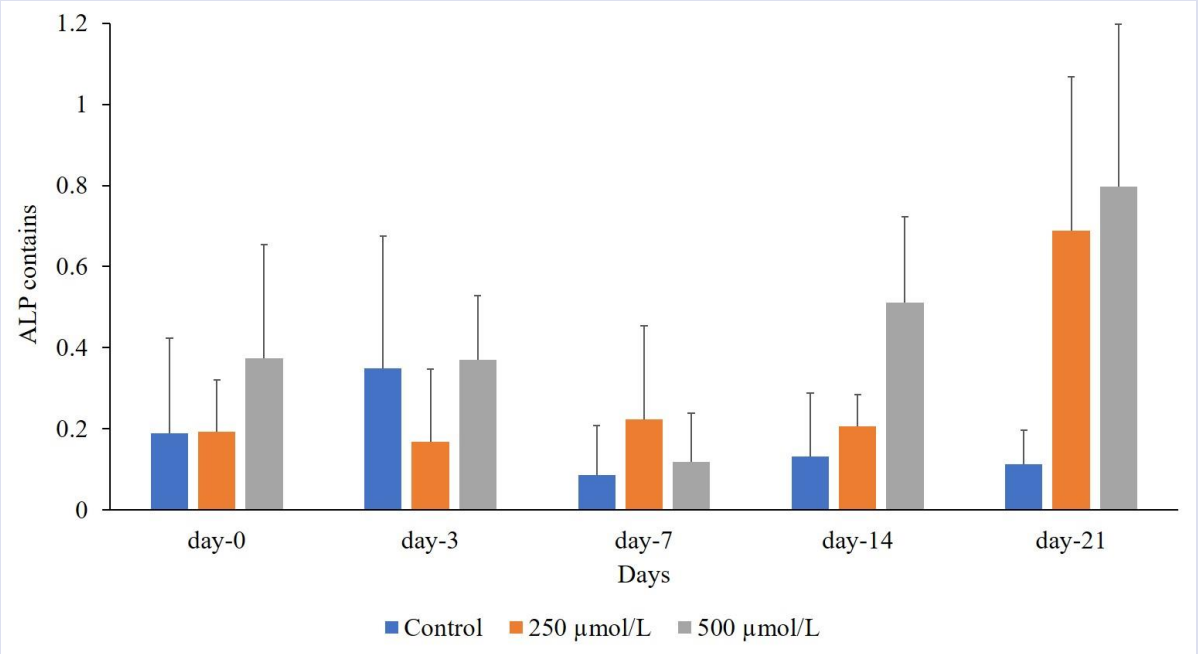

Figure 5. The effect of bisphosphonate risedronate hydrogel treatment to ALP level. There is a significant increase of ALP in 14th and 21st day.

The results of the multiple comparisons (LSD) test showed that there was a significant difference on the 14th day between groups A and C and groups B and C, and on the 21st day between groups A and B and groups A and C (Figure 5). The data is significant if the p-value is <0.05.

Effect of bisphosphonate risedronate hydrogel on alkaline phosphatase levels

The results of measurements of the number of osteoclasts and osteoblasts on days 0, 3, 7, 14, and 21 in groups A, B, and C are shown in Figure 6, as well as the results of the one-way ANOVA test. There were significant differences between groups on days 3 and 14.

The significant difference in the osteoclast/osteoblast ratio only occurred on days 3 and 14; then, it was continued with the multiple comparisons (LSD) test. There was a significant difference on day 3 between groups A and B and groups A and C, and on day 14 between groups A and C and groups B and C (Figure 6).

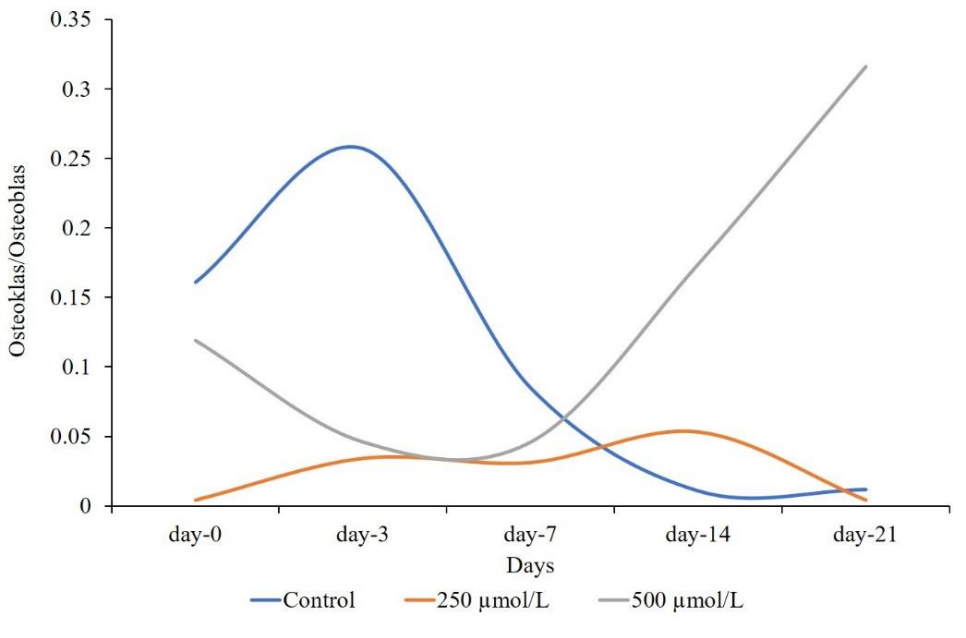

Figure 6. Osteoclast and osteoblast ration in A, B, and C groups. The significant difference was observed in 3rd and 14th day.

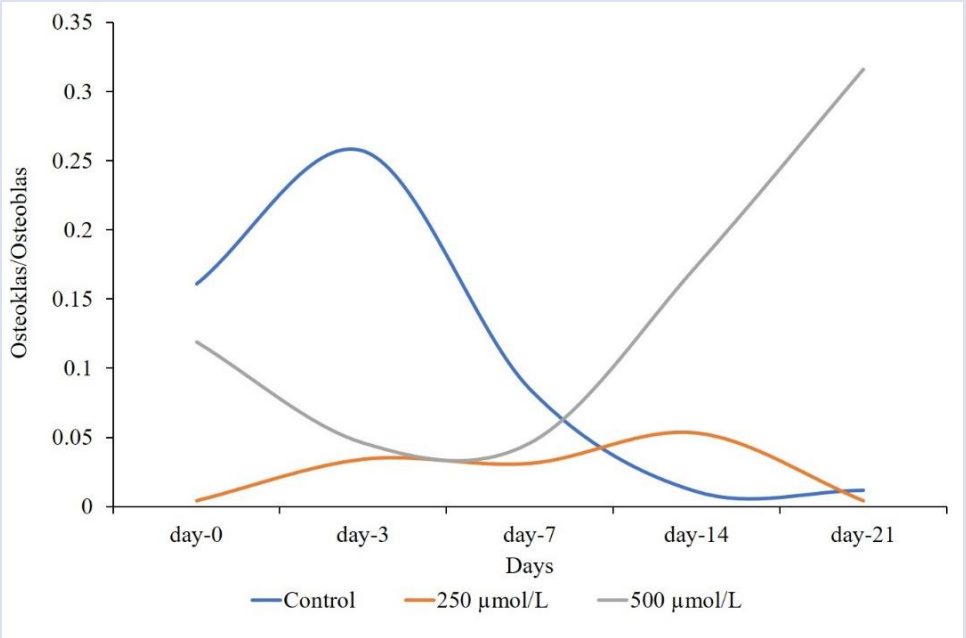

Figure 7. Histological image of osteoclasts and osteoblasts with H&E staining on days 3, 14, and 21 (x400 magnification). Black arrows indicate osteoclasts, and yellow arrows indicate osteoblasts.

The results of statistical tests showed that there was a significant difference on days 3 and 14 where the osteoclast/osteoblast ratio on day 3 in group A (without risedronate) was higher than in groups B (250 µmol/L) and C (500 µmol/L), but on day 14, the ratio was higher in group C than in groups A and B. The number of osteoblasts appeared to be more dominant in all groups (A, B, and C) on days 0, 3, 7, 14, and 21 compared to the number of osteoclasts (with a value of <1). Histological examination with H&E staining showed that the number of osteoblasts was more dominant than the number of osteoclasts (Figure 7).

Discussion

In this study, the results showed that there were no significant differences in ALP levels between groups A, B, and C on days 0, 3, and 7, but there were significant differences on days 14 and 21. The process of bone remodeling was more complex with resorptive activity at its initial phase (3–5 days) and is followed by a reversal (5–7 days). Furthermore, the final phase of bone deposition (7–14 days) occurs in both areas of stress and stress on the alveolar walls. In the early phase, bone resorption occurs more than bone deposition, but in the next phase, resorption and deposition become synchronous.[23]

In this study, ALP levels were measured with the movement of relapse when stabilization has been carried out for approximately 1 week, so there may have been an asynchronous phase between resorption and deposition; therefore, there is no significant difference on days 0, 3, and 7. On days 14 and 21, the effect of the bisphosphonate hydrogel risedronate began to show, where there was a significant difference in both ALP levels between the group without bisphosphonate (group A) and the group that received bisphosphonate injection (groups B and C). This result is not much different from the results of the study of Batra *et al.*[23], which showed that there was a significant change ($p < 0.05$) in ALP activity on days 7, 14, and 21 both on the mesial and distal sides between the experimental side and the control side. The peak of enzyme activity occurred on day 14 from the start of the retraction followed by a significant decrease in activity, especially on the mesial side.

Bisphosphonates increase the proliferation and maturation of osteoblasts.[24] Mature osteoblasts secrete osteoid, type I collagen, growth factors, and ALP. Bone formation occurs through three sequential processes: production (proliferation), maturation of the osteoid matrix, and mineralization.[25,26] During the proliferation, several extracellular matrix proteins (procollagen I, TGF-ß, and fibronectin) can be detected. The matrix maturation phase is characterized by the presence of ALP expression.[27]

The results of this study indicate that bisphosphonate risedronate with gelatin hydrogel as carrier media, caused pure sodium risedronate diffuse out when the hydrogel is degraded, so it can have a local effect. This preparation is also effective in reducing the number of osteoclasts that play a role in the resorption process and is effective in increasing the number of osteoblasts that play a role in the process of forming new bone where bisphosphonates increase the proliferation and maturation of osteoblasts, which is indicated by differences in the increase in ALP levels.[6]

The calculation of the number of osteoclasts and osteoblasts in the stress area during the movement of the relapse aims to obtain the ratio between osteoclasts and osteoblasts to determine the dominance of the activity of the two cells. The results of this study indicated that osteoblasts were more dominant than osteoclasts in the three groups both on days 0, 3, 7, 14, and 21, indicating that osteoblast activity in the bone formation process was more dominant than osteoclasts during tooth relapse movement.

Based on the results of their research, Franzen *et al.*[2] stated that orthodontic tooth movement and relapse would show the same process. On the side which is the tension area (tension side) during active gear movement, it will be changed to a pressure side during the relapses.[28]. After the removal of the orthodontic appliance, the tooth begins to relapse and moves to its original position. This movement is accompanied by changes in the number and distribution of osteoclasts. The number of osteoclasts significantly decreased in both mesial and distal roots of the first molars within 3 days, most likely due to apoptosis and/or decreased vascular density. The number of osteoclasts decreased further on day 14 and stabilized on days 14–21 of the relapse period.[3]

The results of this study showed a significant difference in the osteoclast/osteoblast ratio on days 3 (between groups A and B and groups A and C) and 14 (between groups A and C and groups B and C) and showed that osteoblasts were more dominant than osteoclasts in all three groups. The results of the study of Von Knoch *et al.*[29] using a clinically relevant *in vitro* model showed that bisphosphonates increase bone marrow stromal cell proliferation and initiate osteoblastic differentiation. Although the main action of bisphosphonates is inhibition of bone resorption by osteoclasts, there is increasing evidence that bisphosphonates also interact with osteoblasts.[9]

The effect of bisphosphonates inhibits not only osteoclast activity but also osteoblast formation. Bisphosphonates can stimulate osteoblast proliferation and inhibit osteocyte and osteoblast apoptosis. The results showed that bisphosphonates increased OPG expression in human osteoblastic cells, suggesting that the antiresorptive effect of bisphosphonates was mediated by the influence of osteoblasts.[9] Research by Krishnan *et al.*[6] showed that the application of nitrogenous-type bisphosphonate risedronate increased the number of osteoblasts.

It was concluded that intrasulcular application of bisphosphonate risedronate hydrogel had an effect on the osteoclast ratio of osteoblasts and increased levels of ALP on days 14 and 21. Hydrogel risedronate bisphosphonate increased the proliferation and maturation of osteoblasts, which play an important role in bone formation, thereby increasing tooth stability after orthodontic movement. These results indicate the important role of bisphosphonate risedronate hydrogel in the bone formation process; therefore, it has the potential to inhibit relapse. Although the use of risedronate hydrogel in this

study shows a good effect, it is not easy enough to apply it in the gingival sulcus, so further research is needed to make preparations that are easier to apply and have a local effect.

Conclusions

The intrasulcular application of bisphosphonate risedronate affected the osteoclast/osteoblast ratio and increased ALP levels. These results indicate the important role of bisphosphonate risedronate hydrogel in the bone formation process; therefore, it has the potential to increase tooth stability after orthodontic movement and prevent relapse.

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Conflicts of Interest Statement

There is no conflict of interest with the research results and publication of this manuscript.

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Comparison of Microhardness of Artificial Teeth with Different Contents After Waiting in Various Liquids

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ABSTRACT

Objectives: This study aimed to assess the long-term microhardness of different artificial teeth after waiting in liquids of various pH values.

Materials and Methods: Four different artificial teeth [conventional PMMA (Ivostar) as control group), double cross-linked PMMA(DCL), micro-filled composite resin(VivodentPE), nanohybrid composite resin (PhonaresiII)] were used for the study. After the samples fixed on acrylic blocks were immersed in distilled water at 37˚C for 24 hours, initial microhardness (T0) measurements were performed. Randomly selected samples from each group were immersed in liquids with different pH values (artificial saliva, kefir, orange juice, cola). Measurements repeated on the 7th day on the same samples were recorded as T1, and measurements repeated on the 14th day were recorded as T2. The data obtained were evaluated in the SPSS 22.0 program. Friedman and Kruskall Wallis tests were used to compare of the groups.

Results: While the highest initial microhardness averages were found in the Phonares II group, the lowest average belongs to the Ivostar group. Microhardness findings of all materials measured at different times were obtained in the order of T0>T1>T2. When the data of samples aged in different liquids are compared, significant differences are observed. When the microhardness measurements of a single material exposed in different solutions were compared, no difference was found between the solutions.

Conclusions: A decrease in microhardness of materials that are immersed in liquids with different pH values for a long time was observed, and the microhardness of the materials exposed to these solutions is adversely affected.

Keywords: Acidic Beverages, Artificial Teeth, Hybrid Materials, Microhardness, PMMA

Farklı İçeriklerdeki Yapay Dişlerin Sıvılarda Bekletildikten Sonraki Mikrosertliklerinin Karşılaştırılması

Süreç

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ÖZ

Amaç: Bu çalışmada amaç farklı yapay diş materyallerinin farklı pH değerlerindeki sıvılarda bekletildikten sonraki mikrosertliklerinin uzun dönem karşılaştırmasıdır.

Yöntem: Çalışma için 4 farklı yapay diş materyali [(kontrol grubu olarak konvansiyonel PMMA(Ivostar), çift çapraz bağlı PMMA (DCL), mikrodolduruculu kompozit rezin (VivodentPE) ve nanohibrit kompozit rezin(PhonaresiII)] kullanıldı. Akrilik bloklara sabitlenen örnekler 24 saat 37˚C de distile suda bekletildikten sonra başlangıç mikrosertlik(T0) ölçümleri yapıldı. Her gruptan rastgele seçilen örnekler farklı pH değerine sahip sıvılarda (yapay tükürük, kefir, portakal suyu ve kola) bekletildi. Aynı örnekler üzerinde 7. Günde tekrarlanan ölçümler T1, 14. günde tekrarlanan ölçümlerse T2 olarak kaydedildi. Elde edilen veriler SPSS 22.0 programında değerlendirildi. rupların karşılaştırmasında Friedman ve Wilcoxon testi kullanılırken, bağımsız grupların değerlendirmesinde Kruskall Wallis ve Mann Whitney U testi kullanıldı.

Bulgular: En yüksek başlangıç mikrosertlik ortalamalası PhonaresII grubunda bulunurken, en düşük ortalama Ivostar grubuna aittir. Tüm materyallerin farklı zamanlarda ölçülen mikrosertlik bulguları T0>T1>T2 sıralamasıyla elde edilmiştir. Farklı sıvılarda yaşlandırılan örneklere ait veriler karşılaştırıldığında anlamlı farklılıklar görülmektedir. Aynı zamanda farklı solüsyonlarda muamele edilen tek bir materyale ait mikrosertlik ölçümleri karşılaştırıldığında ise solüsyonlar arasında farklılık bulunmamıştır.

Sonuç: Farklı ph değerlerine sahip sıvılarda uzun dönem bekletilen materyallerin mikrosertliklerinde azalma görülmüştür ve bu solüsyonlara maruz kalan materyallerin mikrosertlikleri olumsuz yönde etkilenmektedir.

Anahtar Kelimeler: Asidik içecekler, yapay diş, hibrit materyaller, mikrosertlik, PMMA

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Introduction

Acrylic artificial teeth (PMMA) used in the treatment of total and partial edentolusness is used in many areas of dentistry due to their low water absorption, high durability, good optical properties, and acceptable dimensional stability.[1] Besides, the good connection with the denture base facilitates discoloration and hygiene maintenance. However, the prosthesis cannot resist parafunctional movements with low wear resistance over time and cannot maintain proper occlusal relationships, resulting in disruptions in closing relationships and loss of vertical dimension.[2]

With the developments in the field of polymer science, to overcome the negative properties of PMMA in the linear polymer structure, the structure of acrylic teeth is highly strengthened by using cross-linking agents (glycolmethacrylate and allylmethacrylate).[3] Cross-linked acrylic teeth, developed with the help of different polymer technologies, can be composed of blended polymer, interpenetrating polymer network (IPN), and double cross-linked (DCL=doublecrosslinked) structures. These developments it is aimed not only to increase the wear resistance but also to increase the structural durability against the formation of cracks in the structure.[4] Cross-links involved in the structures of acrylic teeth have also made them more resistant to organic solvents and heat.[5]

With the improvement in composite materials with higher wear resistance compared to conventional acrylic teeth, the area of use in artificial teeth has also expanded, and modified composite-containing acrylic teeth have been introduced to the market.[3,6] Micro-filled (MF) and nanohybrid composites (NHC) produced to improve the mechanical properties of conventional artificial teeth consist of urethane dimethacrylate (UDMA) matrix as well as PMMA clusters. The "hybrid" means that this composite is formed by the combination of fillers of different types and sizes. NHC contains highly cross-linked inorganic-filled macro filters and highly concentrated inorganic micro fillers[7]. The commercially available composite artificial resin tooth has different properties such as the shape of the filler, the amount of filler, the type of polymer, and the shape of the cross-links.[8] The increase in the amount of organic filler resulted in a decrease in the expansion coefficient and polymerization shrinkage, in addition to an increase in the wear resistance of the resin teeth.

Hardness, defined as the ability of a material to resist locally acting deformation, should be considered in conjunction with wear resistance and is often an indicator of the mechanical property of synthetic, synthetic material.[8,9]

Dental materials are exposed to long-term contact with many liquids in the oral environment, apart from saliva, depending on their consumption habits[10]. Therefore, nutritional habits and their effects on artificial teeth should be evaluated. Besides, when the literature was reviewed, no study was found on the hardness of acrylic and hybrid artificial teeth that evaluated liquids with different acidity in the long term. Therefore, we aimed to evaluate the hardness of artificial teeth immersed in liquids with different pH values in our study. The null hypothesis of our study was determined that liquids with different artificial teeth and pH values would not change the hardness value.

Materials and Methods

This in vitro study was conducted on four different resin materials and beverages (Table 1).Groups were performed according to chemical structure of artificial teeth as follows: GroupI; PMMA (Vivodent Ivostar), GroupII; DCL PMMA (Vivodent DCL), GroupIII; micro-filled composite resin (Vivodent PE), GroupIV; nano-hybrid composite resin (Vivodent Phonares II).

Table 1. Contents of artificial teeth and beverages used in the study

Materials	Components	Manufacturer
Artificial Teeth		
Ivostar	Polimetil metakrilat (PMMA)	
SR Vivodent DCL	Double cross-linked (DCL) PMMA Isosit	
SR Vivodent PE (İt)	Cross-linked inorganic micro-filled composite resin with PMMA pearls	Ivoclar Vivadent (Schaan, Lihtenştayn)
SR Phonares II	Nano Hybrid Composite Resin (UDMA + inorganic fillers + silanated silica prepolymer with inorganic filler + binder PMMA)	
Beverages		
Artificial Saliva	Carboxymethyl cellulose, Xylitol potassium chloride, calcium chloride, potassium sulphate, potassium thiocyanate, distilled ionized water	pH=6.93
Kefir (Ülker İçim, Bursa, Türkiye)	Pasteurized cow's milk, kefir culture	pH=4.5
Orange Juice (Coca-Cola İçecek A.Ş., Istanbul, Türkiye)	Orange juice with orange particles produced from concentrate (100%) water, flavors	pH=3.87
Cola (Coca-Cola İçecek A.Ş., Istanbul, Türkiye)	Water, sugar, CO_2, colorant, cola extract, caffeine, acidity regulator (phosphoric acid)	pH=2.53

The samples were embedded in condensation silicone impression material (Zetaplus, Zhermack, Badia Polesine, Italy) to create negative space with the help of disc-shaped wax with a thickness of 1 cm and a diameter of 2 cm for fixation. Molds were made with auto polymerizing acrylic resin (Panacryl Self Cure Acrylic, Rubydent, Istanbul, Türkiye) with created negative spaces.

The teeth were fixed in these molds by embedding their vestibule surfaces up and parallel to the plane. To facilitate the measurement processes and to standardize the measurement surfaces after the teeth are embedded in the acrylic molds, enamel level correction was made with a precision cutting device (Isomet 1000, Buehler, USA), and then surface treatment was applied with (600-800-1000) grit silicon carbide abrasive paper under permanent water cooling. Each tooth was numbered by writing the abbreviation of the group names on the lower surface of the acrylic bases with a water-proof pen.

After the prepared samples were immersed in distilled water for 24 hours, for microhardness tests, each sample group was prepared with standard metallographic sample preparation methods, and VHN hardness values were measured under 0.1kg-f load using a microhardness device with a diamond square pyramid tip with an apex angle of 136° (Shimadzu HMV-2/HMV-2T Micro Vickers Hardness Tester). The application time was determined as 15 seconds. All of the tests were performed according to ASTM C1327-15(2019) standards. In all hardness tests made, 3 measurements were taken from the specified surface of the samples by the same researcher (by M.Y.). Initial microhardness values were recorded as T0.

After the T0 measurements, all samples were placed in the containers to be used for the experiment, with the vestibule surfaces of the teeth up. The test containers were sufficiently filled with the specified beverages so that all surfaces of the samples were exposed to the liquid. During the test, the teeth were exposed to beverages for 18 hours every day and immersed in distilled water for 6 hours. The samples were kept in an oven (FN 400, Nüve, Türkiye) at a constant temperature of 37˚C throughout the experiment. Drinks were refreshed daily to prevent bacterial contamination throughout the study.

Microhardness measurements were repeated on the 7th (T1) and 14th (T2) days for the same samples. While the measurements were being made, each measurement was made 3 times from the same region of the samples and by the same researcher for the purpose of standardization.

Statistical Analysis

Statistical analysis was performed using computer statistical software (SPSS 22.0 for windows; SPSS Inc., Chicago, IL). After test of normality, nonparametric tests were used. The Friedman test and Wilcoxon tests were used to compare of the groups.

Results

Microhardness results and comparison results of the groups are given in Table 2. Microhardness averages for all groups were found in the order of T0>T1>T2. The initial microhardness (T0) averages decreased for all artificial dental materials compared to the findings after treatment with different liquids. This decrease was significant for all artificial teeth and different fluids ($p<0.05$). While the highest measured T0 value (34.75±0.89) belonged to PhonaresII material, the lowest microhardness value (22.70±0.57) was found for Ivostar material. The order of the microhardness results of the materials at T0, T1 and T2 times is Ph>DCL>PE>Ivostar.

When the T0, T1, and T2 data obtained from the same materials at different times are compared according to the solutions, the difference between all groups was statistically significant ($p<0.05$). In T0, T1, and T2 measurements, in Group I samples, there were differences between artificial saliva-orange juice, kefir-orange juice, orange juice-cola in intragroup comparisons for Ivostar material ($p<0.05$).

Table2. Comparison of initial, 7th and 14th day microhardness findings of different materials

	Beverages	GroupI (Median±Sd)	GroupII (Median±Sd)	GroupIII (Median±Sd)	GroupIV (Median±Sd)	p
T0	Artificial Saliva	25.20±1.10^{A,a,b}	30.30±2.54^{A,a}	24.55±1.43^{A}	31.30±1.81^{A,b}	0.001*
	Kefir	24.94±0.51^{B,C,a,b,c}	31.50±2.01^{B,a}	25.50±0.43^{b,c}	31,15±0,66^{B,C}	0.001*
	Orange Juice	22.70±0.57^{A,B,D,a,b,c}	28.00±1.60^{A,B,a,d,e}	25.50±1.80^{b,d,f}	31.95±1.22^{A,B,D,c,e,f}	0.001*
	Cola	25.53±0.75^{C,D,a,b}	29.70±1.99^{a,c,d}	24.05±1.68^{A,c,e}	34.75±0.89^{C,D,b,d}	0.001*
		0.001*	0.006*	0.043*	0.001*	
T1	Artificial Saliva	24.50±1.58^{A,a,b}	30.06±2.50^{A,B,a}	23.55±1.24^{A}	30.70±2.27^{b}	0.001*
	Kefir	23,80±0,70^{B,a,c}	30.45±2.67^{C,D,a}	23.50±0.90^{B,c}	29.70±0.88^{A,C}	0.001*
	Orange Juice	21.95±0.92 ^{A,B,C,a,b,c}	26.35±1.81^{A,C,a,e}	24.95±1.09^{A,B,b,f}	31.65±0.77^{A,c,e,f}	0.001*
	Cola	24.05±0.73^{C,a,b}	27.20±1.04^{B,D,a,c}	23.40±1.79^{d}	32.35±1.18^{C,b,c,d}	0.001*
		0.003*	0.001*	0.009*	0.003*	
T2	Artificial Saliva	24.29±2.37^{A,a}	29.88±2.78^{A,B,a,b}	23.55±1.24^{A}	30.41±2.35^{b}	0.001*
	Kefir	23.70±0.71^{B,a,c}	30.10±0,71^{C,D,a}	23.42±0.82^{c}	29.30±0.96^{A,B}	0.001*
	Orange Juice	21.86±0.91^{A,B,C,a,b,c}	25.51±2.11^{A,C,a,e}	24.40±1.07^{A,b,f}	31.35±0.46^{A,c,e,f}	0.001*
	Cola	23.950.73^{C,a,b}	26.20±1.02^{BD,a,c,d}	22.95±1.74^{c,e}	31.85±1.26^{B,b,d,e}	0.001*
		0.001*	0.004*	0.036*	0.014*	

*Statistically significance, $p<0.05$, Different capital letters represent the statistical difference between groups in the same column. Different lowercase letters represent the statistical difference between them

In the results of Group II (DCL) samples, while T0 values differ significantly between artificial saliva-orange juice and kefir-orange juice, and between artificial saliva-orange juice, artificial saliva-cola, kefir-orange juice, and kefir-cola in T1 and T2 measurements, it is insignificant in other groups.

In the comparison of Group III (Pe) data, T0 measurements differ between artificial saliva-cola, T1 measurements differ between artificial saliva-orange juice, kefir-orange juice, T2 measurements differ between artificial saliva-orange juice.

While Group IV materials (PhonaresII) were between artificial saliva-orange juice, kefir-orange juice, orange juice-cola, between artificial saliva- orange juice, kefir-orange juice for DCL, and artificial saliva-cola for Pe material ($p<0.05$), the differences between other groups were insignificant ($p>0.05$). While there was a difference in artificial saliva-orange juice, kefir-orange juice, kefir-cola, orange juice-cola groups in T0 data of Phonares II material, in kefir-orange juice, kefir-cola groups in T1 and T2 data, the difference in other groups was insignificant.

While the difference between kefir-orange juice and kefir-cola groups in T0, T1, and T2 measurements in the samples belonging to Group IV (Phonares II) was statistically significant, in addition to these groups, a significant difference was found between artificial saliva-orange juice, orange juice-cola liquids in T0 measurements ($p<0.05$), the difference in other groups was insignificant ($p>0.05$).

According to the comparison data for artificial saliva, kefir, orange juice, and cola liquids of different materials, T0, T1, and T2 data of Group I and Group II were significant for all fluids. While T0 and T1 findings were significant between Ivostar-PhonaresII in artificial saliva and colas, T2 data was significant for Ivostar-DCL in all fluids. There were differences between Ivostar-DCL, Ivostar-Pe, and Ivostar-Ph materials in terms of T0, T1, and T2 data in groups treated with orange juice.

Discussion

The null hypothesis that liquids with different pH values will not cause a change in the microhardness of artificial teeth was rejected in our study. The microhardness values of all artificial teeth decreased after waiting in various liquids. The mean initial microhardness values were found as PhonaresII> DCL>PE>Ivostar. It was concluded that the microhardness of artificial teeth with different features decreased significantly in liquids with different pH values.

In addition to complete and partial dentures, modified acrylic teeth with cross-links and composite resin teeth with micro and nanofillers are also used as an alternative to conventional acrylic teeth, which are mostly used in the construction of implant-supported hybrid prostheses.[8,11,12]

Acrylic polymers can absorb of absorbing water because of the polar properties of the resin molecules.[13] Water acting as a plasticizer reduces the hardness of the material through the formation of microcracks caused by the absorption/adsorption process.[14] As a result of this, the microhardness of materials decreases with exposure to beverages.

Microhardness is defined as the surface property of a material related to its resistance to local deformation. Besides, the hardness value is an indicator of the resistance of dental materials to wear during function.[15] It has been reported that Brinell and Rockwell hardness tests can be used mostly in metal alloys, and Vickers and Knoop hardness tests can be used to measure the hardness of all materials used in dentistry such as gold porcelain, composite resins, and cement. Therefore, we preferred to use the Vickers hardness test in our study.

Goiato *et al.*[16] obtained the result that the microhardness of the polymer, which they immersed in different beverage and cleaning solutions at different times, decreased the most in the cola solution. We concluded that the most changes on the microhardness data we obtained after starting and aging with liquids, similar to these findings, were in cola and orange juice. It was concluded that the microhardness results of the samples aged by immersed in liquids decreased in all artificial tooth groups.

Erosion in dentistry is a chronic condition seen with the loss of substance in hard tissues due to the effect of acids without a bacterial agent.[17] The associations of soda, energy drinks, and food materials with acidic potential with dental erosion are reported in studies.[18,19] Beverages with low pH value not only affect the natural tooth surfaces but also affect the surfaces of resin-containing restoration materials, accelerating their deterioration. Studies have shown that when resin-based restorative materials are immersed in environments with low pH values, the filling components in its structure are separated from the resin material, and degradation in the matrix content is observed.[22,23,24]

In a study in which resin-based restorative materials with different contents were immersed in liquids of different pH values for 7 and 14 days, and the surface roughness and color changes of the resin-based materials were examined by Güler *et al.*[23], samples were immersed in an acidic solution for 18 hours and distilled water for 6 hours. They stated that 14-day aging corresponds to 336 hours, and this aging process corresponds to approximately 13 years.[24] Considering that the mean duration of use of prosthetic rehabilitation is between 10-20 years, we think that the durations we have chosen in our study are acceptable.

Loyaga-Rendon *et al*. attributed the differences in surface hardness of artificial teeth to the presence of cross-links for acrylic resin teeth and the different filling particles and compositions for composite resin teeth.[4] However, no study has been found in the literature evaluating the effect of beverages with different pH values on the surface hardness of artificial teeth with different contents, such as nano filled composite resin, micro filled composite resin, which was newly developed in line with the developments in material technologies and started to be used routinely.

Ersu *et al*. compared the microhardness of artificial teeth (micro-filled composite (Orthosis), acrylic containing cross-links, and conventional acrylic) with different structures. In consequence of the study, the highest values were obtained in the composite artificial tooth group with micro-fill (31 kg/mm^2) and the lowest values in the conventional acrylic resin artificial teeth group (23 kg/mm^2).[25] In our study, when T0, T1, and T2 measurements were compared, they were found to belong to the highest microhardness group. After the NHC resin group, it is DCL>PE>Ivostar, respectively. The results of the researchers are similar with our data despite the differences in materials and methods.

Suzuki *et al*. compared the wear, microhardness, and surface roughness properties of artificial teeth (nano-composite, micro-filled composite, cross-linked acrylic resin, conventional acrylic resin) in four different structures. They concluded that nano-filled composite resin teeth are harder and have higher wear resistance than other teeth.[3] Although the materials and methods used are different, they support our results. The commercial differences in the teeth used and the difference in the application time and strength of the microhardness device used by the researchers for Knoop hardness may have affected the results numerically.

Ünal *et al*.[26] stated that microhardness of different restorative materials were affected gastric acid. They noticed that resin materials should be carefully selected in patients with gastric reflux. It is stated that the decrease in microhardness may be due to the loss of chemical and physical bonds as a result of water absorption and hydrolysis between the resin matrix and the filler particles.

The results obtained within the limitations of our study are that the microhardness of artificial teeth decreases after exposure to acidic beverages. However, it is assumed that cola and orange juice can cause potential changes in some properties of solutions over time, which can be considered a limitation of this study. In addition to this, methodological limitations for in vitro studies are inherent in the evaluation of microhardness and other properties. Therefore, future studies are needed to evaluate differences in a solution's ability to affect acrylic resin hardness over time.

Conclusions

The microhardness of materials can be affected by liquids with different pH values. Compared to conventional artificial teeth, the microhardness results of the new materials are better. Considering the nutritional habits of the patients, it can be recommended to treat patients with low pH consumption habits with new generation resin artificial teeth as an alternative to conventional materials.

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Conflict of Interests

Authors declare that no conflict of interests.

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Micro-Computed Tomographic Evaluation of Dentinal Cracks Caused by Various Recent File Systems

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ABSTRACT

Objectives: The purpose of present study was to evaluate the incidence of dentinal micro-cracks observed after the use of ProTaper Gold (PTG), WaveOne Gold (WOG), OneShape New Generation (OSNG), K3XF nickel-titanium (NiTi) instrumentation systems.
Materials and Methods: Sixty extracted human mandibular first molars were randomly assigned to four groups (*n* = 15). The root canals were instrumented with PTG, WOG, OSNG, and K3XF systems. The cross-sectional images of the roots were screened using high-resolution micro-computed tomography imaging before and after preparation to detect the presence of dentinal cracks.
Results: Although there was no statistically significant difference between PTG and WOG systems, WOG caused lesser micro-crack among all groups. K3XF showed statistically fewer cracks than OSNG. K3XF and OSNG systems caused statistically more dentinal micro-cracks than both Gold systems. WOG and PTG systems caused lesser micro-cracks formation among the systems evaluated in present study.
Conclusions: All used systems have caused different degrees of crack formations. Furthermore, WOG and PTG systems have shown superior features in terms of creating dentinal cracks according to OSNG, and K3XF systems. Preferring PTG and WOG systems during root canal shaping may minimize microcracks.

Keywords: Endodontics, Microcomputed Tomography, Root Canal Preparation.

Çeşitli Yeni Eğe Sistemlerinin Neden Olduğu Dentin Çatlaklarının Mikro Bilgisayarlı Tomografik Değerlendirilmesi

Süreç

Geliş: 02/03/2022
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ÖZ

Amaç: Bu çalışmanın amacı, ProTaper Gold (PTG), WaveOne Gold (WOG), OneShape Yeni Nesil (OSNG), K3XF nikel-titanyum (NiTi) enstrümantasyon sistemlerinin kullanımından sonra gözlenen dentin mikro çatlaklarının insidansını değerlendirmektir.
Gereç ve Yöntem: Altmış adet çekilmiş insan mandibular birinci molar dişi rastgele dört gruba ayrıldı (n = 15). Kök kanalları PTG, WOG, OSNG ve K3XF sistemleri ile enstrümante edildi. Köklerin kesit görüntüleri, dentin çatlaklarının varlığını tespit etmek için hazırlıktan önce ve sonra yüksek çözünürlüklü mikro bilgisayarlı tomografi görüntüleme kullanılarak tarandı.
Bulgular: PTG ve WOG sistemleri arasında istatistiksel olarak anlamlı bir fark olmamasına rağmen, WOG tüm gruplar arasında daha az mikro-çatlamaya neden oldu. K3XF, OSNG'den istatistiksel olarak daha az çatlak gösterdi. K3XF ve OSNG sistemleri, her iki Gold sisteminden istatistiksel olarak daha fazla dentin mikro çatlaklarına neden oldu. WOG ve PTG sistemleri, bu çalışmada değerlendirilen sistemler arasında daha az mikro çatlak oluşumuna neden olmuştur.
Sonuçlar: Kullanılan tüm sistemler farklı derecelerde çatlak oluşumlarına neden olmuştur. Ayrıca WOG ve PTG sistemleri, OSNG ve K3XF sistemlerine göre dentin çatlakları oluşturma konusunda üstün özellikler göstermiştir. Kök kanal şekillendirmesi sırasında PTG ve WOG sistemlerin tercih edilmesi mikro çatlakları en aza indirebilir.

Anahtar Kelimeler: Endodonti, Mikrobilgisayarlı Tomografi, Kök Kanal Hazırlığı.

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Introduction

Root canal preparation is one of the most important steps in endodontic procedures.[1]{Hübscher, 2003 #1} Properly prepared root canals provide enhanced irrigation as well as obturation. Thus, mechanical preparation plays a crucial role in the success of endodontic treatment.[2] However, during mechanical preparation, root canal walls can be exposed to instantaneous stress concentrations through dentine, which causes perforations, zips, iatrogenic defects, dentinal defects and micro-cracks or craze lines, especially in curved canals.[1,3] Minimizing the fractures and micro-cracks became one of the main goals of root canal preparations because these are significant disadvantages of preparations. For this purpose, many instrumentation systems have been introduced and developed in the endodontic field. The K3XF (SybronEndo, Orange, CA) system is an upgraded level of K3 system and one of the most recent instrumentation systems in endodontics. The K3XF system ensures clinicians enhanced flexibility and strength to cyclic fatigue through exclusive R-phase technology, in addition to the core features of the original K3 system. Another recent file system that applies traditional constant rotational movement is OneShape New Generation (OSNG; MicroMega, Besancon, France). The manufacturer of the OSNG files demands that it increases the available volume to eliminate upstream residuals and debris in the root canal system because of its asymmetrical section geometry and larger pitch.[4,5]

The new rotary system called ProTaper Gold (PTG, Dentsply Sirona, Ballaigues, Switzerland) contains a convex triangular cross-section and a changeable progressive pitch. The design of PTG provides high resistance to cyclic fatigue with enhanced flexibility.[4] The manufacturer also asserts that the design of PTG may perform an asymmetric rotary movement aimed to decrease the screwing effect by minimising the contact zone between the file and the dentinal wall. WaveOne Gold (WOG, Dentsply Sirona, Ballaigues, Switzerland) is the modification of the WaveOne single-file reciprocating system. It has been claimed by the manufacturers of WOG that the M-Wire NiTi technology offers an increased cyclical fatigue resistance and lowered screwing effect. The design of WOG is claimed to increase cutting efficiency due to its parallelogram design which contains a triangular-shaped predecessor with one or two cutting edges depending on the location throughout the file. Nonetheless, various features of nickel-titanium (NiTi) files can significantly impact microcrack formation. The relationship between dentinal micro-cracks and the thermal metallurgy and kinematics of new PTG and WOG endodontic instruments has not been examined. Therefore, this study aimed to compare root cracks on the root canals that instrumented with the PTG, WOG, OSNG, and K3XF systems using high-resolution micro-computed tomographic (micro-CT) analysis.

Materials and Methods

Sample Selection and Preparation of Specimens

Approval for the present study was obtained from the Clinical Research Ethics Committee of X University in X, X (2021-08/44). We selected eighty-five mandibular molars with no dentinal fractures extracted for reasons not related to this study. The teeth were extracted both for orthodontic or periodontal reasons. Sixty teeth with no resorptions or visible defects were selected. Possible root canal obstructions, curvature angle of the mesial roots, pre-existing craze lines, and micro-cracks were detected using preoperative micro-CT images. The teeth were examined with Schneider's method and the curvature of mesial roots were ranged between 10°-20°.[6] Extracted teeth were stored at 0.1% thymol until used which is one month after following the removal of surface remnants. According to De-Deus procedure, distal roots were removed by a low-speed saw (Isomet; Buhler Ltd, Lake Bluff, NY). Thus, the mesial root was separated from the tooth.[6] Canal patency has been conducted with a 10 K-file (Dentsply Maillefer, Ballaigues, Switzerland) until the tip was visible from apical foramen and the working length (WL) was 1mm lower than this measurement. After keeping all the specimens in 0.01% thymol, all the roots were covered using a polyether impression material (Impregum F, 3M/ESPE, Seefeld, Germany) as a periodontal ligament space and inserted in acrylic blocks.[7]

Root Canal Instrumentation

The specimens were allocated to 1 of 4 groups: PTG, WOG, OSNG, and K3XF (15 teeth in each group). All the root canal preparations were completed by only one operator, and the instrumentation sequences used were as follows;

PTG Group

The PTG instruments used in a sequence of SX (1/2 of the WL), S1 (size 17, .02 taper; 2/3 of the WL), S2 (size 20, .04 taper; 2/3 of the WL), F1 (size 20, .07 taper; full WL), F2 (size 25, .08 taper; full WL) files. All the PTG instruments were used at 300 rpm with a torque of 3 Ncm for SX and S1 instruments, 1.5 Ncm for F1 instruments, and 2 Ncm for F2 instruments.

WOG Group

The WOG file with a size 25 and taper .08 was used in WO all program. 6: 1 reduction handpiece (Sirona Dental Systems GmbH, Bensheim, Germany) was chosen for this method.

OSNG Group

OSNG (Micro-Mega) instruments (size 25, .06 taper) were used with a torque-controlled endodontic motor (X-Smart, Dentsply Maillefer). The instruments were worked using in-and-out movements and minimal pressure with 2 Ncm torque and 400 rpm at the WL.

K3XF Group

Sybron Elements motor was chosen with K3XF (SybronEndo) instruments to size 25 taper .10 file at the orifice level and the half of WL, at WL, size 25 taper .04 and .06 were used. The speed of the selected motor was 400 rpm and the torque was 3 Ncm. The selected teeth were prepared with a total of 10 ml 5.25% NaOCl solution using a 29-gauge side-vented NaviTip needle (Ultradent, South Jordan, UT, USA). The needle was asserted into the root canals until 1 mm lower than WL.

Dentinal Microcrack Evaluation

Analysis of microcracks before and after root canal instrumentation was carried out by the two examiners. Samples were scanned with micro-CT (Bruker-MicroCT 1172, Belgium) with 100kVa force being used. All samples were scanned using 1000ms exposure time, 0.4 rotation through 360o, and an Aluminum 0.5 mm filter was used. Samples were scanned with 13.7 µm/pixel. All images were taken using 3 frame average. Data were reconstructed with NRecon (Bruker-MicroCT 1172, Belgium) and analysed with CTan (Bruker-MicroCT 1172, Belgium) software. Data viewer (Bruker-MicroCT 1172, Belgium) was used to detect the defect site. To detect the dentinal micro-cracks, 3 pre-calibrated investigators were used in furcation level to apex (n=45 840). When the before and after cross-sectional images of root canal preparations were examined, the dentinal micro-cracks were recorded.

Statistical Analysis

The micro-crack incidence data were analysed using the SPSS statistical software program (version 14.0, SPSS Inc., Chicago, IL). A three-way ANOVA was applied to compare the evaluated NiTi systems in terms of dentinal micro-crack formation. ANOVA with post hoc Tukey's test was used for statistical analysis with a p-value at 0.05.

Results

The mean, standard deviation, and statistical analysis of dentinal defects observed after instrumentation are shown in Table 1. The micro-CT images of dentinal micro-cracks formed in the coronal, middle, and apical thirds of roots are shown for K3XF, OSNG, PTG, and WOG respectively, in Figures 1, 2, and 3. A kappa test was performed and showed 94.6% inter-examiner agreement on the examination of micro-crack formation. Cross-sectional images were examined to compare the condition of the dentinal defect observed in the pre and post instrumentation. The comparison of pre-instrumentation micro-crack observations showed no statistically significant differences among root regions and instrumentation systems (p>0.05). The WOG system produced statistically fewer micro-cracks than any other system (p>0.05).

OSNG caused statistically more cracks formation than the K3XF system (p>0.05). Moreover, K3XF and OSGN exhibited statistically more dentinal cracks than PTG and WOG systems (p>0.05). Furthermore, although there was no statistically significant difference between PTG and WOG systems (p>0.05), considering its average value PTG caused more dentinal micro-crack formation than WOG throughout the entire length of the root canal.

As a result of cross-sectional image examination, the incidence of cracks was higher in the apical thirds than the middle and coronal thirds for the WOG, PTG, OSNG, and K3XF groups (p>0.05).

Discussion

Dentine cracks that do not reach the pulp cavity and on the external surface of roots may be formed as linear micro-cracks. Linear micro-cracks may form from the stress that occurs during mechanical shaping due to excessive tensile strength of the collagen matrix. If the applied force transmitted to the external surface during canal preparation exceeds the force that holds the root dentine together, cracks may form from the dentine to the external root surface.[7] It's been reported that NiTi rotary systems may cause fractures on the dentinal surface.[8,9] Four selected different NiTi systems were compared in the present study and concluded that instrumentation causes micro-cracks depending on the process of producing these instruments. Therefore, the thermomechanical treatment and kinematic features of instrumentation systems must be evaluated in terms of root dentine cracks that occur during preparation. However, no study compared PTG, WOG and OSGN instrumentation systems through their incidence of causing dentinal micro-cracks.

Table 1. The mean, standard deviation and statistical analysis of dentinal defects observed after instrumentation.

	Apical 1/3		Middle 1/3		Coronal 1/3	
	Before Preparation Micro-crack (%)	**After Preparation** Micro-crack (%)	**Before Preparation** Micro-crack (%)	**After Preparation** Micro-crack (%)	**Before Preparation** Micro-crack (%)	**After Preparation** Micro-crack (%)
OSNG	32.25 (1.54)^{aA}	**54.43 (1.80)^{Aa}**	31.16 (1.48)^{aA}	**50.41 (1.21)^{Ba}**	30.12 (1.41)^{aA}	**49.11 (1.21)^{Ba}**
K3XF	31.65 (1.52)^{aA}	**42.35 (2.48)^{Ab}**	30.74 (1.42)^{aA}	**39.15 (1.15)^{Bb}**	29.64 (1.38)^{aA}	**38.73 (1.61)^{Bb}**
PTG	31.05 (1.48)^{aA}	**36.14 (0.94)^{Ac}**	30.55 (1.40)^{aA}	**33.75 (0.77)^{Bc}**	29.48 (1.24)^{aA}	**33.47 (0.85)^{Bc}**
WOG	31.20 (0.83)^{aA}	**35.92 (0.96)^{Ac}**	30.24 (1.28)^{aA}	**33.63 (0.97)^{Bc}**	29.32 (1.18)^{aA}	**33.41 (1.11)^{Bc}**

By the three way ANOVA, F = 283.435; p=0.000 (p>0.05), Different superscript uppercase letters in the same row (same rotary system in different thirds) indicate a statistically significant difference (p>0.05), Different superscript lowercase letters in the same column (different rotary systems in the same third) indicate a statistically significant difference (p>0.05).

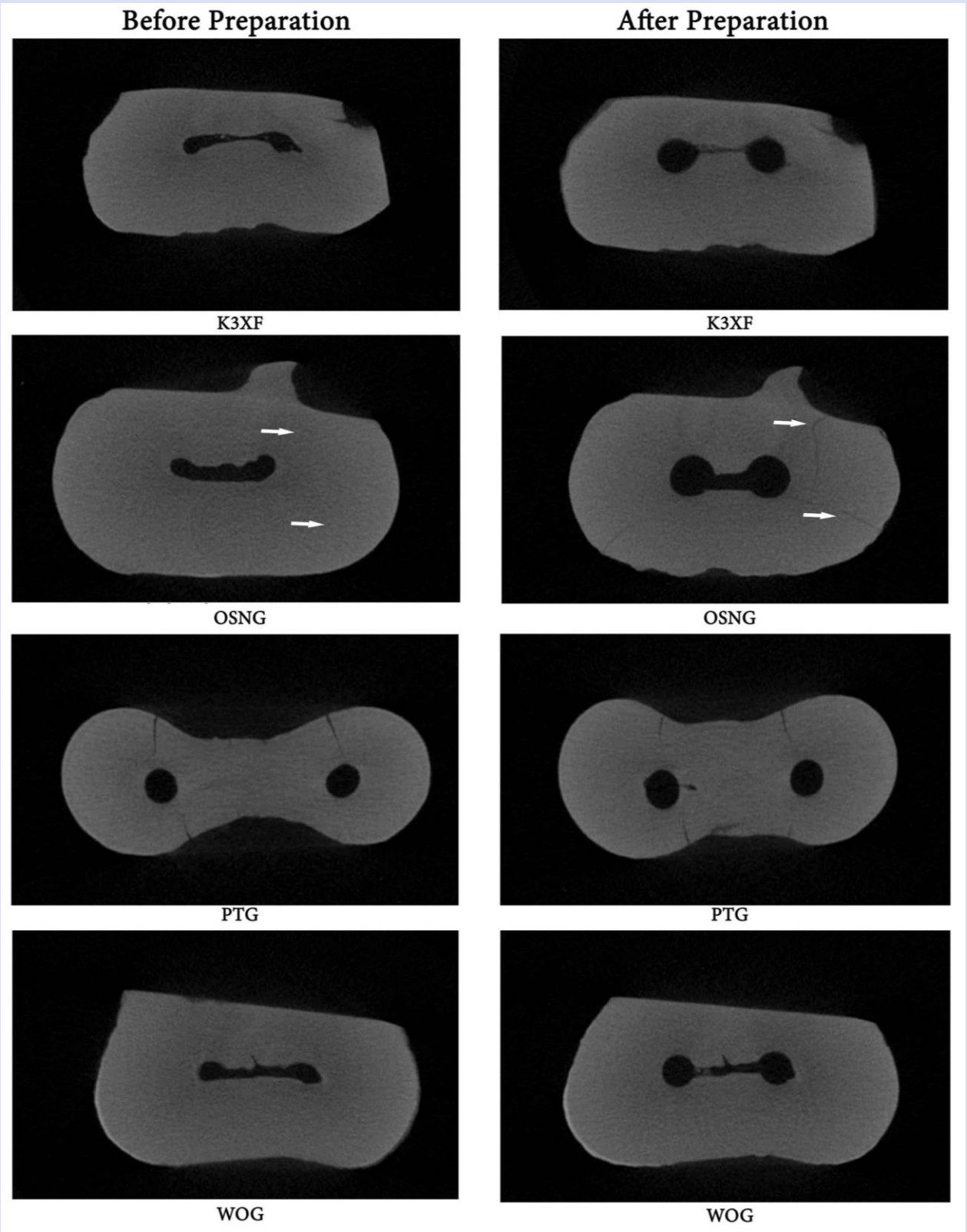

Figure 1. The representative micro-computed tomographic images obtained from the coronal third of roots before and after preparation using instrumentation systems

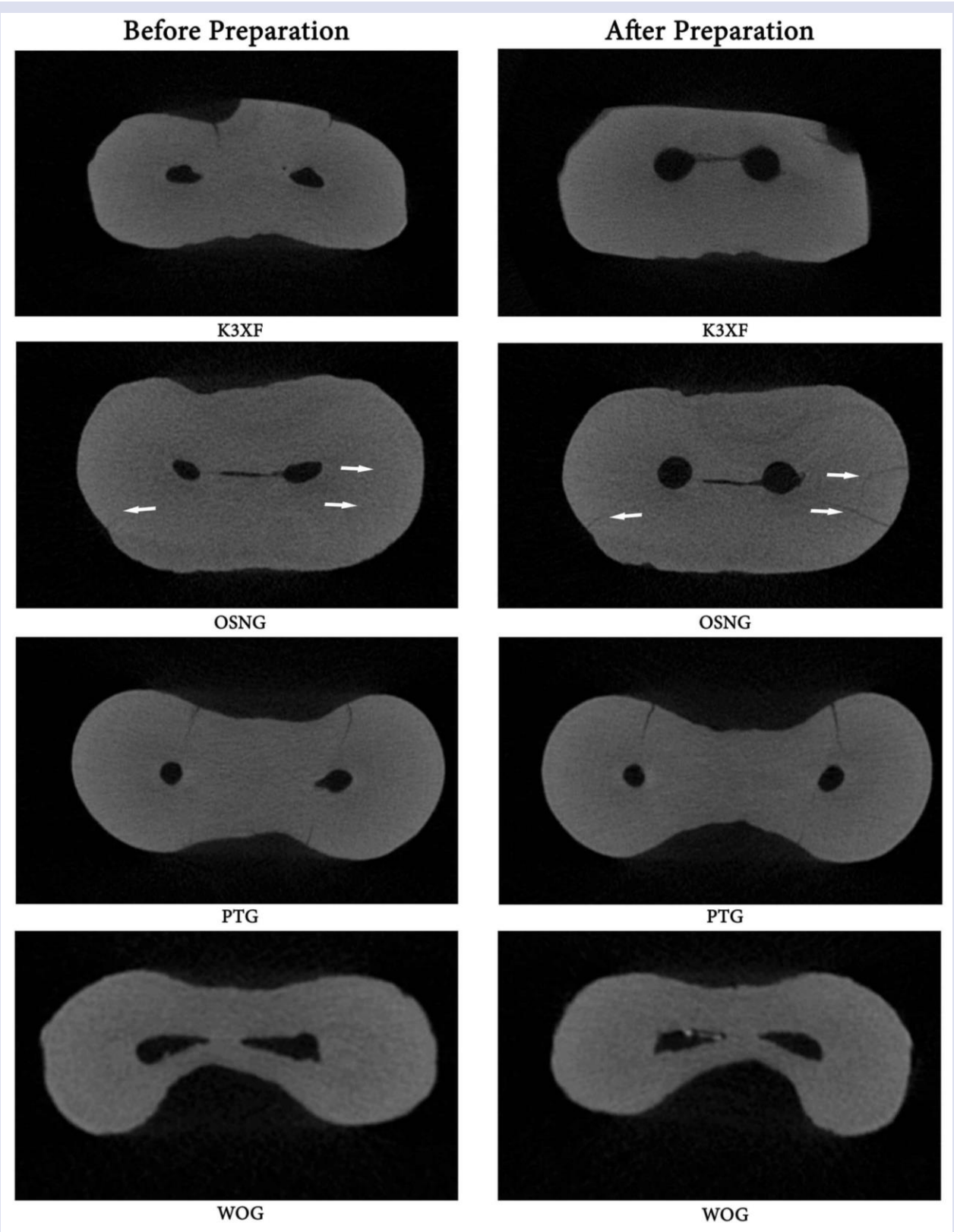

Figure 2. The representative micro-computed tomographic images obtained from the middle third of roots before and after preparation using instrumentation systems

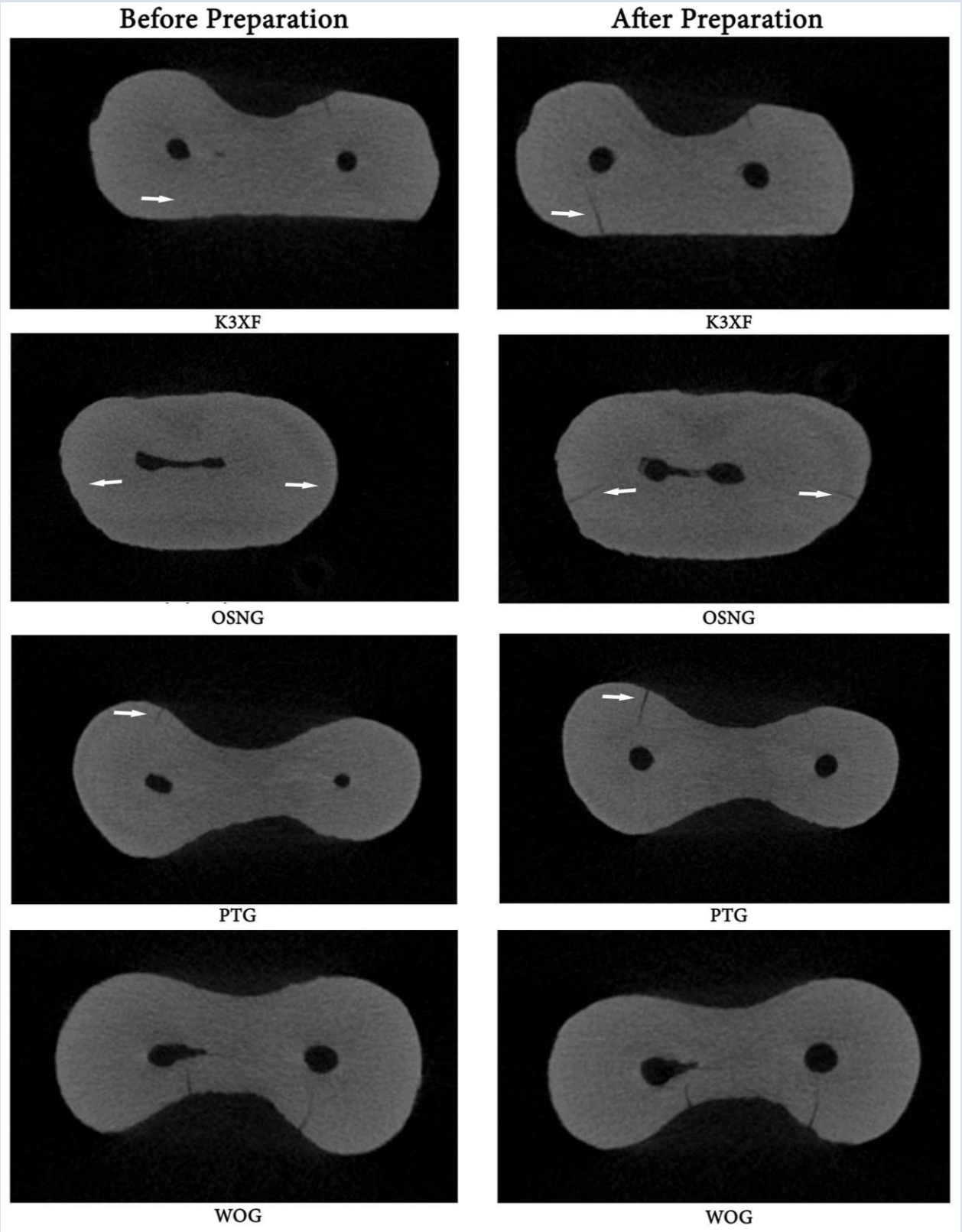

Figure 3. The representative micro-computed tomographic images obtained from the apical third of roots before and after preparation using instrumentation systems

As known, the increase of apical stress and strain may depend on the file design.[10] It's been reported that the PTG and WOG systems cause fewer dentinal micro-cracks at the coronal, middle, and apical thirds compared with the OSNG and K3XF in the present study. The PTG group showed significantly lower micro-cracks than the other groups because the convex triangular cross-section design of PTG instrumentation allows minimal contact of the file on the dentinal walls. Moreover, the micro-crack formation was not reported in the WOG group because of

its offset parallelogram-shaped cross-section design that limits the engagement zone that ensures fewer dentinal crack formations.

As the NiTi systems and instruments develop with the new technologies, the developed NiTi systems became available for usage in different areas as well as different kinematics and alloys. Moreover, it has been claimed that the new systems significantly increase the dentinal micro-cracks with the instrumental origin.[11,12] Also, it has been reported that the reciprocating motion of the file systems causes significantly less damage and micro-cracks than the continuous and rotational motion. Interestingly, middle and coronal thirds were affected less than apical thirds and fewer dentinal micro-cracks were observed. Moreover, continuous rotation produced more micro-cracks in the apical third than in the coronal and middle thirds.[8,13] Comparison of root dentinal crack formation from continuous rotating and reciprocating root canal preparation methods revealed that root canal instruments with reciprocating movements gained better results in terms of dentinal micro-crack formation than instruments with a continuous rotation movement.[14] Nevertheless, continuous rotational movements on root canals can cause micro-cracks and craze lines in root dentine.[15] Also, the continuous rotational motion of the OSNG, K3XF, and PTG caused more micro-cracks to form than the reciprocating motion of the WOG system, which has been designed clockwise and anticlockwise angles. This movement causes stress especially in the apical area of roots and eventually creates micro-cracks at this level. In contrast, continuous rotation of the other instruments may have increased the stress concentration because greater rotational force was adopted to the root canal walls, resulting with more cracks.

The ongoing metallurgic developments in the manufacture of NiTi instrument systems have played a crucial role in improving both flexibility and reducing crack formation. Thermomechanical treatment of NiTi files has been performed using various methods. In time, endodontic instruments have been produced using different metallurgical techniques as M-Wire, then Blue Wire, and recently Gold Wire technology. In the current study, OSNG caused a higher percentage of cracks than the K3XF. In terms of metallurgical evaluation, although OSNG was manufactured conventionally for treated NiTi wire, K3XF was manufactured with R-phase. R-phase is associated with enhanced flexibility and fatigue resistance to instruments. It's the process of heating and cooling until obtaining the final shape of the file which is a twistable and elastic form of NiTi instruments.[16,17] The manufacturer claims that developed NiTi systems are more advantageous than the traditional systems due to their phase transformation according to temperature.[18] This may be the advantage of the K3XF system, which caused fewer microcracks than the OSNG system. Also, several studies support the previous study.[19,20]

PTG and WOG systems were manufactured using the latest metallurgical technology which contains a following heating and cooling process that causes reversing between martensite and austenite. In the present study, both systems caused fewer dentinal cracks compared to the other systems. According to the metallurgical assessment, in both gold systems (PTG & WOG) the phase-transition point between martensite and austenite through heating and cooling cycles was higher compared to previous methods. One of the reasons that make PTG and WOG files more elastic is the Gold Wire alloy material which makes new files more advantageous than traditional NiTi wires. The enhanced flexibility of new systems also promises a better quality of preparation and fewer micro-crack formations during preparation with the PTG system. The PTG systems also show a great ability on more restrictive canals such as curved and long canals.[21] In the present study, the micro-computed tomography experimental model was selected to examine dentinal micro-cracks because it is capable of a qualitative and quantitative assessment of a root canal in three dimensions and a better visualization of root canal morphology.[22] This technique produces highly accurate and clear images.[23] This superior visualisation technology assesses pre and postoperative conditions of root dentine in terms of the presence of cracks. Moreover, the most crucial difference of this approach compared to methods used in previous studies is that roots do not need to be cut for micro-CT evaluation.

Conclusions

Within the limitations of the present study, the WOG system caused the least crack formation amongst the other systems used in the present study. The incidence of dentinal cracks may vary depending on the design of the instrument through kinematic and metallurgic properties.

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None to declare

Conflicts of Interest Statement

The authors declare that they have no conflicts of interest in relation to this study.

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An Investigation of the Metal Fatigue of Different Nickel-Titanium Rotary Instruments After Prolonged Use

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ABSTRACT

Objectives: This study aimed to compare the cyclic fatigue (CF) resistance of nickel-titanium (Ni-Ti) endodontic instruments from ProTaper (PTU), ProTaper Next (PTN), Wave One (WO), and Reciproc (RPC).
Materials and Methods: In our study, PTU, PTN, WO, and RPC rotary files were divided into the experimental and control groups containing an equal number of samples. The experimental group files were used in the shaping of 80 extracted human lower premolar and lower molar teeth. The experimental and control group kits were then placed in the test apparatus and observed until they fractured. Fracture times were recorded and statistically evaluated.
Results: In the one-to-one comparisons of the experimental and control group files, the differences between the fracture times of the experimental and control group files were found to be statistically insignificant in RPC, WO, PTU, and PTN X1 files, fracture time differences were statistically significant in all PTN X2 files. As a result of the pairwise comparison of the experimental and control groups, the difference between the experimental and control groups of the WO and RPC files used with reciprocal movement was found to be statistically insignificant.
Conclusions: The files used with the reciprocal movement were found to be safer in terms of metal fatigue when compared to the other files used with rotational movement after the preparation.

Keywords: Cyclic Fatigue, Ni-Ti Files, Wave One, Reciprocating Movement.

Farklı Nikel-Titanyum Kök Kanal Eğelerinin Uzun Süreli Kullanımı Sonrası Oluşan Döngüsel Yorgunluğunun Araştırılması

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ÖZ

Amaç: Bu çalışmanın amacı ProTaper (PTU), ProTaper Next (PTN), Wave One (WO) ve Reciproc (RPC) nikel-titanyum (Ni-Ti) endodontik aletlerin döngüsel yorgunluk (CF) direncini karşılaştırmaktır.
Gereç ve Yöntem: Araştırmamızda PTU, PTN, WO VE RPC eğeleri eşit sayıda örnek içeren deney ve kontrol gruplarına ayrılmıştır. Deney grubu eğeleri 80 adet çekilmiş insan alt premolar ve alt molar dişlerinin şekillendirilmesinde kullanılmıştır. Sonrasında deney ve kontrol grubu kitleri test düzeneğine yerleştirilerek kırılana kadar gözlemlenmiştir. Kırılma süreleri kaydedilerek istatistiksel değerlendirmeleri yapılmıştır.
Bulgular: Deney ve kontrol grubu eğelerinin bire bir karşılaştırmalarında deney ve kontrol grubu eğelerinin kırılma süreleri arasındaki farklılıklar RPC, WO, PTU, PTN X1 eğelerinde istatistiksel olarak önemsiz bulunurken, PTN X2, eğelerinin tümünde kırılma süreleri farklılıkları istatistiksel olarak önemli bulunmuştur. Deney ve kontrol gruplarının ikili karşılaştırılması sonucunda, resiprokal hareket ile kullanılan WO ve RPC eğelerinin deney ve kontrol grupları arasındaki farklılık istatistiksel olarak önemsiz bulunmuştur.
Sonuç: Resiprokal hareket ile kullanılan eğeler, rotasyonel hareket ile kullanılan diğer eğelerle preparasyon sonrası karşılaştırıldığında, metal yorgunluğu açısından daha güvenli bulunmuştur.

Anahtar Kelimeler: Döngüsel Yorgunluk, Ni-Ti Kök Kanal Eğeleri, Wave One, Resiprokal Hareket.

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Introduction

With the use of nickel-titanium (Ni-Ti) files, significant improvements have been achieved in endodontics. The superelasticity of Ni-Ti files has enabled endodontic files to conform better to canal curvature, have more fracture resistance, and wear less, compared to stainless steel files.[1]

Despite the advantages of Ni-Ti files, their fractures are among the most significant concerns about Ni-Ti files. These fractures may occur without visible signs of previous permanent deformation.[2] Studies demonstrate that the incidence of clinically observed instrument fractures ranges from 0.9% to 21%.[3,4,5] The fracture of Ni-Ti files occurs in two ways, flexural (cyclic) fatigue (CF) and torsional forces. Cyclic fatigue occurs when the metal is subjected to repetitive stress and compression cycles, which causes its structure to deteriorate and, ultimately, fracture.[6,7,8]

Many factors (for example, the radius and degree of root canal curvature, and the design, manufacture, and use of the instrument) are believed to affect the CF resistance of canal files. However, manufacturers have recently attempted to improve the fracture resistance of Ni-Ti files by improving production processes, developing new alloys with superior mechanical properties compared to conventional Ni-Ti, and making changes in their kinematics.[9,10,11]

ProTaper Universal (PTU) (Dentsply Maillefer, Ballaigues, Switzerland) is a rotary file system with a variable conical shape. This design is expected to reduce buckling loads, internal fatigue, and possible fractures.[12] ProTaper Next (PTN) (Dentsply Maillefer, Ballaigues, Switzerland) was developed using the new M-Wire alloy. The design features include variable tapers and an off-centered rectangular cross-section.[13]

WaveOne (WO) (Dentsply Maillefer, Ballaigues, Switzerland), of which cross-sections are produced in a modified convex triangle form, enables the shaping of root canals with a single file. The WO file was produced with the M-wire technology that increases flexural fatigue resistance. In the reciprocal movement, the angle of the counterclockwise (CCW) movement is larger than the angle of the clockwise (CW) movement. The file performs the rotation with 120° CCW and 60° CW movements.[14] While the file performs the cutting procedure in its CCW movement, it becomes free in its CW movement. The full cycle is completed with three reciprocating movements. The conducted studies reported that this reciprocating movement prolongs the life of the file compared to continuous rotation.[15,16]

Reciproc files (RPC) (VDW, Munich, Germany) were produced with the M-wire technology like WO files and have the advantages of the M-wire technology. The files have an S-shaped cross-section, a non-cutting end structure, and two sharp cutting edges.[17,18] The files are designed to be used with a reciprocating movement and can be distinguished from other files by their unique design features. The spirals of the files are reversed, and this feature provides them with the ability to cut in the CCW movement. While the file performs the CCW rotation at a wider angle of 150°, it performs the CW rotation at a narrower angle of 30°.[19,20]

This *in vitro* study aimed to investigate the results of flexural fatigue, which might occur in the use of four different Ni-Ti files (PTU and PTN, which are used with rotational movement, and WO and RPC, which are used with reciprocating movement) in inclined root canals, and to conduct a comparative analysis of metal fatigue occurring after their use. Therefore, by learning to what extent Ni-Ti root canal files were affected by the preparation process, it was aimed to obtain information about fracture behaviors and determine the situations that should be considered.

Materials and Methods

The study was initiated after receiving the ethics committee approval dated 11/11/2018 and numbered 2018-11/05 from Cumhuriyet University Clinical Research Ethics Committee. The study was carried out at the Endodontic Clinic of the Faculty of Dentistry of Cumhuriyet University.

The first stage of our study includes the use of Ni-Ti files in artificial models simulating clinical conditions, while the second stage involves the exposure of unused files and files used in simulated models to fracture in the test apparatus and the calculation of the time to fracture.

Due to the risk of fracture of Ni-Ti root canal files, the root canal shaping process was performed on simulated patients. For this purpose, 20 simulated patients' mandibular models, each of which included lower premolar and lower molar teeth on the right and left sides, were created. During the model building process, the extracted teeth with completed root development, lower premolar teeth having a single root and a single canal, lower molar teeth having two roots and three canals (two canals in the mesial root, a single canal in the distal root), and teeth of which canals conformed to the criteria of curved root canals, were included in the study.

The prepared acrylic models were placed on simulated patients, and endodontic access cavities were opened. Digital radiographs (Trophy Trex, CCX Digital, Marne-La-Vallée, France) were obtained using K-file number 10 (Dentsply Tulsa, Oklahoma City, USA), and the working length of each tooth was determined and recorded. Rubber-dam (OptiDam Kerr, Bioggio, Switzerland) was applied to the models before starting the mechanical preparation of the root canals of the teeth on all models (Figure 1).

The experimental groups consisted of PTU (Group 1), PTN (Group 2), WO (Group 3), and RPC (Group 4) files. The files in each group were used in one lower premolar and one lower molar tooth (in four root canals). In the file changes, irrigation was performed with 2 ml of 5.25% NaOCl (Sultan Healthcare, USA).

Figure 1. The simulated patients used in our study and the rubber-dam applied state

Figure 2. Test apparatus used for the evaluation of flexural fatigue

The files used were then tested in the device simulating the root canal slope of 40° at the torque and speed values recommended by the manufacturers. During the preparation of the test apparatus, to minimize friction and to provide the standardization of each file at a certain angle, the test apparatus of Cheung and Darvell[21] was used by performing modifications (Figure 2).

For a more precise calculation of the fracture time of files, an electronic system was installed in the apparatus, and a stopwatch with a 1/100 precision was added. When the file contacts the pins, the circuit is completed, the circuit breaks as soon as the file fractures, and the stopwatch calculates the fracture time accurately by stopping at the same time. The time to fracture was recorded separately for each file. For each file group, the values in seconds that elapsed until the files fractured were multiplied by the files' number of rotations per second, and thus, the files' number of cycles to failure (NCF) was calculated.[22,23]

The control groups consisted of PTU (Group 5), PTN (Group 6), WO (Group 7), and RPC (Group 8) files. The files not used in the control group were placed in the test apparatus like the files in the experimental groups and subjected to fracture tests under air cooling at the torque and speed values recommended by the manufacturers. The time to fracture was recorded separately for each file, and the NCF values were calculated.

Statistical analysis

The data obtained from our study were analyzed using SPSS (Statistical Package for Social Science) version 22.0. In the data analysis, the Kolmogorov-Smirnov significance test of the difference between the two means in independent samples, analysis of variance, and Tukey's test were used when the parametric test assumptions were fulfilled, and the Kruskal-Wallis test and the Mann-Whitney U test were used when the parametric test assumptions were not fulfilled. The significance level was considered to be 0.05.

Results

In our study, the means of the NCF values for the experimental and control groups consisting of 4 different Ni-Ti file systems were presented in Table 1.

When the NCF values were compared in the comparison and statistical evaluation of the experimental and control group results of all groups, minimum values were observed in the experimental group.

Table 1. The means of the NCF values for the experimental and control groups consisted of 4 different Ni-Ti file systems in the study.

	PTU (Mean±SD)					PTN (Mean±SD)		WaveOne (Mean±SD)	Reciproc (Mean±SD)
	S1	S2	F1	F2	F3	X1	X2		
Experimental Group (n=10)	193.66 ±50.96	399.44 ±88.47	333.31 ±54.83	238.62 ±58.46	210.68 ±61.57	1459.65 ±777.54	1385.27 ±458.34	632.67 ±196.98	3928.25 ±1210.26
Control Group (n=10)	204.92 ±41.19	428.15 ±85.39	412.71 ±213.13	245.30 ±121.87	234.28 ±67.10	1821.88 ±489.58	2349.60 ±665.64	777.45 ±250.14	4831.63 ±894.85
RESULT	**P= 0.593**	**P= 0.470**	**P=0.280**	**P=0.878**	**P=0.423**	**P= 0.229**	**P= 0.001***	**P= 0.168**	**P= 0.082**

The mean NCF values of the files in the control group were found to be higher than the mean NCF values of the files in the experimental group. However, the difference in the NCF values between the experimental and control groups was found to be statistically insignificant for all file numbers ($p>0.05$). While the difference between the PTN experimental and control groups was statistically insignificant for the X1 file ($p>0.05$), the difference in the X2 file was statistically significant ($p<0.05$).

Discussion

The metal fatigue of Ni-Ti files can be evaluated in two different ways in the test apparatus torsional and flexural fatigue. In some studies, file fractures occurring due to CF were reported to be more than fractures caused by torsional stress.[24,25,26,27] For this reason, flexural fatigue, which frequently appears in clinical treatments and constitutes a risk factor for file fractures by shortening the life of files, was also investigated in our study.

The CF values of Ni-Ti files can be evaluated clinically with studies carried out on patients, as well as with studies carried out on extracted teeth. Furthermore, different studies have been conducted on the number of uses of files clinically or on extracted teeth. Gambarini [24] investigated flexural fatigue after the prolonged clinical use of thirty ProFile files. Twenty ProFile files, which constituted the experimental group, were used in a total of 10 teeth, including six to seven molars and three to four single-rooted teeth, and an average of 26.7 canals. In the study, in which Aydin *et al.*[28] evaluated flexural fatigue of used and new RaCe files, experimental group RaCe files were used clinically in the root canals of five molar teeth. Yared *et al.*[29] evaluated in their study the metal fatigue of ProFile files clinically after use in the preparation of 4 molar teeth. In another study, the same researchers evaluated the flexural fatigue of ProFile files after using them under conditions simulating clinical conditions.[30] They used the files in the preparation of the mesial canals of the extracted lower molar teeth. They performed the opening of the entrance cavity, the determination of the canal size, and all preparation processes by hand. As is observed in these studies, the use of files for the preparation process of root canals clinically on the patient or on extracted human teeth reflects stresses that will occur on the file most naturally. However, in the studies carried out with the use of extracted teeth by hand, the procedures are performed with direct vision and cannot adequately provide the clinical conditions. Therefore, transferring files to the test apparatus after their clinical use may provide more accurate results. However, it should be kept in mind that during clinical use, files may fracture even at first use. For this reason, in our study, we tried to transfer the clinical conditions to the laboratory environment. Acrylic mandibular models were obtained by using extracted teeth and placed on phantom heads. Thus, the preparation process was performed in vitro on simulated patients, in the working positions under clinical conditions, and under the same visual conditions.

In our study, the files were used at different speed values in line with the recommendation of the manufacturers. Therefore, the number of cycles per second of the files in different groups also differs. For this reason, the NCF values of the files were calculated after the fracture time was determined, and statistical evaluations were made over the NCF values. The NCF values of the files used with the reciprocal movement were calculated over the rpm values specified by the manufacturer without considering the kinematic differences, as in the study by Higuera *et al.*[31]

Nguyen *et al.*[32] evaluated the flexural fatigue of PTN, PTU, and Vortex Blue files in their study. Although Vortex Blue and PTU files are used with the crown-down technique, in PTN files, the apical shaping is performed first. Moreover, although the PTU file was produced from a conventional Ni-Ti alloy, the PTN file was produced with the M-wire technology. As a result, it was determined that the Vortex Blue file was more resistant to flexural fatigue than the PTN file, and the PTN file was more resistant than the PTU file. In our study, similarly to this study, the PTN file fractured at higher NCF values than the PTU file.

In a study, the researchers investigated metal fatigue differences between files by using files with different tapers, and they reported that the file with the highest taper fractured within the shortest time. They attributed this result to the increase in the tensile strength depending on the increase in the diameter of the file, even the curvature remained the same, and to the more free movement of the file with a small taper in the canal than the file with a large taper.[32,33] In our study, the NCF values of ProTaper files were evaluated within the group. Both in the experimental and control groups, among the finishing files of F1, F2, and F3, the file F3 with the highest apical diameter fractured at the minimum number of cycles, while the file F1 with the lowest apical diameter fractured at the maximum NCF value. These results are parallel with the results of other studies. Fife *et al.*[34] investigated CF, which occurred as a result of the prolonged continuous use of PTU files, and they reported that S1 files fractured in a shorter time than S2 files. In parallel with this study, in our study, when shaper files were compared, it was found that while the S1 file with the smallest apical diameter fractured at the least NCF value, the S2 file with the second smallest apical diameter fractured at the maximum NCF value. We think that this result is because the S1 file is the first file used and that files undergo more deformation due to the narrowness of the canal mouths.

When the NCF values of the PTN file were compared within the group, the difference between X1 and X2 files was not found to be statistically significant in both the experimental and control groups. However, in the statistical comparison of the files between the groups, while the difference between the groups for X1 files was found to be statistically insignificant, the difference between the groups for X2 files was found to be statistically significant in favor of the control group. As a result, after the preparation of one lower premolar and lower molar tooth, the X1 file was

not significantly affected by flexural fatigue, whereas the X2 file was significantly affected by it. We think that the X2 file, which was thick, was more affected by the user due to the accumulation of more internal stress and, thus, fractured in a shorter time. The studies on factors such as core thickness and cross-sections of root canal files reported that flexural fatigue resistance decreased, and torsional fracture resistance increased, as core thickness increased. Some researchers reported that files with a large diameter were more vulnerable to flexural fatigue than files with a small diameter due to internal stress accumulation.[24,32]

In our study, following the recommendations of the manufacturer, file S1 was used at the highest torque value, and file S2 was used at the lowest torque value. The studies have reported that the use of endodontic motors with low torque values increases the flexural fatigue resistance of Ni-Ti files. It is stated that the mechanical stress on Ni-Ti files is proportional to the torque of the motor, that the specific torque limit of the file is frequently exceeded when high torque motors are used, and thus, the risk of deformation or fracture due to mechanical stress increases.[24,33] In another study conducted by using different types of motors, the researchers stated that low torque-controlled motors were more reliable than other motors and reported that the slight pressure applied to the apical could reduce the risk of fracture.[34]

There have been many studies investigating the effect of the use of kinematics on instrument fractures.[35,36,37,38] In our study, RPC and WO files, which are used with reciprocal movement and produced with the M-wire technology, and also PTN files, which are used with rotational movement and produced with the M-wire technology, were used. Therefore, it was possible to compare the files produced with the same alloy technology but used in different kinematics.

Castello-Escriva *et al.*[14] compared the flexural fatigue resistance of PTU, WO, and Twisted File files and used each file in the proprietary movements and speeds recommended by the manufacturer. They performed statistical evaluations after calculating the NCF value of each file, and as a result, they found that the WO file used with reciprocal movement was more resistant to flexural fatigue than other files.

We think that this is caused by the fact that RPC and WO files are produced with the M-wire technology, which has been shown to provide the increased cyclic fatigue resistance to files in various studies, and the fact that the reciprocal movement, which occurs in CW and CCW, reduces the files' risk of screwing inside the canal, the compressive and tensile forces to which they are exposed, and the risk of cyclic fatigue. In our study, among the single-file systems, WO and RPC files, which are used with the same kinematics and have the same alloy technology, were compared, and it was observed that RPC fractured at a higher number of cycles than the WO file, which has the modified convex triangular cross-section, similar to the geometry of the PTU file. We think that these similar results are caused by the fact that, unlike the other two files, the RPC file has two cutting-edged S-shaped geometry and a smaller cross-sectional area and that its flexibility increases due to these properties.[39]

We think that this is caused by the fact that RPC and WO files are produced with the M-wire technology, which has been shown to provide the increased cyclic fatigue resistance to files in various studies, and the fact that the reciprocal movement, which occurs in CW and CCW, reduces the files' risk of screwing inside the canal, the compressive and tensile forces to which they are exposed, and the risk of cyclic fatigue.[40,41,42]

As a result, the M-wire technology can increase the flexural fatigue resistance of files. However, factors, such as the file design and the cross-section of files, also affect file fracture. In our study, when the flexural fatigue resistance of the Ni-Ti files produced conventionally and with the M-wire technology was compared, the files produced by the M-wire technology were observed to have more flexural fatigue resistance. It was observed that the flexural fatigue resistance of the Ni-Ti canal files we used decreased as their diameters increased. In our study, it was determined that the reciprocal movement reduced the compressive and tensile forces affecting the files inside the canal and the risk of screwing the files inside the canal and that the flexural fatigue resistance of the files used with reciprocal movement was higher compared to Ni-Ti files used with other rotational movements.

Conclusions

Instead of the direct use of large-diameter files in very narrow and curved canals, we find it safer in such canals firstly to use files with a low taper and then with a high taper, and to use files with reciprocal movement. Further studies, ex vivo or clinical, are highly recommended to verify the clinical efficacy of these instruments for shaping the root canal and for ways to minimize the risk of fracture.

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Conflicts of Interest Statement

None.

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Evaluation of Marginal Adaptation and Microleakage of Differant All-Ceramic Porcelain Systems

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ABSTRACT

Purpose: This study evaluated the marginal adaptation and microleakage of the In-Ceram Alumina, In-Ceram Zirconia and Finesse press all-ceramic porcelain systems.
Material and methods: Thirty maxillary central teeth extracted for periodontal reasons without caries and cracks were divided equally into three groups and there was no control group; only the three systems were compared. Sample teeth cemented were stored in distile water for 24 hours. Then, they were applied to a repeated thermal cycle for 500 times. The samples were left in 5% of basic fuchsin dye for 24 hours. For the marginal adaptation rankings, all of the sample teeth for which cross-sections were made were moved into the metal microscope (Scherr Turico St. James/Minn./USA) and the marginal adaptation degrees were measured in both the palatinal and vestibul regions by measuring twice with x10 enlargement at micron level. For the statistical evaluations of marginal adaptation and microleakage values, Kruskal Wallis test has been used.
Results: The differences between the three all-ceramic porcelain systems are not significant. The Finesse porcelain system caused the least leakage in both regions. In second place in both regions was In-Ceram Alumina. In-Ceram Zirconia caused the most leakage in bothregions. The biggest magrin gap in the palatal region was seen in the Finesse porcelain system, In-Ceram Zirconia in second place. Theleast marginal gap was caused by the In-Ceram Alumina porcelain system.
Conclusions: When the microleakage scores of the In-Ceram Alumina, In-Cream Zirconia and Finesse groups are compared, the differences between the groups are not significant. When the marginal adaptation values of the In-Ceram Alumina, In-Ceram Zirconia and Finesse groups are compared in terms of palatal and vestibular values, the differences are not statistically significant.

Key words: Marginal adaptation, Microleakage, All-Ceramic Porcelain Systems.

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Introduction

New ceramic materials for restorative dentistry have been developed and introduced in recent years.[1] Dental ceramics are known for their natural appearence and their durable cemical and optical properties. However, dentists have remained suspicious of marginal adaptation and microleakage of ceramic restorations.[2]

Along with physical properties of the materials and esthetics of the definitive restoration, a critical clinical parameter is the quality of adaptation to the prepared tooth. Marginal adaptation is one of the important criterions used in the clinical evaluation of fixed restorations. The presence of marginal discrepancies in the restoration exposes the luting agent to the oral environment. The larger the marginal discrepancy and subsequent exposure of the dental luting agent to oral fluids, the more rapid is the rate of the cement dissolution. The resultant microleakage permits the percolation of food, oral debris, and other substances that are potential irritants to the vital pulp. The longevity of the tooth could be compromised, not only by caries, but also by periodontal disease. Clinical studies have shown that poor marginal adaptation of a restoration correlates with increased plaque retantion and reduced gingival health, as indicated by a higher Plaque Index (PI), an elevated Gingival Index (GI), and increased Pocket Depth (PD). A change in the subgingival microflora is also attributed to inadequate marginal adaptation.[4] Inaccurate margins can lead to changes in the periodontal tissues and/or to recurrent caries, and so it is important to assess the accuracy of margins resulting from the use of new, improved materials or techniques[5], however, the adaptation of complete ceramic crowns is a matter of concern to the dentist despite the manufacturer's claim of their superior adaptation.[6]

All-ceramic dental restorations provide esthetics seldom revealed by metal-ceramic restorations. One all-ceramic System is fabricated using a slip-cast technique (In-Ceram, Vita/Zahnfabrik, Bad Säckingen, Germany) and another by a heat-press technique (Finesse, Ceramco, Burlington, NJ, Germany)[4] Alumina ceramic (In-Ceram, Vita/Zahnfabrik, Bad Säckingen, Germany) was recently introduced to create all-ceramic substructures for individual crowns and fixed partial dentures. This ceramic materiai, known originally as Slip-cast, was developed in 1985 by Dr. Sadoun of the biomaterials research laboratory at the University of Paris.[7]

The aim of this study evaluates the marginal adaptation and microteakage values of three all- ceramic porcelain systems.

Materials and Methods

The marginal adaptation and microleakage of 3 different all-ceramic porcelain systems were examined: In-Cream Alumina (In-ceram Alumina, Vita/Zahnfabrik, Bad Säckingen, Germany), In-cream Zirconia (In-ceram Zirconia, Vita/Zahnfabrik, Bad Säckingen, Germany) and Finesse (Finesse, Ceramco, Burlington, NJ, Germany). Thirty maxillary central teethextracted for periodontal reasons without decay and cracks, were used. Teeth were divided equally into three test groups (In-Cream Alumina ten exams (n=10), In-cream Zirconia ten exams (n=10), Finesse ten exams (n=10). The teeth were placed into an autopolymerizing acrylic resin mold for preparation processes for adaptation to the parallelometer table.

The teeth were cut so as to form a 90 degree shoulder in the marginal region with a reduction of 1.2 mm -1.5 mm from the facial, 1.5-2 mm from the incisal, 1.2-1.5 mm from the lingual and interproximal surfaces using a grooved diamond bur (Z-Rex, Diatec Dental AG, Heerbrugg, Germany) and the parellelometer (Parallelometer, Marathom M103, Murcia, İspanya) was externally cooled with an injector, and thus the tooth preparations were performed.

Preparation of In-Cream Alumina and In-Cream Zirconia Porceiain System Samples According to the manufacturer's instructions, the In-Cream Alumina and In-Cream Zirconia processes were made using the same impression materials and the putty-wash technique, after tooth preparation.

To form the casts, phosphate bonded revetment (In-cream Spezialgips revetment, Vita/Zahnfabrik, Bad Säckingen, Germany) was used by mixing 20 g of revetment with 4.6 g of water in revetment mixing. However, before the preparation procedure, servicalregions on the teeth of the cast were determined and the die spacer material (Die spacer Versiegler, Vita/Zahnfabrik, Bad Säckingen, Germany) was applied according to the manufacturer's instructions, over the teeth on the cast, by forming 30-50 microns of cement space in order to make it easier to work. For the In-Ceram Alumina, alumina porcelain powder and for the In-Ceram Zirconium, zirconium porcelain powder were mixed with a glass spatula in a glass tube and then the mixing procedure was completed in a VıtasonicII (VıtasonicII, Vita/ Zahnfabrik, Bad Säckingen, Germany) device for 5-10 minutes according to the manufacturer's instructions.

Then the mixture obtained was moved from the glass tube into a plastic one. The porcelain powder and liquid mixture made as if performing wax modeling over the cast with dies previously made were applied in the form of coatings using a number 5 sable brushes (Vident brushes, Vita/Zahnfabrik, Bad Säckingen, Germany) and the initial conditions of the teeth forms started to be processed. Fore each coating, the same processes were applied. Following the coating process, the overflowed sections were corrected with respect to their form using a number 15 lancet.

The In-Ceram Alumina and In-Ceram Zirconia porcelain samples over the casts with dies were put into an oven manufactured by the same firm (Inceremat, Vita/Zahnfabrik, Bad Säckingen, Germany). The samples were kept for 6 hours at 120 °C with an 8.33 °C increase per minute. They were kept there for another 2 hours and then for a further 2 hours at 1120 °C, and thus the samples were made.

The temperature of the öven was 200°C for 30 minutes for In-Ceram Alumina porcelain samples and after 2.5 hours it reached 1110°C. The oven was at 200 °C for 50 minutes for In-Ceram Zirconia porcelain samples and after 2.5 hours it reached 1140°C. When the temperature reached 400°C, the oven was opened and left to cool to room temperature. Diamond burs were used to level samples removed from the oven, and under 6 atmospheres pressure, they were subjected to 30-50 microns aluminum oxide sanding. The samples were then placed into the oven on the oxide program at 960°C for 10 minutes to discharge the excess glass.

The porcelain (Vitadur Alpha porcelain set, Vita/Zahnfabrik, Bad Säckingen, Germany) was applied with the coating technique after the last leveling process, according to the manufacturer's instructions, and then the glazing material was applied. Following 4 minute preheating, the oven, kept at 600°C with a 107°C increase over 3 minutes immediately after the preheating, was raised to 920°C and the porcelain samples waiting for 1 minute at this temperature were subjected to 5 minute-cooling and were taken from the oven, thus the glazing process was completed.

Preparation of Finesse Porcelain System Samples, According to the manufacturer's instructions, the Finesse process was made using the same impression materials and the putty-wash technique, after tooth preparation.

In order to prepare porcelain samples of Finesse with heat pressure technique, the necessary wax samples were made by melting and pouring the wax into the mold. The wax samples were made according to the manufacturer's instructions by using refractory die material from the same manufacturer. It was mixed in the revetment mixing machine and sprued into the cylinder plastic casting path and was taken into the investment ring. Then, these rings were placed first into the pre-heating oven and with the rise of 5°C per minute and heated until the temperature reached 850°C and wax removal process was made for 60 minutes.

Without keeping the investment rings waiting, they were moved into the oven and placed into the manchet

anchorage. According to the baking conditions, with the 700°C initial starting time and 60°C minute rise in heat process continued and at 930°C vacuum was put into use. The oven at 1180°C for 7 minutes was left for self cooling and kept in cooling by itself for 5 hours.

The Vitadur Alpha porcelain was applied with the coating technique after the last leveling process, according to the manufacturer's instructions, and then the glazing material was applied. Following 4 minute preheating, the oven, kept at 600°C with a 107°C increase over 3 minutes immediately after the preheating, was raised to 920°C and the porcelain samples waiting for 1 minute at this temperature were subjected to 5 minute-cooling and were taken from the oven, thus the glazing process was completed.

Measuring Margial Adaptation of Porcelain Teeth Samples and the Microleakage Values

In the cementation process of the 30 maxillary central teeth samples (10 each prepared by the three methods), glass ionomer based cement was mixed according to the manufacturer's directions (Meron Glass ionomer luting cement, Voco, Cuxhaven, Germany). All of the sample teeth were cemented under a 2 kg of load 5 minutes. Excess cements at the borders of the porcelain crowns were cleaned with hand tools after cementation and then the samples were kept for 24 hours in distilled water at room temperature.

The experimental samples prepared were subjected to 500 repeated thermal cycles, keeping each of them 30 seconds at 5±2°C and 55±2°C. The apex of all sample teeth were coated with a thick coating of sticky wax (Cerawax, Spofa Dental, Jicin, Czechoslovakia) and four coatings of die spacer was applied, forming a gap of 1 mm from the marginal borders of the sample teeth. After the die spacer dried, the sample teeth were kept for 24 hours in 5% basic fuchsin dye.

The teeth were removed form the dye and washed under running water for 15 minutes to completely remove the dye. The die spacer and the sticky wax at the end of the root were cleaned completely with a spatula. They were placed into transparent autopolymerizing acrylic resin so that one third of the teeth roots was in the resin (Ortoplast resin, Vertex, Soesterberg, Holland). Later, smooth cross-sections were taken in the insizo-gingival direction in such a way that they would pass trough the mid central direction of the teeth. For this process, from the sample teeth on the acrylic plates assembled on cross-section making machine, manufactured to operate at low speed (Isomet cutter, Buehler, Ilinois, USA) and under water cooling, the cross-section making processes was completed wıth the aid of a diamond spiral disk. The surfaces of the cross-sections were smoothened using sandpaper.

All samples were examined with a surface microscope (Microscope, Nikon MM-400M, Tokyo, Japon). Following x10 enlargement and zooming adjustments, microscope images of all samples were taken in millimeters using a camera (Panasonic Microskope camera, Panasonic Lumix M 4/3 Adapter, Osaka, Japan) placed into the microscope. In the same microscope, of the sample teeth for which cross-sections were made the microleakage ranked in both the palatal and vestibular directions according to the amount of leakage by repeating the process twice (without distinguishing leakage between the tooth-cement and cement- porcelain structures) and gradation ranking was achieved by looking at dye penetration amounts. On the scale formed, the gradation ranking was performed according to the followings:

Microleakage Rankings

There is no leakage at all

There is leakage to $^{1/4}$ of the intermediate surface (Only in the step regions)

There is leakage to $^{1/2}$ of the intermediate surface (At upper region of the step)

There is leakage to $^{3/4}$ of the intermediate surface (Below the incisal region)

There is leakage to entire intermediate surface (Including the incisal region)

For the marginal adaptation rankings, all of the sample teeth for which cross-sections were made were moved into the metal microscope (Scherr Turico St. James/Minn./USA) and the marginal adaptation degrees were measured in both palatal and vestibular regions by measuring twice with x10 enlargement at micron level.

Statistical Assessment on Marginal Adaptation and Microleakage Values

The data obtained in the study was evaluated with SPSS (Version 7.5) program and Kruskal-Wallis (KW) test was carried out.

Results

When microleakage values of the In-Ceram Alumina, In-Ceram Zirconia and Finesse groups are compared the differences between the groups are not statistically significant (p>0.05) (Table 1) (Figure 1,2,3,4).

The least leakage was in the Finesse porcelain system in both regions. In the second place, again in both regions, was In-Ceram Alumina. In-Ceram Zirconia caused the most leakage in both regions.

When the marginal adaptation values of the In-Ceram Alumina, In-Ceram Zirconia and Finesse groups are compared in terms of palatal and vestibular values, the differences are not statisticaily significant (p>0.05). (Table 3 and 4)

The most margin opening in the palate is given by Finesse, followed by In-Ceram Zirconia. The smallest margin opening was given by In-Ceram Alumina. In the vestibule, the largest margin opening was given by In-Ceram Alumina, followed by In-Ceram Zirconia. The smallest margin opening was given by Finesse.

In all of the three groups of In-Ceram Alumina, In-Ceram Zirconia and Finesse groups in palatinal and vestibul regions, marginal openings were determined to be at certain values.

Table 1. Statistical Assessment of Microleakage Values in Groups.

Groups	Palate	Median	Vestibule	Median
	X±Se	Values	X±Se	Values
In-Ceram Alumina n=10	1.40 ±0.22	1.50	1.50 ±0,16	1.50
In-Ceram Zirconia n=10	1,10 ±0.31	1.50	1.70 ±0.33	1.50
Finesse n=10	0.80 ±0.24	1.50	0.90 ±0.17	1.50

KW = 2.76 KW = 5.20, p>0.05 p>0.05, p-0.251 p=0.074

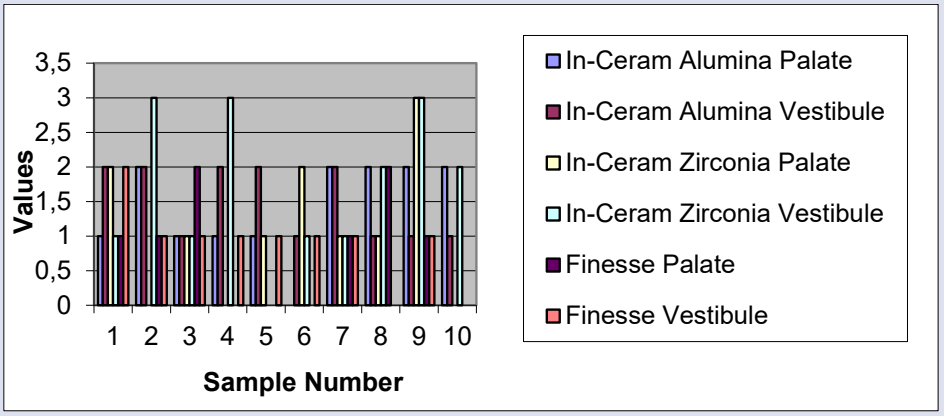

Figure 1. Microleakage values.

Figure 2. Microscopic image taken with x10 enlargement from the sample prepared with the Finesse porcelain system.

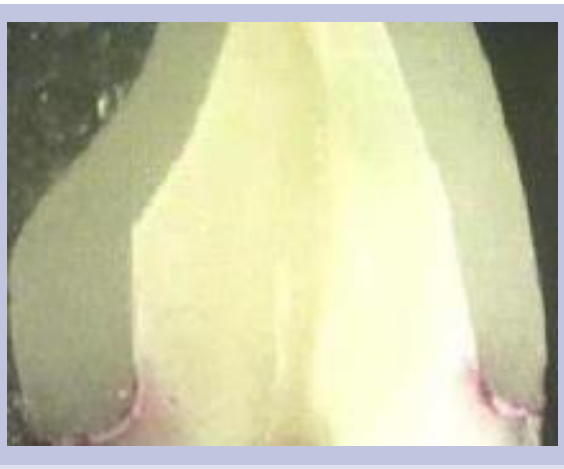

Figure 3. Microscopic image taken with x10 enlargement from the sample prepared with the In-Ceram Alumina porcelain system.

Figure 4. Microscopic image taken with x10 enlargement from the sample prepared with the In-Ceram Zirconia porcelain system.

Table 2. Marginal adaptation values (Measuring twice with xlO enlargement at micron level).

In-Ceram Alumina (Palate)	In-Ceram Alumina (Vestibule)	In-Ceram Zirconia (Palate)	In-Ceram Zirconia (Vestibule)	Finesse (Palate)	Finesse (Vestibule)
200	186	274	82	136	260
36	44	88	134	246	68
144	154	128	236	388	52
94	52	118	118	148	38
72	96	170	30	198	44
72	140	120	68	334	62
194	194	50	56	42	124
122	124	96	140	100	184

Table 3. Statistical evaluation of marginal adaptation in the groups.

Groups	Palate	Palate	Vestibule	Vestibule
	X±Se	Min-Max	X±Se	Min-Max
In-Ceram Alumina n-10	123.80±18.13	36.00-200.00	118.80±17.49	44.00-194.00
In-Ceram Zirconia n=10	130.40±20.84	50.00-274.00	106.80±23.51	30.00-236.00
Finesse n=10	191.20±33.27	42.00-388.00	91.80±26.21	44.00-260.00

Discussion

Microleakage may be defined as the passage of bacteria, fluids, molecules or ions between a cavity wall and the restorative material applied to it. Many different techniques have been used to demonstrate that, despite what clinicians may like to think, the margins of restorations allow the active movement of ions and molecules. These techniques include the use of bacteria, compressed air, chemical and radioactive tracers, electrochemical investigations, scanning electron microscopy and, perhaps most commonly of all, the use of dye penetration studies.

Investigations of leakage have been carried out both in vivo and in vitro, but the latter is more common. In vitro experiments fail broadly into two categories: those that use a clinically relevant cast which attempts to reproduce the oral situations, and those in which the cast does not represent this and is purely a test of the materials behavior.[8]

Thermal changes are cyclic in nature and their effect can lead to material fatigue and early bond failure. Before establishing marginal adaptation and microleakage, the teeth should be exposed to cold and hot food as in the oral cavity.[9]

Different investigators subjected samples to different numbers of thermal cycles: Beznos 600[10], Ceballos et al. 500[11], and Cardoso 700.[12] Generally, the number of thermal cycle varies between 1 and 2500[13]. According to the Standard ISO/TS 11405: 2003[14] that we used, we executed the process 500 times between the 5±2°C and 55±2°C.

Wendt et al. evaluated the effect of thermocycling on dye penetration during the in vitro microleakage analysis of composites. According to their findings, there was no significant increase of microleakage in restorations when thermocycling was used to simulate temperature extremes, either in dye or water baths, as opposed to restorations that were not thermocycled.[15]

Beznosevaiuated the microleakage at the cervical margins of Class II composite resin restorations restored with different techniques. The results showed that all of the techniques worked well for enamel, with almost no leakage. However, on cementum, all techniques demonstrated moderate to severe leakage.[10]

Sorensen et al. evaluated the marginal fidelity and microleakage of porcelain veneers made with platinum foil and refractory dies techniques. The platinum foil veneers had significantly better vertical marginal fidelity but significantly more overcontouring than had the refractory die veneers. Universal microleakage at the tooth-composite resin interface and negligible microleakage at the porcelain-composite resin interface were observed. No relationship was found between the amount of vertical marginal opening and the amount of microleakage.[16]

Schaerer et al. compared the marginal adaptation of three cast ceramic crown Systems (Cerestore, Dicor, and Ceplatec). Cerestore produced an impressive marginal adaptation without technique sensitivity. Dicor produced rounded marginal openings, while Ceplatec produced suitable marginal adaptation.[17]

Holmes et al. measured the marginal adaptation of castable ceramic versus gold crowns. They found no statistically significant difference in the combined absolute marginal adaptation between ceramic and gold crowns. Randomized block ANOVA demonstrated statistically significant differences among individual gold crown samples, but none among individual ceramic crown samples.[18]

Gardner et al. compared the load necessary to cause porcelain failure on traditionally fabricated metal-ceramic crowns cemented to metal tooth analogs with two different types of margins. They found that the load

required to cause porcelain fracture in the crowns with porcelain facial margins was statistically significantly greater than that required to cause porcelain fracture for crowns with metal collars.[19]

Weaver et al. evaluated the variable effects of cementation on the marginal adaptation of Dicor, Cerestore, and porcelain fused to metal crowns. They found that marginal adaptation was not improved with a gingival bevel preparation or an increased seating force. The best marginal adaptation was recorded for Cerestore crowns.[20]

The marginal adaptation values determined are higher than the normal values in the literature.

An ideal restorative possesses perfect marginal adaptation and should not be the cause of microleakage. The results of this study indicate that under simulated conditions of thermocycling, all-ceramic porcelain systems have not improved in terms of marginal adaptation or microleakage properties. However, it is necessary to examine long-term clinical data to understand the characteristics of these all-ceramic porcelain systems. When using all- ceramic porcelain systems for prosthetic restorations in clinical practice, the influence of marginal adaptation and microleakage should be taken into consideration.

Conclusions

With the research conducted, the marginal adaptation and microleakage of different all-ceramic porcelain systems (In-Ceram Alumina and In-Ceram Zirconia porcelain systems made on refractor dies in form of core material, and Finesse porcelain system with the heat pressure technique), that can play a role in failure of the same porcelain systems were compared and the results are indicated below.

When the microleakage scores of the In-Ceram Alumina, In-Cream Zirconia and Finesse groups are compared, the differences between the groups are not significant ($p>0.05$).

When the marginal adaptation values of the In-Ceram Alumina, In-Ceram Zirconia and Finesse groups are compared in terms of palatal and vestibular values, the differences are not statistically significant ($p>0.05$).

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Conflicts of Interest Statement

None.

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Accuracy of 3 Electronic Apex Locators in Nonsurgical Retreatments of Teeth with Root-Ends Resected at Different Angles: In-Vitro Study

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ABSTRACT

Aim: The accuracy of three electronic apex locators (EALs) during retreatment of root-end resected teeth with different resection bevel angles were evaluated in the present study.
Materials and Methods: Forty mandibular premolar teeth were divided into two groups regarding resection bevel angle after root canal filling. In the first group, the apical 3 mm of each specimen was resected at a 0-degree bevel angle using a diamond bur. The resection bevel angle was approximately 45-degree in the second group. Electronic length measurements were obtained with a size 15 K-file advanced apically in dissolved gutta percha using Dentaport ZX, Propex Pixi, and Apit 15. The filling materials were then completely removed from the root canals, and the actual lengths up to the resection region were determined. The actual length was subtracted from the electronic length measurements for each specimen. Measurements were analyzed statistically using independent sample t-test, repeated-measures analysis of variance, and Bonferroni tests. The level of statistical significance was defined as $p<0.05$.
Results: In the 45-degree group, a significant difference was found between Propex Pixi and Apit 15. Measurements at 0- and 45-degree resection bevel angles were not statistically different from each other in any EAL groups.
Conclusions: The resection bevel angle did not affect the accuracy of the tested EALs. More accurate measurements were obtained with the Propex Pixi at a 45-degree resection bevel angle compared with the Apit 15.

Keywords: Electronic Apex Locator, Resection Bevel Angle, Retreatment, Root Canal.

Kök Uçları Farklı Açılarda Rezeke Edilmiş Dişlerin Cerrahi Olmayan Yeniden Tedavilerinde 3 Elektronik Apeks Bulucunun Doğruluğu: In Vitro Çalışma

Süreç

Geliş: 14/04/2022
Kabul: 07/06/2022

ÖZ

Amaç: Bu çalışmada, farklı rezeksiyon eğim açılarıyla kök ucu rezeke edilmiş dişlerin yeniden tedavileri sırasında üç elektronik apeks bulucunun (EAB) doğruluğu değerlendirildi.
Gereç ve Yöntem: Kırk mandibular premolar diş rezeksiyon eğim açısına göre kanal dolgusu sonrası iki gruba ayrıldı. Birinci grupta, her örneğin apikal 3 mm'si elmas frez kullanılarak 0-derecelik bir eğim açısında rezeke edildi. İkinci grupta rezeksiyon eğim açısı yaklaşık 45-dereceydi. Elektronik uzunluk ölçümleri, Dentaport ZX, Propex Pixi ve Apit 15 kullanılarak çözünmüş güta perka içinde apikal olarak ilerletilmiş 15 numaralı bir K-tipi eğeyle elde edildi. Daha sonra dolgu maddeleri kök kanallarından tamamen uzaklaştırıldı ve rezeksiyon bölgesine kadar olan gerçek kanal uzunlukları belirlendi. Her örnek için gerçek uzunluk, elektronik uzunluk ölçümlerinden çıkarıldı. Ölçümler independent sample t-test, tekrarlı ölçümlerde varyans analizi ve Bonferroni testleri kullanılarak istatistiksel olarak analiz edildi. İstatistiksel anlamlılık düzeyi $p<0.05$ olarak tanımlandı.
Bulgular: 45-derece grubunda Propex Pixi ve Apit 15 arasında anlamlı fark bulundu. 0- ve 45-derecelik rezeksiyon eğim açılarındaki ölçümler, hiçbir EAB grubunda istatistiksel olarak birbirinden farklı değildi.
Sonuçlar: Rezeksiyon eğim açısı, test edilen EAB'ların doğruluğunu etkilemedi. Propex Pixi ile 45-derecelik rezeksiyon eğim açısında Apit 15'e göre daha doğru ölçümler elde edildi.

Anahtar Kelimeler: Elektronik Apeks Bulucu, Rezeksiyon Eğim Açısı, Yeniden Tedavi, Kök Kanalı.

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Introduction

At present, all reliable endodontic techniques are based on the thorough cleaning, disinfection, and filling of root canals. For a successful root canal treatment, the infected root canal contents must be completely removed, microorganisms and their products must be eliminated, and the root canal system must be sealed hermetically.[1] Although nonsurgical root canal treatment has become a routine dental procedure, long-term healing is not observed in all treatments. Due to the high number of treatments performed, the small number of failed cases turn into relatively large number of patients requiring further treatment.[2]

Many reasons are reported in the endodontic literature for the failure of initial nonsurgical root canal treatment. These are inadequate access cavity planning; untreated main and/or accessory canals[3]; poorly cleaned and filled canals[4]; errors during root canal instrumentation such as ledges, perforation, or instrument fracture[5,6]; and procedural errors such as overfilling.[7] Coronal leakage due to inadequate coronal restoration is also responsible for post-treatment failure.[8]

Orthograde root canal retreatment, surgical endodontic treatment, transplantation, tooth replantation, extraction with no prosthetic replacement, extraction and replacement by using a dental prosthesis, and extraction and replacement with single implant-supported crown are the treatment approaches that can be preferred in the failure of the initial root canal treatment.[9-11]

Although it is not a routine procedure, an orthograde revision may be required for root-end resected teeth in case of persistent infection or secondary root canal infection.[12,13] Root-end resection alone cannot usually initiate the recovery of apical periodontitis caused by intraradicular infection. It can be achieved by nonsurgical revision (orthograde retreatment) of insufficient or infected root canal filling.[13] Therefore, the first step should be to remove filling material completely and clean and shape the root canal system adequately.[14]

The determination of the radiographic working length is often a problem in the procedures for revising the root canal filling of resected teeth because it is difficult to identify the apical terminus of the root canal on radiographs depending on the resection bevel angle.[13] Apical microsurgery procedures performed with an operating microscope and surgical ultrasonic tips reduce the need for inclined cutting of the root-end. However, when the resection bevel angle is different from 0-degree, the apical terminus of the root canal will be shorter than the radiographic apex, and the working length will generally be determined longer.

Electronic apex locators (EALs) accurately determine the working length in initial root canal treatments and retreatments.[15-18] However, the large apical terminus size of the root canal may affect the accuracy of EALs in the resected teeth, as the apical anatomy is changed and apical narrowing of the canal is removed by root resection.[12,13]

Different generations of EALs have been introduced to measure working length by locating the root apex. The DentaPort ZX (Morita, Tokyo, Japan) is a combined device that measures the working length by simultaneous measurement of impedance values in the same canal using two different frequencies (8 kHz and 0.4 kHz).[19] The Propex Pixi (Dentsply Maillefer, Ballaigues, Switzerland), on the other hand, is a pocket-sized, multifrequency type EAL.[15] The Apit 15 (Osada Electric Co., Ltd., Tokyo, Japan) also measures at two frequencies. It determines the apical constriction by comparing the impedances of two different frequencies.[20] It has been shown in previous studies that EALs determine the apical terminus within a clinically acceptable range in root-end resected teeth.[12,13] The purpose of this in-vitro study is to evaluate the accuracy of three different EALs in determining the apical terminus during retreatment of root-end resected teeth with different resection bevel angles.

Materials and Methods

The study design was approved by the Non-Interventional Clinical Research Ethics Committee of Sivas Cumhuriyet University, Sivas, Türkiye (2018-05/17). Forty human mandibular premolars with single straight root canals extracted for orthodontic or periodontal reasons were used in the study. Root canal morphology were determined via buccolingual and mesiodistal preoperative radiographs. After the teeth were kept in 5.25% sodium hypochlorite (NaOCl) for 15 minutes to remove organic debris, the soft and hard tissue residues were removed from the root surfaces using a periodontal curette. Teeth with root fractures/cracks, open apices, resorption, caries, or calcified root canals were excluded from the study. Selected teeth were stored in distilled water until used. Access cavities were prepared and apical patency was checked with a 10 K-file. To obtain approximately 17 mm standardized root length and a constant reference point for all measurements, the coronal parts of the teeth were removed. The working length of each root canal was determined by subtracting 0.5 mm from the measured length after the tip of a size 15 K-file was visible at the major foramen.

All root canals were instrumented with the S5 system (Sendoline, Täby, Sweden) up to size 30/.04 using EndoTouch TC2 (SybronEndo, Glendora, CA, USA). New instruments were used for every 4 canals. 2 mL of 2.5% NaOCl were used as an irrigation solution after each instrument change. After shaping, the canals were rinsed with 5 mL of 17% ethylene-diaminetetraacetic acid for 1 minute followed by 5 mL of NaOCl. A final rinse with 5 mL of distilled water was performed. Root canal obturation was done using AH Plus (Dentsply DeTrey, GmbH, Konstanz, Germany) and gutta percha (Diadent, Chongju, Korea) with cold lateral compaction technique. Finally, temporary filling material was placed into the access cavity, and all samples were stored under 100% humidity at 37 °C for seven days to provide complete hardening of the sealer.

The samples were then randomly divided into two groups of 20 specimens each according to the resection

bevel angle. In the first group, the apical 3 mm of each specimen was resected at a 0-degree bevel angle using a diamond bur. The resection bevel angle was approximately 45-degree in the second group. All samples and lip clips of the EALs were embedded in an alginate mould. The filling material was removed from the coronal thirds with a size 3 Gates-Glidden bur. Eucalyptol was then introduced into each root canal to soften the gutta percha. The electronic canal lengths (ELs) were measured with a size 15 K-file advanced apically in the dissolved gutta percha using a digital caliper. ELs were recorded with the Dentaport ZX device at the last green bar, with the Propex Pixi at the 0.0 mark and with the Apit 15 at the meter readings "APEX" line in each group.

After all EL measurements were obtained, the root canal filling materials were completely removed. The actual lengths (ALs) were measured by visualization of the tip of a size 15 K-file at the resection site using a dental loupe with 3.5× magnification. Measurements were repeated three times for each tooth by the same operator, and the mean of these measurements was calculated. The AL was subtracted from the EL measurements for each specimen. Respectively, positive and negative values represented measurements that were long and short of the AL, whereas 0.0 showed coinciding measurements.

Statistical analysis was done with IBM SPSS Statistics version 22.0 (IBM Corp., Armonk, NY). The Kolmogorov-Smirnov test was used to assess the normality of data, and measurements were analyzed statistically using independent sample t-test, repeated-measures analysis of variance, and Bonferroni tests. The level of statistical significance was considered as $p<0.05$.

Results

The mean and standard deviation (SD) values of the difference between EL and AL for each EAL in root-end resected teeth with different resection bevel angles are shown in Table 1. According to the data obtained, no statistically significant differences were observed between the EALs evaluated in teeth resected at an angle of 0-degree ($p=0.250$). There was a significant difference between the EALs when the measurements were taken in teeth resected at an angle of 45-degree ($p=0.002$). The Propex Pixi was more accurate than the Apit 15 at a 45-degree resection bevel angle. Measurements at different resection bevel angles were not statistically different in any EAL groups ($p>0.05$).

Discussion

In a nonsurgical retreatment procedure, which is among the treatment options in case of failed apical surgery, the working length determination may have some hardships as the resection level or angle cannot be exactly determined on the radiograph.[21] When the apex was resected with an angle different from 90-degree to the long axis of the root, it may not be possible to accurately establish the radiographic working length.[22] The present study investigated the reliability of the Dentaport ZX, Propex Pixi, and Apit 15 in the presence of root canal filling material in teeth resected with different resection bevel angles**.**

Previous studies reported that these devices could accurately determine the working length.[15,23-25] Furthermore, other studies showed that these EALs determined the working length accurately after removing the root canal fillings during retreatment procedures.[18,26,27] However, as in apically resected teeth, apical constriction is not always present in teeth with apical root resorption or in teeth with open apices.[28] EAL readings differ from the actual working length for teeth with apical foramina exceeding 0.5 mm, such as immature permanent teeth.[29] Herera *et al.*[30] stated that the accuracy of the Root ZX device within ± 0.5 mm was 87% in 0.6 mm foramen diameter and 84% using files size 45 or larger in 0.7 mm foramina. However, when the foramen diameter was 0.9 mm or 1.0 mm, the accuracy of the device was 73% or 63%, respectively, even within a tolerance of ±1.0 mm. In teeth with simulated apical root resorption, within ± 0.5 or ± 1.0 mm, a previous study reported the accuracy of 76.6% or 96.9% for the Root ZX, 82.8% or 96.9% for the Apit, respectively.[31] In another study, within the margin error of ± 0.5 and ± 1.0 mm, the Root ZX was precise in 77% and 94% of the primary molar teeth with root resorption, respectively.[32]

In the present study, the accuracies of the tested EALs were not affected by different cutting angles. However, the SD value of the Dentaport ZX was lower at 0-degree resection bevel angle than 45-degree resection bevel angle, and a low SD is obtained when the EAL measurements are consistent. These findings cannot be compared with existing data. To the best of our knowledge, no reports on the accuracy of EALs for determining apical terminus in teeth resected with different resection bevel angles are available.

Although no significant differences were noted among the tested EALs in the 0-degree group, the Propex Pixi gave more accurate measurements than the Apit 15 in the 45-degree group. Dentaport ZX is based on the same principle as the original Root ZX. ElAyouti *et al.*[13] reported that the Root ZX (90%) was the most accurate in detecting the apical terminus of the root-end resected teeth within ± 1.0 mm compared with the Raypex 4 (78%) and Apex Pointer (75%) devices. They concluded that all the EALs tested were able to determine the apical terminus of resected teeth within an acceptable range. Uzun *et al.*[12] also claimed that the EAL function of the Tri Auto ZX which features the same electronics as the Root ZX useful for WL determination in orthograde retreatment procedures of root-end resected teeth. However, the auto-reverse function is not useful for these procedures. Similar to the observations of ElAyouti et al.[13] and Uzun *et al.*[12], the present study showed that the three devices were reliable because the greatest mean difference value was 0.238 mm and the accuracy of detecting the resection site within ± 1.0 mm was 100% for all tested devices.

Table 1. Mean and standard deviation (SD) values of the difference between the electronic length and the actual length for each Electronic Apex Locator in root-end resected teeth with different resection bevel angles (mm)

	0-degree Mean ± SD	45-degree Mean ± SD	p values
Dentaport ZX	0.180 ± 0.244^{Aa}	0.209 ± 0.373^{ABa}	0.776
Propex Pixi	0.181 ± 0.332^{Aa}	0.103 ± 0.325^{Aa}	0.454
Apit 15	0.235 ± 0.323^{Aa}	0.238 ± 0.323^{Ba}	0.973
P values	0.250	0.002*	

Different superscript uppercase letters in the same column indicate a statistically significant difference (*p<0.05). Different superscript lowercase letters in the same row indicate a statistically significant difference (*p<0.05).

Table 2 Frequency [n (%)] of the measurements relative to the resection site (0.0).

	0-degree			45-degree		
	Dentaport ZX	Propex Pixi	Apit 15	Dentaport ZX	Propex Pixi	Apit 15
<-1.0	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
-1.0 to -0.51	0 (0)	0 (0)	0 (0)	1 (5)	2 (15)	0 (0)
-0.50 to 0.0	3 (15)	5 (25)	4 (20)	4 (20)	3 (15)	4 (20)
0.01 to 0.50	15 (75)	12 (60)	14 (70)	10 (50)	14 (70)	13 (65)
0.51 to 1.0	2 (10)	3(15)	2 (10)	5 (25)	1 (5)	3 (15)
>1.0	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Negative values indicate measurements short of the actual length.

Within ± 0.5 mm of the resection site, the accuracies of three EALs (Dentaport ZX, Propex Pixi, and Apit 15) were 90, 85, and 90% for 0-degree resection bevel angle, and 70, 85, and 85% for 45-degree resection bevel angle, respectively (Table 2).

The strictest tolerance limit of ± 0.5 mm[22,33,34] and the more lax tolerance margin of ± 1.0 mm[15,16,27] have been used to evaluate the accuracy of the EALs in many studies. In the present study, difference values falling within these limits were deemed clinically acceptable since it was difficult to visually check the relationship between the rubber stop and the reference point, the rubber stop and the caliper, or the file tip and the caliper. Also, it was difficult to visualize the exact point where the tip of the file reached the resection site, even with magnification, especially in teeth resected with a 45-degree angle. In the 0- or 45-degree groups, the Dentaport ZX resulted in overestimation in 85% or 75% of the canals, respectively. In both 0- and 45-degree groups, the percentages of overestimation were 75% for the Propex Pixi and 80% for the Apit 15. This present result differed from the study of ElAyouti *et al.*[13], who reported that the Root ZX exhibited high accuracy without over-instrumentation of the root canal. The different methodologies might explain this discrepancy; ElAyouti *et al.* determined the electronic measurements with a small size file by taking the average of the two readings (apical 0.0 and coronal 0.0 readings) after root canal filling removal and canal enlargement. A root canal with a large apical size may cause underestimation of the root canal length, especially when using a small size file.[23,35-37]

Conclusions

According to the findings of our study, the mean values of the tested EALs were within the tolerance range of ± 0.5 mm according to the actual length, so the measurements obtained were clinically acceptable. The working length can be successfully determined with electronic apex locators even in the presence of root canal filling in the orthograde revision of root-end resected teeth. The accuracies of the Dentaport ZX, Propex Pixi, and Apit 15 in resected teeth were not affected by the different resection bevel angles. However, Dentaport ZX was accurate to ±0.5 mm in 90% of teeth resected at a 0-degree angle and 70% of the teeth resected with a 45-degree angle. Propex Pixi responded more successfully than the Apit 15 at a 45-degree resection bevel angle

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Conflicts of Interest Statement

The authors declare no conflict of interest.

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The Menstrual Cycle Phase and Effect of Aromatherapy on Orthodontic Debonding Pain

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ABSTRACT

Objectives: The aim of this prospective clinical study was to evaluate the effects of the menstrual cycle phases and aromatherapy on women's perception of orthodontic debonding pain.

Materials and Methods: The materials of this study were consisted of randomly selected 48 female patients (mean age: 19.00±3.40 years). Four different study groups were performed. LA+; the patients in the luteal phase and received aromatherapy (n=12), LA-; the patients in the luteal phase and did not receive aromatherapy (n=13), FA+; the patients in the follicular phase and received aromatherapy (n=11), FA-; the patients in the follicular phase and did not receive aromatherapy(n=12). Debonding was performed and the pain experience for each tooth was scored by the patient on a visual analogue scale (VAS). Also, participants' general responses to pain were assessed with the Pain Catastrophizing Scale (PCS). The aromatherapy protocol was to inhale lavender oil from approximately 30 cm for 3 minutes, 3 minutes before debonding.

Results: It was found that the mean VAS scores were higher in the luteal phase than in the follicular phase, however this difference was not statistically significant. There was no statistically significant difference between the groups with and without aromatherapy in terms of VAS scores. The correlation between total PCS scores and total VAS scores was statistically significant (r=0.310).

Conclusions: Debonding in female patients is recommended for the comfort of patients on days when the patient's menstrual phase is in the follicular phase. It should be considered that patients with a lower pain threshold will experience more pain during the orthodontic debonding procedure.

Keywords: Aromatherapy, Menstrual Phase, Orthodontic Debonding, Pain.

Menstrüel Döngü Evresi ve Aromaterapinin Ortodontik Debonding Ağrısına Etkisi

Süreç

Geliş: 02/06/2022
Kabul: 21/04/2022

ÖZ

Amaç: Bu prospektif klinik çalışmanın amacı, menstrüel siklus evrelerinin ve aromaterapinin kadınların ortodontik debonding ağrı algısı üzerindeki etkilerini değerlendirmektir.

Yöntem: Çalışmamızın materyallerini rastgele seçilmiş 48 kadın hasta (ortalama yaş: 19,00±3,40 yıl) oluşturmuştur. Dört farklı çalışma grubu gerçekleştirilmiştir. LA+; luteal fazda olup aromaterapi alan hastalar (n=12), LA-; luteal fazda olan ve aromaterapi almayan hastalar (n=13), FA+; foliküler fazda olup aromaterapi alan hastalar (n=11), FA-; folliküler fazda olan ve aromaterapi almayan hastalar (n=12). Debonding işleminden sonra, her diş için ağrı deneyimi hasta tarafından görsel analog skalada (VAS) puanlanmıştır. Ayrıca, katılımcıların ağrıya genel tepkileri Ağrı Felaketleştirme Ölçeği (PCS) ile değerlendirilmiştir. Aromaterapi protokolü, debonding işleminden 3 dakika önce yaklaşık 30 cm'den 3 dakika boyunca lavanta yağını soluyarak gerçekleştirilmiştir.

Bulgular: Ortalama VAS skorlarının luteal fazda foliküler faza göre daha yüksek olduğu bulunmuştur; ancak bu fark istatistiksel olarak anlamlı değildir. Aromaterapi alan ve almayan gruplar arasında VAS skorları açısından istatistiksel olarak anlamlı fark bulunmamıştır. Toplam PCS puanları ile toplam VAS puanları arasındaki korelasyon istatistiksel olarak anlamlıdır (r=0.310).

Sonuç: Ortodontik tedavi gören kadın hastalarda debonding işleminin, daha az ağrı hissetmeleri için menstrüel evrenin foliküler fazında olduğu dönemlerde yapılması önerilmektedir. Ağrı eşiği düşük olan hastaların ortodontik debonding işlemi sırasında daha fazla ağrı duyabileceği göz önünde bulundurulmalıdır.

Anahtar Kelimeler: Aromaterapi, Menstrüel Evre, Orthodontik Debonding, Ağrı.

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Introduction

The sensation of pain is an important physiological and emotional experience that can vary according to factors such as gender, age, past experiences with pain, emotional stress, and cultural background.[1] Different levels of pain sensation accompany the process depending on the applied biomechanical principles in various stages of orthodontic treatment. Approximately 95% of patients undergoing orthodontic treatment reported that they experience varying degrees of pain.[2] There is not enough literature data on the presence, causes, and severity of pain in the debonding phase when brackets, tubes and/or bands are removed. The debonding phase is a painful procedure of varying severity from person to person. It has been reported that while some individuals feel very low levels of pain, some individuals feel a higher level of pain.[1] Many studies have reported that female patients feel more pain than male patients and this is related to gonadal hormones.[3,4]

The menstrual cycle of women consists of two consecutive phases: the follicular and luteal phases. Although the length of a cycle varies among women, it is 28 days on average.[5] The luteal phase is 14 days before the first day of menstrual bleeding and the remaining days of the cycle are the follicular phase. While the follicular phase may show different durations according to the cycles (14-21 days), it is stated that the luteal phase has more stable periods.[6] It is known that fluctuations in hormonal, physical and psychological symptoms occur in the follicular and luteal phases of the menstrual cycle.[7] Thermal, pressure and ischemic pain perceptions increase in the luteal phase compared to the follicular phase.[8]

Aromatherapy is the practice of using natural aromatic essential oils for a range of applications that have been shown to improve mood, relieve pain, and improve cognitive function.[9] Aromatherapy is performed by releasing the volatile scent of essential oils into a certain environment. Aroma compounds are converted into chemical signals via the nasal mucosa and these are transferred to the brain.[10] This practice with plant-based fragrances has a very low application cost, has no side effects reported in the literature, and does not tend to cause addiction.[11-13]

Some studies have reported that aromatherapy can be used among non-pharmacological treatment methods for dental anxiety, since it reduces dental anxiety levels.[14,15] While the scents of natural essential oils are diffused into the air by candles or dispensers, inhalation of scent molecules stimulates the limbic system of the brain through the olfactory system.[10] This may enable patients to relax their bodies and tense mental states[16] the implementation of various planned dental treatments may become easier and more comfortable for the patient.[14] Moreover, it has been reported that the application of aromatherapy in dental clinics also masks the unpleasant eugenol odour reported by the patient as one of the main sources of anxiety.[17]

When we searched the literature, we could not find a study investigating the menstrual cycle phase and the effect of aromatherapy on orthodontic debonding pain perception. The aim of this study was to evaluate the effects of the follicular and luteal phases of the menstrual cycle and aromatherapy on women's perception of orthodontic debonding pain. There are 2 hypotheses tested in this study:

- Aromatherapy reduces the level of pain during the orthodontic debonding process.
- Women feel less pain in the follicular phase during orthodontic debonding.

Materials and Methods

The research protocol of this clinical study was approved by the Nevsehir Hacı Bektas Veli University Ethics Committee (No: 2020.13.142, Date: 23 June 2020). The scope of the study was explained to all patients participating in the study and a signed and informed consent form was obtained from the patient/parents. Patients with a history of ongoing psychiatric treatment, history of mild to severe periodontal disease, difficulty in communication, irregular menstrual cycle, amenorrhea, pregnancy, history of combined oral contraceptive use, any pain sensation in the orofacial region and using analgesics within 24 hours before the appointment were excluded from the study. Patients in the debonding phase of orthodontic treatment and treated with fixed orthodontic treatment using metal brackets, patients with regular menstrual cycles, and without systemic disease were included in this study.

The sample size was determined using the G*Power software program (Version 3.1.9.2, Universität Düsseldorf, Germany) with an alpha error probability of 0.05 and a power of 95% (effect size 0.5). Power analysis showed that a total of 45 patients were adequate. The material of this study consists of 48 patients (average age: 19.00±3.40 years) who were randomly selected from female patients who were treated at the Department of Orthodontics, Faculty of Dentistry of Ordu University and met the inclusion criteria. Four different study groups were designed depending on whether aromatherapy was applied or not and whether the menstrual phase was in the follicular or luteal phase. LA+; the patients in the luteal phase and received aromatherapy (n=12), LA-; the patients in the luteal phase and did not receive aromatherapy (n=13), FA+; the patients in the follicular phase and received aromatherapy (n=11), FA-; the patients in the follicular phase and did not receive aromatherapy (n=12).

Debonding was performed by the same orthodontist (T.A.) and debonding was started after taking medical anamnesis. The researcher interviewed all patients and debonding was performed using a torque action with the same debonding device (Ixion™, DB Orthodontics). The brackets were removed one by one from right to left in the

maxilla and mandible and a 100 mm VAS was prepared for each tooth (Figure 1). According to this scale, a score of 0 means "no pain" and scores increasing from 0 to 100 represent an increase in pain. Patients were asked to mark according to the level of discomfort experienced after bracket/tube/band removal from each tooth, and the pain experience for each tooth was scored by the patient in VAS.

Figure 1. Removal of brackets with finger pressure and torque movement during the orthodontic debonding process.

Figure 2. Aromatherapy process applied by inhalation and lavender oil used in this study.

Participants' general responses to pain were assessed with the Pain Catastrophizing Scale (PCS). PCS is one of the basic scales that also includes cognitive and emotional components related to pain.[18,19] To assess the link between personal characteristics and actual pain during debonding, PCS consisting of 13 statements describing participants' general response to any painful situation, different thoughts and feelings that may be associated with pain, was used. PCS questionnaires were administered to patients after debonding.

The aromatherapy group was randomly selected among patients who met the criteria. The patient inhaled the aroma in a glass godet by dropping 5 drops of lavender oil into 10 cc water, 3 minutes before the debonding process at about 30 cm[20] (Figure 2). Skin contact is avoided. Lavender natural essential oil (100% pure Lavandula angustifolia Mill. NU13950, lot number 9133, Code APE 7490B) was purchased from Nu-KA Defne Essencia (Antalya, Türkiye). The origin country of the lavender plant is France. The other group was the control group and aromatherapy was not applied.

Statistical analysis was performed using the statistical analysis program (SPSS Inc., version 20 for Windows; Chicago, IL, USA). The distribution of the data was evaluated by the Shapiro-Wilks normality test. Mann Whitney U-test was used to compare VAS values between groups and Spearman's rank correlation coefficient analysis was used to evaluate the correlation between total VAS score and PCS. Statistical significance level was determined as $p<0.05$.

Results

The distribution of ages by groups shown in Table 1. The comparison of the VAS and PCS scores of the subjects who did not receive aromatherapy are shown in Table 2, and the data of the subjects who received aromatherapy are shown in Table 3. The higher VAS scores were observed in both the upper and lower jaws in both the groups that received and did not receive aromatherapy in the luteal phase. While the total VAS score of the LA+ group was 211.83, this value was 143.64 in the FA+ group. The comparison of the VAS and PCS scores of the individuals who received and did not receive aromatherapy in the luteal phase is shown in Table 4. Although there was no statistically significant difference in VAS scores between the LA+ and LA− groups, all VAS scores were higher in the LA+ group. The comparison of VAS and PCS scores of individuals who received and did not receive aromatherapy in the follicular phase is shown in Table 5. Although there was no statistically significant difference in VAS scores between the FA+ and FA− groups, all VAS scores were higher in the FA+ group. Spearman correlation values between VAS scores and PCS scores are given in Table 6. The correlation between total PCS scores and total VAS scores was statistically significant ($r=0.310$, $P<0.05$), regardless of menstrual stage and aromatherapy application.

Discussion

It was concluded that the application of aromatherapy in female patients did not reduce the level of pain during the orthodontic debonding procedure. However, the level of pain felt by female patients when orthodontic debonding is applied in the follicular phase less than in the luteal phase. Accordingly, while the first hypothesis of this study was rejected, the second hypothesis was accepted.

Many factors have been identified that may cause pain during the orthodontic debonding procedure. General health status of the patient, gender, tooth structure, mobility in teeth, direction of force applied during debonding are some of these factors.[21] It has been reported that the most effective of these factors are the mobility of the teeth and the direction of force applied during orthodontic debonding. It has been reported that patients feel less pain during debonding in intrusive forces than in mesial/distal, facial/lingual or extrusive forces.[21]

Table 1. Comparison of the ages of individuals between groups

	Groups				Pα
	LA+ (n=12) Mean (SD)	LA− (n=13) Mean (SD)	FA+ (n=11) Mean (SD)	FA− (n=12) Mean (SD)	
Age (years)	19.14 (3.03)	18.43 (3.28)	18.67 (2.52)	19.79 (4.63)	0.778

LA+: the patients in the luteal phase and received aromatherapy, LA−: the patients in the luteal phase and did not receive aromatherapy, FA+: the patients in the follicular phase and received aromatherapy, FA−: the patients in the follicular phase and did not receive aromatherapy, SD: Standard deviation, α Results of One-way analysis of variance.

Table 2. Comparison of VAS and PCS scores of subjects without aromatherapy

	LA−	FA−	p*
	Mean (SD)	Mean (SD)	
Upper tooth VAS scores	59.92 (102.47)	40.58 (45.71)	0.478
Lower tooth VAS scores	82.00 (138.34)	36.42 (39.67)	0.870
Total VAS scores	141.92 (232.13)	77.00 (75.73)	0.913
PCS scores	8.46 (12.87)	4.08 (5.45)	0.464

LA−: the patients in the luteal phase and did not receive aromatherapy, FA−: the patients in the follicular phase and did not receive aromatherapy, SD: Standard deviation, *Results of Mann-Whitney U test.

Table 3. Comparison of VAS and PCS scores of aromatherapy subjects

	LA+	FA+	p*
	Mean (SD)	Mean (SD)	
Upper tooth VAS scores	109.00 (123.95)	79.36 (164.58)	0.116
Lower tooth VAS scores	120.83 (160.78)	64.27 (106.71)	0.708
Total VAS scores	211.83 (272.37)	143.64 (233.84)	0.267
PCS scores	4.42 (8.27)	2.73 (4.88)	0.699

LA+: the patients in the luteal phase and received aromatherapy, LA−: the patients in the luteal phase and did not receive aromatherapy, SD: Standard deviation, *Results of Mann-Whitney U test.

Table 4. Comparison of VAS and PCS scores of subjects without aromatherapy

	LA+	LA−	p*
	Mean (SD)	Mean (SD)	
Upper tooth VAS scores	109.00 (123.95)	59.92 (102.47)	0.113
Lower tooth VAS scores	120.83 (160.78)	82.00 (138.34)	0.956
Total VAS scores	211.83 (272.37)	141.92 (232.13)	0.265
PCS scores	4.42 (8.27)	8.46 (12.87)	0.315

LA+: the patients in the luteal phase and received aromatherapy, LA−: the patients in the luteal phase and did not receive aromatherapy, SD: Standard deviation, *Results of Mann-Whitney U test.

Table 5. Comparison of VAS and PCS scores of subjects with and without aromatherapy in the follicular phase

	FA+	FA−	p*
	Mean (SD)	Mean (SD)	
Upper tooth VAS scores	79.36 (164.58)	40.58 (45.71)	0.734
Lower tooth VAS scores	64.27 (106.71)	36.42 (39.67)	0.734
Total VAS scores	143.64 (233.84)	77.00 (75.73)	0.735
PCS scores	2.73 (4.88)	4.08 (5.45)	0.769

FA+: the patients in the follicular phase and received aromatherapy, FA−: the patients in the follicular phase and did not receive aromatherapy, SD: Standard deviation, *Results of Mann-Whitney U test.

Table 6. Spearman correlation values between VAS scores and PCS scores

	Upper tooth VAS scores	Upper tooth VAS scores	Total VAS scores
PCS scores	0.330*	0.201	0.310*

* The correlation level is significant at the P<0.05 level

In this study, the fact that all patients were female and the debonding procedure was performed by the same orthodontist and using the same direction of movement (torque movement) allowed us to obtain pure study data. It has been stated that the short handle of the tool to be used in the debonding process with torque movement and the application of finger pressure during disassembly create a more tolerable pain level in the patient.[21] In this study, a standard short-handled removal forceps was used in all patients and the teeth were supported by finger pressure during the procedure.

The results of this prospective clinical study show that menstrual cycle phases affect the severity of orthodontic pain perceived by the patient during orthodontic debonding. Although there was no statistically significant difference, it was observed that the VAS scores obtained in the luteal stage were higher than the follicular stage. Although there are many side effects in orthodontic

treatments, pain is one of the leading side effects.[22] As far as we have researched, there is no study in the literature on the menstrual phase and the perception of pain that develops with orthodontic debonding procedure. The studies investigating the relationship between the menstrual cycle and orthodontic pain are also limited. Riley *et al.*[8] emphasized that the effects of the menstrual cycle on the perception of pain are too obvious to be ignored. Estrogen levels decrease and progesterone levels increase during the luteal phase. Pain sensation is higher in the luteal phase than in the follicular phase and during menstruation.[23] According to molecular biology studies, decreased estrogen causes the hypothalamus to release norepinephrine, which triggers a drop in acetylcholine, dopamine, and serotonin, which can lead to premenstrual syndrome with common symptoms such as pain sensitivity, insomnia, fatigue, and depression.[24] The fact that the GABAergic system, which affects neuronal excitability, is associated with estrogen and progesterone levels that change during menstrual phases explains the change in perception of pain sensation during menstrual phases.[25] Ileri *et al.*[5] investigated the relationship between menstrual phase and pain level following lace-back procedure in female patients during orthodontic treatment, they stated that there is a higher pain level in the luteal phase and that menstrual cycle phases may have an important role in how women perceive orthodontic pain in clinical applications.

The length of the menstrual cycle is determined by the rate and quality of follicular growth and development, and it is normal for the cycle to vary in everyone. It is known that between the ages of 25-35, more than 60% of the cycles are between 25 and 28 days.[26] Progesterone levels normally rise after ovulation and peak around 8-10 days after the luteinizing hormone surge.[27] In this study, we included patients in the follicular phase and luteal phase of the menstrual cycle in order to see the maximum effect of hormonal changes. One of the limitations of this study is that methods such as determining the hormonal level from the blood level or ultrasonographic examination were not used. Since these procedures, which can be considered as interventional, are difficult to implement in terms of ethics, menstrual phases were determined with the calendar method.

Aromatherapy is a form of therapy that uses aromatic compounds such as essential oils for therapeutic or medicinal purposes and has been in use for nearly 6000 years to improve the mood or health of individuals with both physical and emotional effects.[28] Aromatic oils are obtained from various parts of plants, herbs, trees and flowers for medicinal purposes, and there are more than forty different types of oils. These oils have varying degrees of antimicrobial activity and are thought to have effects with antiviral, antifungal, and antioxidant properties.[29] Aromatherapy works in connection with the sense of smell, and it has been stated that its possible mechanism of action is by acting on the olfactory nerve cells in the nasal cavity and sending impulses to the limbic system, which stimulates the nervous and circulatory system.[30] Lemon, chamomile, lavender, orange, apple, cedarwood and bergamot are a few sources of essential oils often used in aromatherapy, and it is known that these aromatic oils should be used in very small amounts.[29,31] Aromatherapy treatments can be done through massage, topical applications or inhalation. In this study, the protocol of applying lavender oil by inhalation,[20] as followed in the groups treated with aromatherapy. Although many studies have been conducted in the literature on aromatherapy and dental anxiety, there is no study evaluating the relationship between orthodontic treatment-induced pain and aromatherapy. While some studies concluded that aromatherapy did not affect dental anxiety,[32] it was concluded that aromatherapy reduced the level of dental anxiety in some studies.[14,15] According to this study findings, there was no statistically significant difference in terms of debonding pain levels between the groups with and without aromatherapy at different menstrual phases.

In this prospective study, two scales were used to evaluate pain levels after orthodontic debonding; VAS and PCS. The VAS is one of the most used tools to measure patient-perceived discomfort during orthodontic treatment or other clinical practice.[33,34] Scott and Huskisson[35] reported that the VAS is a scale that is easily understood by most patients, it is reliable, and it has high reproducibility. On the other hand, there are also studies reporting that the VAS has some practical limitations in clinical practice and that many patients have difficulty in assessing the distance accurately.[36] When assessing pain and disability, not only physical characteristics such as frequency, duration and severity of pain should not be considered, but also cognitive and emotional components should be considered.[18,19] In this context, the PCS has been a very useful scale to assess the link between personal pain perception and actual pain during debonding. Also, it was observed that there was a significant correlation between the total VAS scores and the total PCS scores. If we interpret it for clinical applications; it was found that individuals who are more sensitive to pain in their daily life have higher pain levels than other patients during the orthodontic debonding procedure.

Conclusions

Based on the findings of this prospective clinical study;

- Orthodontic debonding should be performed between the days when the patient's menstrual phase is in the follicular phase to reduce the patient's pain level and increase comfort.
- It has been observed that the application of aromatherapy does not reduce the pain levels during the orthodontic debonding procedure in female patients.
- It should be considered that patients with a lower pain threshold will experience more pain during the orthodontic debonding procedure, and orthodontic debonding should be done in female patients by considering individual differences.

Conflict of Interests

The authors of the present study declare no conflict of interest.

Ethical standards

The research protocol of this clinical study was approved by the Nevsehir Hacı Bektas Veli University Ethics Committee (No: 2020.13.142, Date: 23 June 2020). This study has been conducted in full accordance with the World Medical Association Declaration of Helsinki.

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Effect of Anti-Halitosis-Mouth Rinses on Surface Properties of Resin Based Restorative Dental Materials

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ABSTRACT

Objectives: This *in-vitro* study aimed to investigate the effect of five different types of mouth rinses used for halitosis on color stability and surface roughness of two types of restorative materials.

Materials and Methods: In this study, a total of 120 disc-shaped samples (10x2mm) were prepared with nano-hybrid resin composite (Filtek Z550) and giomer (Beautifill II) materials. Randomly selected samples were divided into six groups as five different mouth rinses (Listerine Fresh Burst, Listerine Total Care, Colgate Plax, Oderol, Halitosil) and a control group (distilled water). Initial color values were measured by spectrophotometer (Easyshade Compact) according to the CIELAB system, and roughness values (Ra) were measured by contact profilometer (Surtronic 25). All specimens were incubated in mouth rinses at 37°C for 12 hours and measurements were performed in the same procedure. Data were analyzed by using Kruskal-Wallis H and Bonferroni Post Hoc tests with the SPSS 24.0 program at a significance level of 0.05.

Results: The results of this study showed that there was not a statistically significant increase in surface roughness values. There was a significant change in CIELAB values in all of the Beautifil II materials after the immersion in mouth rinses. There was a statistically significant difference between the color change values of Beautifil II and Filtek Z550 materials kept in the same mouth rinses. Beautifil II was exhibited color change with values above the clinically acceptable limit (ΔE>3.3).

Conclusions: Color changes occurred in both of the restorative materials kept in different mouth rinses.

Keywords: Halitosis, Mouth Rinses, Resin Composite, Giomer, Surface Roughness.

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Introduction

Halitosis is bad breath from the mouth due to oral or non-oral conditions (Table 1).[1,2] It is usually (80-90%) caused by oral situations such as poor oral hygiene, dental caries, or periodontal disease. The sulfur-containing substrates exist in the different surfaces of the oral cavity, such as the dorsum of the tongue, periodontal pockets, desquamated epithelial cells, serum, or saliva. Gram-negative anaerobic bacteria degrade them, and volatile sulfur compounds are produced.[3-5] Periodontal treatments, mechanical therapies, and mouth rinses are utilizable for controlling chronic halitosis. Antibacterials in mouth rinses target volatile sulfur compound producer bacteria (porphyromonas gingivalis, prevotella intermedia, fusobacterium nucleatum) and reduce their numbers in the oral cavity.[1] Chlorhexidine (CHX), quaternary ammonium compounds (cetylpyridinium chloride (CPC), benzalkonium chloride), triclosan, essential oils, chlorine dioxide, zinc salts, hydrogen peroxide, sodium bicarbonate, amine fluoride/stannous fluoride are antibacterial agents that are used in different concentrations in mouth rinses. Chlorhexidine is a cationic agent that increases bacterial cell membrane permeability. That produces cell lysis and death and thereby reducing VSC production.[6,7] Cetylpyridinium chloride is a cationic quaternary ammonium antiseptic compound that suppresses the expression of specific genes of VSC production in anaerobic periodontal pathogens.[8-10] Triclosan has a broad spectrum of antimicrobial activity against bacteria, especially the gram-negative anaerobic species. Metal ions, such as stannous, mercury, copper and zinc can bind to the sulfur radicals and reduce the expression of the volatile sulfur compounds. Particularly zinc ions in zinc salts have a strong affinity for thiol groups present in the volatile sulfur compounds and converting volatile sulfur compounds to non-volatile sulfides that have low solubility.[7,10-12] In a study comparing the anti-VSC effect of different concentrations of zinc ions (0.1%, 0.3%, 1.0%), chlorhexidine (0.025% and 0.2%) and cetylpyridinium chloride (0.025% and

0.2%); all concentrations of Zn reduced hydrogen sulfide production by 80% during the first hour after use of the solutions. The anti-VSC effect of a 0.2% solution of chlorhexidine increased after the first hour. The anti-VSC effect of 0.2% chlorhexidine after 3 hours was significantly higher than 0.2% cetylpyridinium chloride. In addition, the anti-VSC effect of 0.025% chlorhexidine was significantly higher than the 0.025% cetylpyridinium chloride at the end of all periods. After 3 hours, 0.2% CHX was found to be the most effective agent.[13]

Minimally invasive dentistry is currently the most effective treatment option. Due to the superior aesthetic and mechanical properties of the composites and thanks to the developments in resin composite technology, the preference and use of composites in anterior and posterior teeth are increasing day by day compared to ceramics. Despite all these superior properties, composite restorations may become discolored due to factors; such as lack of oral hygiene, foods, drinks, mouth rinses, which may cause long-term clinical aesthetic failures and shorten the life of the restoration. Color stability in composite materials is related to the chemical properties of the resin matrix and the proportion and properties of the inorganic filler contents. In other words, color change tendency depends on factors such as degree of polymerization, surface characteristics, moisture absorption, diet, and oral hygiene habits.[14,15]

It was reported that the chemical contents and the pH degree of the mouth rinses change the surface properties of the dental restorations. In resin composites, the adsorption of staining agents can cause discoloration due to the increase in the degradation and roughness on the surface.[16-18] The aim of this *in-vitro* study was to evaluate the color and surface roughness changes of recent composite resins when exposed to different anti-halitosis-mouth rinses. The null hypothesis was that there would be statistically significant differences in surface roughness values and color changes values of restorative materials between baseline and after immersion.

Materials and Methods

The properties of the test materials used in this study are shown in Table 2. One hundred twenty disc-shaped specimens of 10 mm in diameter and 2 mm in thickness were prepared in a cylindrical metal mold by the following materials: nano-hybrid resin composite (Filtek Z550, 3M ESPE, St. Paul, MN, USA) and giomer (Beautifill II, Shofu Dental Inc, Kyoto, Japan). A2 shade was chosen as the base color for all materials. The specimens were polymerized with the halogen light-device (Optilux 501, Kerr, West Collins Orange, CA) at a distance of 1 mm for 40 seconds after gently pressing the material between two glass slides to the thickness of 1 mm and a polyester strip (Mylar strip; SS White Co., Philadelphia, PA, USA) for the removing of excess material. All the specimens were incubated in distilled water (Ph 6.55) at 37°C for 24 hours. To mimic clinical conditions and achieve a standardized polished surface 600 (P1200) grit silicon carbide paper (Metaserv SIC Paper, Buehler, Illinois, USA) was applied by polisher machine (Metaserv 250 Grinder/ Polisher, Buehler, Illinois, USA). Silicone finishing polishing discs (Super-Snap Rainbow Technique Kit, Shofu Dental, Kyoto, Japan) were performed for 30 seconds using minimal pressure by a low-speed handpiece at 5000 rpm.

To evaluate surface roughness and the color stability, 60 specimens of each restorative material were randomly divided into six subgroups (n=10) which will be treated with five different types of mouth rinses and distilled water (control group). Baseline surface roughness values (Ra, µm) were measured by using a contact profilometer (Surtronic 25, Taylor-Hobson, Leicester, UK). The cut-off and evaluation lengths of the device were set at 0.25 mm and 1.25 mm, respectively. Three measurements were performed in the center of each sample in different directions and the average value of these three measurements was regarded as the average surface roughness value.[19]

Table 1: Causes of Halitosis1, 2

Oral Conditions	Poor oral hygen, tongue-coating, decreased salivary flow rate (xerostomia), tooth caries, chronic periodontal diseases, oral ulcerations, acute oral infections, oral malignancies, prothetic restorations, bacterial retention areas in oral cavity.
Non- Oral (Systemic) Conditions	-Respiratory system diseases (respiratory tract infections, sinusitis, cleft palate, tonsilloliths, foreign bodies, tonsillitis, lung infections, bronchitis, malignancies), -Gastrointestinal diseases (duodenal obstruction, hypertrophic *pyloric stenosis*, hiatal hernia, gastroesophageal reflux disease, achalasia, *Helicobacter pylori* infection, gastric ulcers), -Hepatic diseases, -Hematological diseases, -Leukemia, -Renal diseases, -Endocrine system disorders (diabetic ketoacidosis) -Menstruation -Metabolic disorders (trimethylaminuria and hypermethioninemia).
Others	Sulfur compounds producer dietary products, drugs, alcohol, tobacco, psychogenic factors (halitophobia).

Table 2: The properties of the test materials.*

a. Mouth Rinses

Product Name	Brand	Contents
Listerine Fresh Burst (LFB) (Ph: 4.88) Alcohol Content: 26%)	Johnson & Johnson Limited, Maidenhead, UK, SL6 3UG. Johnson & Johnson (Ireland) Limited, Airton Road, Tallaght, Dublin 24, Ireland.	[PR-009045], Aqua, Alcohol, Sorbitol, Poloxamer 407, Benzoic Acid, Sodium Saccharin, Eucalyptol, Methyl Salicylate, Aroma, Thymol, Menthol, Sodium Benzoate, CI 47005, CI 42053
Listerine Total Care (LTC) (Ph: 3.43 Alcohol Content: 22%)	Johnson & Johnson Limited, Maidenhead, UK, SL6 3UG. Johnson & Johnson (Ireland) Limited, Airton Road, Tallaght, Dublin 24, Ireland.	[PR-017429], Aqua, Alcohol, Sorbitol, Poloxamer 407, Benzoic Acid, Zinc Chloride, Eucalyptol, Aroma, Sodium Saccharin, Methyl Salicylate, Thymol, Menthol, Sodium Fluoride, Sodium Benzoate, Sucralose, Propylene Alcohol, CI 16035, CI 42090, Contains Sodium Fluoride (220 ppm F)
Colgate Plax (CP) (Ph: 6.05) Alcohol Content: 7.2%)	Colgate-Palmolive Company Limited, Krung Thep Maha Nakhon 10110, Thailand	Aqua, glycerin, Propylene Glycol, Sorbitol, Poloxamer 407, Aroma, Cetylpyridinium Chloride, Potassium Sorbate, Sodium Flouride (225 ppm), Sodium Saccharin, Menthol, CI 42051.
Oderol (O) (Ph: 5.6 No Alcohol Content)	Helba Ilac Ic Dis San. Tic. A.S. Serifali Mh. Kule Sk. No: 27/5 Umraniye, Istanbul, Türkiye	Chlorhexidine Digluconate 0.025%, Zinc Lactate, Mentha Piperita, Sucralose, Deionized Water.
Halitosil (H) Zn (Pharmol) (Ph: 5.84 No Alcohol Content)	IMK Farma, Tarabya Mh, Aydınevler Bostan Sk. No: 15/1A- 1A Sarıyer, Istanbul, Türkiye.	Aqua, Glycerin, Zinc Chloride, Sodium Chloride, Boric Acid, Potassium Sorbate, Sodium Benzoate, CL 42090

b.Composites

Product Name	Brand	Organic Matrix	Inorganic Fillers	Classification
Filtek Z550	3M ESPE, St.Paul, MN, USA	Bis- GMA, UDMA, Bis-EMA, TEGDMA, PEGDMA	Surface-modified zirconia/silica fillers, non-agglomerated/non-aggregated surface modified silica particles. 81.8%(wt), 68%(vol) (Particle size: 3µm- 20nm)	Nano-hybrid
Beautifil II	Shofu Dental Inc, Kyoto, Japan	Bis-GMA, TEGDMA	S-PRG filler, multi-functional glass, fluoroboraluminosilicate glass. (Particle size: 0.01 µm–4µm) 83.3% (wt), 68.6%(vol)	Giomer

Bis-GMA= bisphenol A glycol dimethacrylate; UDMA= urethane dimethacrylate; PEGDMA= polyethylene glycol di-methacrylate; TEGDMA= triethylene glycol dimethacrylate; Bis-EMA= ethoxylated bisphenol A glycol di-methacrylate; S-PRG= surface reaction type pre-reacted glass-ionomer
*Data obtained from manufacturers.

Baseline color coordinates of specimens were measured with a spectrophotometer (Easyshade Compact, VITA Zahnfabrik, Bad Säckingen, Germany) according to CIELAB system which was introduced by the Commission Internationle d'Éclairage (CIE) in 1976.[28] CIELAB provides representation of a color stimulus by dimensions of lightness, chroma, and hue and produce a three-dimensional color space where the a*(red-green), b*(yellow/blue) axes form one plane to which the L *(White/black) axis is orthogonal. Color changes (ΔE*) were calculated by the followed formulation: [19,20]

$$\Delta E^*_{ab}=[(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2]^{0.5}$$

The spectrophotometer was calibrated using the calibration block according to the manufacturer's instructions. Probe tip for measurement was placed facing and perpendicular to the centers of the sample surfaces and measurement repeated three times for each sample. After initial measurements all specimens were immersed distilled water and mouth rinses at 37°C for 12 hours. Then color and surfaces roughness measurements were performed in the same procedure. All the measurements were obtained by single operator.

Statistical Analysis

Data were analyzed with the SPSS (IBM SPSS for Windows, Ver.24) program at the significance level of 0.05 (α). The Shapiro-Wilk test (n <50) was used to determine whether the mean values were normally distributed. Non-parametric tests were performed because the measured values of some of the groups of variables were not normally distributed. Kruskal-Wallis H test was used to compare the measurements according to the groups, and Bonferroni Post Hoc (multiple comparison) test was used to determine the different groups that were significant.

Table 3. Means and standart deviations for surface roughness values (Ra in µm) of the tested restorative materials in different mouth rinses.

Tested Materials	Filtek Z550	Beautifil II
Base	0.14(0.15)	0.16(0.01)
After Halitosil	0.16(0.02)	0.17(0.02)
Base	0.16(0.03)	0.15(0.02)
After Oderol	0.17(0.03)	0.17(0.02)
Base	0.15(0.03)	0.15(0.02)
After Colgate Plax	0.17(0.02)	0.17(0.02)
Base	0.17(0.02)	0.16(0.01)
After Listerine Fresh Burst	0.18(0.01)	0.17(0.02)
Base	0.15(0.04)	0.16(0.02)
After Listerine Total Care	0.19(0.05)	0.21(0.03)
No statistical differences between the groups (p>0.05).		

Table 4. Means and standart deviations for color changes (ΔE) of the tested restorative materials in different mouth rinses.

Tested Materials	Listerine Total Care (N=10)	Halitosil (N=10)	Oderol (N=10)	Colgate Plax (N=10)	Listerine Fresh Burst (N=10)	Control Group (Distilled Water) (N=10)
Filtek Z550	1.92(1.01)^{aA}	1.30(0.42)^{abA}	1.40(0.93)^{abA}	1.66(0.60)^{abA}	1.84(1.90)^{aA}	0.60(0.20)^{bA}
Beautifil II	6.47*(1.88)^{aB}	5.26*(1.46)^{bB}	5.79*(0.63)^{abB}	4.15*(0.89)^{cB}	6.24*(1.37)^{abB}	0.78(0.29)^{dA}

*Clinically acceptable color change value is below ΔE * = 3.3.; a, b, c: Shows the difference between groups in same row; A, B, C: Shows the difference between groups in same column; (according to Bonferroni Post hoc comparison test, p<0.05).

Results

As a result of the Kruskal-Wallis H analysis, p<0.05 was accepted as significance level. The average surface roughness values obtained before and after immersion in mouth rinses of the composite materials are given in Table 3. Initial average roughness values of composites; Ra(µm)=0.167(±0.01) for Filtek Z550 and Ra(µm)=0.161(±0.01) for Beautifil II. When the surface roughness values obtained before and after immersion in the mouth rinses were compared, no statistically significant difference was found in Filtek Z550 or Beautifil II (p>0.05). Listerine Total Care was produced the highest surface roughness change for the Z550 (ΔRa=0.041µm) and Beautifill II (ΔRa=0.052µm).

Means and standard deviations for color changes (ΔE) of the tested materials are given in Table 4. It was found that the color changes after immersing in the mouth rinses were statistically significant between Filtek Z550 and Beautifil II groups (p<0.001). For Filtek Z550 there was a significant difference between control groups and LTC groups; control groups and LFB groups (p<0.05). For Beautifil II statistically significant differences were found between the control and all the mouth rinse groups (p<0.05). The highest ΔE values were consistently observed in the Beautifil II composite regardless of the mouth rinses used. The lowest color change values for both materials were found in control groups (distilled water). The color change values obtained for Beautifil II were from highest to lowest respectively, Listerine Total Care, Listerine Fresh Burst, Oderol, Halitosil and Colgate Plax. For Filtek Z550 composite; the highest color change values were obtained in Listerin Total Care and Listerin Fresh Burst mouth rinses, respectively.

Discussion

This *in-vitro* study evaluated the effect of anti-halitosis-mouth rinses on color stability and surface roughness of nano-hybrid and giomer restorative materials for a period of 12 hours. It was stated that the immersing time of 12 hours is equivalent to 2 minutes per day/total of 1-year mouth rinse usage.[21,22] The null hypothesis was that there would be statistically significant differences in surface roughness and color changes values of composites between baseline and after immersion, partially accepted. Mouth rinses produced a significant color change but did not cause a statistically significant increase in surface roughness values.

In this study there was no statistically significant difference was found in surface roughness values for Filtek Z550 or Beautifil II materials after immersion. In terms of microbiologically, the acceptable surface roughness limit for restorative materials is considered to be 0.2µm[23] and the surface roughness values obtained in this study did not exceed this limit. The researchers stated that the surface characteristics of the materials affect the optical properties, and the increasing surface roughness changes the color coordinates.[24,25] In our study, similar to the Celik *et al.*[26], although there was no significant change in surface roughness, statistically significant color change occurred in Filtek Z550 samples kept in LTC and LFB, and in all samples of Beautifill II kept in mouth rinses.

Listerine Total Care has the highest alcohol content after LFB and the lowest pH among all. Almeida *et al.*[27] indicated that the low pH of mouth rinses may cause catalysis of ester groups from dimethacrylate monomers in the resin matrix composition. Hydrolysis of these ester groups would result in the release of alcohol and carboxylic acid which may increase the degradation of the

resin composite. It was stated that alcohol, which was a dimetacrilate solvent causes plasticization in the resin matrix and therefore softens and accelerates degradation and discoloration.[27,28] This degradation process in the structure of the material also causes an increase in surface roughness.[29] In this study, similar to the Cengiz *et al.*[18] the mouth rinse with the lowest pH (LTC) was produced the highest surface roughness change (ΔRa) for both of the restorative materials.

The color change of materials is one of the factors that shorten the life of the resin composite restorations, and it is a reason for the restoration repair or change, especially in the anterior region. Vichi *et al*.[30] stated that the color change threshold that the human eye can perceive is ΔE * = 1 and the clinically acceptable color change value is below ΔE * = 3.3. In our study, the most color change in Filtek Z550 material occurred in LTC and LFB groups, but it was below the clinically acceptable limit. In Beautifill II, all ΔE * values exceeded the clinically acceptable limit and there was a statistically significant difference between the ΔE* values of Filtek Z550 and Beautifil II, after immersion of mouth rinses. In previous studies investigating color stability, fluoride in materials such as Beautifil II, a giomer, has been reported to significantly increase water absorption and color change (ΔE) values due to its water solubility.[31,32]

Festuccia *et al.*[33] reported that the color stability of resin composite materials was related to monomer conversion degree and water absorption tendency of polymer matrix. Filtek Z550 contains Bis-GMA, UDMA, Bis-EMA, TEGDMA, PEGDMA, and Beautifil II contains Bis-GMA, TEGDMA monomers in the matrix structure. Bis-GMA (bisphenol A-glycerolate dimethacrylate) is a methacrylate with a high viscosity provided by the hydroxyl groups and the aromatic core. [34,35] To reduce the disadvantages of Bis-GMA such as high viscosity, low mobility, and to increase the degree of conversion, it is combined with diluting high mobility bifunctional co-monomers such as TEGDMA (triethylene glycol dimethacrylate), EGDMA (ethylene glycol dimethacrylate), UDMA (urethane dimethacrylate) and BisEMA (ethoxylated bisphenol A dimethacrylate).[34-37] Bis-EMA monomer, which is the ethoxylated form of Bis-GMA, is less hydrophilic and less viscosity due to lack of secondary functional hydroxyl groups. Longer ethylene glycol spacer produces higher flexural strength and higher mobility. Because of it's higher viscosity, Bis-GMA reaches the gelation point earlier in the polymerization reaction, which leads to a lower degree of conversion than Bis-EMA based materials. [37-39] Low viscosity monomer UDMA presents an aliphatic urethane chain that high flexibility, higher flexural strength, elastic modulus, and hardness.[35,37] UDMA monomers were significantly more reactive and has higher conversion rates than Bis-GMA monomers.[40] TEGDMA is a highly flexible monomer, it has a low molecular weight, low viscosity, and high mobility during polymerization and this reason it has great monomer conversion rates. However, due to its hydrophilic properties, it increases the water absorption of the structure, which accelerates degradation, decreases the mechanical properties and negatively affects the color stability.[34,37] In a study Fonseca *et al.*[35] investigated the degree of conversion, water sorption and optical properties of experimental dental composites composed of BisGMA, BisEMA, BisEMA 30, and two UDMA-based monomers, that mixtured with TEGDMA. BisEMA mixed with TEGDMA presented the synergistic effect with TEGDMA and had the best performance in terms of all the parameters tested. Ranking of the conventional base monomers for color stability was BisEMA>UDMA>BisGMA. This informations may explain that the color stability of the Filtek Z550, which contains UDMA, Bis-EMA monomers in the matrix structure, was better than Beautifil II.

Filtek Z550 is a nanohybrid resin composite with surface-modified zirconia/silica fillers in its structure[19]. Beautifil II is a giomer material that provides fluoride-releasing through the S-PRG fillers (surface pre-reacted glass filler particles) it contains. The water absorption properties of resin-based restorative materials affect the amount of coloring agents entering the resin matrix and the color change values[16]. Gonluol *et al*.[32] (2015) also stated in their study that Beautifill II has higher solubility and water absorption properties than Filtek Z550 and other composite types. In addition, in the same study[32], similar to our study, a statistically significantly more color change occurred in Beautifil II than in Filtek Z550. On the other hand, Park *et al.*[31](2007) stated that in materials with fluoride release, the place of the filler dissolved from the surface is covered with water, and this causes hole formation and softening on the surface. However, no significant difference was found in the surface roughness values in our study, and the microhardness parameter was not tested either. For these reasons, it is necessary to carry out additional studies examining the color change, surface roughness and microhardness values together.

Chlorhexidine, zinc lactate, zinc chloride, stannous fluoride, essential oils (eucalyptol, menthol and methyl salicylate) and cetylpyridinium chloride are the most commonly used anti-microbial agents in anti-halitosis effective mouth rinses.[8,41] Chlorhexidine is a broad spectrum and most preferred cationic agent, but it has side effects such as calculus formation, altered taste perception, and yellow-brown extrinsic staining.[13,42] These discolorations are formed by processes such as protein denaturation, which leads to the formation of metal sulfide, or the Maillard reaction, which creates melanoid substances that cause brown staining.[41] Like Chlorhexidine, cetylpyridinium chloride is a broad-spectrum cationic agent with side effects such as ulceration, burning sensation and discoloration.[13] The most important side effect of zinc lactate or zinc chloride is that it's metallic taste. Stannous fluoride has a discoloration feature due to the Sn it contains.[8,13]

In this study, the most color change was expected from Oderol that containing chlorhexidine digluconate 0.025% and Colgate Plax that containing cetylpyridinium chloride. But the mouth rinses that produced the statistical significant color change in Filtek Z550 material were LTC and LFB. And the mouth rinses that produced the highest color change in Beautifil II material were Listerine Total

Care, Listerine Fresh Burst, Oderol, Halitosil and Colgate plax respectively. This could be explained by lower pH value and higher alcohol content than other mouth rinses. In previous studies [43,44], it was stated that mouthwashes containing alcohol showed better results in wound healing and plaque control. In our study, the chosen alcohol-containing mouthwashes are the most widely used mouthwashes for the relief of halitosis in the market. But Aydın *et al.*[45] stated that alcohol is not necessary in halitosis mouth rinses as it dries the oral mucosa and exacerbates bad breath and has no effect on sulfur gases. Almeida *et al.*[27] stated that alcohol-free mouth rinses presented a similar effectiveness on plaque control and gingival inflammation reduction compared to mouth rinses containing alcohol.

Conclusions

In this study, immersion of mouth rinses for 12h had no significant effect on the surface roughness values. Immersion of Listerine Total Care and Listerine Fresh Burst mouth rinses had a significant effect on the color changes in the Beautifil II and Filtek Z550 specimens. Beautifil II showed higher discolorations than Filtek Z550. Clinicians should consider the effects of pH degrees and alcohol contents of mouth rinses used for halitosis on restorative materials.

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Conflicts of Interest Statement

The authors declare no conflict of interest in this study.

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Shear Bond Strength of Chairside CAD-CAM Blocks to Eroded Dentin

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ABSTRACT

Objectives: To assess the shear bond strength (SBS) of chairside computer-aided design and computer-aided manufacturing (CAD-CAM) blocks to dentin subjected to simulated gastric erosion when cemented with self-etch and self-adhesive resin cements.

Materials and Methods: One hundred eighty dentin samples were assigned to two groups: sound and eroded dentin. In the eroded dentin group, samples were eroded with HCl (0.01 M, pH 2, 2 min) and stored in artificial saliva for 60 min then, brushed using a power brush (2N, 15 s). This cycle was repeated three times. CAD-CAM blocks (3x3x3 mm^3, n=15/group) of Lava Ultimate (LU), Vita Enamic (VE), and Vita Suprinity (VS) were cemented to sound and eroded dentin with self-etch Multilink N (MN) and self-adhesive RelyX U200 Automix (RU) resin cements. SBS was measured after 24 hours. The failure mode was assessed by using a stereomicroscope. Data was analyzed with 3-way ANOVA and Bonferroni correction.

Results: The SBS was significantly affected by the main factors: tooth structure, resin cements, and CAD-CAM blocks. When LU was cemented with RU to sound dentin, a higher SBS was obtained compared to eroded dentin. MN revealed significantly higher SBS than RU. When using MN in sound dentin LU showed lower bond strength than VE and VS. The predominant failure mode was mixed for all groups.

Conclusions: It was determined that the bond strength of dentin was affected by simulated gastric erosion. The use of Multilink N resin cement in both sound and eroded dentin can be recommended. For a reliable bond to eroded dentin, selection of the proper cement system and material type are necessary.

Keywords: Dentin; CAD-CAM blocks; Shear Bond Strength; Gastric Erosion; Resin Cement.

Hastabaşı CAD-CAM Blokların Eroze Dentine Makaslama Bağlanma Dayanımı

Süreç

Geliş: 28/03/2022
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ÖZ

Amaç: Bu çalışmada hastabaşı bilgisayar destekli tasarım-bilgisayar destekli üretim (CAD-CAM) bloklarının self-etch ve self-adeziv rezin simanlar kullanılarak gastrik erozyona uğratılmış dentine olan makaslama bağlanma dayanımlarının değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Yüz seksen dentin örneği sağlam dentin ve eroze dentin olmak üzere iki gruba ayrılmıştır. Eroze dentin grubunda örnekler HCl (0,01 M, pH 2, 2 dk) ile erozyona uğratılmış ve 60 dk yapay tükrükte bekletilmiş, sonrasında, elektrikli diş fırçası kullanılarak (2N, 15 s) fırçalanmıştır. Bu döngü üç kere tekrar edilmiştir. Lava Ultimate (LU), Vita Enamic (VE) ve Vita Suprinity (VS) CAD-CAM blokları (3x3x3 mm3, n=15/grup) self-etch Multilink N (MN) ve self-adeziv RelyX U200 Automix (RU) rezin simanları kullanılarak sağlam ve eroze dentin örneklerine simante edilmiştir. Makaslama bağlanma dayanımı 24 saat sonra ölçülmüştür. Başarısızlık tipi stereomikroskop kullanılarak değerlendirilmiştir. Veriler üç-yönlü ANOVA ve Bonferroni düzeltmesi kullanılarak analiz edilmiştir.

Bulgular: Makaslama bağlanma dayanımı ana faktörlerden önemli ölçüde etkilenmiştir: diş yapısı (p=0,011), rezin simanlar ve CAD-CAM bloklar LU sağlam dentine RU ile simante edildiğinde, eroze dentinle karşılaştırıldığında daha yüksek bağlanma dayanımı elde edilmiştir. MN kullanıldığında, RU'dan daha yüksek bağlanma dayanımı değerleri elde edilmiştir. Sağlam dentinde MN kullanıldığında LU, VE ve VS'den daha düşük bağlanma dayanımı göstermiştir. Tüm gruplarda baskın olan başarısızlık tipi karma başarısızlık olarak belirlenmiştir.

Sonuçlar: Dentinin bağlanma dayanımının gastrik erozyondan etkilendiği belirlenmiştir. Hem sağlam hem de eroze dentinde Multilink N rezin siman kullanımı önerilebilir. Eroze dentinde güvenilir bir bağlanma için uygun siman ve restoratif materyal seçimi gerekmektedir.

Anahtar Kelimeler: Dentin; CAD-CAM Blok; Makaslama Bağlanma Dayanımı; Gastrik Erozyon; Rezin Siman.

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Introduction

Dental erosion is the devastation of dental hard tissue caused by extrinsic (environment, diet and drugs) and intrinsic (gastric juice) acids without the influence of bacteria.[1] Tooth surfaces can be affected by acidic gastric content as a result of chronic vomiting, regurgitation, rumination, or gastroesophageal reflux. In these patients, loss of the mineral by intrinsic acid on tooth structure can be explained by the erosive potential of hydrochloric acid (HCl). HCl in gastric juice is a strong acid with high erosive potential.[2-4]

Erosive challenges to tooth structure lead to loss of structural integrity, greater wear and loss of microhardness.[4-6] The opening of the dentin tubules, the removal of the organic part of the intertubular dentin and the dentin plugs, increasing the diameter of the tubule, and causing collagen exposure have been reported when erosive lesions reached dentin.[7] If dentin is chronically exposed to acids, mineral loss increases and the organic dentin matrix is gradually exposed. If demineralization proceeds, mineral loss decreases over time with the protective effect of the developing organic dentin matrix.[8]

Restorative procedures are essential to recover function and esthetics, maintaining tooth structure and preventing dentin hypersensitivity in the teeth where erosive tooth wear occurs.[9] Computer-aided design and computer-aided manufacturing (CAD-CAM) system allows clinicians to independently design and process high quality, highly esthetic dental restorations, allowing the procedure to be completed in a single visit.[10] Chairside CAD/CAM blocks can be used to make inlays, onlays, veneers and crowns. Within chairside CAD/CAM blocks, Lava Ultimate (3M ESPE) is a resin nano-ceramic material, that contains a polymer network (20% wt) strengthened by 80% wt zirconia-silica nanofillers.[11] Vita Enamic (Vita Zahnfabrik) is a polymer-infiltrated ceramic network material that contains strengthened polymer network (14% wt) and ceramic network (86% wt). The ceramic and polymer networks completely penetrated each other.[12] Vita Suprinity (Vita Zahnfabrik) is a zirconia-reinforced lithium silicate ceramic. The incorporation of zirconia particles strengthens the ceramic structure and helps prevent crack progression.[13,14]

It is recommended to use adhesive luting to bond CAD-CAM blocks to tooth structure.[15,16] Self-etch cements are used with self-etch primer on prepared tooth surfaces. Self-adhesive resin cements eliminate adhesive or acid application steps and offer a simplified application procedure with one-step use. They provide chemical bonding to the tooth surface due to the acidic monomers in the structure.[17,18] Several studies have evaluated the changes that occur on the dentin bond strength after erosive challenge.[19-24] In this studies, the extrinsic erosion was simulated by using citric acid[19,20] or acidic drinks[21-23] and intrinsic erosion was simulated by using HCl-pepsin solution.[24] To our knowledge, no previous study has investigated the bond strength of chairside CAD-CAM blocks to dentin exposed to intrinsic erosion. Therefore, the present study aimed to evaluate the shear bond strength (SBS) of current chairside CAD-CAM blocks to dentin exposed to simulated gastric erosion when cemented with self-etch and self-adhesive resin cements. The null hypothesis was that there would be no effect of intrinsic dental erosion, of resin cements, or of CAD-CAM blocks on the SBS to dentin.

Materials and Methods

In this in vitro study, three types CAD-CAM blocks-Lava Ultimate (LU), Vita Enamic (VE), and Vita Suprinity (VS)-were cemented to sound and eroded dentin with self-etch Multilink N and self-adhesive Rely X U200 Automix resin cements to evaluate the SBS (Table 1).

Ethical approval was received from the Ethical Research Committee of the Karadeniz Technical University in Trabzon, Türkiye (ID: 2018/71 and decision date 07.05.2018).

Preparation of Dentin Samples

Human third molars without cracks, fractures, or defects were used. After extraction, ninety teeth were kept in +4 °C 0.5% chloramine-T aqueous solution for 1 week and then kept in +4 °C distilled water for a maximum of one month. The buccal and lingual enamel was removed using a slow-speed diamond saw (Microcut 150; Metkon Instruments), and the flat dentin surfaces were exposed. One hundred eighty dentin samples were embedded in autopolymerizing acrylic resin (SC; Imıcryl Dental, Türkiye) in cylindrical silicone molds. After removal mold, grinding was performed under running water with silicon carbide abrasive paper up to 1200-grit in a polishing machine (Beta Grinder-Polisher, Buehler) to create standardized smear layers. Dentin samples were assigned to two groups: sound dentin and eroded dentin. A schematic flow chart of the experimental procedure is shown in (Figure 1).

Table 1. CAD-CAM blocks used in this study

Materials	Batch Numbers	Composition
Lava Ultimate (3M ESPE, USA)	N894706	80% ceramic (69% SiO_2, 31% ZrO_2), 20% polymer (Bis-GMA, UDMA, Bis-EMA, TEGDMA)
Vita Enamic (VitaZahnfabrik, Germany)	59711	86% ceramic (58-63% SiO_2, 20-23% Al_2O_3, 9-11% Na_2O, 4-6% K_2O, 0-1% ZrO_2), 14% polymer (UDMA, TEGDMA)
Vita Suprinity (VitaZahnfabrik, Germany)	63323	56-64% SiO_2, 1-4% Al_2O_3, 15-21% Li_2O, 8-12% ZrO_2, 1-4% K_2O

SiO_2: silicon dioxide, ZrO_2: zirconium dioxide, Bis-GMA: bisphenol-A-glycidylmethacrylate, UDMA: urethane dimethacrylate, Bis-EMA: bisphenol-A-ethoxylate glycidyl methacrylate, TEGDMA: triethylene glycol dimethacrylate, Al_2O_3: aluminium trioxide, Na_2O: sodium oxide, K_2O: potassium oxide, Li_2O: lithium oxide

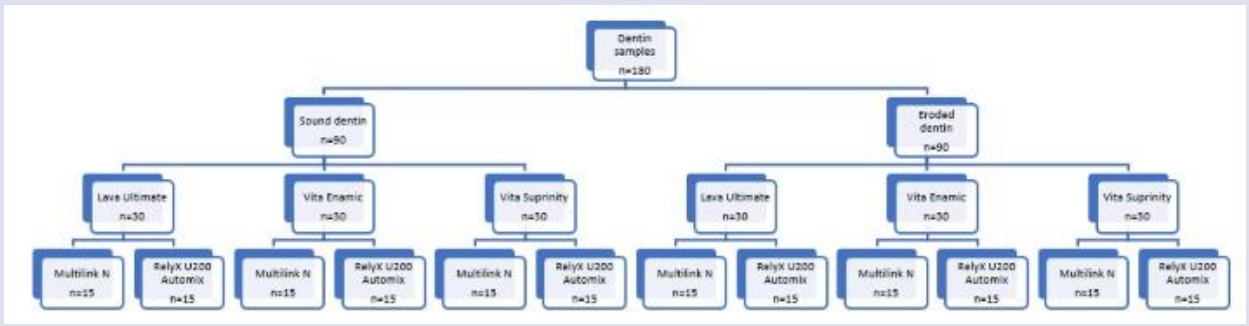

Figure 1. Shematic flow chart of the experimental procedure.

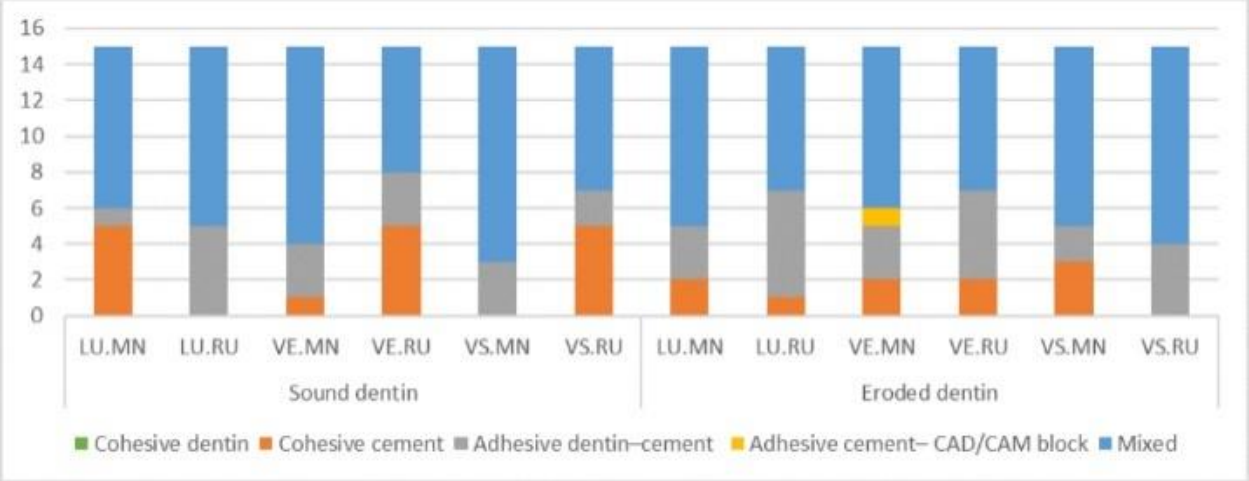

Figure 2. Distribution of failure modes after shear bond strength test.
LU.RU: Lava Ultimate + RelyX U200 Automix; LU.MN: Lava Ultimate + Multilink N; VE.RU: Vita Enamic + RelyX U200 Automix; VE.MN: Vita Enamic + Multilink N; VS.RU: Vita Suprinity + RelyX U200 Automix; VS.MN: Vita Suprinity + Multilink N.

Erosion-Abrasion Procedure

Samples in eroded dentin group were subjected to three cycles of erosion-abrasion procedure. One cycle consisted of erosion and brushing.[25] To simulate gastric erosion, 0.01 M HCl (Noratex Kimya) with a pH of 2 applied to the dentin samples with 2 minutes (min).[26] Samples were rinsed in distilled water and kept in artificial saliva for 60 min for remineralization then samples were brushed using a power brush (Triumph Professional Care, Oral B Braun GmbH) which was settled on a custom-made holder and a brushing force of 2 N[8] for 15 seconds. Soft-bristles toothbrush head (Oral-B Sensitive, Braun) was selected. Slurry was prepared with toothpaste (ProNamel, Sensodyne; RDA value 34) and artificial saliva (3:1). After toothbrushing, samples were rinsed in distilled water for 1 min, then the other cycle was carried out. Three cycles were performed, one after the other. [25,26]

Preparation of CAD-CAM Blocks

The blocks were cut with a slow-speed, water-cooled diamond saw (Microcut 150; Metkon Instruments). A total of 180 samples, 60 samples from each block type, of 3 x 3 x 3 mm³ dimensions were obtained. LU, VE, and VS CAD-CAM blocks were cemented with RelyX U200 Automix (RU) and Multilink N (MN) resin cements to sound and eroded dentin surfaces (n=15).

Pretreatment of CAD-CAM blocks and application procedures of the resin cements were used according to the corresponding manufacturer's instructions (Tables 2, 3). Resin cements were applied to the surface of the blocks and seated to the dentin with finger pressure then polymerized with light (Elipar S10, 3M ESPE, 1200 mW/cm²). After cementation, samples were kept in 37 °C, 100% humidity for 24 hours (h), then shear bond strength (SBS) was tested by using a universal testing machine (Instron 3382) with 0.5 mm/min crosshead speed. The maximum force (N) was recorded at the time the fracture occurred, then N divided by the surface area of the sample to calculate SBS values (MPa). The fractured surface of each sample was examined by stereomicroscopy (Leica MZ16) at 40x magnification, and the failure modes were categorized as cohesive in dentin, cohesive in cement, adhesive in dentin–cement interface, adhesive in cement–CAD-CAM block interface, and mixed.

Statistical Analysis

The data was analyzed by SPSS for Windows 17.0 (SPSS Inc.). The Shapiro–Wilk test was used for testing normality. SBS data was evaluated by three-way ANOVA. The Bonferroni correction was used for multiple comparisons. Statistical significance was considered at $p<0.05$.

Table 2. Pre-treatment of CAD-CAM blocks

CAD-CAM material	Pretreatment steps
Lava Ultimate	Sandblasting with Cojet sand, at 2 bars Removing sand with alcohol, air-drying Applying Single Bond Universal Adhesive (scrubbing 20s)
Vita Enamic	Conditioning (HF 5%, 60 s), rinsing (60 s), drying (20 s), silanization
Vita Suprinity	Cleaning ultrasonic bath with distilled water Crystallized at 840 °C for 8 min in ceramic furnace (Programat P300), Conditioning (HF 5%, 20 s), rinsing with water, cleaning with 98% alcohol (1–3 min), drying, silanization

*HF: Hydrofluoric acid.

Table 3. Application procedures of resin cements

Resin cement	Application procedure
Multilink N (Ivoclar Vivadent Liechtenstein)	Tooth surface: Clean, rinse, dry with air that is free of water and oil. Mix Multilink N Primer A and B in a 1:1 ratio. Apply the mixed Multilink N Primer A/B with disposable microbrush to the entire bonding surfaces, scrub (30 s), and disperse excess with blown air until the mobile liquid film is no longer visible. Dispense Multilink N catalyst and base from the double-push syringe and mix in a 1:1 ratio. Remove the excess cement.Light-polymerize (all margins 20 s).
RelyX U200 Automix (3M ESPE, Germany)	Tooth surface: Clean, rinse, lightly air dry in only 2–3 bursts of water-free and oil-free air. Dispense RelyX U200 Automix catalyst and base from the double-push syringe and mix in a 1:1 ratio. Remove the excess cement. Light-polymerize (single surface 20 s; any other surface, additional 20 s).

Table 4. Results of three-way ANOVA

Source	Type III sum of squares	df	Mean square	F	p value
Tooth structure (A)	87.340	1	87.340	6.649	.011
Resin cements (B)	1411.635	1	1411.635	107.464	.000
CAD-CAM blocks (C)	191.300	2	95.650	7.282	.001
A × B	0.278	1	0.278	0.021	.885
A × C	9.914	2	4.957	0.377	.686
B × C	33.771	2	16.886	1.285	.279
A × B × C	38.427	2	19.213	1.463	.235

Table 5. SBS (MPa) means and standard deviations for all experimental groups

	Sound dentin		Eroded dentin	
	Multilink N	RelyX U200 Automix	Multilink N	RelyX U200 Automix
Lava Ultimate	11.06±2.33^{Aa}	7.73±1.59^{Ab*}	11.35±2.61^{Aa}	5.90±1.04^{Ab*}
Vita Enamic	15.86±4.62^{Ba}	8.27±2.32^{Ab}	13.16±5.28^{Aa}	7.97±2.97^{Ab}
Vita Suprinity	15.06±3.31^{Ba}	8.95±3.24^{Ab}	13.06±7.09^{Aa}	7.14±2.49^{Ab}

Different uppercase letters indicate a statistically significant difference among CAD-CAM blocks ($p<0.05$). Different lowercase letters indicate a statistically significant difference between resin cements ($p<0.05$). * indicates a statistically significant difference between sound and eroded dentin ($p<0.05$).

Results

The analysis of variance and significant differences for different factors and interactions are presented in Table 4. The 3-way ANOVA showed that the three main factors, tooth structure (sound dentin or eroded dentin) ($p=0.011$), resin cements (RU or MN) ($p<0.001$), and CAD-CAM blocks (LU or VE or VS) ($p=0.001$) significantly affected the SBS.

SBS means and standard deviations for all groups are presented in Table 5. The highest values were obtained when VE was used with MN (15.86 ± 4.62 MPa) in sound dentin and (13.16 ± 5.28 MPa) in eroded dentin. The lowest values were obtained when LU was used with RU (7.73 ± 1.59 MPa) in sound dentin and (5.90 ± 1.04 MPa) in eroded dentin. Generally, higher SBS values were obtained in sound dentin than in eroded dentin, but the difference was significantly only when the LU was used with RU in sound dentin($p=0.001$).

MN showed higher SBS than RU. The difference was significantly for all groups ($p<0.05$). When LU, VE, and VS were used with MN in sound dentin, LU showed lower SBS than VE ($p=0.002$) and VS ($p=0.011$). When LU, VE, and VS were used with MN in eroded dentin, LU showed lower SBS than VE and VS, but the difference was not significantly. When LU, VE, and VS were used with RU in sound and eroded dentin, LU showed lower SBS than VE and VS, but the difference was not significantly. There was no significantly difference between the SBS of VE and VS in all groups. The failure modes are shown in Figure 2. For LU, VE, and VS, the predominant failure mode was mixed.

Discussion

In the present study, it was aimed to assess the shear bond strength of three chairside CAD-CAM blocks to dentin subjected to simulated gastric erosion when cemented two resin cements. The null hypothesis that

there would be no effect of intrinsic dental erosion, resin cements, and CAD-CAM blocks on SBS to dentin was rejected. Significant differences were found for the three main factors.

Erosion, abrasion, and attrition are not usually seen alone but interact with each other. Abrasion of dental hard tissues affected by erosion is considered the most important interaction.[27] Therefore, in this in vitro study, the erosion protocol of Hove et al. was used to simulate intrinsic gastric erosion[26], and erosion-abrasion protocol was applied together to simulate better conditions in daily life.[27]

In this study for erosion procedure HCl (0.01 M, pH 2, 2 min) was applied to dentin samples, then samples were stored in artificial saliva for 60 min. For abrasion procedure a power brush was used for 15 s. A demineralization period of 2 min shows the duration of the pH drop in saliva after the acid attack.[3] Although the pH of pure gastric acid is between 0.9 and 1.5, it is rarely lower than 1.5 due to the buffering effect in the esophagus and the dilution effect of food and drinks. It is more convenient to use 0.01 M HCl than 0.1 M HCl for clinical conditions.[26] Not to brush immediately after contact with acid may represent better conditions in daily life, because people are unlikely to brush their teeth immediately after every erosive attack, so in this study, after-erosion dentin samples were stored in artificial saliva for 60 min.[27] In this study, a brushing force of 2N was used in accordance with ISO 14569-1 820075.[5]

Bond strength to eroded dentin has been evaluated in few studies.[19-24] It has been shown that the bond strength of adhesive systems to eroded dentin is lower than sound dentin.[20,21,23] In some studies, no significantly difference was found in the bond strength of sound and eroded dentin.[19,22] There is no consensus among studies regarding the erosion procedures used. In these studies, citric acid[19,20], acidic drinks[21-23] and HCl-pepsin solution[24] were used while performing the extrinsic erosion procedure. In this study, unlike existing studies, HCl was used to simulate intrinsic erosion, then abrasion procedure was performed. According to the findings of this study, eroded dentin exhibited lower bond strength values than sound dentin. When dentin is eroded, changes such as opening of dentin tubules, removal of the organic part of intertubular dentin and dentin plugs, increased tubule diameter, and collagen exposure may occur.[7] It becomes difficult for the adhesive to infiltrate into exposed collagen.[20] In addition, when dentin is eroded, the mineral components dissolve and the organic dentin matrix is released.[7,8] The presence of a thickened superficial organic layer could lead to the assumption that adhesive penetration would be impaired, producing lower bond strengths in eroded dentin.[19]

In this study, as reported by previous studies, self-etch resin cement showed higher bond strength in all groups than self-adhesive resin cement.[28-30] The reasons the bond strength of self-adhesive resin cements is lower than conventional cements are that the acidic monomers in resin have limited etching potential for demineralization, insufficient pH neutralization after curing[18], the higher viscosity of the cement prevents deeper resin penetration[17], and non-removal or incomplete removal of the smear layer creates a weaker bond at the interface.[30] In addition, self-adhesive resin cement's increased hydrophilicity can compromise mechanical strength[17], which may be one reason for reduced bond strength. Furthermore, chemical composition differences, surface wetting properties, viscosity and mechanical properties of resin cements may be among the factors affecting bond strength.[31]

Flury et al. cemented LU and VE to dentin with five resin cements and reported that after 24-h storage, SBS did not significantly differ between LU and VE.[32] A previous study stated that the bond strength of LU was lower than that of VE.[33] In this study, LU showed lower SBS in all groups than VE and VS. The difference was significantly only when used with MN in sound dentin. This finding can be explained by the differences in the microstructural properties such as filler type and concentration, material composition and mechanical properties of the LU, VE, and VS. It has been reported that hydrofluoric acid (HF) etching and silane application is an effective surface preparation protocol for VE and VS.[14,33] HF enhances bond strength due to the glass matrix structure in VE and VS.[33,34] Bellan et al. evaluated the dentin bond strength of LU, VE, and VS and reported that LU and VE showed significantly higher μTBS than did VS, which may be due to the differences in the modulus of elasticity of restorative materials.[15] The difference from the present study is that different surface preparation protocols were applied to the blocks. LU, VE, and VS were sandblasted with 50 μm aluminum-oxide (Al_2O_3) particles. In the present study, only LU was sandblasted with Cojet. VE and VS was etched with hydrofluoric acid, then silane was applied to the blocks surfaces. According to the manufacturer's instructions, the Cojet sandblasting application was recommended in the surface preparation protocol of LU (Table 2), but there was no clear indication about the application time. The difference made at this stage may cause a decrease in the surface energy of the LU. These reasons can explain lower the SBS when LU was used in this study.

According to Elsaka, mixed failure is associated with increased bond strength, whereas adhesive failure indicates low bond strength.[35] In this study for all groups, the most commonly observed mode of failure was mixed. Increased adhesive failure when LU, VE, and VS with RU were used in eroded dentin can be expressed by the lower bond strength that self-adhesive cement exhibits.

In the present study, SBS after 24 h was examined. The main limitation of this study was the lack of aging procedures. Therefore, clinical and laboratory studies are needed to assess the long-term effect of erosion on the SBS of CAD-CAM blocks to dentin.

Conclusions

Within the limitation of this in vitro study, it can be concluded that dental erosion affected the SBS to dentin, and eroded dentin showed generally lower SBS. The use of self-etch resin cement system, Multilink N can be

recommended due to higher SBS values compared to self-adhesive cement. In terms of material type, Vita Enamic and Vita Suprinity showed higher SBS in comparison to Lava Ultimate. The type of material and cement system chosen by the clinician is important to provide better bond strength to the eroded dentin structure.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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Assessment of DMFT Indexes, Salivary Flow Rate, pH, and Detections of S.Mutans Salivary Levels by a Quantitative Real-Time PCR in Polycystic Ovary Syndrome

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ABSTRACT

Objectives: PCOS is an endocrine disorder that is common in women. However, PCOS effects on oral and dental health have not been stated clearly. The aim of this study is to examine the effects of Polycystic Ovary Syndrome (PCOS), which is common in women of reproductive age, on saliva and dental tissues in these women.
Materials and Methods: One-hundred individuals who were / were not diagnosed with PCOS and insulin resistance were included in this study (n=100). Subsequently, individuals, with PCOS and insulin resistance (PCOSID +), with PCOS and non-insulin resistance (PCOSID-), without PCOS and insulin resistance (ControlID +) and without PCOS and non-insulin resistance (ControlID-) were divided into 4 groups (n=25). DMFT (Decayed, Missing, Filled Teeth) index was used for dental health evaluation, while pH meter was used for saliva pH measurement. Also, Streptococcus Mutans (S. Mutans) numbers were analyzed by the real-time Polymerase Chain Reaction (PCR) method. In statistical analysis $p<0.05$ was considered significant.
Results: In comparison among the groups, significant differences were found in terms of DMFT index, S. Mutans, and salivary pH values. Among the compared groups, the highest DMFT index, S. Mutans values were found in the PCOSID(+) group, the lowest in ControlID(-) group, while the lowest saliva pH value was found in the PCOSID(+) group.
Conclusions: S. Mutans and DMFT index values were found highly in the saliva of PCOS patients, which is a multifactorial syndrome, and it is determined that salivary parameters have an effect on this situation.

Keywords: PCOS, Real-Time PCR, S. Mutans, Salivary pH

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Introduction

Polycystic Ovary Syndrome (PCOS) is an endocrine disorder of unknown etiology, which is common among women of reproductive age. With a prevalence of approximately 6-8%, PCOS is a clinical picture characterized by chronic anovulation, clinical and/or biochemical hyperandrogenism and polycystic appearance in the ovaries.[1] Several systems are affected by this syndrome and it is presented by menstrual irregularities (oligo-amenorrhea, dysfunctional uterine bleeding), signs of hyperandrogenism (hirsutism, acne, sebaceous skin), obesity and metabolic syndrome.[2]

Insulin resistance (IR) plays a key role in the pathogenesis of PCOS. Insulin resistance is the failure to induce adequate biological response although the insulin is at normal concentration. IR and hyperinsulinemia are some of the common conditions in PCOS patients.[3] Although IR is not a diagnostic criterion of PCOS, it is detected in 50-80% of women with PCOS, regardless of their Body Mass Indices (BMI), and it accelerates the development of diabetes by making patients more susceptible to prediabetes.[4]

In recent years, the relationship between PCOS, which has different complications, and periodontal diseases caused by chronic low-grade inflammation has become a noteworthy issue for reproductive endocrinology. The relationship between PCOS and inflammation, similar to periodontal diseases, and its long-term metabolic consequences has led to the hypothesis that it may be associated with periodontal parameters.[5] Although the underlying biological connections have not been clarified yet, the hyperestrogenic and hyperandrogenic states that occur in PCOS are thought to cause structural changes in the gums and gingival inflammation, and these changes cause bacteria to colonize the gums more easily, increasing the risk of periodontal disease. Therefore, studies report that the detection of periodontal diseases in their early period in PCOS cases and initiation of treatment are crucial for reducing the metabolic complications that may occur in the long term.[6]

If chronic inflammation in periodontal tissues is not treated, tooth-supporting tissues will be destroyed over time and, as a result, dental cavity and loss will occur.[7] Bacteria in the oral cavity play a significant role in the increase of such dental caries. One of these bacteria is Streptococcus mutans (S. Mutans).[8] S. Mutans damages dental hard tissues due to

its acidogenic properties.[9] Studies report that S. Mutans is generally localized in the superficial layers of caries, and facultative bacteria such as lactobacilli colonize towards dentin. [10] A limited number of studies are available in the literature focusing on its relationship with periodontal tissues, but there are no studies investigating the dental hard tissue or oral microbiology.

In the previous limited number of studies investigating PCOS and periodontal state and carious lesions, it remains elusive exactly when dental health starts to deteriorate in PCOS since patients within a wide range of ages are included in the study. Thus, this study aims to investigate bacteria that cause dental cavities in young adults diagnosed with PCOS in their early reproductive period, when metabolic problems are observed to a lesser extent, using the real-time Polymerase Chain Reaction (PCR) method.

Materials and Methods

This clinical study was carried out in Gaziantep University, Faculty of Dentistry, Department of Restorative Dentistry as a multidisciplinary study in collaboration with Gaziantep University Medical Faculty Hospital Gynecology and Obstetrics Department, Microbiology Department and Endocrinology Department. Approval was obtained from Gazianatep University Ethics Committee (2019/311). In the study, serum findings of patients and individuals referred to us were evaluated retrospectively to form groups, and the clinical findings of a total of 100 patients/individuals, 50 of whom were diagnosed with PCOS and 50 were healthy individuals, were evaluated prospectively. All participants were given information about the research, and oral and written informed consent was obtained from all participants.

Experimental Groups

Using 3.1.9 G*Power software analysis, a significance level of 5% (α = 0.05) at 0.80 (1-β) for an effect size of 0.41 was calculated as the sample size. The minimum number of patients was determined as 25 for each group. The results of biochemical parameters were obtained from the patient files, and the groups were standardized according to serum levels of FSH, LH, LH/FSH, HOMA and estrogen.

A total of 100 female patients (n = 100) were included in the study, who were aged 18-33, did not have any systemic disease, were diagnosed with PCOS and had insulin resistance and were categorized as follows: 25 PCOSID (+) patients diagnosed with PCOS but without insulin resistance; 25 PCOSID (-) patients without PCOS but with insulin resistance; 25 ControlID (+) patients without PCOS but with insulin resistance and, finally, 25 ControlID (-) female individuals without PCOS and insulin resistance.

Study groups were formed as follows:

- PCOSID (+) (G1): 25 female patients (n = 25) with PCOS diagnosis and insulin resistance.
- PCOSID (-) (G2): 25 female patients (n = 25) with PCOS diagnosis but without insulin resistance.
- ControlID (+) (G3): 25 healthy volunteers (n = 25) without PCOS but with insulin resistance.
- ControlID (-) (G4): 25 healthy volunteers (n = 25) without PCOS and insulin resistance.

Measurement of saliva flow rate

Saliva samples were taken at 9.00-10.00 in the morning in order to ensure standardization in our study. Individuals were asked not to eat, drink or brush their teeth for at least 2 hours before stimulated and unstimulated saliva samples were taken. Stimulated saliva flow rate, unstimulated saliva flow rate and saliva pH were evaluated.

Measurement of Unstimulated saliva flow rate

Unstimulated saliva flow rate was measured according to the following scores:

- Score 1: Low saliva flow rate; < 60 sec
- Score 2: Normal saliva flow rate; > 60 sec

Measurement of Stimulated saliva flow rate

In order to stimulate the salivary flow, patients were asked to chew a paraffin gum and swallow the first saliva formed in the mouth and then spit the saliva accumulated in the mouth for 5 minutes into a measured container. Saliva flow rate was scored as follows:

- Score 0: Low saliva flow rate; < 0.7 ml/min
- Score 1: Normal saliva flow rate; 0.7-1.1 ml/min
- Score 2: High saliva flow rate; > 1.1 ml/min

Determining the DMFT Index

According to the DMFT index, the total number of decayed (decay, D), missing (M) and filled (F) teeth is divided by the number of people examined, and thus filled, missing & decayed teeth per person are calculated (D+M+F/N = DMFT). Congenital missing teeth, unerupted teeth and supernumerary teeth were not included in this index calculation.

The DMFT index evaluation was performed prior to the study by two physicians and calibrated on 100 patients. Cohen's Kappa coefficient was used to make the clinical evaluation among the physicians. As a result of the examination, the Kappa coefficient for reliability was 0.74 for all variables and the Kappa coefficient for repeatability was 0.80.

Real-time PCR method

Stimulated saliva samples were collected with the help of a pipette and transferred to Eppendorf tubes. They were stored in the freezer (-80ºC) until the study day. Subsequently, the samples were immediately transferred to the microbiology laboratory with an ice battery and kept frozen at -20°C until the PCR analysis.

After the study samples were collected, DNA isolation was performed for S. Mutans with the Genesig S. Mutans detection kit (United Kingdom) according to the manufacturer's instructions.

To investigate the presence of S. mutans bacteria and determine the bacterial load in the isolated eluates, the forward and reverse (forward: 5'-CCGGTGACGGCAAGCTAA-3', reverse; 5' TCATGGAGGCGAGTTGCA-3') primers (Genesig Primer Design, United Kingdom) were designed and

supplied. In our study, S. Mutans strains ATCC 25175 and ATCC 35668 were used as positive controls. Standards were optimized for use in the real-time PCR. First, the master mix was prepared for the real-time PCR. 525 µl of re-suspension buffer solution was added to the lyophilized 2X qPCR master mix in a glass vial and diluted. 165 µl of distilled water from the kit was added to dilute S. mutans primer/probe mix. 500 µl of the buffer solution from the kit was added to dilute the lyophilized S. Mutans positive controls. Six standards were established separately for each strain. An amount of the diluted positive control was put into the first tube of 6 sterile 250 µl Eppendorf tubes.

90 µl of buffer solution was added to the tubes numbered 2, 3, 4, 5 and 6. 10 µl of positive control was taken from the Tube No. 1 and added to the Tube No. 2 and diluted, and similarly, 10 µl of positive control was taken from the Tube No. 2 to be added to the Tube No. 3 and dilute it and thus, standards were established sequentially, including the Tube No. 6. The master mix for PCR was prepared by mixing in a sterile Eppendorf tube, taking into consideration the negative control and standards, and 15 µl of this mixture was added to each tube. 5 µl of sample, negative control and standards were each added to the tubes, the tubes were capped and amplified in Rotor Gene (Qiagen, Germany) to obtain the quantitative analysis result.

Statistical Analysis

Normally distributed numerical variables were expressed as mean ± standard deviation, and non-normally distributed numerical variables were presented as mean values. Frequency analysis was applied to determine the percentage distribution of categorical variables in the groups.

ANOVA - LSD tests and Kruskal-Wallis pairwise tests were used for the statistical analysis. Pearson's Chi-square test/Fisher's exact tests were used to compare the inter-group categorical variables. Pearson's/Spearman's Rho tests were used for correlation calculation. r>0.06 was considered high correlation; r=0.3-0.6 was considered as medium correlation and r < 0.3 was considered low correlation. p<0.05 was considered significant for all values.

Results

Findings related to saliva parameters

No statistically significant difference in unstimulated and stimulated saliva flow rate was found between the groups (p > 0.05).

In inter-group comparison of saliva pH values, the statistical differences between PCOSID (+) and ControlID (+), PCOSID (+) and ControlID (-), PCOSID (-) and ControlID (+) and PCOSID (-) and ControlID (-) groups were found to be statistically significant (p<0.05).

The highest mean pH value of saliva was observed in the ControlID (-) group and the lowest value was observed in the PCOSID (+) group.

Unstimulated and stimulated saliva flow rate distributions of the groups are shown in Table 1, saliva pH mean and standard deviation (±SD) values are given in Table 2, and p values in the inter-group comparison are shown in Table 3.

Findings of S. Mutans value

S. Mutans counts of the saliva samples taken from individuals in all groups were determined by PCR method. In the inter-group comparison, a statistically significant difference was found between PCOSID (+) and ControlID (+), PCOSID (+) and ControlID (-), PCOSID (-) and ControlID (+) and PCOSID (-) and ControlID (-) groups (p<0.05).

The highest mean saliva S. Mutans value was observed in the PCOSID (+) group and the lowest value was observed in the ControlID (-) group.

The mean and standard deviation (±SD) values of S. Mutans in the saliva of the groups are shown in Table 4 and the p values in the inter-group comparison are shown in Table 5.

Findings regarding the DMFT index value

Based on the clinical examination of all individuals in the groups, the DMFT values were recorded.

In the inter-group comparison, a statistically significant difference was found between PCOSID (+) and ControlID (-) groups and PCOSID (-) and ControlID (-) groups (p<0.05).

The highest mean DMFT index value was observed in the PCOSID (+) group and the lowest value in the ControlID (-) group.

The mean and standard deviation values (±SD) of DMFT index values of the groups are shown in Table 6 and the p values for the inter-group comparison are shown in Table 7.

The relationship between saliva parameters and DMFT index values

In the PCOSID (+) group, a negative, moderate and statistically significant correlation was observed between unstimulated saliva flow rate and the DMFT index values (p<0.05).

No significant relationship was observed between stimulated saliva flow rate and the DMFT index values in all groups (p>0.05).

No significant relationship was observed between saliva pH value and the DMFT index values in all groups (p>0.05).

The correlation analysis of the DMFT index values with S. Mutans and saliva parameters is shown in Table 8.

The relationship between the S. mutans count and the DMFT index values

In the PCOSID (+) group, a positive, high and statistically significant relationship was observed between the S. Mutans count in saliva and the DMFT index values (p<0.05).

The correlation analysis between the S. Mutans count in saliva and the DMFT index values is shown in Table 8.

The relationship between saliva parameters and S. Mutans count

In the PCOSID (+) and ControlID (-) groups, a negative, low and statistically significant correlation was observed between the unstimulated saliva flow rate and the S. Mutans count in saliva and a negative, moderate and statistically significant correlation was observed between the PCOSID (-) and ControlID (+) groups (p<0.05).

Table 1. Frequency (n) and Percentage (%) values of unstimulated and stimulated salivary flow rate for all groups

	PCOSID(+)		PCOSID(-)		Control ID(+)		Control ID(-)		p
	n	%	n	%	n	%	n	%	
Unstimulated Salivary Flow Rate									0.934
Low	12	48	11	44	10	40	11	44	
Normal	13	52	14	56	15	60	14	56	
Total	25	100	25	100	25	100	25	100	
Stimulated Salivary Flow Rate									0.631
Low	14	56	12	48	9	36	10	40	
Normal	11	44	13	52	16	64	15	60	
Total	25	100	25	100	25	100	25	100	

* p <0.05 is significant

Table 2. Mean Saliva pH values of groups (±SD)

	PCOSID(+)	PCOSID(-)	CONTROLID(+)	CONTROLID(-)	P
SALIVARY PH	6.82±0.09	6.96±0.09	7.34±0.08	7.42±0.06	**0.001***

* p <0.05 is significant

Table 3: P values of Saliva parameters in the inter-group comparison

	STIMULATED SALIVARY FLOW RATE	UNSTİMULATED SALIVARY FLOW RATE	SALIVARY PH
PCOSID(+) - PCOSID(-)	1.000	0.777	0.160
PCOSID(+) - CONTROLID(+)	0.569	0.569	**0.001***
PCOSID(+) - CONTROLID(-)	0.258	1.000	**0.001***
PCOSID(-) - CONTROLID(+)	0.569	0.774	**0,007***
PCOSID(-) - CONTROLID(-)	0.258	0.777	**0.001***
CONTROLID(+) - CONTROLID(-)	0.569	0.569	0.493

* p <0.05 is significant

Table 4. Mean S. Mutans values of groups (±SD)

	PCOSID(+)	PCOSID(-)	CONTROLID(+)	CONTROLID(-)	P
S. MUTANS	121176.68±78698.41	119189.12±50476.39	13544.57±6036.52	4774.06±3046.02	**0.001***

p <0.05 is significant

Table 5. P values of S. mutans in the inter-group comparison

	S. MUTANS
PCOSID(+) - PCOSID(-)	0.432
PCOSID(+) - CONTROLID(+)	**0.042***
PCOSID(+) - CONTROLID(-)	**0.001***
PCOSID(-) - CONTROLID(+)	**0.013***
PCOSID(-) - CONTROLID(-)	**0.001***
CONTROLID(+) - CONTROLID(-)	0.393

* p <0.05 is significant

Table 6. Mean DMFT index values of groups (±SD)

	PCOSID(+)	PCOSID(-)	CONTROLID(+)	CONTROLID(-)	P
DMFT	5.72±3.84	5.64±3.32	4.60±2.82	3.72±2.47	**0.046***

* p <0.05 is significant

Table 7. p values of DMFT index in the inter-groups comparison

	DMFT
PCOSID(+) - PCOSID(-)	0.929
PCOSID(+) - CONTROLID(+)	0.214
PCOSID(+) - CONTROLID(-)	**0.028***
PCOSID(-) - CONTROLID(+)	0.248
PCOSID(-) - CONTROLID(-)	**0.034***
CONTROLID(+) - CONTROLID(-)	0.328

* p <0.05 is significant

Table 8. DMFT index correlation values (r) between S.mutans and saliva parameters values among the groups

	DMFT							
	PCOSID(+)		PCOSID(-)		ControlID(+)		ControlID(-)	
	p	r	p	r	p	r	p	r
S. MUTANS	**0.001***	0.798	0.077	0.360	0.539	0.129	0.562	0.122
STİMULATED SALIVARY FLOW RATE	0.194	-0.269	0.382	-0.183	0.770	-0.062	0.748	-0.068
UNSTİMULATED SALIVARY FLOW RATE	**0.025***	-0.448	0.267	-0.231	0.849	-0.040	0.811	-0.050
PH	0.983	-0.004	0.483	-0.147	0.879	-0.032	0.968	-0.009

* p <0.05 is significant, r> 0.6 is high.

Table 9. S.mutans correlation values (r) between DMFT index and saliva parameters values among the groups

	S. MUTANS							
	PCOSID(+)		PCOSID(-)		ControlID(+)		ControlID(-)	
	p	r	p	r	p	r	p	r
DMFT	**0.001***	0.798	0.077	0.360	0.539	0.129	0.562	0.122
STIMULATED SALIVARY FLOW RATE	0.302	-0.215	0.090	-0.246	0.165	-0.644	0.239	-0.510
UNSTİMULATED SALIVARY FLOW RATE	**0.021***	-0.255	**0.015***	-0.481	**0.002***	-0.578	**0.026***	-0.244
PH	0.897	-0.027	0.317	-0.209	0.600	-0.110	0.575	-0.118

* p <0.05 is significant, r> 0.6 is high

No statistically significant relationship was found between the stimulated saliva flow rate and the S. Mutans count in saliva in all groups (p>0.05).

No statistically significant relationship was found between saliva pH value and the S. Mutans count in saliva in all groups (p>0.05).

The correlation analysis of the S. Mutans count in saliva and the DMFT and saliva parameters is shown in Table 9.

Discussion

Symptoms of a large number of systemic, bacterial, viral and genetic diseases emerge primarily in the mouth. With the diagnosis of oral symptoms that develop due to these diseases, severe complications that may occur in the future will be prevented.

One of the most common reasons why patients with PCOS apply to the clinic is menstrual irregularity, and most patients present with oligomenorrhea or amenorrhea.[2] In this patient group, GnRH sensitivity decreases against the negative feedback effect of estradiol and progesterone, and the increasing GnRH release frequency results in increased LH in particular. These changes in the central gonadotropin dynamics observed in PCOS can occur primarily or secondarily (due to peripheral hormonal disorders). [11] In PCOS, an increase in serum LH level and, thus, serum LH/FSH ratio is observed due to the disorder in the hypothalamus-pituitary-ovarian axis. Although the LH/FSH ratio is usually high in PCOS patients by approximately 60-70%, a LH/FSH ratio of > 2 helps in the diagnosis of PCOS.[12] Serum FSH, LH and LH/FSH and estrogen levels of our study groups were standardized.

Insulin resistance occurs in women with PCOS by 50-80%. The presence of insulin resistance in PCOS can cause both metabolic disorders and reproductive disorders. The process that starts at an early age with insulin resistance predisposes to several diseases such as cardiovascular diseases, dyslipidemia, hypertension, obesity and Type II DM.[13] It is important to diagnose insulin resistance, which is common in women with PCOS, at an early stage to control possible metabolic disorders.[14] In the literature, the HOMA-IR method is used to assess insulin resistance, and any value that is higher than 2.5 is associated with insulin resistance.[15] In this context, our study groups are divided into subgroups and standardized based on the presence of insulin resistance.

The primary cariogenic bacteria that cause tooth decay is S. Mutans, which secretes lactic acid and produces intense extracellular polysaccharides. [16] Although it is very difficult to determine the level of S. Mutans in dental plaques, the level of S. Mutans in saliva gives an idea about the level of microorganisms in the plaque. A proportional increase is thought to exist between the S. Mutans count in saliva and plaque and tooth decay.[17] For this reason, various studies utilize stimulated saliva sample to determine the S. Mutans level. [18,19] Several methods have been developed to determine the level of S. Mutans in saliva. Non-practical methods such as microbiological culture and other methods with high contamination risk are used in the detection of S. Mutans.[20] S. Mutans kits that provide practical and quick results are also available on the market.[21] The real-time PCR method, which has been used frequently in recent years, is an accurate and precise method for detecting S. Mutans. Studies conducted on S. Mutans demonstrate that real-time PCR method gives more specific and accurate results than other methods.[22] In our study, real-time PCR technique was used to ensure accurate and precise S. Mutans count in stimulated saliva samples.

Although it is effective on the amount of saliva, risk of caries and caries activity, reduced saliva flow rate adversely affects oral health.[23] Several studies on saliva functions report that stimulated saliva is used more advantageously than unstimulated saliva. This is because the stimulated saliva sample is more resistant to daily pH changes.[24]

No consensus was reached in various studies evaluating patients in terms of saliva flow rate in diabetes, which is one of the systemic diseases.[25,26] Malicka *et al.*[27] found that the

unstimulated saliva flow rate was lower in patients with Type II DM than in the control group. On the other hand, in their study in which stimulated saliva flow rates are examined, Boyce *et al.*[28] report that patients with Type II DM have a lower flow rate than the control group; however, statistically significant results could not be obtained. These conflicting results may result from the differences in age, treatment protocols and medications used.[29]

In our study, the highest unstimulated saliva flow rate value was observed in the ControlID (+) group and the lowest value was observed in the PCOSID (+) group; however, no statistically significant difference was found between all groups ($p > 0.05$). In all groups, a significant correlation was found between unstimulated saliva flow rate values and S. Mutans values in saliva ($p<0.05$).

In our study, the highest stimulated saliva flow rate value was observed in the ControlID (+) group and the lowest value was observed in the PCOSID (+) group, however, no significant difference was found between the groups ($p>0.05$). In all groups, there was no significant relationship between stimulated saliva flow rate values and S. Mutans values in saliva and the DMFT index values ($p>0.05$).

Chronically high levels of unmet free estrogen are present due to hypothalamic-pituitary dysfunction observed in patients with PCOS. Estrogen is effective in maintaining the integrity of the oral cavity as well as regulating reproductive functions.[30] High estrogen levels in patients with PCOS affect the vascular permeability of the oral mucosa, which reduces the immune competence of the oral cavity.[31] Zhang *et al.*[32] found that estrogen was present in the cells in the salivary gland ducts and suggested that the salivary glands were one of the estrogen target organs. Another study reported that serum estrogen level and saliva flow rate decreased during ovulation and increased during menstruation. In addition, unstimulated and stimulated saliva flow rates were found to be lower in women compared to men.[33] This suggests that estrogen plays a crucial role in suppressing the saliva flow rate.[34] Findings about the saliva flow rate can be explained this way.

There are studies in the literature evaluating the relationship between various systemic and autoimmune diseases and saliva pH.[35,36] Mumcu *et al.*[37] reported in their study on patients with Behcet's disease that saliva pH was lower compared to the control group. Additionally, Loyola *et al.*[38] reported in their study on Systemic Lupus Erythematosus (SLE) patients that the stimulated saliva flow rate and saliva pH values were lower than the control group, which caused an increase in the DMFT index values.

In our study, the highest mean pH value of saliva was observed in the ControlID (-) group and the lowest value was observed in the PCOSID (+) group ($p<0.05$). These results provided similar results with the DMFT index values and S. Mutans values. Similarly, no significant relationship was observed between saliva pH and the DMFT index values and S. Mutans values in all PCOS and Control groups ($p>0.05$).

Increased estrogen levels in patients with PCOS have an inhibitory effect on parathyroid hormone (PTH) and cause calcium (Ca^{+2}) retention in salivary glands. Thus, any increase in the estrogen level^{+2} results in decreased concentration.[31] Decrease in Ca^{+2} in saliva results in decreased saliva pH and increased incidence of caries.[39] Likewise, the oral environment becomes more acidic as a result of the decreasing pH level of saliva and the level of S. Mutans, one of the cariogenic microorganisms in saliva, increases.[40]

When it is considered that the dental plaque is the primary factor of periodontal diseases, it is important to evaluate periodontal diseases for preventive dentistry.[41] Although few studies are available on the periodontal health of individuals with PCOS[42,43], there is no study in the literature on the effect of PCOS on oral microflora and its relationship with tooth decay, except the study conducted by Surmelioglu *et al.*[44].

In the literature, several studies focus on the relationship of S. Mutans with a majority of systemic diseases.[45,46] Siudikiene *et al.*[45] report that the number of S. Mutans in saliva was higher and tooth decay was more common in diabetic patients. Moreover, the S. mutans count is closely related to saliva pH, saliva flow rate and the DMFT index values.[46]

In our study, the highest saliva S. Mutans value was found in the PCOSID (+) group and the lowest value in the ControlID (-) group ($p<0.05$).A positive and significant correlation was observed between the number of S. Mutans in saliva and the DMFT index values in the PCOSID (+) group ($p<0.05$). In all groups, a negative and significant correlation was found between the number of S. Mutans in saliva and unstimulated saliva flow rate values ($p<0.05$). These results should be interpreted within the DMFT index values and saliva flow rate values.

The insulin sensitivity of tissues varies in patients with insulin resistance. In insulin resistance, glucose breakdown primarily decreases in the muscle and postprandial hyperglycemia occurs. Later, glucose output from the liver increases with the effect of insulin resistance. Thus, fasting hyperglycemia and all-day hyperglycemia begin to emerge.[47] In these cases, the presence of glucose in the oral cavity increases with hyperglycemia and thus, the amount of acid-producing bacteria increases, pH decreases and hyposalivation occurs.[40] Low saliva flow rate causes changes in the oral microbiota. This change results in a higher number of S. Mutans in the oral cavity.[48] In our study, the effect of insulin resistance on oral flora can be thus explained.

An increase in vascularization and inflammatory reactions are observed with estrogen receptors in the gingiva in patients with PCOS due to the increased level of estrogen.[31] Due to the increased level of estrogen, the oral microflora becomes more acidic, the microorganism count in the saliva and the level of S. Mutans increases.[49] Studies suggest that irritability and depression occurring in women in the premenstrual period due to changes in the estrogen and progesterone levels may be reflected in saliva components.[50] Depression reduces saliva secretion, while

positive mood increases the saliva flow rate.[51] An increase in the S. Mutans count is detected in the oral microflora when saliva flow rate decreases.[48] In our study, the effect of PCOS on the oral flora can be explained based on these reasons.

Although general inter-oral parameters do not give any clear result, more accurate results can be achieved by increasing the number of patients. These results showed that insulin resistance alone did not have any effect on S. mutans values in the oral flora. PCOS, a multi-factorial syndrome, is found to significantly increase the level of S. Mutans regardless of interoral factors.

The large number of S. Mutans in the oral microflora paves the way for the formation of caries.[45] In the literature, a large number of studies revealing the relationship between systemic and autoimmune diseases and the DMFT index value can be found.[36,52] Erdem *et al.*[53] report that patients with Behcet's disease had higher DMFT index values than the control group. Glodny *et al.*[54] report in their study on patients with metabolic syndrome that the patients have a higher number of caries than the control group. This may result both from dental caries and the pathophysiological mechanism of Metabolic Syndrome associated with chronic low-grade inflammation and from insulin resistance.

In our study, the highest DMFT index value was observed in the PCOSID (+) group and the lowest in the ControlID (-) group ($p<0.05$).

Previous studies report that the DMFT index is associated with insulin resistance.[55] The presence of glucose in the oral cavity increases with hyperglycemia caused by insulin resistance, and thus, the amount of acid-producing bacteria increases, pH decreases and hyposalivation occurs.[40] Studies report that a relationship exists between hyperglycemia and the DMFT index.[56,57] An increase in the incidence of caries is observed as hyperglycemia increases the risk of hyposalivation.[39] Nevertheless, the mechanisms that give these results are not clear and various theories have been put forward. These include reduced mineralization of enamel and predisposition to tooth decay due to the co-existing hyperglycemia and hyposalivation, decreased salivary gland function due to the resulting inflammatory response and changes in the neuroendocrine response of the salivary glands due to the immune reaction (Allushi, Bagavant, Papinska, & Deshmukh, 2019). Findings related to insulin resistance from our study results can be thus explained.

The high DMFT index values in patients with PCOS are closely associated with the saliva pH, saliva flow rate and S. Mutans values.[58] When we evaluate our results in general, the data obtained from all groups varied. Nonetheless, PCOS significantly increased the DMFT index values, regardless of inter-oral factors.

There were some limitations in our study. Since the patient groups in the study comprised of women in their reproductive period, their effects on saliva parameters and caries lesions in women with PCOS in older age groups are unclear.

Conclusion

When all results were analyzed, the salivary S. Mutans counts and the DMFT index values of the PCOS groups were higher than the control groups. Hyperglycemia caused by insulin resistance and estrogen levels increased with PCOS syndrome are thought to be primarily effective in obtaining these data from our study. The oral health data obtained in this study we conducted on PCOS patients, which are common in our society, are the initial data in the literature. We think that the data obtained from our study will serve as a reference to future studies, and thus, contribute to the literature.

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Comparative Evaluation of the Effect of Different Rotary Instrument Systems on the Amount of Apically Extruded Debris

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Research Article

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ABSTRACT

Objectives: The purpose of our study is to examine in vitro the amount of debris extrusion from the apical after root canal preparation with different rotary instruments.
Materials and Methods: In the present study, 60 single roots single-canal lower premolar human teeth were used. The teeth were randomly selected and divided into 4 main groups (n=15). Root canals are shaped by using 2Shape, One Curve, and XP-3DEndo Shaper working in rotational motion and WaveOne Gold working in reciprocal motion. Later, the weight of each eppendorf tube was weighed on a precision scale and the amount of debris extrusion from the apical was determined with 10¯4 precision by subtracting the empty weight of the tube. Since the parametric test assumptions were fulfilled in the evaluation of the data obtained regarding the amount of debris extrusion from the apical of file systems by loading them into the SPSS 22.0 program, One-Way Variance analysis was used and the level of error was taken as 0.05.
Results: When the amount of debris extrusion from the apical is ordered from high to low, it was seen that there are 2Shape, One Curve, XP-Endo Shaper, and WaveOne Gold. However, the difference between study groups was not statistically significant.
Conclusions: Considering the results obtained in terms of debris extrusion from the apical about the new generation files with different metallurgy, kinematics, structural features, designs, and different configurations that we used in the present study, it was seen that these systems would not show any difference in terms of the effect of debris on the success of endodontic treatment.

Keywords: Root Canal Treatment, Debris Extrusion, Rotary Systems, Endodontics, Endodontic Treatment

Hastabaşı CAD-CAM Blokların Eroze Dentine Makaslama Bağlanma Dayanımı

Süreç

Geliş: 10/06/2022
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ÖZ

Amaç: *Çalışmamızın amacı, farklı döner aletlerle kanal hazırlığı sonrası apikalden çıkan debris miktarını in vitro olarak incelemektir.*
Gereç ve Yöntemler: *Bu çalışmada 60 adet tek köklü tek kanallı alt premolar insan dişi kullanıldı. Dişler rastgele seçilerek 4 ana gruba ayrıldı (n=15). 2Shape, One Curve ve XP-3DEndo Shaper rotasyonel hareket ile WaveOne Gold ise resiprokal hareket ile kullanılarak kök kanalları şekillendirildi. Daha sonra her bir eppendorf tüpünün ağırlığı hassas bir terazide tartıldı ve tüpün boş ağırlığı çıkarılarak apikalden çıkan debris miktarı 10¯4 hassasiyetle belirlendi. Eğe sistemlerinin apikalinden debris ekstrüzyon miktarına ilişkin elde edilen verilerin SPSS 22,0 programına yüklenerek değerlendirilmesinde parametrik test varsayımları karşılandığından, Tek Yönlü Varyans analizi kullanılmış ve hata düzeyi olarak alınmıştır. 0,05.*
Bulgular: *Apikalden gelen debris ekstrüzyon miktarı yüksekten düşüğe doğru sıralandığında 2Shape, One Curve, XP-Endo Shaper, WaveOne Gold olduğu görüldü. Ancak çalışma grupları arasındaki fark istatistiksel olarak anlamlı değildi.*
Sonuçlar: *Bu çalışmada kullandığımız farklı metalurji, kinematik, yapısal özellikler, tasarımlar ve farklı konfigürasyonlara sahip yeni nesil eğeler hakkında apikalden debris ekstrüzyonu açısından elde edilen sonuçlara bakıldığında, bu sistemlerin artıkların endodontik tedavinin başarısına etkisi açısından herhangi bir farklılık göstermeyeceği görülmüştür.*

Anahtar kelimeler: *Kanal Tedavisi, Kalıntı Ekstrüzyonu, Döner Sistemler, Endodonti, Endodontik Tedavi*

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Introduction

One of the most important stages of endodontic treatment is root canal preparation. Chemomechanical preparation made with different root canal files and techniques is the removal of the necrotic or infected pulp tissue, bacteria, toxins, and another immunological removal in the root canal system, as well as shaping the narrowest part of the canal in the apical foramen in a form that narrows from the coronal to the apical.[1] Chemomechanical preparation of the root canal, removal of infected residues can be achieved by mechanical shaping of the root canal and washing with chemical solutions.[2,3]

It has been supported by many studies that the debris extrusion from the apical that can occur during endodontic treatment is closely related to the irrigation agents used, the preparation techniques applied, and the preferred root canal ınstruments.[4-8] It has been determined in the researches that the technique used in root canal preparation, the type and size of the canal ınstruments, the point where the mechanical shaping in the apical area will be terminated, the irrigation method, and the amount of solution used affect the amount of debris extrusion from the apical in different rates.[4,9-14] Also it has been reported that none of the existing preparation systems can shape root canals without apical extrusion.[15,16]

Infected debris extrusion from the apical with the rotary instrument systems used during root canal preparation disrupts the microbial balance and may cause host defense and exacerbations that lead to acute inflammations. However, on account of the different structural features, metallurgy, kinematics, and designs of the new generation files produced, they will be able to minimize the complications that may occur by causing less debris extrusion compared to conventional rotary ınstrument systems.[17]

The purpose of this invitro study is the evaluation of comparatively, examined the amount of debris extrusion from the apical during root canal preparation by rotary instruments with different metallurgy, kinematics, structural properties, and design.

Material and Methods

Selection and Collection of Teeth

In this study, when $\alpha = 0.05$, $\beta = 0.10$, $1-\beta = 0.90$, 15 teeth in total were processed into each group and 60 teeth in total were processed, and in this case, the power of the test was found to be p=0.90919. To be used in the study, 60 pieces of apical development were completed for orthodontic and periodontal reasons and a single apical foramen with a slope less than 15º according to the Schneider method, without caries and restoration, lower premolar human extracted teeth were used.[18] Considering the current approaches, digital radiography was taken from the buccal and approximal surfaces of the teeth and single-rooted, single-canal teeth without any anatomical difference were included in the study.

The hard and soft tissue residues on the root surfaces of the selected teeth were cleaned with the help of a crescent. Teeth were kept in 2.5% NaOCl for 2 hours for disinfection and then kept in distilled water at room temperature until the time of the experiment.

Determination of Working Length of Teeth

All teeth are standardized by occlusal abrasion with the help of a fissure diamond bur under water cooling and the working length is adjusted to 16 mm. Again, the entrance cavities are opened with a diamond rond bur under water cooling. Under a dental microscope (Olympos 4477, Tokyo, Japan); The tip of the K-type file (Mani Inc., Tochigi, Japan) number 15 placed in the root canal is advanced in the canal until the tip can be seen through the major apical foramen and the canal length is confirmed 17mm with a rubber washer, and the working length is retracted by 1 mm and at 16 mm fixed.[19]

Preparation of Experiment Setup

While preparing the experimental setup, the experimental setup developed by Myers and Montgomery (1991) and modified by Tınaz *et al.*[13,20] was used. Teeth by prepared and run lengths determined, by providing suitable perforations in the coronal diameter of the stem to the center of the lid of the Eppendorf tube to remain in the tube when the apices door is closed, placed cyanoacrylate to (Pattex Instant Adhesive, Turkish Henkel, Istanbul, Türkiye) debris extrusion thereby rendered stable is intended to collect here. Each cover is sterilized and numbered after matching the teeth. In order to balance the air pressure inside the tube and the outside air pressure, the 27 G injector needle is placed in the caps so that the tip remains in the tube.

The tooth-cannula-cap unit was placed in the eppendorf tube and the excess fluid in the tube was ejected through the cannula. The eppendorf tube, whose initial weight was measured, was then mounted to the 15 cc bottle to hold the unit during the operations, thus preventing possible contact with the eppendorf tube and preventing any residue that would increase its weight. To prevent the extrusion debris from being seen by the physician during the procedures, a 15 cc bottle and plastic part of the cannula are wrapped in aluminum foil. The initial weights of the tubes were measured three times on a precision scale (Precisa, Dietikon, Switzerland) with a sensitivity of 10^{-4} g and averaged and the average weight of each tube was recorded.

Creating Working Groups and Shaping Root Canals

Teeth standardized in terms of root curvature, apical foramen widths, and working lengths were randomly selected as 15 in each group. 4 working groups were formed to use different rotary tool systems in each group;

Group 1: 2 Shape (Coltene micro mega, Besançon, France)

Group 2: One Curve (Coltene micro mega, Besançon, France)

Group 3: WaveOne Gold (Dentsply Maillefer, Baillagues, Switzerland)

Group 4: XP-3D Endo Shaper (FKG Dentaire SA, La Chaux-de-Fonds, Switzerland)

Group 1: 2 Shape

Before starting to shape, working length was checked with K-type file number 15. The files were used in the form of 3 waves with an up-down progressive movement, at a speed of 250-400 rpm in continuous rotation, and the torque was adjusted to be 2-2.5 N.cm. The rotary was placed in the root canal until resistance was felt in the file and 2/3 of it was shaped by removing the initial resistance areas by using a circumferential brushing motion. It consists of 2 Shape, TS1 (0.4 taper, number 25) and TS2 (0.6 taper, number 25) shaping instruments and the instruments were used in the canals respectively.

Group 2: One Curve

The full length has been progressed with 8 and 10 files in the One curve system. Then, before starting the shaping, the working length was checked with a K-type file number 15. With continuous rotation, the endo motor was shaped so that its speed was 300 rpm and the torque was 2.5 N.cm. The coronal part was enlarged with the One Flare in the set. One curve was prepared by creating a leading canal path with a working length with a One G glide path. One curve preparation was made with a direct downward movement up to the working length in continuous rotation at the specified speed and torque.

Group 3: Wave One Gold

In shaping with Wave One Gold files, the Wave One Gold mode was used at a speed of 300 rpm and a torque of 2 N.cm. Working length was checked with no 15 K type file before starting to shape. Root canals were shaped using Small and Primary files in accordance with the manufacturer's instructions. The shaping was made by reciprocating movement (150° counterclockwise, 30° clockwise). Styling is terminated with Wave One Gold Primary.

Group 4: XP-3D Endo Shaper

Working length was controlled with 10 and 15 K-type files in the XP-3D Endo Shaper system. The instrument was operated with a speed of 800-1000 rpm and the endo motor adjusted to 1 N.cm of torque. In accordance with the manufacturer's instructions first before proceeding until after a maximum of 5 seconds along the longitudinal study was conducted within the channel 15 additional strokes.

During shaping, the canals were washed with distilled water at every exit of the file from the canal mouth or after every three back and forth movements. In total, irrigation was performed using 10 ml of distilled water for each sample. In all groups, root canal shaping was performed by a single operator, following the manufacturer's instructions and using the X-Smart Plus (Dentsply, Maillefer, Ballaigues, Switzerland) endodontic motor.

Identification and Measurement of Extrusion Debris

After the shaping was completed, the lids of the eppendorf tubes were opened and the root surfaces of the teeth were washed with 1 ml of distilled water so that the adhering debris residues were collected into the tube. Thus, debris residues stuck on the root surface were also collected in the tube. The tubes were then placed in the incubator with their mouths open. The tubes were kept in a dry oven at 37°C until the distilled water evaporated completely. After the liquid evaporated, in order to determine the amount of extrusion debris, the tubes were weighed three times on the digital scale where the first measurements were made with a sensitivity of 10^{-4} and the average values were calculated and the measurements were recorded. The difference between the initial weight of the Eppendorf tube and the weight measured after preparation was recorded as the amount of extrusion debris.

Statistical Evaluation

Since the parametric test assumptions were fulfilled in the evaluation of the data by loading the data obtained in the present study into the SPSS 22.0 program (Kolmogorov-Smirnov) when comparing the measurements obtained from more than 2 independent groups, One-Way Variance analysis was used and the level of error was taken as 0.05.

Results

When the weight of the tube and the amount of debris were measured together, the difference between the groups was found to be insignificant ($p>0.05$) (Table 1). Although the difference between groups is statistically insignificant, when the total amount of extrusion debris with the weight of the tube is examined from maximum to minimum; 2 Shape, One Curve, XP-Endo Shaper, and Wave One Gold.

In addition to this result, when the rotational rotary instrument systems were evaluated within themselves, it was determined that the maximum extrusion was 2 Shapes, while the least extrusion was the XP-Endo Shaper.

Table 1. Extrusion Debris Amounts

		n	Average	Standard Deviation	Result
Tube Weight and Amount of Debris	2 Shape	15	0.7207	0.0097	F=2.48
	One Curve	15	0.7153	0.0099	P=0.070
	Wave One Gold	15	0.7122	0.0086	
	XP-Endo Shaper	15	0.7136	0.0083	
Amount of Overflowing Debrice	2 Shape	15	0.022893	0.0097	F=2.50
	One Curve	15	0.017420	0.0099	P=0.069
	Wave One Gold	15	0.014333	0.0086	
	XP-Endo Shaper	15	0.015713	0.0082	

Discussion

The success of endodontic treatment depends on accurate diagnosis, effective dissolution of root canals, disinfection, and a tight apical and coronal occlusion data filling.[2] Success in root canal preparation depends on the length of the root canal, the type of tooth used, the width of the root canal, the curvature of the root canal, the size of the minor and major diameters of the apical foramen, the irrigation solution and method used, the kinematics and design of the root canal tools, the distance of the apical border of the preparation to the apical foramen, the design of the instrument used. may vary depending on the amount of debris extrusion from the apical.[11,12,21-26]

In the present study, two systems with rotational and reciprocal movements were chosen as the rotary tool systems we preferred. While the 2 Shape, One Curve, and XP-Endo Shaper rotary tool systems are rotational moving systems, the Wave One Gold system is included in the present study as a reciprocating rotary file system. Crown-down shaping method has been used in all rotary ınstrument systems in accordance with the recommendations of the manufacturers.

It has been observed that the method used during root canal preparation in rotary file systems has an effect on debris extrusion from the apical. Considering all these studies, this method was also preferred in the present study because of the advantage of the Crown down method, which reduces the amount of debris extrusion from the apical by shaping a part of the coronal region first and then gradually descending to the apical.[14,27]

From the studies carried out using files with different cones in the production of rotary ınstrument systems; In a study by Kuştarcı *et al.*[8], It was observed that the ProTaper Universal file system with a larger taper angle caused significantly more debris extrusion than the K3 file system. In the study of Pedrinha *et al.*[28,29], It was seen that WO (0.08) carries more debris than WOG (0.07). Contrary to our work, these studies have shown that files with larger taper angles carry more debris. In both studies, rotary files with reciprocal motion were compared among themselves, and ın present study, rotary file systems with different kinematic features were evaluated together. At the same time, while the file systems developed with Gold Wire used in the present study have exactly the same properties, it has been observed that other file systems developed with M Wire have different structural features. Accordingly, the main difference is that the XP-3D Endo Shaper, which has been developed with M-Wire heat treatment in the same way as the studies described above, has a different design (Booster type design / Adaptive core technology), and its S-shaped design is suitable for the expansion and contraction of the walls. We think that it arises due to its structural and design advantage, which enables the formation of less debris than files with more taper by abrading dentin evenly from the walls.

When other studies using files with different cones in the production of rotary instrument systems are evaluated, In a study conducted by Haridas *et al.*[30], It was observed that Wave One Gold (0.07) had a higher taper than Protaper Next (0.06), but it caused less debris extrusion. In the study conducted by Zan *et al.*, During root canal preparation of PTG (0.08) and WOG (0.08) rotary file systems, it was less than K3TMXF (0.06), OSNG (0.06), and TFA (0.08). It has been observed to carry an amount of debris.[31] Considering these studies, it was seen that, unlike other studies, the effect of the taper angle on the debris extrusion from the apical was not significant. Similar to these studies, in the present study, the Wave One Gold (0.07) with the highest taper angle carries the least debris, then the 2nd least debris is compared to the XP-3D Endo Shaper (0.04), without showing a correlation depending on the taper angle, 3. The least debris has One Curve (0.06) and the 4th most debris extrusion is shown by the 2 Shape (0.06) file system having the same taper angle. Although it is not statistically significant, this difference between the debris extrusion amounts is not due to the difference in the taper angle, but due to the metallurgical advantages of the rotary file systems used by different heat treatments such as T-Wire, C-Wire, M-Wire, and Gold technology, provided by increased flexibility. In addition, the amount of debris extrusion from the apical was found to be different due to the triple helix, variable, convex triangle, parallel side cross-section, and different knife-file designs.

When looking at the studies on the use of rotary file systems used for root canal preparation with different kinematics; As a result of the study conducted by Bürklein *et al.*[32], the most debris extrusion amount was seen in the Reciproc group, but no significant difference was found between the other groups. In the study conducted by Şerefoğlu *et al.*[33], It was revealed that the Reciproc group carried significantly more apical debris than the PTU-R and R-Endo rotary file systems during the preparation of seriously curved root canals, except for the H file system where manual preparation was made. In our study, it was observed that the reciprocating system caused less debris extrusion than the rotational movement systems. This different result causes different teeth selected in the studies, the flexibility provided by the production of rotary file systems with T-Wire, C-Wire, and Gold technology and heat treatment, with the 2-blade design with a parallelogram cross-section, causes less debris extrusion from the apical with the increase of the area created to carry the debris coronally and We think it depends on the use of different preparation procedures.

When looking at other studies on the use of rotary file systems used for root canal preparation with different kinematics; In a study by Haridas *et al.*[30]; The instrumentation technique with reciprocating motion has been shown to carry less debris compared to continuous rotation and backward- forwards motion. In a study by Silva *et al.*[34], They compared reciprocal (WaveOne and Reciproc) and rotational (ProTaper Universal and ProTaper Next) file systems and observed that the most debris extrusion was caused by the ProTaper Universal system. Although there is no significant difference between other systems, Reciproc showed the least debris burst. In the preparation performed with the Wave One Gold with reciprocal

movement, as in these studies, the preparation made with the rotational movement with 2 Shape, One Curve, and XP-Endo Shaper instrument systems was supported by the data with less debris extrusion than the preparation made with 2 Shape, One Curve and XP-Endo Shaper instrument systems. By its design, the off-center design of WOG due to its parallel cross-section and its friction-reducing two-blade design, with only one cutting edge in contact with the canal wall, the file attaches less to the canal wall and creates more space to move debris coronally creating more space to carry debris coronally during root canal treatment. Helped to minimize the amount of debris. We also think that the reciprocal movement is due to the fact that it moves with a pressure that imitates the known balanced force technique and removes less debris from the apical.[35]

Since it is thought that the metallurgical properties of the rotary instrument systems used during root canal preparation may affect the amount of debris extrusion from the apical, the studies should be evaluated. According to this; In a study conducted by Surakanti *et al.*[36], when the amount of debris extrusion from the apical during root canal preparation was evaluated, it was observed that the WaveOne and ProTaper rotary file systems were significantly higher than the Hyflex CM rotary file. In a study by Bürklein *et al.*, One file system with reciprocal movement Reciproc, a single file system with rotational motion F360 and OneShape were compared with the Mtwo system, which is a rotationally moving multiple file system, in one of the studies of apical extrusion. As a result of the study, while the amount of debris extrusion was mostly seen in the Reciproc group, no significant difference was found between the other groups.[32] When the metallurgical properties of the files used in the studies were examined, it was seen that the files developed with M-Wire and CM-Wire heat treatment technologies were used and the files developed with M-Wire technology carried more debris. Considering the metallurgical properties of the files in the present study, it was seen that the file system developed with Gold Wire technology carries less debris than the M-Wire system in preparations made using files developed with T-Wire, C-Wire, M-Wire, and Gold heat treatment and technologies. In this case, the flexible structure of the Gold file system and the double blade design, which reduces friction, cause a decrease in the amount of apical debris. In addition, although they were developed with similar heat treatment technologies such as M-Wire, according to Resiproc and Wave One, the XP-3D Endo Shaper used in our study was produced with adaptive core technology due to its superelastic feature, causing less pressure, and dentin evenly and in a small amount from the walls. We think that it causes less debris extrusion due to its removal.

There is an important study revealing the effect of metallurgical properties of rotary instrument systems used during root canal preparation on the amount of apically extruded debris. In a study by Sarıçam *et al*., the roots were randomly divided into 3 groups in the study: OneShape; One Curve; and 2Shape. It has been observed that the amount of extrusion debris produced by the One Curve rotary tool system is similar to that produced by the One Shape system and lower than that of the 2 Shape system.[37] In the present study, when the amount of debris extrusion from the apical during root canal preparation, like those of Sarıçam *et al.* It was observed that One Curve carried less debris than 2 Shape. This is due to the use of the glide path in preparation according to the manufacturer's instructions in One Curve, the use of a single file, the patented variable cross-section along the blade, its design, metallurgical (C-Wire technology) structure different from 2 Shape (T-Wire), especially in the apical. It is thought that the amount of debris extrusion as a result of the decrease in the pressure created on the canal walls causes less debris amount to extrusion than the apical compared to 2 Shape.

In the study conducted by De-Deus *et al.*[38], when looking at the amount of debris carried by single and multiple file systems from the apical during root canal treatment of teeth divided into 3 groups G1 (ProTaper), G2 (Wave One), and G3 (Reciproc); It has been observed that there is no significant difference between two single-file systems and they carry less debris than the multiple file system. In the present study, Wave One Gold, in which two files are used, caused the least debris extrusion, while the most debris extrusion was seen in 2 Shapes where two files were used, and the amount of debris extrusion was seen in single file systems was among these systems using two files. In the present study, as in the study of De-Deus *et al.*, single and multiple systems were evaluated together with different kinematics. However, the different results obtained from our study can be attributed to the different types of teeth selected in the study and the lack of a large difference between the number of files used. At the same time, while M-wire heat treatment technology was used in the above-mentioned study, we think that the superior features such as the reduction of friction with less pressure to the apical due to the more flexible file produced with Gold Wire technology depend on the prevention of the number of files.

In the study of Bürklein *et al.*[32], no difference was found between single and multiple rotary file systems and the amount of debris extrusion from the apical after preparing the root canals. In the study of Özsu *et al.*[39], it was observed that the SAF group carried the least debris, and the ProTaper Next and Wave One groups were associated with less debris than the ProTaper Universal group. In the single and multiple file groups, there was no direct ranking in relation to the number of files. Considering the results obtained, systems with different numbers of files as in the above-mentioned studies were used in our study. Considering the results obtained, in our study, while Wave One Gold, in which two files were used, caused the least extruded debris, the highest extruded debris was observed in 2 shapes using two files, and the amount of extruded debris seen in single file systems was determined by this study. The fact that it is among the systems has shown that there is no direct proportional distribution with the number of files. Accordingly, when the studies mentioned above are evaluated, we think that the use of single or multiple file systems during root canal treatment does not have a direct effect on debris extrusion from the apical if the difference

in the number of files is not too much, but the effect may be minimal. We think that the minimal amount of extrusion debris increases the amount of debris removed from the canal walls during the use of systems with a higher number of files in continuously rotating file systems, in parallel with the number of files. However, in cases where there is a large difference in the number of files, we think that the amount of debris extrusion from the apical may be higher due to the longer preparation time with the file in root canal preparation made with the rotary file system.

In our study, 2 Shape, One Curve, XP-3D Endo Shaper, and Wave One Gold rotary file systems used in root canal preparation were used together for the first time in a study, we believe that the results obtained in this context can be very useful.

Conclusions

Considering the results between the new generation file systems, it is thought that these systems, which have different metallurgical and structural features, different designs, and different kinematic features and configurations, have advantages that can affect the long-term success of root canal treatment. In the light of this information, we think that endodontic treatment should be started by choosing the most ideal file system suitable for the diagnosis and structural characteristics of the tooth to be treated, considering the superior properties of different new generation files.

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Ethical Approval

This article does not contain any studies with human participants or animals performed by any of the authors. This experimental study was conducted in conformity with the principles set forth in the WMA Statement on Animal Use in Biomedical Research.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Covid-19 Vaccination and Dentistry: Are we Facing New Challenges or Working within our Possibilities? Analytical Review

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ABSTRACT

Objective: To systematize available data regarding COVID-19 vaccination aspects among dental specialists and highlight relevant occupationally-related features of vaccination challenges.

Materials and Methods: Search of pertinent literature sources associated with above-formulated objective was provided via PubMed Central database (https://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com/). Criteria of publication date included 2020-2022 years period. Publications in English or at least with English abstract/summary were collected within primary sample for further preliminary content-analysis. All articles collected for in-depth content-analysis were evaluated due to the text-mining, text-identification and text-extraction principles with further clusterization and systematization of outcomes at the Microsoft Excel 2019 software (Microsoft Office, Microsoft, 2019).

Results: After full reading of articles' texts 28 of them were categorized as those containing new and/or unique information, interpretations or facts, out of which 12 were cross-sectional online surveys, 4 were editorials, 7 were literature/systematic/clinical reviews, 1 was brief report, 1 was opinion article, 1 was ethical moment, 1 was advice article, and 1 was web-source. New challenges related with COVID-19 vaccination within dental field are represented by personal hesitancy of dental professionals and students, which in turn associated with such factors as provided information support, previous COVID-19 experience, fear of getting infected or transmit disease to the patients or family members, fear of potential post-vaccination side-effects development, changes of occupational status, and interaction within dental team.

Conclusions: Further improvements of dental care field possible only after vaccination of dental professionals. Vaccination of dentists is widening window of their possibilities regarding inclusion as members of COVID-19 vaccine's delivery team and participation within "behaviorally informed strategies" and public motivational programs, which in turn is aimed at amplification of positive willingness for COVID-19 vaccination among general public.

Keywords: COVID-19, Vaccination, Dentistry

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Introduction

Due to the international COVID-19 vaccination dataset by the 13th of May 2021 near 4.4% of population worldwide have been fully vaccinated against COVID-19, which equals to near 346 million people.[1] Nevertheless, while some countries demonstrating progressive increase tendency of vaccination rate (62.75% in Israel, 53.20% in UK, 48.39% in Bahrain, 46.23% in USA, 46.94% in Chile, 46.41% in Hungary, 35.70% in Germany and 28.56% in France on the 13th of May 2021), other countries, like Ukraine, which is native for corresponding author, characterized with only 13,661 persons fully vaccinated, and near 2.1% of population received 1 dose of vaccine.[1] Such great differences among above analyzed vaccination levels argumented by the influence of various economical, national, social and technical-related factors and reasons, which are remaining under ongoing public health research as urgent and relevant investigation topics.[2]

Despite relative availability of different vaccines including Oxford/AstraZeneca, Pfizer/BioNTech, Sinopharm/Beijing, Johnson&Johnson, Moderna, Sinovac, impact of personal and occupationally associated factors also should not be excluded during analysis of vaccination coverage rates.[3] Moreover, vaccination issues among healthcare providers of different specialties seeking for more in-depth analysis considering direct contact of medical personnel with significant number of patients.

Even though telemedicine has widened possibilities for qualified medical care during COVID-associated quarantine period with elimination of direct physical contact[4], but only vaccination supported a new phase arising within classical pandemic pattern which could be interpreted as transitional to quazi-normal.

Dentistry as a peculiar branch of medicine has undergone its fundamental changes under pandemic restrictions, while some of them have been similar to those within all medical fields, while others were characterized with specific occupationally-related pattern.[4,5,6,7] Number of publications have presented dental specific measures regarding prevention of COVID-19 spread, while the most relevant studies reported about COVID-19 oral symptoms which could be used for early and comprehensive diagnostics of patients affected by coronavirus disease.[4,5,7] Such manifestation include tongue's color changes, tongue's plaque changes, salivary glands' functional and structural alterations, loss of taste and possible dysesthesia, which demonstrated various connections with mild, moderate and severe form of COVID-19 infection.[4,7]

Another COVID-19 related aspect, which is of high clinical importance in dental practice, includes vaccination of dental specialists and their role in the promotion of COVID-19 vaccination programs among dental patients. In 2021 vaccination progression among dental specialists demonstrated some issues regarding hesitancy aspects, which impact the readiness of dental field in general to transfer into new on-going vaccination era of COVID-19 pandemic.

Objective

To systematize available data regarding COVID-19 vaccination aspects among dental specialists and highlight relevant occupationally-related features of vaccination challenges.

Protocol of provided analytical review

Protocol of present study, its' design and realization phase were reviewed and approved by Ethical Committee of Medical Faculty #2 at Uzhhorod National University (Ukraine) (#26020221) on 26/02/2021 due to the principles with Helsinki Declaration of 1975, as revised in 2008.

Search of pertinent literature sources associated with above-formulated objective was provided via PubMed Central database (https://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com/). Search algorithm using Mesh-terms in PubMed was provided in the following form: ("covid-19 vaccines"[MeSH Terms] OR ("covid-19"[All Fields] AND "vaccines"[All Fields]) OR "covid-19 vaccines"[All Fields] OR "covid 19 vaccine"[All Fields]) AND ("dentistry"[MeSH Terms] OR "dentistry"[All Fields]).[8,9] Search within Google Scholar was held by the following keywords: "dentistry", "COVID-19", "vaccination".[10] Criteria of publication date included 2020-2022 years period. Publications in English or at least with English abstract/summary were collected within primary sample for further preliminary content-analysis.

Aim of preliminary content-analysis was oriented on the systematization of final publications study sample strictly associated with formulated objective of present research. Preliminary consistent content-analysis included following phases: 1) evaluation of publication title; 2) assessment of provided abstract/summary; 3) separation of keystone research aspects and exploring their relation to the COVID-19 vaccination issues within dentistry based on abstract/summary analysis. Preliminary content-analysis was held due to the basic principles of intellectual filtering and text mining, while absence of any relation to the topic of COVID-19 vaccination within dentistry was dominant reason for article exclusion from the further research.

Final (in-depth) content-analysis was provided among articles that positively undergone procedure of preliminary content-analysis due to the standard protocol, categories of which included: aspects of COVID-19 vaccination problems among dentists, personal hesitancy/willingness of dental specialists to undergone COVID-19 vaccination, potential outcomes of undergoing COVID-19 vaccination or refusal to such.

All articles collected for in-depth content-analysis were evaluated due to the text-mining, text-identification and text-extraction principles with further clusterization and systematization of outcomes at the Microsoft Excel 2019 software (Microsoft Office, Microsoft, 2019). Phased process of in-depth content analysis included following steps:

1. Formulation of content-analysis categories ("Bibliographical record of the analyzed article", "Origin of an article: Journal, Database", "Type of the Research", "Key points and main findings", "Unique information provided within the article considering COVID-19 vaccination and dentistry", "Repetitive/previously provided information duplicated within article considering COVID-19 vaccination and dentistry");

2. Categorization of unique and repetitively provided information considering COVID-19 vaccination and dentistry due to its relationship with specific article or articles;

3. Diagramming of connections between different articles considering uniqueness or repetitive nature of relevant information and clustering of such with further comparison;

4. Grouping of outreached findings and their Interpretation with formulation of contextual conclusions.[11,12,13,14]

For the evidence-expansion purpose Connected Papers service (https://www.connectedpapers.com/) was additionally used,[15] which helped to analyze related, prior and derivates researches for all targeted publications, included for the in-depth content analysis (Figure 1).

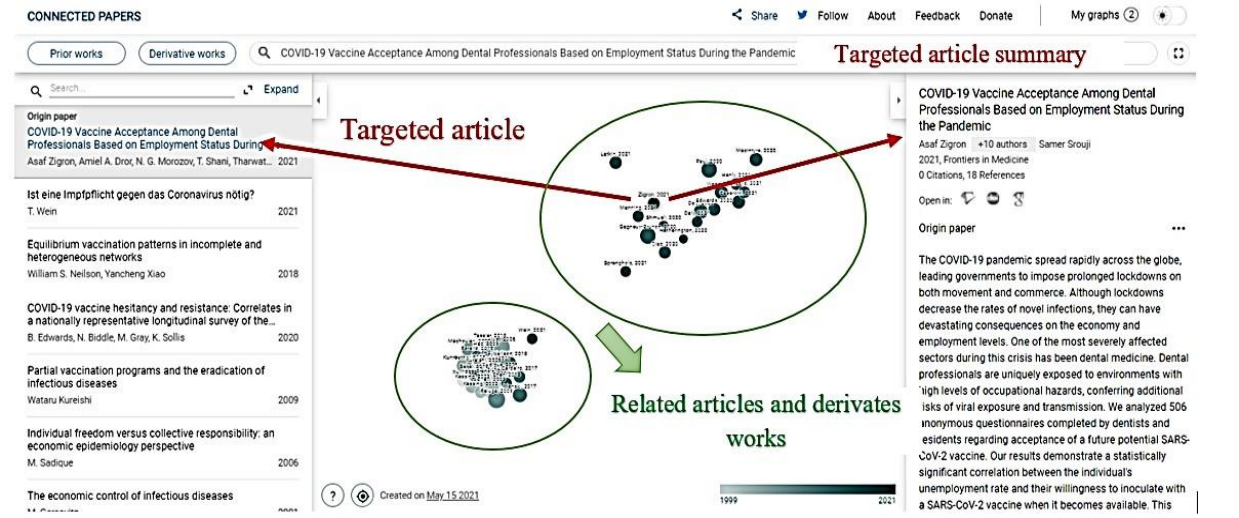

Figure 1. Interface of Connected Papers Service used for accompanied literature sources.

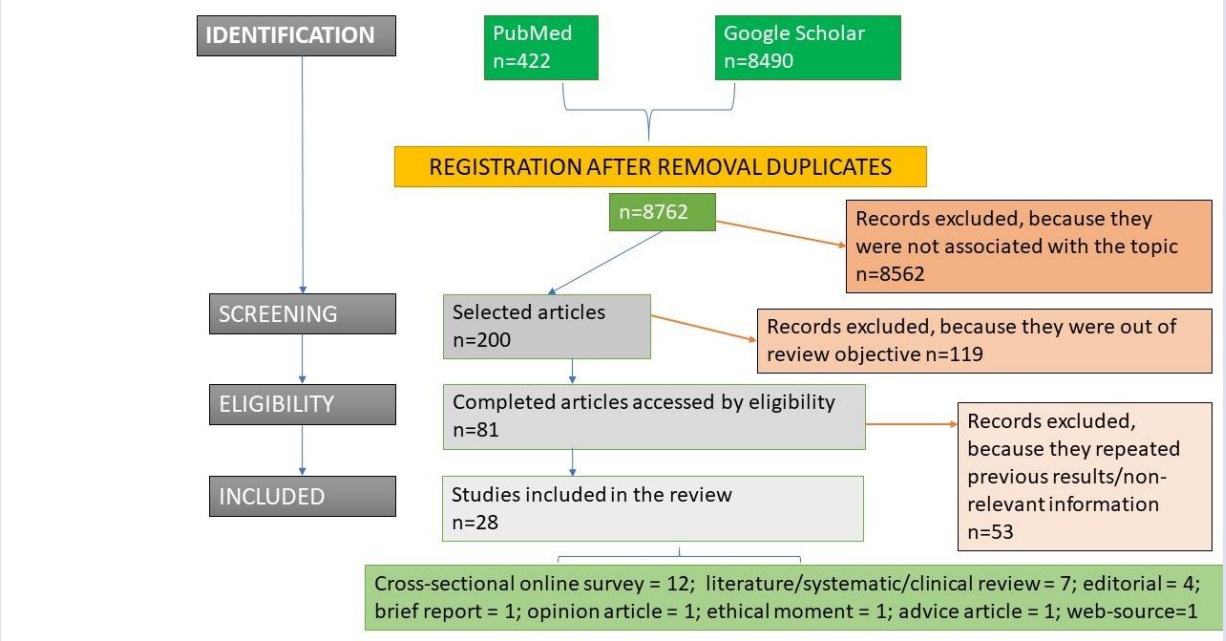

Figure 2. Flowchart of provided literature search

Studies collected for in-depth analysis

8912 results of the search were found and distributed as follows: 422 in PubMed and 8,490 results in Google Scholar.

After removing duplicates and articles not associated with the objective of the study, only 200 publications remained. In-detail analyses of titles and summaries/abstracts helped to optimize study sample of article to 81, all of which were analyzed in full manner during in-depth content-analysis. After full reading of articles' texts 28 of them were interpreted as those containing new and/or unique information, interpretations or facts. Other 53 completed articles accessed by eligibility were excluded because of duplicating results or demonstrating data analogically or similarly represented in other articles, or not representing results relevant to up-to-date actual continuity regarding COVID-19 vaccination issues within dentistry field. At the end, 28 articles were included in this review, out of which 12 were presented by cross-sectional online surveys, 4 – by editorials, 7 – by literature/systematic/clinical reviews, 1 – by brief report, 1 – by opinion article, 1– by ethical moment, 1 – by advice article, 1 – by web-source (Figure 2)

General aspects of COVID-19 and dentistry

COVID-19 impact on dental field could be nominally categorized on such before vaccination phase and such of on-going vaccination phase.[16] While data on before vaccination phase is processing through progressive detalization, analysis and systematization, data on on-going vaccination phase is still collecting and could be structured only sometime after.

Coronavirus disease changed not only dental care system itself with stratification of dental appointments based on emergency need, while post-ponding non-urgent dental visits and implementing hygienic restrictions during dental treatment (at the level of different national accepted protocols and expert recommendations), but also directly impacted oral health of infected persons regarding pathological changes of tongue, mucous, salivary gland and different kind of dysfunctions.[17,18,19] Also COVID-19 made a tremendous impact on dental practice and education associated with personal and financial losses and limitations,[20] and changed tendencies of ongoing laboratorial and clinical dental studies.[21]

COVID-19 vaccination has not only personal pathogen-targeted protection effect, which could spread to the level of public immunization, but it also demonstrates socio-economic impact, while helping to re-establish usual public interaction and communication, educational and academical activities, community's national and international ecosystems. Nevertheless, vaccination is not the only one available instrument in translation to quazi-normal post-vaccination pandemic period, but other social marketing and promotion strategies should also take place.[22] Previously researchers highlighted the importance of so-called "behaviorally informed strategies" for effective COVID-19 vaccination and slowdown of further pandemic spread.[23]

Hesitancy of dental specialists regarding COVID-19 vaccination

Study provided within Israel, which characterized with the highest vaccination rate so far, found that dental hygienists demonstrated greater level of hesitancy regarding COVID-19 vaccine compare to dentists and general population, while all analyzed samples demonstrated more negative attitudes regarding COVID-19 vaccine compare to other forms of vaccine.[24] Turkish dentists demonstrated 84.1% positive respondents' willingness to receive COVID-19 vaccine. Dentists who were agreed on vaccination also were characterized with statistically higher means of "Fear of COVID-19" scores compare to those who didn't want to get vaccinated.[25] Among Greek health care providers dental specialists demonstrated the highest rate of COVID-19 vaccination acceptance (near 83%) compare to physicians and pharmacists.[3] Also outcomes obtained in above mentioned studies demonstrated that provision of official information regarding safety and low risks of possible side-effect development after COVID-19 vaccination helped to decrease level of hesitancy among medical care employees.[24,25]

Cross-sectional study demonstrated that healthcare workers had higher willingness to get vaccinated in comparisons with control group (82.95% against 54.31%), while fear of passing coronavirus infection, fear of getting infected and previous infection in anamnesis were the main factors of motivation for immunization.[26] Despite that average of 22.51% (ranging within 4.3-72%) healthcare workers demonstrated hesitancy regarding COVID-19 vaccination.[27] Fear of post-vaccination side-effects was the main factor of reduced personal motivation for COVID-19 vaccination.[26] Nevertheless, it should be kept in mind that factor of fear regarding development of post-vaccination side-effects is modifiable by the adequate informational assistance and provision of supportive results obtained after targeted studies.

Observational research dedicated to the COVID-19 vaccination experience among United States-based dental professionals and students demonstrated that over 80% of all respondents felt moderately to very safe while practicing after the COVID-19 vaccine was made available. Also, more than 75% of dental students and specialists had shown moderate or high levels of confidence regarding protection they have received after vaccination within the pandemic conditions.[28]

Study provided among United States hygienists reported the highest level of vaccine hesitancy among specialists aged 26-39 years and those who had been infected with COVID-19 during the time of the survey. Factor of being contracted by the COVID-19 was statistically associated with higher adjusted odds ratio of hesitancy regarding COVID-19 vaccination.[29] The need for COVID-19 vaccination promotion among dental hygienists was specifically highlighted in previous study as such specialists categorized as those who could effectively promotes COVID-19 vaccination programs among general population.[29]

Hesitancy of dental and medical students regarding COVID-19 vaccination

Survey provided among medical and dental students found that dental students were characterized with near two-time higher prevalence of hesitancy to receive COVID-19 vaccine, even though greater portion of dental students-respondents reported of having COVID-19 or know somebody who was infected.[30] Medical students represented higher belief in the need of mandatory vaccination both among public and health care providers and greater willingness to participate in COVID-19 vaccine trials compare to dental students.[30] Such outcomes demonstrated occupationally specific trend regarding vaccination hesitancy, which should be taken into account while developing different targeted motivational strategies for reaching wider COVID-19 immunization effect.

In other study only 55.8% dental students were agreed on COVID-19 vaccination right after FDA vaccine approval, while only 32.9% demonstrated the will to take part in COVID-19 vaccine trials.[31] Out of number of dental students who were not motivated to take vaccine, 63% would be agreed on vaccination if such was mandated by health care system, while 16.3% would refuse to vaccinate even under mandatory regime.[31] Interpretation of such outcomes must be provided considering the fact that nearly 95% respondents agreed that they have a pronounced risk of getting infected with coronavirus disease.

In both studies dental and medical students agreed with the level of more than 90% that they need to learn about

vaccine as future healthcare providers for theirselves safety and for the safety of their patients, but in COVID-19 vaccine hesitant group only 36.7% of respondents would recommend vaccine for their patients and only 34.0% would give vaccine for their patients, which was statistically lower compare to the analogical results reported in COVID-19 vaccine acceptance group.[30,31]

A health care student-based online survey reported also that concerns about possible side effects and use of personal protective behavior as an alternative to the COVID-19 vaccination could be categorized as factors associated with higher level of hesitancy regarding COVID-19 vaccination.[32] Systematic review dedicated to the global COVID-19 acceptance evaluation demonstrated that mains reasons behind vaccine hesitancy mostly based on insufficient levels of education, deficiency of awareness, and inefficient government efforts and initiatives.[33]

Considering above-mentioned information implementation of additional educational strategies aimed to improve knowledge of students regarding COVID-19 vaccines are of high relevance, since such approach would support increase of positive attitudes towards COVID-19 public immunizations not only among health care providers, but also among patients.

Oral side effects of COVID-19 vaccination

Cirillo reported about such orofacial COVID-19 vaccine-associated side effects as peripheral facial paralysis, swelling of face, lips or tongue related with anaphylaxis reaction.[34] Description of such adverse effects were characterized with high level of heterogeneity, and frequency of their occurrence was generally rare.[34] Vaccine side effects registered among health care workers in Czech Republic included blisters and ulcers occurrence in 36% and 14% cases respectively, development of halitosis in 14% cases, bleeding gingiva in 11.4% cases and accumulation of plaque in 10.5% cases.[35] Most of oral reactions developed either in 1-3 days or within 1 week after vaccination, while lesions were predominantly localized on the lips, and with relatively analogical frequency at the buccal mucosa, tongue, palate and gingiva. Occurrence of side effects located within oral cavity was statistically associated with development of general side effects and duration of such.[35]

But if broadly speaking no significant oral side effects of COVID-19 vaccination have been reported so far, which evidently could be related with vaccination process. It is recommended to use Hill's criteria of causal inference and provide in-depth analysis of patients' anamnesis data to make some definitive conclusion about potential significance of side effects after vaccination and its connection with vaccine injection.[35,36,37]

Occupational status changes and COVID-19 vaccination

In questionnaire-based study it was found that changes within occupations status (from being employed to getting unemployed) statistically correlates with higher acceptance of COVID-19 vaccine among dentists: the highest acceptance level of 94-95% for COVID-19 vaccination was registered among orthodontists, general dental practitioners and endodontists, among which only 5%, 14% and 7% respectively were providing dental care during quarantine period; while among maxillofacial surgeons, 87% of which were still working during lock-down, only half of respondents positively reacted to the willingness of vaccination.[38]

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Dentists and COVID-19 vaccine delivery: window of opportunities

Due to present window of opportunities dentists should be evaluated as additional personal for delivering COVID-19 vaccines with possibility to implement such approach within different immunization models.[37,40] There are several positive interlinks between oral mucosa immunity and perspectives of COVID-19 vaccine developments, which associated with specific humoral and cell responses, simpler route of administration and minimized risk of needle usage. Nevertheless, immune exclusion pattern should be taken into account, since direct delivery of vaccine through oral mucous may support tolerance rather than corresponding immunization effect.[41] Fair enough that adaptation of vaccination delivery strategies should preliminary get corresponding approvals from different regulatory institutions and agencies and should be organized within complex clinical databases and nets for unification of income and outcome parameters.

Dentists and vaccination priority

Ethical argumentation for vaccination of dentists as primary health care providers and doctors with high risk of exposure to COVID-19 by the first level priority principle based on the several facts: 1) dental health is a component of quality of life, that is why proper dental treatment enhances high level of general quality of life; 2) dentists have ethical responsibilities to provide specific interventions within pandemic conditions and respond to the challenges caused by the spread of coronavirus disease; 3) dentists could motivate their patients to get vaccinated which will support general immunization strategies.[42] Moreover, vaccination of dentists would support proper provision of dental care, and latter is

associated with improvement of oral microbiome among dental patients with enhancing of its resistance to the viral and pathogenic bacterial influence.[43]

Federal USA guidance on vaccination priority stratification does not includes any difference in order among healthcare workers in hospitals, those who directly contacting with COVID-19 patients and doctor of other specialties, including dentists.[44] While in six states physicians of other specialties different from those working within hospitals or directly with COVID-19 patients were categorized with lower priority to vaccination.[44]

In cases where dental employee is not agreed to get COVID-19 vaccinated, then by the Dawson dental team, employer and employee must found similar point of interaction regarding that dentist should have argumented reason to refuse vaccination; moreover infection controlling measures must be fully implemented within a practice and all responsibilities regarding infection transmission must be precisely validated and distributed due to the relevant legislation bases.[45]

Future of dentistry and COVID-19

Primary developed protocols for dental care provision during COVID-19 pandemic before vaccine era may now look too strict and rigid, nevertheless it's too early to conclude that they are overly limiting during vaccination period. Most likely that such protocols should be modified and adapted due to present reality while considering all the infection-restricting requirements.[46] Control of dental clinic environment, maintenance of strict hygienic restrictions and infection control precautions, temperature screening, pre-treatment questionnaires regarding COVID-19 experience, routine use of face masks and respirators possibly may stay as obligatory adaptational measures until full resolution of pandemic, and even after it.[47] Prognostically vaccination against COVID-19 would support return to the greater prevalence of conservative procedures in dental practice and relative decrease of emergency surgeries and associated interventions. Future model of dental education in turn seems to get modified into hybrid one rather than in strictly distant online mode.[48]

Oral COVID-19 vaccines and antiviral drug for treatment of COVID-19

Recent studies demonstrated possible strategies of using so-called oral vaccines or specific anti-viral treatment against COVID-19, which could be delivered orally. Among different vaccination strategies emerging nowadays RPS-CTP vector system was described as perspective for the development of oral mucosal COVID-19 vaccine and as a promising vaccine platform for resolving clinical challenges regarding optimal vaccine delivery.[49] Saccharomyces cerevisiae surface display system, Salmonella strains and Bacillus subtilis spores were described as perspective platforms for the development of effective oral COVID-19 vaccines, even though results of implementing such were obtained only in experimental conditions within the animal-based models.[50,51,52] At the end of 2021 FDA authorized first oral antiviral drug for treatment of COVID-19, which could be prescribed for adults and children with mild-to-moderate forms of coronavirus disease. Recent meta-analysis reported that three novel oral antiviral drugs for COVID-19 associated with reduced levels of mortality and hospitalization rates, while demonstrating high safety levels.[53]

Conclusions

Experience received during pre-vaccination period of COVID-19 pandemic should be considered through the re-establishment of usual dental practice modes and adaptation to the new realities of dental care while vaccination is in progress. COVID-19 vaccine should not be interpreted as only possible universal mechanism for restitution of "as it used to be" dental practice because of differences of vaccination rates worldwide, new mutations of virus, and hesitancy of dental specialists and dental students regarding vaccination. Social distancing, infection controlling measures, routine use of masks and respirators with rigid adherence to hygienic restrictions and disinfection arrangements over dental clinical environment remain relevant and essential for on-going vaccination phase of COVID-19 pandemic.

New challenges related with COVID-19 vaccination within dental filed are represented by personal hesitancy of dental professionals and students, which in turn associated with such factors as provided informational support, previous COVID-19 experience, fear of getting infected or transmit disease to the patients or family members, fear of potential post-vaccination side-effects development, changes of occupational status, and interaction within dental team.

Vaccination of dentists is widening window of their possibilities regarding inclusion as members of COVID-19 vaccine's delivery team and participation within "behaviorally informed strategies" and public motivational programs, which in turn is aimed at amplification of positive willingness for COVID-19 vaccination among general public.

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Conflicts of Interest Statement

Authors declare no conflicts of interest

Ethical approval

This study represented in the form of review article with no experience provided. But Helsinki declaration was considered for all steps of manuscript preparation. The authors claim that no part of this paper is copied from other sources, and all the fragments of the text

interpreted from other publications supported with corresponding citations and references.

Authors' contributions

MGK, AC and YY contributed in searching, reviewing the literature, summarizing the results, and writing up the manuscript. RP and MS also contributed to reviewing the literature and summarizing the results. MGK, AC and MP contributed to the design and finalize the manuscript.

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Intelligent Systems for Precision Dental Diagnosis and Treatment Planning – A Review

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ABSTRACT

Machines have changed the course of mankind. Simple machines were the basis of human civilization. Today with humongous technological development, machines are intelligent enough to carry out very complex nerve-racking tasks. The ability of a machine to learn from algorithms changed eventually into, the machine learning by itself, which constitutes artificial intelligence. Literature has plausible evidence for the use of intelligent systems in medical field. Artificial intelligence has been used in the multiple denominations of dentistry. These machines are used in the precision diagnosis, interpretation of medical images, accumulation of data, classification and compilation of records, determination of treatment and construction of a personalized treatment plan. The article aims to review the current and potential applications of intelligent systems in dentistry. Artificial intelligence can help in timely diagnosis of complex dental diseases which would ultimately aid in rapid commencement of treatment. Research helps us understand the effectiveness and challenges in the use of this technology. The apt use of intelligent systems could transform the entire medical system for the better.

Keywords: Deep Learning, Artificial Intelligence, Convolutional Neural Networks, Dentistry

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Introduction

Conventional medicine has had a 'one size fits all' approach towards ailments. Precision medicine is a set of strategies that help in the customization of both the diagnosis and the treatment plan to the likes of an individual.[1,2] A shift from conventional traditional outlook towards diseases to a more contemporary personalized outlook is bound to happen in the very near future. Personalized medicine is possible, by applying, superior knowledge of the disease and the deeper nuances of the factors associated, along with the extensive exploitation and consolidation of limitless data, through massive data analyzing tools, with the help of artificial intelligence (AI).[3,4]

Intelligent systems are machines with the ability to have a deeper understanding of the data, which is often comparable to the zeniths of human understanding.[5]These systems were profoundly invested in, to seek their role in modern medicine. Two approaches of learning has been instituted, one follows the case history type questions asked by the system and subsequently correlating it to the various symptoms, on the basis of the available huge data base in a short span of time. The other involves the use of neural networks and deep learning often yielding credible results which are superior.[6] Intelligent systems in the medical and dental field are either virtual or physical.[7,8] Virtual intelligent systems are used in health record maintenance, medical education, disease diagnosis and treatment planning. Physical systems have been used in robotic procedures. The data accumulation is further enhanced with the use of image analyzing artificial intelligence where raw data in the form of images could be interpreted for accurate results.[9] Dental diseases are often associated with morphological alterations of the tissues, such as the teeth, periodontium, oral mucosa and bone. The changes, as a consequence of various disease processes can be studied/predicted by AI in a standardized accurate manner and a short time frame. The exorbitant rise in oral pathoses and the need for quick and reliable diagnosis warrants more use of AI to assist dental practitioners. Intelligent systems have been previously used in several aspects of the dental field, nevertheless, the objective of this review is to highlight and understand the current and potential applications of these systems in the various clinical ramifications of dentistry.

History of Intelligent Systems

AI has witnessed vast developments in the past 50 years.[10] However, the view that the human mind is a set of syllogism has been set forth in motion by ancient Greek philosophers like Aristotle.[11] A pivotal point in the development of AI is the Turing test of 1950.[12,13] This marked the ability of a machine to make decisions comparable to that of the human mind. The history of development includes two lag phases called AI winters.[10,13] These periods mark developmental hurdles that artificial intelligence had to confront. The timeline of artificial intelligence in medicine is chiefly influenced by the rapid digitalization of the medical literary data. The shortcoming of the early developed machines was lack of data for input. This was eventually overcome with the availability of voluminous, easily accessible data through online databases. Intelligent systems grew by leaps and bounds with the development of the Convoluted Neural Network (CNN). CNN constitutes a network of algorithms which help the machines learn in a layered pattern. Figure 1 shows the various milestones in the development of artificial intelligence.[14,15]

Principle of Intelligent *Machines*

Machine learning is the ability of a system, to undertake elaborate functions by virtue of complex algorithms in the absence of definitive commands.[16]In the medical fraternity, machine learning is of limited use and often turns obsolete. The algorithms have shown great potential in processing data that is explicitly standardized, which is extremely challenging when it to comes to the medical field. Deep learning is the use of a layered model abstraction, enabling the system to comprehend from various inputs like images or texts.[17]

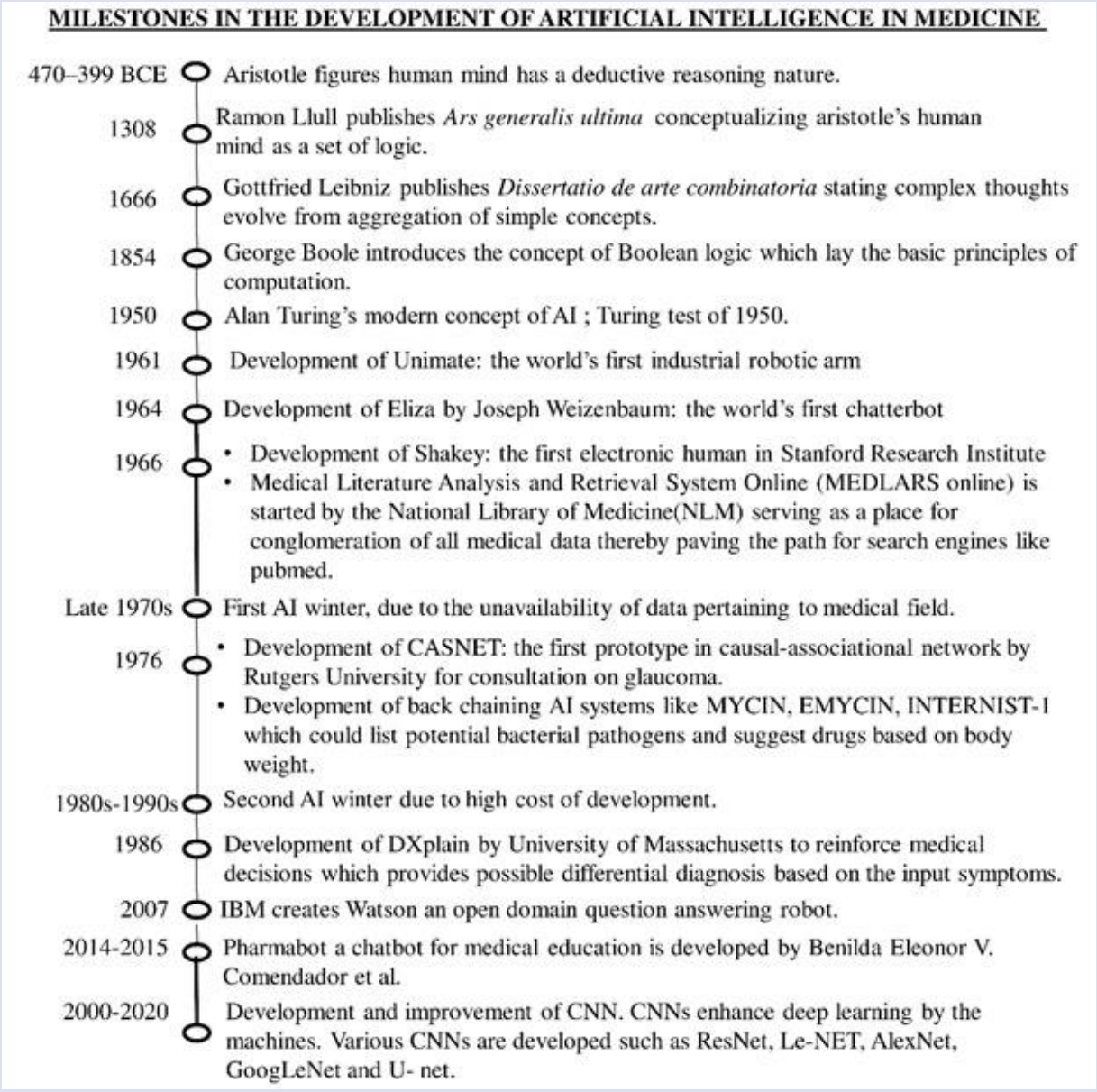

Figure 1. The various milestones in the development of artificial intelligence in medicine.

Deep learning is associated with two attributes; the multilayered non-linear processing of the data and the learning feature presentations in the layers.[18,19] The learning process could be supervised or unsupervised. This deep learning is facilitated by the use of artificial neural networks (ANNs). The inspiration for these neural networks is the cortical neural connections in the human brain. The neural networks were constructed in a similar pattern. Medical application of neural networks would not be possible without 'big data'.[20,21] Big data is the conglomeration of all relevant data. A few examples in the medical field include genomic sequences, medical imaging technology and micro-molecular structure of proteins. ANNs were reinstated with deeper and more hidden layers to improve efficiency. Though the increase in number of layers is desirable, in order to improve the efficiency of the system, it presents with the disadvantage of reducing the magnitude of the input variables required to arrive at a final prediction, which affects the result. To overcome this, layer wise pre-trained deep auto-encoder has been employed.[22,23] Image recognition, segmentation, video recognition is processed using CNN.[24,25] Tabular data is processed efficiently by the ANN. The significant layer in CNN includes the convolution layer and the pooling layer.[26] The image is scanned and each receptive field is checked by the convolution layer and the resultant input variables are pooled into the pooling layer.[27] Through this procedure the image can be analyzed. Through pattern recognition the resultant image is tagged with valuable information which guides the clinician to make decisions, aiding in precision diagnosis and advocating a personalized treatment plan.

Intelligent Systems in Dentistry

The role of intelligent systems in dentistry is based on the paradigm that any medical decision requires the physician to have adequate knowledge on the subject matter which can be reinforced by AI.[28] Data in the healthcare field is aggregated universally, and is available in heterogeneous clumps such as demographic data, socioeconomic data, medical history, clinical and investigational data all of which can be integrated and correlated by AI.[29] Artificial intelligence plays a role in research and interactive patient care. The ability of the patients to monitor their own heart rate, blood pressure or oral status through wearables, acts as a strong motivation factor. Continuous monitoring allows shortening of the lag between disease development and medical intervention. This immediate medical/dental attention could help reduce chronic illnesses which wreaks havoc and burdens the society.[30] Nevertheless without appropriate patient compliance the use of any monitoring device is futile.AI in the form of deep learning has been applied in various aspects of dentistry which will be discussed further. A summary of all the applications of artificial intelligence in dentistry has been included in Table 1. Several deep learning systems have been employed for this feat such as U-Net (CNN), MLPNN (Mutli layer perceptron neural network (ANN)), AlexNet (CNN), DetectNet (CNN), VGG16 (Visual geometry group also called Oxford Net with 16 layer depth(CNN)), ResNet50(Residual neural network(ANN)), Inception-v3 (CNN), EfficientNet-B0 (CNN), InceptionResNet-v2 (CNN), Xception (CNN), and MobileNet (CNN).[31,32]

Various studies have hypothesized the potential of AI to assist in the diagnosis of oral lesions. A deep learning network, EfficientNet-B0 has been trained to classify oral lesions into benign and malignant using real time clinical images. The system showed results with an increased accuracy of 85%.[31] Speight PM *et al.* (1995) have used ANNs to screen for the likelihood of the presence of premalignant lesions in the oral cavity among 2027 adults with a history of tobacco and alcohol abuse.[33] The results gained from the study proved the ANNs to have a comparable specificity and sensitivity to that of a dental expert.ResNet-101 and R-CNN (Region-based Convolutional Neural Networks) has been employed for the detection of oral lesions and the need for referral for such lesion with better accuracy of 87.07%.[31] According to McCartney S *et al.* (2014) the diagnosis of facial pain could be assisted by AI. This is achieved by collecting a questionnaire with various historical data. The inputs when processed through the neural networks are able to identify and differentiate the facial pain into nervus intermedius neuralgia (NIN), atypical facial pain (AFP), glossopharyngeal neuralgia (GPN) and temporomandibular joint disorder (TMJ) with a specificity of 99-100%.[34] Song A *et al.* (2018) used a CNN to detect the presence of facial nerve paralysis from 1049 clinical images of the patients.[35] The AI system was able to identify the presence of facial nerve paralysis with 97.5% accuracy which was up to neurologist standards. In a study by Men K *et al.*[36] (2019) rCNN (Residual CNN) deep learning architecture has been exploited to predict the development of xerostomia after radiation therapy in oral squamous cell carcinoma in 784 patients. The functioning of the salivary gland is checked using Tc-99m pertechnetate through scintigraphy. The manual interpretation of the scans were highly reproducible but on an average it took 15 mins per SPECT/CT scan, which was effectively interpreted in under 1 minute by deep learning architectures.[37] Temporomandibular joint pathology is often best visualized and diagnosed using magnetic resonance imaging(MRI). The ability to diagnose a disc perforation from an MRI, rests totally on the expertise of the radiologist and is deemed a challenging task by many. The deep learning architectures help in the diagnosis of disc perforation from MRI scans with high accuracy.[38]

Table 1. Applications of artificial intelligence (AI) in the various branches of dentistry

BRANCH OF DENTISTRY	APPLICATION OF ARTIFICIAL INTELLIGENCE
Oral Medicine	• Classification of malignant and benign lesion[31] • Correlation between tobacco, alcohol abuse and development of oral premalignant lesion[33] • Identification and classification of facial pain[34] • Detection of facial nerve paralysis[35] • Predicting xerostomia post radiotherapy[36] • Detection of TMJ disc perforation[38]
Oral Radiology	• Classification of dental radiographs[39] • Tooth identification from radiographs[40] • Diagnosis of Sjogren's syndrome[42,43]
Forensic Odontology	• Identification of age and gender by tooth morphology[32] • Identification of age from hand-wrist radiograph[45,46]
Oral Surgery	• Diagnosis of maxillary sinusitis[47] • Identification of supernumerary teeth[49] • Prediction of swelling following extraction of third molar[51]
Oral Cancer	• Early diagnosis of oral cancer[53] • Prediction of oral cancer survival rates[55]
Prosthodontics	• Identification of prosthesis and restorations[57] • Classification of implant systems based on radiographs[58]
Orthodontics	• To decide the need for extraction in the treatment plan[59,60] • Identification of various orthodontic problems such as overbite, crossbite,etc[61] • Identification of radiographic landmarks[63]
Endodontics	• Diagnosis of accessory root canal[64] • Identification of apical constriction[65] • Identification of early dental carious lesions[67]
Periodontics	• Prediction of oral malodour[68] • Development of smart tooth brush[69,70] • Prediction of periodontal bone loss[71]

Artificial intelligence has been employed in various aspect of oral radiology. The large pools of dental radiographs often gets accumulated in the clinical setting, which can be efficiently classified in a retrospective pattern.[39] AI was capable of classifying a huge number of the radiographs into periapical, bitewing, cephalogram and panoramic radiographs with utmost accuracy.The radiographs can be processed to label the teeth with the appropriate tooth numbering system.[40] This will help in the quick compilation of dental records. Sur J *et al.* have found a remarkably positive response to the use of AI in dental radiology in India.[41] With 69% of the participants looking forward for AI systems to aid in the radiological diagnosis. Literature review reveals employment of deep learning systems to diagnose Sjorgren's syndrome from CT scans and ultrasonography.[42,43] The research concluded with the deep learning systems diagnosing Sjorgren's syndrome as efficiently as an experienced radiologist.

Forensic odontology has identified various areas where the augmentations with intelligent systems prove effective. The scope into forensic odontology is based on the perpetuity of teeth against the pangs of time.[44] Avuçlu E *et al.* (2019) used 1315 dental x-ray images for the identification of age and gender based on the tooth morphology using a CNN called multilayer perceptron neural network (MLPNN).[32] This yielded a 100% accurate correct classification of the dental radiographic images which could be used in the identification of individuals. CT skull and hand-wrist radiographs have predicted the age of an individual with utmost accuracy.[45,46] Panoramic radiographs have been used to identify individuals, with much accuracy based on the presence of edentulous spaces, using deep learning systems such as VGG16, ResNet50, Inception-v3, InceptionResNet-v2, Xception, and MobileNet-v2 of which VGG16 has shown 100 % accuracy.

The intelligent systems show futuristic potential in oral surgery. A deep learning system, using panoramic images for diagnosis of maxillary sinusitis, revealed 87.5% diagnostic performance.[47] This was comparable to the experienced radiologist and significantly higher than the junior dental residents. The identification and classification of supernumerary teeth have been effortlessly produced by various deep learning systems such as AlexNet, DetectNet, VGG-16. These systems, using panoramic images, are able to identify the presence of supernumerary teeth and the number of teeth present. Kuwada C *et al.* (2020) tested 550 panoramic images for detection of supernumerary teeth in the maxillary incisor region, with 96% accuracy.[48] Diagnostic precision, AI reinforced treatment planning, custom manufacturing of surgical appliances and equipment, post-operative follow-up by superimposing pre and post operation images have all been applied for the betterment of orthognathic surgeries, in the form of deep learning.[49,50] The necessity for an orthoganthic surgery can be predicted by deep learning systems by means of cephalograms. Artificial neural networks were able to predict very accurately the

occurrence of facial swelling following extraction of a third molar, based on the anatomy of the wisdom teeth and the surgical procedure done.[51] This helps the surgeon to follow a personalized treatment plan for the patient including an appropriate pain alleviation protocol.

Oral cancer has been regarded as one of the most common neoplasm in the world.[52] Oral cancer is best tackled when diagnosed early like most other cancers. AI can help in the early diagnosis of oral cancer by the use of hyperspectral images of the lesions driven to map the presence of oral squamous cell carcinoma.[53] Fu Q *et al.* used 1469 intraoral photographic images to detect oral cancer using a cascaded convolutional neural network which resulted in accuracy, sensitivity and specificity comparable to that of an oral cancer expert and significantly better than a medical student.[54] Cancer survival rates can be predicted using log-rank test and Cox proportional hazard which use cancer prognostic factors for their prediction.[55] However these models are found to be unsatisfactory and hence a deep learning survival rate prediction using DeepSurv has been employed. DeepSurv produced better more accurate prediction of the survival rates of oral cancer patients.Various multinomic data such as genetic, proteomic, radiologic, clinical, histopathologic and biochemical data related to oral cancer can be accumulated and congregated by AI.[56] With the conglomeration of all this data each cancer could be traced to its origin and each individual will receive a personalized treatment crafted for the specific cancer.

AI has played a role in the identification of prostheses and restorations in the dentition thereby assisting in the treatment planning process.[57] The AI system shows very high accuracy for identifying metallic restorations and moderate accuracy for tooth coloured restorations. AI has been trained and tested to identify and classify various implant systems from radiographs.[58] This could help in the identification of dental implant brand just from the radiograph, which is a tedious task even for an experienced radiologist. Such identification of the implant can be exploited for the identification and classification of fractured dental implants.

Literature review reveals that neural networks have been used for deciding the need of extraction as part of orthodontic treatment using data from various indices such as 'IMPA (Incisor to Mandibular Plane Angle Index)'.[59, 60] These systems showed 100% accuracy in the training sets and showed 80% accuracy in the test set. Artificial intelligence has been employed to identify the various variables such as missing tooth, overbite, anterior openbite, posterior openbite, diastema, overjet thereby aiding in orthodontic treatment decision.[61] Choi HI *et al.* found that deep learning could help in making the choice between surgical or non-surgical management.[62] Radiographic landmarks in cephalograms, hand- wrist radiographs and cervical vertebrae are efficiently identified by artificial neural networks.[63] This has a two-fold use in orthodontics in that the growth and development of the individual and the level of bone maturity can be identified. Additionally it is also used to plot cephalometric landmarks to identify dental or skeletal malocclusion thereby assisting treatment planning.

In endodontics, artificial neural networks have been used in the diagnosis of accessory root canals from panoramic radiographs, which was counter checked using CBCT images.[64] This saves valuable time and ensures the success of endodontic therapy. Apical constriction can be identified very precisely by these neural networks thereby assisting in the effective cleaning and shaping of the root canals.[65]The detection of caries from dental radiographs is one of the most significant and straight forward application of neural networks in dentistry. This could be due to the fact that dental caries is the most common disease affecting man.[66] The ability for AI to effectively identify early lesions, lessens the burden of dental caries on humanity by leaps and bounds.[67] Various models of neural networks like GoogLeNet, Inception v3 CNN, MLPNN have been employed in research to evaluate the accuracy, sensitivity and specificity in the diagnosis of caries from radiographs.The results from all such studies reveal that a highly accurate, sensitive and specific diagnosis of dental caries can be yielded by AI.

Oral malodour has been predicted by neural networks by evaluating saliva samples for the presence of operation taxonomical units in the 16s RNA of the bacteria thereby differentiating the malodourous bacteria from healthy commensals.[68] This opens the potential to develop oral malodour screening, aiding in the diagnosis of halitosis. Artificial intelligence has been employed in the development and fine tuning of smart toothbrush which makes a colossal difference in the lives of the debilitated and bedridden patients.[69,70] This is made possible by continuous motion tracking systems, aiding in the development of a completely autonomous smart tooth brush. Krois J *et al.* using 1456 images of panoramic radiographs trained a 7 layer deep learning CNN which estimated periodontal bone loss with a mean accuracy of 81%.[71]

Challenges of AI in Dentistry

In comparison to other branches of medicine, dentistry is one of the most suitable areas where the applications of AI are limitless. Yet surprisingly, although the origin of AI was as early as 1950s, it is still being applied more only for the purpose of research.[72] The reasons behind this compromised growth could be, the discord among various dental clinical data sources and their incompatibility.[73]Secondly, this data could be biased and might not represent the whole population.[74]Data validation requires a huge number of experts, which is tedious to procure.[75] The results generated might not be directly applicable to patient needs.[76] In dentistry, like any other medical field, the responsibility of the physician channels alongside the need of the patient.[77]With the employment of huge data base, especially in case of a sensitive patient there is a need for an ironclad security to

respect the individual's autonomy and privacy. This goes parallel with the need of adaptability of AI to the current effective legal, ethical and governing bodies.[30,78] Use of a federated AI might mitigate the said concern. The lack of standardization of AI especially in the dental field is yet another hurdle. Besides this, there will be a lacuna that is always felt in terms of the human touch comprising of empathy and care.[79] The practical applications of AI as a part of the normal life will see light of day only when these challenges are addressed today.

Conclusions

Artificial intelligence has the potential to make the diagnosis of complex dental diseases swifter and more precise which would ultimately aid in timely commencement of treatment. The ability to determine treatment routes, craft a personalized treatment plan and predict the outcome of the treatment given, could make the role of AI indispensable to health care.

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Conflicts of Interest Statement

The authors declare no conflict of interest.

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Oral Soft Tissue Keratocyst: A Review of Cases from 1975 to 2021

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Reviews

History

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ABSTRACT

The odontogenic keratocyst be a developmental cyst that's important due to its specific clinical behavior and histopathology. They arise from remnants of the epithelial structures that are related to the event of teeth and occur predominantly intraosseous. However, they occasionally can appear extraosseous in the gingiva as peripheral counterparts. The gingiva is the most common location of peripheral keratocyst, but other sites like mucosal, and intramuscular, epidermal sites have also been reported. The origin of soft tissue OKCs is still under controversy. In this article will be discussing the Oral soft tissue keratocysts reported so far in the literature.

Keywords: Soft Tissue Keratocyst, Odontogenic Keratocyst, Peripheral, Gingiva, Alveolar Mucosa.

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Introduction

The odontogenic keratocyst is a developmental cyst that is important due to its specific histopathologic features and clinical behavior arising from the cell rests of the dental lamina. It can be seen anywhere in the jaw but is most commonly seen in the posterior part of the mandible, whereas they occasionally can appear extraosseous in the gingiva as peripheral counterparts.[1] The gingiva is the common location of peripheral OKC, but other sites like epidermal, mucosal, and intramuscular sites have also been reported. Initially, it was thought of as a gingival cyst of adults but Yih *et al*. demonstrated considerable immunohistochemical differences between soft tissue OKCs and gingiva cysts using markers Ki 67 and p53.[2] De Oliveira reported the immunopositivity for CK17, CK19, and CK14 which support an odontogenic epithelial origin for oral soft tissue keratocysts. Although, further studies are required in molecular and multicentric approaches to determine the exact origin of soft tissue keratocyst.[1]

Clinical Presentation

OKCs may be associated with pain, swelling, or discharge. At times, they experience paraesthesia of the lower lip, this extends in the medullary cavity, and a clinically observable bone expansion occurs later. Dayan *et al*. in 1988 have described the occurrence of OKC in the gingiva, which resembled the gingival cyst of adults clinically but the histological features were similar to that of an OKC. Two cases with similar features have also been reported, which showed no recurrence after a simple enucleation procedure [Ide *et al*, 2002]. Authors have suggested the term 'peripheral odontogenic keratocyst' and included it as the histological spectrum of gingival cyst in the adult, which was not a good idea. Chi *et al*. in 2005 have also reported two cases and supported the view that these lesions should be regarded as peripheral OKCs and not as gingival cysts of the adult.[2] Yih *et al*. [2000] demonstrated substantial immunohistochemical differences between a sample of six gingival cysts in adults and three soft tissue OKCs, which showed moderately positive staining for p53 and strongly positive staining for Ki-6[7] in the parabasal and basal cells of the epithelial linings of the peripheral OKCs, whereas the six gingival cyst epithelial linings were all completely negative for Ki-67 and p53. The BCL-2 expression was strongly positive in the basal and parabasal cells of the three peripheral keratocyst and showed weak positivity in some of the gingival cysts, this view supported that gingival cyst and peripheral OKC were of distinct entities.[2]

Histopathology

Oral soft tissue keratocysts, despite their unusual sites, reveal the same pathognomic microscopic features of intraosseous odontogenic keratocysts, hence they can

only be diagnosed histologically due to their unusual sites of clinical presentation. Solid epithelial rests, basal budding, and Satellite micro-cysts, which may be present in intraosseous odontogenic keratocysts, were all absent in oral soft tissue keratocysts.[3,4]

Source search criteria: The review search is done using the following combinations of keywords peripheral tissue keratocyst, OKC, soft tissue keratocyst, POKC, and keratocyst using the search engine PubMed and google scholar from the year 1975 to 2021 based on the soft tissue presentation of the lesion without any bony involvement.

Cases Review

Stoelinga *et al*. (1975); Buchner and Hansen (1979) reported cases of peripheral keratocyst which had no follow-up.[5,6] Dayan *et al*. (1988) reported a 42-year-old male patient with a 1cm nodule on the gingival area between the left upper cuspid and the first bicuspid that was treated by enucleation and curettage which showed recurrence when followed up for 10 months.[5-7] In 1994 Chehade et al. reported six cases, two in maxillary gingiva and four in mandibular gingiva, in which the patient's follow-up was lost in all of them.[6] In the same year, Fardel and Johannessen reported a case of a 41-year-old female patient with a mandibular and maxillary gingival lesion with histological features of keratocyst, but she was not followed upon.[6]

In 2002, Ide *et al*. reported two cases in female patients- with an asymptomatic left maxillary gingival lesion that has been present for two years in a 38-year-old with no recurrence in 60 months follow-up and an asymptomatic 5mm sessile swelling in the right maxillary gingiva of a 46-year-old patient which was resected, no recurrence was reported in 72 months.[5,6,8] Chi *et al*. 2004, reported two cases- an asymptomatic 1 cm nodule in the left mandibular gingiva which is fluctuant slightly blue with recurrence after enucleation and curettage in 6 months and a 64-year-old female with an asymptomatic, slowly enlarging 1.5 cm bluish nodule in left maxillary gingiva with no recurrence after enucleation when followed for 21 months.[5]

Chi *et al*, in 2005, reported two cases in females- one in the left maxillary gingiva with a blue mucosal nodule measuring 1.5 cm in diameter, the lesion was enucleated with no recurrence when followed for 21 months, and another case with submucosal nodule 1 cm in diameter involving the facial attached and unattached gingiva. The lesion was excised, after three months, the patient showed no evidence of disease.[5,6] In the same year, Preston and Narayana reported a case in maxillary gingiva of an 83-year-old female, and no recurrence was noted when followed up for six months.[6]

In 2008, Ide *et al*. reported a 53-year-old male with left mandibular gingival soft tissue keratocyst with histomorphology consistent with an OKC and no recurrence in 84 months. In the same year, Faustino *et al*. reported a case with a left mandibular gingival lesion in a 57-year-old female with recurrence in 12 months.[6] Precheur and krolls in 2009 reported a case of a 59-year-old male patient with pain and swelling in his left cheek consisting of multiple episodes of swelling and pain with increasing severity over the past 6 months. The histologic diagnosis was consistent with ectopic odontogenic keratocyst when an incisional biopsy was performed.[3,6,9]

Ide *et al*, in 2010 reported two cases-a case of painless swelling in the left buccal mucosa posterior to the parotid papilla measuring 3x2x2 cm in a 60-year-old. Histologically, a multilocular cyst with the conventional OKC lining was found, which is diagnosed as soft tissue OKC, and a 16-year-old boy with a 5 mm nodule in the right buccal mucosa. His Microscopic examination revealed a unilocular microcyst (3 mm) and a cyst lining which showed features of conventional OKC.[5,6,9]

Vij *et al*. 2011 reported a left maxillary gingival soft tissue keratocyst in a 56-year-old male patient.[6] Grobe *et al*. 2012reported a 52-year-old male patient with a painless swelling in the right cheek, significantly increasing in size over the previous six months. On the panoramic x-ray, there was no evidence of an odontogenitically-induced process and when mass was excised, the histopathological examination led to the diagnosis of a KCOT, and no recurrence has been reported when followed for four months.[6,9,10] Kaminagakura *et al*, 2013 reported a case of a left buccal mucosal lesion in a 37-year-old male with no recurrence reported in 12 months.[6,9] In the same year, Yamamoto *et al*. reported a 74-year-old male patient with an elastic firm movable mass of 50mm in the right buccal mucosa with no recurrence in 4 months.[6,9,11]

In 2014 Abe *et al*, reported a case of a submucosal nodule in the left temporalis muscle in a 46-year-old male measuring 21 mm in diameter, covered with red-colored mucosa with no recurrence was noted in 12 months.[6,9,12] In the same year Sakamoto *et al*. reported a case of a mandibular gingival lesion in a 24-year-old female with multiple KCOTs removed at ages 10, 12,14,15, and 21 from her maxilla and mandible. The present lesion is 3mm, which did not enlarge or diminish in size over four months and it was surgically removed with a 1-mm margin.[6] Zhu *et al*. also in the same year reported a lesion with Solid swelling, non-mobile, measuring 2 cm in diameter in the right buccal mucosa of a 69-year-old male.[6,9]

Makarla *et al*, 2015 reported a case in the right buccal mucosa of a 62-year-old male with histological features similar to keratocyst, with no recurrence in 24 months follow-up period.[6,9] Vazquez-Romero *et al*, 2017 reported a left maxillary gingival soft tissue OKC in a 32-year-old male with no recurrence reported over 12 months.[6] In 2018, Witteveen ME reported two cases-a nodule in the right buccal mucosa measuring 2.5 cm in diameter in a 63-year-old male patient in which an excisional biopsy was performed, and a case of a 48-year-old female with a swelling on the inside of the left cheek, which showed a histomorphology consistent with OKC. In both cases, no recurrence was reported.[6,9]

Bruno-Teixeira-Gonçalves Rodrigues MS, 2020 reported two cases-a single painless well-defined nodular, sessile, non-tender swelling covered by normal oral mucosa, measuring 15 mm in a 48-year-old female, excisional biopsy was performed which showed recurrence in 48 months, and a case of a 63-year-old female with an anterior mandibular gingival lesion with histological features of POKC. The patient recovered in one week and didn't return for follow-up.[6] In the same year, De Oliveira EM reported a submucosal nodule on the buccal mucosa in a 64-year-old male patient, which is a painless mid-cheek swelling lasting for about 18 months which is diagnosed as soft tissue keratocyst considering histological features. Beena V T, 2021 reported a case with a well-defined solitary swelling of size 2.5 cm×2.5 cm, firm in consistency, non-tender, slightly compressible nodular mass extending from below the zygoma to the lower border of the lower lip superior-inferiorly. Under general anesthesia, the lesion was excised intraorally and the tissue sections showed features of OKC with no possible recurrence on follow-up for six months.[13] (Table 1a, b)

Table 1a. Cases reported from 1975- 2021

A	Year	Age	Sex	Site	Clinical Feautures	Histopatholgy	Treatment	Recurrence
A1	1975	NS	NS	S1	NS	NS	NS	NS
A2	1979	NS	NS	S2	Reported as the gingival cyst of the adult, keratocyst type	NS	Surgical exploration	NS
	1988	42	M	S3	1 cm nodule b/w cuspid & bicuspid	H1	Enucleation & curettage	Recurrence in 10 months
A3	1994	37	M	S4	Raised, fluctuant 3X3mm, Greyish.	H2	Excision	NS
	1994	66	F	S1	Pale yellow, raised.	H2	Excision	Lost follow-up
	1994	35	F	S4	Mobile nodule, 10 X 10 mm	H2	Excision	Lost follow-up
	1994	70	M	S5	White nodule	H2	Excision	Recurrence in 7 years
A4	1994	57	F	S1	Slowly enlarging, 7 X 5 mm, raised	H2	Excision	Lost follow-up
	1994	42	M	S4	Bone fenestration, saucerization	H2	Excision	Lost follow-up
	1994	41	F	S6	Large fibromatous masses in the maxillary molar regions	H3	Incisional biopsy	No follow-up
A5	2002	38	F	S3	Asymptomatic, present for two years	H4	Enucleation	No recurrence in 60 months
A6	2002	46	F	S7	Asymptomatic 5mm, sessile swelling	H4	Resection	No recurrence in 72 months
	2005	64	F	S3	Blue mucosal nodule 1.5 cm in diameter	Keratocystic features	Enucleation	No recurrence in 21 months
A7	2005	81	F	S1	Submucosal nodule of 1 cm	Keratocystic features	Excised	Recurrence Re-excised, no recurrence in 3 months
A8	2005	83	F	S3	Round yellow nodule on the maxillary gingiva between the left canine and first premolar	Similar Features of OKC	conservative surgical treatment	No recurrence in 6 months
A9	2008	53	M	S5	Fluctuant nodule, measuring 6 mm in diameter.	Similar Features of OKC	-	No recurrence in 84 months
A10	2008	57	F	S5	Asymptomatic small nodule, soft, nonmobile, 5 mm in diameter	Similar Features of OKC	Surgical removal, enucleation	No recurrence in 12 months
A11	2009	59	M	S8	Firm, slightly tender, mobile, 3-4 cm mass	Consistent with OKC	Incisional biopsy	NS
	2010	60	M	S9	Painless welling measuring 3*2*2 cm	Multi-locular cyst with conventional OKC lining	Excised	No recurrence
A12	2010	16	M	S10	5 mm nodule near parotid papilla	Unilocular micro-cyst and cyst lining Features of OKC	-	No follow-up
A13	2011	56	M	S3	swelling was soft in consistency and had well-defined borders measuring. 2.5×2.0 cm	Similar Features of OKC	Excisional biopsy	NS
A14	2012	52	M	S11	Painless swelling over 6 months	Features of OKC	Excision	No recurrence in 4 months
A15	2013	37	M	S9	solitary nodule posterior to the parotid papilla	Similar Features of OKC	Excisional biopsy	No recurrence in 12 months

Table 1b. Cases reported from 1975- 2021

A	Year	Age	Sex	Site	Clinical Feautures	Histopatholgy	Treatment	Recurrence
A16	2013	74	M	S10	Elastic, firm movable mass of 50 mm	Similar Features of OKC	Intraorally extirpated under general anaesthesia	No recurrence in 4 months
A17	2014	46	M	S12	Submucosal nodule 21 mm in diameter non tender	Similar Features of OKC	surgically removed under general anaesthesia.	No recurrence in 12 months
A18	2014	24	F	S4	3mm lesion which did not enlarge or diminish for 4 months	Similar Features of OKC	Excisional biopsy	NS
A19	2014	69	M	S10	Solid swelling, non-mobile, measuring 2 cm in diameter.	Similar Features of OKC	Extensive resection of the mass & reconstruction with sternocleidomastoi d flap	NS
A20	2015	62	M	S10	Asymptomatic swelling with reduced mouth opening, soft to firm measuring 6 × 6 cm in size	Similar Features of OKC	excision	No recurrence in 24 months
A21	2017	32	M	S3	Non painful whitish lump, fluctuant	Similar Features of OKC	A full-thickness incision	No recurrence in 12 months
	2018	63	M	S10	Firm mobile nodule measuring 2.5 cm in diameter.	Consistent with OKC features.	Excision biopsy	No recurrence in 4 years
A22	2018	48	F	S9	Swelling on the inside of the left cheek.	Histomorphology consistent with an OKC.	Incisional biopsy	No recurrence in 1 year
	2020	43	F	S13	Well-defined, sessile, nontender, measuring 15 mm	Similar Features of OKC	Excisional	No recurrence in 48 months
A23	2020	63	F	S14	Asymptomatic, single elevated lesion,tense on palpation with yellowish coloration	Similar Features of OKC	Excisional	No follow-up
A24	2020	64	M	S15	painless mid-cheek swelling lasting for about 18 months	showed Similar features of OKC	Excision	No recurrence in 10 months
A25	2021	61	M	S16	swelling was firm in consistency, non-tender, slightly compressible nodular mass	showed Similar features of OKC	Excision	No recurrence in 6 months

M: Male; F:female; A: Author; A1: Stoelinga et al; A2: Buchner & Hansen; A3: Dayan et al; A4: Chehade et al; A5: Fardel & Johannessen; A6: Ide et al, A7: Chi et al; A8: Preston and Naryana; A9: Ide et al; A10: Faustino et al; A11: Precheur and Krolls; A12: Ide et al; A13: Vij et al; A14: Grobe et al; A15: Kaminagakura et al; A16: Yamamoto et al; A17: Abe et al; A18: Sakamoto et al; A19: Zhu et al; A20: Makarla et al, A21: Vazquez-Romero et al; A22: Witteveen; A23: Bruno-Teixeira-Gonçalves Rodrigues MS; A24: De Oliveira EM; A25: Beena V T; S1: Maxillary gingiva; S2: Buccal mucosa; S3: Left maxillary gingiva; S4: Mandibular gingiva; S5: Left mandibular gingiva; S6: Maxillary & mand gingival lesion; S7: Right Maxillary gingiva; S8: Left cheek; S9: Left buccal mucosa; S10: Right buccal mucosa; S11: Right cheek; S12: Submucosa; S13: Right maxilla; S14: mandibular gingival lesion; S15: Mid cheek; S16: Lower lip region, H1: Features of cystic lining; H2: uniform, thin stratified squamous epithelium with palisading of the basal layer and superficial keratosis; H3: Multiple gingival cysts, some containing keratin. The cyst lumens were filled with fibrin; H4: Stratified squamous epithelium with palisading basal cells & superficial corrugated layer; *NS- not stated

Discussion

OKC being classified as a cyst of odontogenic origin for about five decades, histological character, the pathogenesis, and progress of entity eventually resulted in a transformation from a cyst to an odontogenic tumor in 2005.[10,14] In the 2017 classification, it was moved back into the cyst category because most of OKC's are documented to completely regress, following decompression, and mutations in OKC are not just limited to the PTCH gene alone.[15]

The term Peripheral odontogenic keratocyst was coined by Dayan *et al*. The occurrence of a keratocyst within the oral soft tissues is exceedingly rare. These lesions usually appear as a nodule or a swelling and can occur with or without symptoms. Oral soft tissue keratocysts can be present with a different clinical profile. They have been suggested to arise from remnants of the dental lamina that become entrapped within the mucosa during embryogenesis.[2]

Despite its unusual location, oral soft tissue keratocysts reveal an equivalent pathognomic microscopic feature of intraosseous odontogenic keratocysts. Therefore, a histopathological diagnosis should not present any difficulties. Satellite microcysts, solid epithelial rests, and basal budding, which can be present in intraosseous odontogenic keratocysts, were all absent in oral soft tissue keratocysts with some exceptions.[2-4]

The differential diagnosis usually includes other odontogenic cysts that could affect this region, especially the gingival cyst of the adult and the peripheral calcifying odontogenic cyst as most POKC are located in the gingiva. Both may produce a painless swelling filled by a bluish-gray or bluish fluid and superficial resorption of cortical bone. The second most common location is the buccal mucosa where other lesions like cystic and cystic-solid salivary gland lesions are considered in the clinical differential diagnosis. Histological analysis is the gold standard for POKC diagnosis. In the extraosseous location, an equivalent histological pattern described for conventional OKC should be present.[6] keratocysts can be found in other parts of the body, including skin lesions but their origin is not confirmed and requires further clarification.[1]

The recurrence rate of POKC is very low. This is not in line with the higher recurrence rate of intraosseous OKCs (up to 62.5%). This could be due to better resectability in soft tissues or the fact that they are two separate entities with different biological behaviors.[9] In a patient with NBCCS, a higher recurrence rate may be attributed to artificial inflating for a given treatment. OKCs are among the most consistent features of the syndrome along with skeletal anomalies occurring in 65–75%.[16,17]

Conclusions

The clinical evaluation of soft tissue keratocysts is very difficult, they often present different clinical entities, but they have to be evaluated histopathologically to be diagnosed as keratocyst. The radiographic evaluation to rule out the bony involvement may help in diagnosis. The origin of soft tissue keratocyst is not yet known. The histogenesis and pathogenesis of oral soft tissue keratocysts should be further investigated to clarify whether it represents a type of intraosseous odontogenic keratocyst or whether it is a distinct entity.

Abbreviations

OKC-Odontogenic keratocyst, POKC–Peripheral odontogenic keratocyst, NBCCS-Nevoid basal cell carcinoma syndrome.

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The Role of Statins in Periodontal Therapy- A Review

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Reviews

History

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ABSTRACT

Periodontitis is an inflammatory mechanism causing step by step destruction of the periodontal tissues and alveolar bone. Periodontal treatment is intended to restore the tissues damaged by the disease. Various periodontal procedures have been introduced to lower the destruction; statins are being one among them. They are cholesterol-reducing drugs which have shown to promote bone formation and proven to be effective in periodontal therapy. However, statins have numerous actions, with anti-inflammatory and immunomodulatory effects, as well as the capacity to accelerate new bone formation. The pleiotropic effects of statins have been assessed for their prospective advantage in the therapy of several inflammatory and immune-mediated diseases including periodontitis. Such features could be beneficial for periodontal therapies. This article goes through the history and effects of statins and explores its potential role in periodontal regenerative therapy.

Keywords: Statins, Periodontitis, Simvastatin, Rosuvastatin, Periodontal Regeneration.

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Introduction

Periodontal disease is an incendiary infection affecting the aiding tissues of the dentition, produced by a group of pathogens. In 2017, the World Workshop classified Periodontitis based on multidimensional staging and grading system, Periodontitis as a manifestation of systemic diseases and necrotizing periodontal diseases. The prevalent form of periodontitis is chronic periodontitis, which is usually associated with the pocket formation and depletion of bone but the terminologies as “chronic” or “aggressive” has been grouped under a single category as Periodontitis.[1] Elimination of bacterial infection and restraining the advancement of inflammatory process are the fundamental treatment objectives. Traditional non-surgical periodontal therapy primarily involves scaling and root planing. However, it has its own limitations as it is difficult for debridement to approach fields like deep pockets, furcations, and grooves on the tooth surfaces, which concludes in partial debridement of these areas. Local application of antiseptics, antibiotics and laser assisted therapy are some of the alternative options that have been recommended to traditional non-surgical therapy. Controlled device containing tetracycline which desired for placement into the periodontal pocket and deliver the effective agent into the periodontal pocket.[2] Other antibiotics such as doxycycline and minocycline are also approved for the local drug delivery systems.

Lately, some statins like simvastatin (SMV), atorvastatin (ATS) and rosuvastatin (RSV) also have been considered as an ancillary remedy to non-surgical periodontal therapy. Statins were initially imported as cholesterol-reducing drugs, which performed by hindering the 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase by intruding into liver and interfering in cholesterol synthesis and reduces the prevalence of cardiovascular disease. Excluding their cholesterol-lowering property, statins also have additional properties such as:

1. Anti-inflammatory properties
2. Antioxidative properties
3. Antibacterial properties
4. Pleiotropic effects, such as blocking the release of pro-inflammatory mediators and matrix metalloproteinases (MMP’s)

Due to the pleiotropic, non-hypolipidemic effects of statins, these could potentially be utilized as an adjunct therapeutic agent for periodontal disease therapy. By employing either systemic or local delivery systems, few studies have explored the biological mechanisms that may be involved in the anti-inflammatory effects of statins on periodontal tissues. In this way, the conventional periodontal treatment approach could be augmented with statins to decrease periodontal inflammation and promote bone tissue formation.[3] Local delivery of statins has proven to have additional assistance to traditional non-surgical periodontal treatment by few studies in contrast to conventional scaling and root planing alone.[4] Thus, the objective of the review is to appraise the usage of statins that showed additional benefits with non-surgical periodontal treatment in contrast to phase 1 therapy alone

Table 1. History of Statins

YEAR	INVENTION
1784	François Poulletier, a French doctor-chemist obtained real cholesterol from gallstones. Later after three years, another French physicist, Michel E. Chevreul, termed them cholesterin
1888	Friedrich Reinitzer, an Austrian botanist formulated the atomic formula of cholesterol
1927–1928	Heinrich O. Wieland and Adolf Windaus gave the structure of cholesterol
1950	The fundamental objective of the trial done by Dawber was to constrain the biosynthesis of cholesterol in the human system and HMG-CoA reductase (HMGR) develop into a pure objective
1959	Triparanol, the first cholesterol-reducing agent that constrained cholesterol formation was popularized into medical use in the United State of America
1964	Bloch and Lynen - The cholesterol formation pathway
1976	An HMG-CoA reductase inhibitor named Compactin was identified
1978	Alfred Alberts and colleagues discovered a new HMG-R inhibitor and later named it has lovastatin
1986–1987	Lovastatin was inured FDA approval for the initial commercial use
1989	Different statins named simvastatin and pravastatin were formed
2003	Atorvastatin turned into the popular statin in the history of pharmaceutics
2010	Atorvastatin, Fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, and simvastatin all these statins become available in markets

History of statins

The history of statins goes back to the late 1950s where Triparanol was the first cholesterol reducing agent that was popularized in medical use in the USA. In 1978, Alfred Alberts and his colleagues discovered a new HMG-CoA reductase inhibiting agent named Lovastatin and by 1980s it got the Food and Drug Administration (FDA) approval for commercial use. Late 1980s was the discovery of simvastatin and pravastatin and by 2000, atorvastatin became the popular drug in use. All the statins were made available in the markets by 2010. (Table 1)

Classification of Statins

The classification of statins was processed according to certain criteria which are differences in structure and ring structure that affect the pharmacological properties of statins then the capability of drug to lower the cholesterol levels (Fluvastatin is least effective and Atorvastatin and Rosuvastatin are the most effective)[5]

The different criteria for classification of statins are:

1. *According to the methods of manufacture of statins:*
   a. Type 1 Fermentation (Simvastatin, Lovastatin, Pitavastatin, and Pravastatin)
   b. Type 2 Synthetic (Atorvastatin, Fluvastatin, and Rosuvastatin).
2. *According to the solubility of statin:*
   a. Hydrophilic (Pravastatin, Rosuvastatin and Pitavastatin)
   b. Lipophilic (Fluvastatin, Atorvastatin, Simvastatin and Lovastatin).

The interaction of these drugs with other drugs were included as Rosuvastatin and Pravastatin counts in the human body are minor and cannot be altered by alternative drugs considering the enzymes present in the liver that eradicate Rosuvastatin and Pravastatin are not inhibited through innumerable number of the drugs when compared to other statins. Because of this mechanism, the levels of these drugs are inhibited from elevating and prominently to increasing toxicity like myopathy. Recently, Rosuvastatin and Atorvastatin are seen as the exceedingly puissant and Fluvastatin the slightest puissant statins.

Statins are soluble in both aqueous environment and viscous environment. The water-soluble statins are eliminated from the body and unmetabolized by the liver. Fat soluble statins are fragmented down in the liver by cytochrome P450 system and water-soluble statins contribute to minor interactions with other drugs.

Structure of Statin

The structures of statins can be generally categorized into three parts as a target enzyme substrate analog, HMG-CoA, the substrate analogue linked to an intricate hydrophobic ring framework involved in the reductase enzyme which is conclusive of the statin and the solubility properties of the drugs is defined by side groups on the rings.

Mechanism of Action

Cholesterol is synthesized in the cytoplasm and membrane of the endoplasmic reticulum of virtually all tissues in humans including the liver, intestine, adrenal cortex, and reproductive tissues. The mode of action of statins is by inhibiting a process in the body's formation of cholesterol. The common output of the liver is cholesterol but occasionally when the liver produces excessive amount of cholesterol. This reaction is inhibited by statins that commences with the abridgment of acetyl-CoA with acetoacetyl-CoA to form HMG-CoA in a reaction catalyzed by HMG-CoA synthase. The HMG-CoA reductase enzyme then converts HMG-CoA to mevalonate. After the production of mevalonate there are various reactions that follow to produce cholesterol. Statins inhibit the HMG-CoA reductase enzyme associated with liver's cholesterol production thus hinder the liver's capability to produce low-density lipoprotein. This process causes an elevation

in count of the low-density lipoprotein receptors on the periphery of liver cells, proceed in more cholesterol being eliminated from the blood and decrease in risk for high cholesterol-associated diseases. (Figure 1)

Pleiotropic Effects of Statins

Apart from lipid lowering properties, this drug has additional non-lipidic effects that are responsible for its pharmacological silhouette demonstrated in clinical trials. New studies have shown various properties of statins on non-lipidic biological scopes known as "pleiotropic effects" of statins, which include the antioxidant effect,[6] antithrombotic effect[7], anti-inflammatory effect[8], immunomodulatory properties[9] and the osteo-modulatory effects.[10]All these properties of statins indicate that it is enhancing one of the first host modulation agents in periodontics. The biologically significant amount of antioxidant and anti-inflammatory effects of SMV is accepted to be important in treatment of periodontitis.[11] Free radical scavenging activity of statins in human body have been established in few studies. Interaction with lipids, proteins and deoxyribonucleic acid is prevented by direct scavenging of reactive oxygen species. In this regard, Fluvastatin is more active against peroxyl radical, and SMV and ATS are more active against hydroxyl radical. Various pleotropic effects of statins prove that it is a possible host modulating agent in the regimen of periodontal infections in humans.

Application of Statins in Periodontal Therapy

The primary aim of periodontal therapy is inhibiting the fragmentation and replacing periodontal apparatus to their initial form and structure. SMV proves to hinder bone resorption which is negligible compared to its anabolic effect on maturation of osteoblasts and new bone formation.[12] It also carries antioxidant as well as anti-inflammatory properties that facilitate healing of periodontal intrabony defects. The anti-inflammatory effect could be due to the depletion of isoprenoids by statins that inhibit the IL-1 and IL-6 mediators along with lowering the LDL cholesterol levels.[13] A study conducted by Meisel et al explained that the statins were effective modifiers in the relationship between periodontitis and its inflammatory counterparts in systemic circulation.[14] The locally delivered statins such as SMV and ATS possess potential benefits in periodontal regenerative therapy due to the above-mentioned properties.[15,16] Moreover, solutions of SMV in adequate concentration have been added with bone grafts to increase the regenerative potential.[17,18]

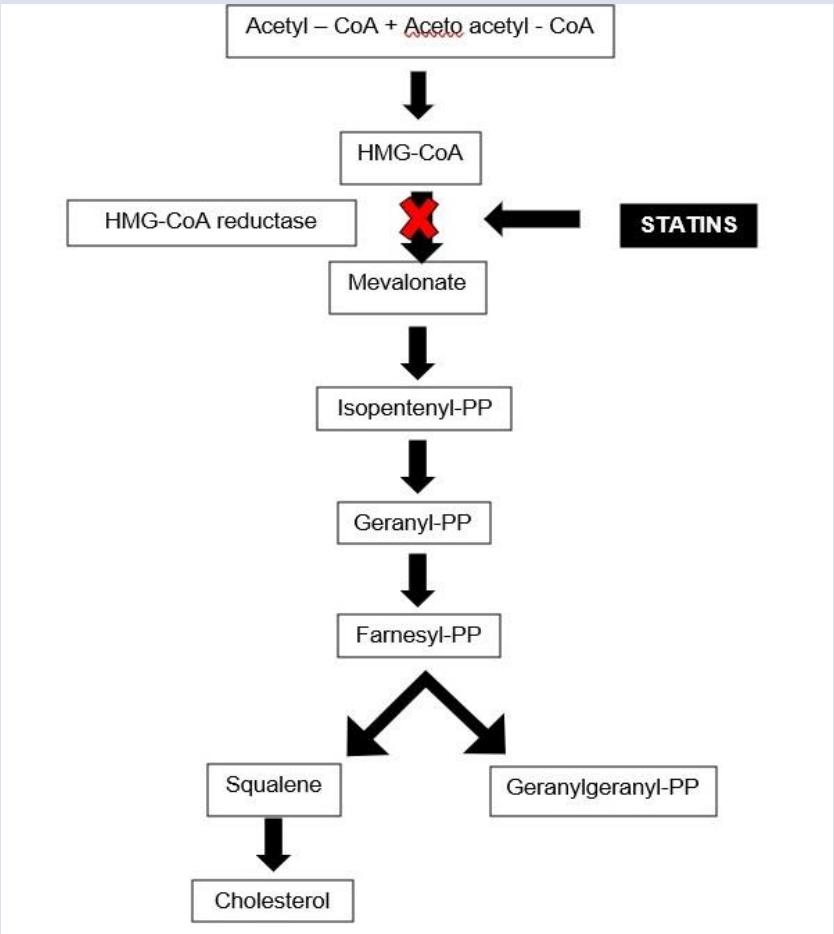

Figure 1. Melvonate Pathway.

Obesity is generally in conjunction with dyslipidemia with increased blood triglyceride levels and low-density lipoprotein levels. The excess release of proinflammatory cytokines may develop damage to the periodontal tissue; meantime, the increased systemic inflammation seen in obesity is contributed by the cytokines released in periodontitis. In a large patient population this overlap of obesity, hyperlipidemia, and periodontal disease have found benefits from statin therapy.[19]

Comprehensive research has been operated on the link uniting periodontal diseases and cardiovascular diseases.

A study was conducted to assess the relation among periodontal health and common parameters like probing depth (PD) and gingival index (GI).[20] It was illustrated that the parameters were greater in subjects with dyslipidemia, whereas subjects employed with ATS had lesser GI scores and PD levels which were correlated with reduction in total cholesterol and blood triglyceride levels.

In yet another study conducted on patients with atherosclerosis and managed with high doses of atorvastatin, it was concluded that there was a convincing reduction in periodontal inflammation when measured by c reactive protein levels and a positron emission tomography scan after 12 weeks of therapy.[21] Few other studies have observed the molecular effects of statins in periodontitis, and it has been demonstrated that administration of statins led to decreased levels of interleukin 1β, tumor necrosis factor α and MMP's in periodontitis patients.[10,22]These proinflammatory mediators are responsible for most of the host tissue damage seen in periodontitis patients. Few studies have proven that statins have the capability to elevate levels of both osteoprotegerin (OPG) levels and bone morphogenetic protein 2 (BMP-2), that play a major developmental component in the formation of bone.[23,24] A clinical trial based on the effect of local statin administration on periodontal disease was illustrated that the use of topical simvastatin gel in adjunct to non-surgical periodontal therapy resulted in greater intra bony defect fill and clinical attachment level (CAL) with decreased PD level and GI scores than the placebo group.[25] Local employment of statins such as RSV and ATS achieved clinical improvements such as PD reduction and CAL gain in addition to non-surgical periodontal regime when compared to scaling and root planing alone.[26]

Osteogenic properties of statin in periodontal therapy

SMV has been recorded to promote osteoblastic activity and hinder osteoclastic activity. Short-term exposure of alveolar bone to stains was enough to commence a cascade of bone regeneration by inducing the local generation of the BMP-2. The BMP-2 promoter has been employed as a mark to recognize new compounds that initiate the transcription and differentiation of osteoblasts.[27]

On oral administration of SMV, lowered action of serum tartrate-resistant acid phosphatase 5b was recorded, expressing the lowered osteoclast activity. Since osteoblasts and marrow adipocytes originate from a common mesenchymal progenitor, few adipogenic agents have recorded to overcome osteoblast differentiation. SMV augments alkaline phosphatase action and mineralization, including increasing the expression of bone sialoprotein, osteocalcin and Type I collagen, and it has demonstrated to have anti-inflammatory action by depleting the formation of IL-6 and IL-8.[28] Some of the recent studies involve comparing the efficacy of local delivery of 1.2 mg of ATV, RSV, or placebo gels for the regimen of intraosseous defects in subjects with chronic periodontal disease. A re-application of the gels was performed after 6 months to increase the bioavailability of the drug at the site. The mean reductions in the modified sulcus bleeding index (mSBI) and PD, the gain in the CAL, and the reduction in the intrabony defect depth were considerably more in the statin subjects than in the placebo gel subjects. At the same time, RSV treatment illustrated a larger beneficial effect than ATV at 6 and 9 months.[29] The clinical potency of locally administered 1.2% RSV and 1% Metformin (MF) gel as an addition to phase 1 periodontal treatment in the reduction of intraosseous defects in chronic periodontal patients concluded that additional local delivery of 1.2% RSV and 1% MF gel caused critical clinical attachment level gain, decline in probing pocket depths and enhanced bone fill compared to the placebo group.[30] The correlation capability of 1.2% ATV and 1.2% SMV, in addition to phase I therapy, in the regimen of intrabony defects inferred that ATV showed improved clinical measurements and greater proportion of radiographic defect depth reduction as compared to sites treated with SMV.[31]

Statins effect on periodontium

An important factor considered in healing of alveolar bone is the cells derived from periodontal ligament. The osteoblast like properties have been shown with help of in vitro studies and are accountable not only for osteogenesis and osteoclasia, but also for fibrogenesis and fibroclasis, and cementogenesis and cementoclasis.[32] The periodontal condition and immunoglobulin IgG subclasses against *Porphyromonas gingivalis* in subjects with pre- rheumatoid arthritis and early rheumatoid arthritis were compared to control group to institute a link between periodontal disease markers and rheumatic activity and the results showed that individuals with pre-rheumatoid arthritis (pre-RA) had increased inflammatory periodontal involvement and a critical link between IgG and *Porphyromonas gingivalis* and ACPAs in pre-RA and markers of rheumatoid arthritis (RA) activity in individuals with early rheumatoid arthritis (e-RA).[33] Another study compared the effect of phase I treatment on clinical measurements and GCF levels of tissue or blood vessel-type plasminogen activator (t-PA) and plasminogen activator inhibitor-2 (PAI-2) with periodontal subjects, presence, or absence of RA and results illustrated that phase 1 reduced the pretreatment GCF PAI-2 levels creating a link with the GCF plasminogen activator

inhibitor-2 amounts.[34] The considerable increased t-PA and PAI-2 GCF levels in periodontal subjects proposed that the plasminogen triggering action plays an aspect in the infection pathway of periodontal disease. By evaluating the effect of phase I therapy on the serum levels of RA-related inflammatory markers in subjects with chronic periodontal disease presented that phase I therapy may help in the regulation of RA-related inflammatory markers in subjects with chronic periodontitis.[35]

Retrospective studies have evaluated the possible effect of daily statin dose on periodontal clinical parameters and/or tooth loss which were inconclusive.[36,37]Whereas various preclinical and clinical studies studied the action of local and/or systemic benefit of statins as addition to non-surgical and/or surgical periodontal treatment have been published.[38,39] The studies concluded by proving that statins are effective against *A. actinomycetemcomitans* and *Porphyromonas gingivalis* which are the important species of bacteria involved in periodontal pathogenesis. Moreover, statins have proven to hinder the tissue degrading enzymes and in exerting a pro-proliferative action on mesenchymal stromal cells and endothelial progenitor cells. Statins have a positive effect on differentiation of osteoblasts, bone morphogenetic protein and vascular endothelial growth factor expression and it hinders with resorption of bone and the process of osteoclastogenesis.[40] In a systematic review of randomized controlled clinical trials, including meta-analyses, the administration of local statin as an addition to phase I periodontal treatment resulted in sufficient clinical and radiographic enhancement compared to SRP alone. There was a positive impact of intra-surgical statin administration, whereas there was no positive impact with systemic statin administration with addition to non-surgical periodontal treatment.[41] The introduction of local drug delivery help in stimulating alveolar bone regeneration. Large- scale studies have been carried out to state these findings such as the efficacy of statins as potential inhibitors of bone resorption and their anabolic effects on bone to further regeneration.[42]

Conclusions

Analysis of the available scientific evidence demonstrates that statin administration may represent a new approach and a valuable tool as an addition to periodontal treatment. Local delivery proved to be ideal by providing high concentrations at target site and decreases the disadvantages of systemic delivery, such as adverse reactions and low patient compliance. We can consider topically delivered statins as an adjunct treatment for the hindrance of periodontal disease in high-risk patients because it enhances the resolution of periodontitis, reverses the associated defects, and represents a form of periodontal maintenance. This drug can accomplish the objective of regeneration without any intrusive methods, thereby producing minimal distress to the patients. It is proved that the antioxidant and anti-inflammatory effects of this agent could promote healing of osseous deformity. Studies conclude that statins have potential effect on alveolar bone present in both preclinical and clinical field and some have opposing results of SMV effects. Nevertheless, long-duration clinical research in human patients are necessary to demonstrate the mode of application, optimum therapeutic threshold and the effectiveness in humans for regeneration of bone and assess the capable benefits of statin in periodontal regeneration.

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Conflicts of Interest Statement

No conflicts of interest

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