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EDİTÖRDEN

Bilimsel bilgi birikimine katkıda bulunma sorumluluğuyla sürdürdüğümüz yayın hayatımıza, yeni sayımızla birlikte bir adım daha eklemekten büyük mutluluk duyuyoruz. Editör ekibimizin yoğun ve titiz çalışmaları neticesinde hazırlanan bu sayımızda, siz değerli okuyucularımıza güncel, özgün ve nitelikli bilimsel içerikler sunmayı hedefledik.

Bu sayımızda, Periodontoloji, Ağız Diş ve Çene Cerrahisi, Restoratif Diş Tedavisi ve Epidemiyoloji alanlarında yürütülmüş beş özgün araştırma makalesinin yanı sıra, Endodonti, Protez alanında iki derleme makalesi yer almaktadır. Ayrıca, klinik pratiğe ışık tutacak nitelikte Çocuk Diş Hekimliği, Protez, Ağız Hastalıkları alanında üç olgu sunumu da dikkatle seçilerek sizlerin beğenisine sunulmuştur. Her bir çalışma, ilgili alanlarda çalışan araştırmacı ve klinisyenlere değerli bilgiler sağlamayı amaçlamaktadır.

Dergimizin, Scilit, ROAD Index, Crossref gibi uluslararası saygın indekslerdeki yerini koruyor olması, bilimsel niteliğimizin ve yayın kalitemizin bir göstergesi olmanın yanı sıra, bizlere geleceğe yönelik daha büyük hedefler için ilham vermektedir. Yılda üç sayı olarak düzenli bir şekilde yayınlanan dergimizin bu başarısında, özverili çalışmalarıyla sürece katkı sağlayan editörlerimize, hakemlerimize ve yazarlarımıza teşekkürü bir borç biliriz. Ayrıca, bilimsel üretimi destekleyen anlayışlarıyla her zaman yanımızda olan Dekanlığımıza, Rektörlüğümüze ve Mütevelli Heyetimize içten teşekkürlerimizi sunarız.

Dergimizin her yeni sayısında, bilim dünyasına katkıda bulunacak özgün ve güncel içerikler sunmaya devam edeceğimizi taahhüt ederken, tüm meslektaşlarımıza sağlıklı, verimli ve başarılı çalışmalar dileriz. Gelecek sayımızda daha da zenginleştirilmiş bir içerikle yeniden buluşmak dileğiyle, Dergimizin Editörler Kurulu adına saygı ve sevgilerimizi sunarız.

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The Effects of Biotics Derived from *Lactiplantibacillus* plantarum EIR/IF-1 on the Modulation of Periodontal Inflammation

Lactiplantibacillus plantarum EIR/IF-1 Kaynaklı Biyotiklerin Periodontal İnflamasyonun Modülasyonu Üzerindeki Etkileri

Hikmet Can[1], Hazal Kibar Demirhan[2], Emine Omer Oglou[2], Fadime Kiran[3*]

ABSTRACT

Objective: This study aims to investigate the immunomodulatory effects of postbiotics and paraprobiotics derived from Lactiplantibacillus plantarum EIR/IF-1.

Materials and Methods: Human periodontal ligament fibroblast (hPDLF) cells were co-incubated with the release and bound forms of exopolysaccharides (10-1,000 µg/mL), cell lysate (0.1-1,000 µg/mL), cell surface proteins (0.1-100 µg/mL), and inactivated cells (10^6-10^{10} CFU/mL) derived from Lactiplantibacillus plantarum EIR/IF-1 for 24 hours. Cell viability was assessed by MTT assay. Lipopolysaccharide (LPS) from Porphyromonas gingivalis, a key pathogen involved in periodontal disease, was used to induce inflammation in hPDLF cells. Non-toxic doses of the biotics were subsequently tested for their impact on cytokine production in LPS induced hPDLF cells. Cytokine levels (IL-10, IL-8, and IFN-γ) were quantified using the ELISA protocol.

Results: After 24 hours incubation of hPDLF cells with 1 µg/mL LPS and selected concentrations of the biotics derived from the EIR/IF-1 strain that did not exhibit toxic effects, it was observed that LPS from P. gingivalis induced IL-8 production. However, the biotics extracted from the EIR/IF-1 strain significantly reduced IL-8 production (p<0.0001). Furthermore, these biotics increased the production of the anti-inflammatory cytokine IL-10 (p<0.0001).

Conclusion: The obtained data suggest that the biotics have the potential to counteract the pro-inflammatory effects induced by LPS. The findings highlight the potential of postbiotics and paraprobiotics, containing biologically active and effective components, as a promising natural and reliable approach for reducing and preventing periodontal inflammation. In conclusion, our results suggest that microbiota-derived biotics could serve as effective adjuncts in the management of periodontal diseases.

Keywords: *Inflammation, Periodontal Diseases, Cytokine, Probiotic*

ÖZET

Amaç: Bu çalışma, Lactiplantibacillus plantarum EIR/IF-1 suşundan elde edilen postbiyotiklerin ve paraprobiyotiklerin immünmodülatör etkilerini araştırmayı amaçlamaktadır.

Gereç ve Yöntemler: İnsan periodontal ligament fibroblast (iPDLF) hücreleri, Lactiplantibacillus plantarum EIR/IF-1 kaynaklı salınan ve bağlı formlarda bulunan eksopolizakkaritler (10–1.000 µg/mL), hücre lizatı (0,1–1.000 µg/mL), hücre yüzeyi proteinleri (0,1–100 µg/mL) ve inaktif hücreler (10^6–10^{10} KOB/mL) ile 24 saat süreyle birlikte inkübe edilmiştir. Hücre canlılığı MTT testi ile değerlendirilmiştir. Periodontal hastalıkla ilişkili önemli bir patojen olan Porphyromonas gingivalis'ten elde edilen lipopolisakkarit (LPS), iPDLF hücrelerinde inflamasyonu indüklemek için kullanılmıştır. Biyotiklerin, LPS ile uyarılmış iPDLF hücrelerinde sitokin üretimine olan etkisi, toksik olmayan dozlarla birlikte inkübasyon neticesinde test edilmiştir. Sitokin seviyeleri (IL-10, IL-8 ve IFN-γ) ELİZA protokolü ile belirlenmiştir.

Bulgular: Hücreler 1 µg/mL LPS ve toksik etkisi olmayan seçilen biyotik dozları ile 24 saat inkübe edildikten sonra, P. gingivalis kaynaklı LPS'nin IL-8 üretimini indüklediği gözlemlenmiştir. Ancak, EIR/IF-1 suşundan elde edilen biyotikler, IL-8 üretimini önemli ölçüde azaltmıştır (p<0.0001). Ayrıca, bu biyotikler anti-inflamatuvar bir sitokin olan IL-10 üretimini artırmıştır (p<0.0001).

Sonuç: Elde edilen veriler, biyotiklerin LPS'nin oluşturduğu pro-inflamatuvar etkileri azaltabilecek potansiyele sahip olduğunu göstermektedir. Bu bulgular, biyolojik olarak aktif ve etkin bileşenler içeren postbiyotikler ve paraprobiyotiklerin periodontal inflamasyonu azaltmak ve önlemek için umut verici, doğal ve güvenilir bir yaklaşım olarak kullanılabileceğini vurgulamaktadır. Sonuç olarak, mikrobiyota kaynaklı biyotiklerin periodontal hastalıkların yönetiminde etkili yardımcı bir tedavi olarak kullanılabileceği önerilmektedir.

Anahtar Kelimeler: *İnflamasyon, Periodontal Hastalıklar, Sitokin, Probiyotik*

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Introduction

Periodontal diseases, which refer to inflammation and infection of the tissues that surround and support teeth, are reported as the second most prevalent chronic disease worldwide, after cardiovascular diseases. Additionally, periodontal diseases are recorded as the sixth most common disease among 291 diseases reported within the scope of Global Burden of Disease studies and are considered an important current public health problem when their prevalence, treatment costs, and negative effects on the patients are taken into consideration.[1] In 2022, World Health Organization (WHO) highlighted the fact that more than 1 billion people worldwide suffer from periodontal diseases.[2] In general, it is estimated that 15% of the human population has experienced periodontitis at some point in their lives, and more than 47% of adults aged 30 and over have been diagnosed with periodontal disease at least once. Periodontal diseases, which increase with age, affect more than 70% of adults aged 65 and older. Among individuals between the ages of 35 and 44, tooth loss occurs at a rate of 5% to 15% following aggressive periodontitis.[3] In addition to the damage they cause to oral tissues and tooth loss, periodontal diseases have also been linked to various systemic conditions such as cardiovascular diseases, diabetes, and Alzheimer's disease.[4] Therefore, considering both their direct effects on dental or oral tissues and their indirect role in predisposing individuals to other diseases, as well as their high global prevalence and socio-economic impact on societies, periodontal diseases are currently referred to as a "silent" global pandemic.[5]

Periodontal diseases are generally characterized as chronic, infectious, and inflammatory pathological conditions initiated by a dysbiotic subgingival biofilm (plaque). Although the etiopathology of the disease is influenced by various factors, it can be broadly described by the interactions between microorganisms responsible for dental biofilms and host's immune system response.[6] In light of these processes, periodontal diseases are classified into categories: gingivitis and periodontitis. The accumulation of bacteria from microbial dental plaque in the subgingival tissues, followed by inflammation of the surrounding tissues, is referred to as gingivitis (gum inflammation). When the dental biofilm caused by microorganisms is not eradicated, the infection in the gum progresses to other tissues of the periodontium, ultimately reaching the alveolar bone and leading to periodontitis, which is defined as an aggressive pathological condition. The progression of the disease results in advanced attachment loss and alveolar bone resorption, culminating in progressive periodontal bone loss. Failure to implement an effective treatment approach for healing or biofilm eradication leads to early tooth loss.[7] In conclusion, both tooth loss resulting from periodontal inflammation and its connection with systemic diseases underline the need for development of new and effective treatment strategies for periodontal diseases.[8] Considering that the existing damage is caused by inflammation resulting from excessive activation of the host's immune cells, targeted treatment strategies are expected to not only focus on biofilm removal but also aim to reduce inflammation.

Biotics, defined as an umbrella term encompassing probiotics, prebiotics, postbiotics, and paraprobiotics, have gained considerable attention in recent years within both health and food industries. The terms postbiotics and paraprobiotics are emerging as current concepts that are not included in the traditional definitions of probiotics (microorganisms that confer health benefits to the host when consumed in adequate amounts) and prebiotics (non-digestible dietary components).[9] Postbiotics, a novel area within the biotics family, are defined as "bacterial or metabolic end products produced by microorganisms that possess biological activity in the host", and may include any substance or combination of substances that provide synergistic benefits to the host, either directly or indirectly.[10,11] These metabolic end products may consist various components such as short-chain fatty acids, microbial cell fractions, functional proteins, exopolysaccharides (EPS), cell lysates, teichoic acids, peptidoglycan-derived muropeptides, and pili-type structures. It has been noted that postbiotics produced by

beneficial microorganisms can exert their positive effects attributed to the producer strain through the similar mechanisms.[12] They have been reported to possess antibacterial, anti-biofilm, anti-inflammatory, hypocholesterolemic, antioxidant, and immunomodulatory effects on the host organism.[13] Additionally, they contribute to microbiota homeostasis by positively influencing host metabolism and signaling interactions.[14] The fact that postbiotics exert their potential effects on the host by modulating biological signaling pathways underscores their significance as key mediators of the beneficial effects of microbiota members. Another group of biotics that has attracted attention in recent years, "paraprobiotics," is defined by the Food and Agriculture Organization/World Health Organization as "inactive (non-living, ghost) microbial cells that provide benefits to consumers when applied in sufficient amounts".[10,15]

This study aims to investigate the potential effects of postbiotics and paraprobiotics derived from Lactiplantibacillus plantarum EIR/IF-1 on inflammation associated with periodontal disease under *in vitro* conditions. This bacterium was selected due to its previously observed biological activities (antimicrobial, anti-biofilm, and anti-quorum sensing) against significant periodontal pathogens, as reported in our earlier studies.[16-18]

Materials and Methods

Lactiplantibacillus plantarum EIR/IF-1 (NCBI GenBank Accession Number: MW057714.1), isolated from the infant fecal microbiota and identified through 16S rRNA sequencing, was kindly provided by the bacterial culture collection of the Pharmabiotic Technologies Research Laboratory (Faculty of Science, Ankara University) and used as the source of biotics. Bacterial glycerol (50%) stock solution was transfered to De Man-Rogosa-Sharpe (MRS) broth medium and incubated at 37ºC for 24 hours (Nüve, Turkey). After two passages for activation, the purity and phenotypic validation were performed through streak plating and Gram staining and the strain was used for further assays.[19]

To obtain inactive cells, EIR/IF-1 strain was inoculated into MRS broth at a 1% concentration and incubated at 37ºC for 24 hours. After incubation, the culture was centrifuged at 15,000x*g* for 20 minutes at 4ºC (Nüve, Turkey) and the pellet was suspended in sterile physiological saline solution. Serial dilutions were performed to determine the number of cells. 10 µL from each dilution were drop-plated on MRS agar plates and incubated at 37ºC for 24 hours. Following incubation, the colonies were counted and calculated as colony-forming units (CFU)/mL. The cells were then inactivated by heat treatment in a water bath (Nüve, Turkey) at 60ºC for 3 hours. Inactivation efficacy was confirmed by culturing the cells in MRS broth and agar for 48 hours at 37ºC.[20]

Following the culture procedures mentioned in the previous step, the pellet obtained from the EIR/IF-1 strain was dissolved in 1 mL of a solution containing 5 mM ethylenediaminetetraacetic acid (EDTA, Merck, USA) and 5 mM magnesium chloride ($MgCl_2$, Merck, USA) in 50 mM Tris (pH 7.5) buffer (Merck, USA). Sonication was performed three times at 40W (QSonica, USA). The cell lysate was obtained after centrifugation at 14,000×*g* for 10 minutes at 4ºC. To confirm cell lysis, cell lysate was inoculated into MRS broth and onto MRS agar, and incubated for 48 at 37ºC. After confirming the absence of microbial growth, the cell lysate was subsequently lyophilized (Buchi, Switzerland).[21]

Exopolysaccharides (EPS) from the EIR/IF-1 were obtained in two different stages. To extract the release form of exopolysaccharides (EPS-r), the EIR/IF-1 strain was inoculated into MRS broth and incubated at 37ºC for 24 hours. After incubation, the culture was centrifuged at 15,000×*g* for 20 minutes at 4ºC, and supernatant (upper phase) was subsequently heated in a water bath at 100ºC for 15 minutes. After centrifugation at 15,000×*g* for 15 minutes, 20% trichloroacetic acid (TCA, Sigma, USA) was added to the supernatant. The mixture was incubated with shaking at 4ºC for 2 hours, and then centrifuged at 25,000x*g* for 20 minutes at 4ºC. The supernatant was mixed with two volumes of 95% ethanol (Merck, USA) and incubated overnight. After a final centrifugation

at 6,000×*g* for 30 minutes at 4ºC, the obtained EPS-r was lyophilized.[22] For the extraction of cell surface-bound exopolysaccharides (EPS-b), the cells obtained from the previous step were washed with 10 mL of sterile physiological saline and resuspended in 5 mL of 1 M sodium chloride (NaCl, Merck, USA). The suspension was sonicated at 40W for 3 minutes. After centrifugation at 6,000×*g* for 30 minutes at 4ºC, the supernatant was mixed with two volumes of 95% ethanol (Merck, USA) and incubated overnight. After a final centrifugation at 6,000×*g* for 30 minutes at 4ºC, the obtained EPS-b was lyophilized.[22] The total glucose content of EPS-b and EPS-r was determined according to the method of Dubois et al.[23] 1 mL of 5% phenol solution (Merck, USA) and 5 mL of 96% sulfuric acid (Merck, USA) were mixed with the EPS-b, EPS-r and standard solutions containing different concentrations of glucose, separately. The mixtures were incubated at room temperature for 10 minutes, followed by incubation at 37ºC for 15 minutes. The color change was measured by spectrophotometrically (BioTek Epoch, USA) at a wavelength of 490_{nm}.

For the extraction of cell surface proteins, the EIR/IF-1 strain was inoculated into 1% MRS broth and cultured at 37ºC for 24 hours. Following incubation, the culture was centrifuged at 15,000×*g* for 20 minutes at 4ºC. The obtained pellet was washed twice with 25 mL of cold phosphate-buffered saline (PBS; 0.12% K_2HPO_4, 0.022% Na_2HPO_4, 0.85% NaCl, pH: 7.4). Next, 10 mL of 5 M lithium chloride (LiCl, Merck, USA) solution was added, and the mixture was stirred at 4ºC for 15 minutes. After centrifugation at 9,000×*g* for 10 minutes at 4ºC, the supernatant was transferred to a molecular weight cut-off (MWCO) membrane with a 12,000 Da pore size (Sigma, USA), and dialysis was performed against cold distilled water (dH_2O) for 24 hours. During the dialysis process, water was exchanged every 2 hours. The dialyzed solution was centrifuged at 20,000×*g* for 30 minutes at 4ºC. The resulting pellet was resuspended in 10 mL of 1 M LiCl solution and stirred at 4ºC for 15 minutes. After centrifugation at 20,000×*g* for 10 minutes at 4ºC, the supernatant was transferred to the dialysis membrane and dialyzed again for 24 hours. The final dialyzed solution was centrifuged at 20,000×*g* for 30 minutes at 4ºC and the obtained cell surface proteins were lyophilized.[24] The total protein content of the cell surface proteins was determined using the bicinchoninic acid (BCA) Protein Assay Kit (Smith method; TaKaRa, Japan) according to the manufacturer's instructions. Briefly, standard solutions of bovine serum albumin (BSA) at concentrations of 125-2,000 µg/mL were prepared from a 2 mg/mL BSA stock solution. Standard solutions and cell surface proteins were separately mixed with 200 µL of BCA reagent and incubated at 37ºC for 30 minutes. Following incubation, a purple-colored product was formed as a result of the reaction between the copper ions of the BCA reagent and the peptide bonds of the proteins. The color change was measured spectrophotometrically at a wavelength of 562_{nm}.

The immunomodulatory effects of the biotics were evaluated using human periodontal ligament fibroblast (hPDLF) cells, which were kindly provided by the cell culture collection of the Pharmabiotic Technologies Research Laboratory (Faculty of Science, Ankara University). These cells were isolated and characterized from healthy human periodontal tissues during our previous studies.[25] The cells were cultured in alpha-MEM medium (Sartorius, Germany) supplemented with 10% fetal bovine serum (BI, Germany), 1% penicillin-streptomycin (Gibco, USA), 1% L-glutamine (Sartorius, Germany), and 1% non-essential amino acids (Gibco, USA) at 37°C with 5% CO^2 and 80-90% relative humidity in T75 flasks. The medium was refreshed every 3 days. During culturing, cells were visualized under an inverted phase contrast microscope (Olympus, Japan), as shown in Figure 1. When 85-90% confluence was observed, the culture medium was removed, and the cells were washed with PBS buffer, followed by trypsinization. After centrifugation at 200×*g* for 5 minutes, the cells were counted using an automatic cell counter (Bio-Rad, USA) following trypan blue staining, and were subsequently seeded in 96-well tissue culture plate at a density of 10,000 cells per well to assess the non- cytotoxic doses of biotics. After a 24-hour incubation period, the culture

medium was completely removed, and media containing EPS-r (10-1,000 µg/mL), EPS-b (10-1,000 µg/mL), cell lysate (0.1-1,000 µg/mL), cell surface proteins (0.1-100 µg/mL), and inactivated cells (10^6-10^{10} CFU/mL) were added to the wells in triplicate. Wells without biotics used as the control. After an additional 24-hour incubation period, the culture medium was removed, and cell viability was assessed using the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) assay. Briefly, 10 µL of MTT solution (5 mg/mL, Serva, USA) was added to each well, and after a 4-hour incubation at 37ºC, the MTT solution was removed. Subsequently, dimethyl sulfoxide (DMSO, Sigma, USA) was added to each well, and the optical density was measured at a wavelength of 550_{nm} using a microplate reader (BioTek Epoch, USA).[26]

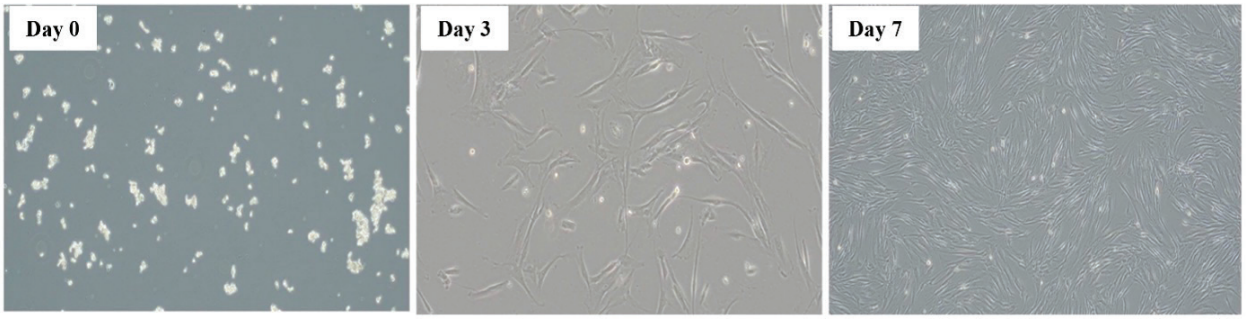

Figure 1. Microscopic images of human periodontal ligament fibroblast cells

To determine the immunomodulatory effect of the biotics, an inflammation was induced in hPDLF cells using lipopolysaccharide (LPS) from Porphyromonas gingivalis (Sigma, USA). First, the dose of LPS that did not exhibit cytotoxic effect on cells was determined through MTT analysis, as previously described. Next, the highest non-cytotoxic dose of LPS was co-incubated with biotics derived from the EIR/IF-1 strain. After a 24-hour incubation period, the levels of interleukin (IL)-10, IL-8, and interferon (IFN)-γ in the cell supernatants were determined using ELISA (Enzyme-Linked Immunosorbent Assay) kits (MabTech, Switzerland), following protocols recommended by the manufacturer.

All analyses in this study were performed in triplicate and analyzed using GraphPad Prism v.8.0 (GraphPad Software, San Diego, CA, USA). Differences between groups were evaluated with Tukey's test one-way analysis of variance (ANOVA) and $p<0.05$ was considered significant.

Results

Among the biotics extracted from EIR/IF-1 strain, heat-inactivated cells were applied in the cell culture studies with their concentration as CFU/mL. Therefore, the number of bacterial cells prior to inactivation was determined through microbiological assays. The results indicated that the viable cell count was 2×10^{11} CFU/mL, which was then used for dose calculations. After heat inactivation, no growth was observed in either broth or agar media which confirming the successful inactivation of the cells. Similar results were also observed for the lysed cells, indicating that cell lysis was also successfully achieved. The total glucose content of EPS-b and EPS-r was determined based on the glucose standard curve (Figure 2a). Our results showed that the glucose content of EPS-b was 140.71±2.4 mg/L, while that of EPS-r was 741.63±18.2 mg/L. Similarly, the total protein amount of cell surface proteins extracted from the EIR/IF-1 strain was evaluated using the BSA standard curve (Figure 2b). According to the results, the total protein content of the cell surface proteins was determined to be 1.1±0.4 mg/mL.

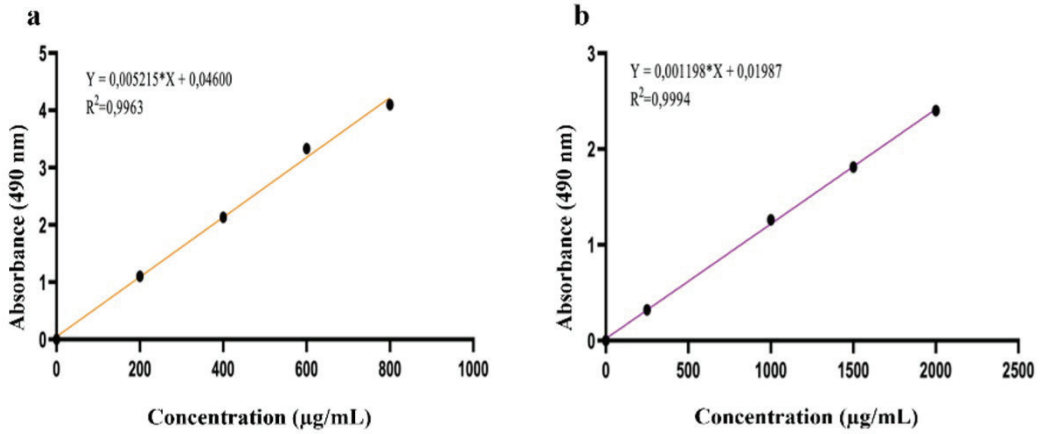

Figure 2. The standard curves used in the study for total sugar (a) and total protein content (b)

hPDLF cells were co-incubated with EPS-r (10-1,000 µg/mL), EPS-b (10-1,000 µg/mL), cell lysate (0.1-1,000 µg/mL), cell surface proteins (0.1-100 µg/mL), and inactivated cells (10^6-10^{10} CFU/mL) for 24 hours. Cell viability was assessed based on the absorbance values obtained from the test groups and control groups using the MTT assay. Upon evaluating the MTT data, it was observed that the 1,000 µg/mL doses of EPS-b, EPS-r and cell lysate, the 100 µg/mL dose of cell surface proteins and the 10^{10} CFU/mL dose of inactivated cells exhibited toxic effects on the hPDLF cells (Figure 3). Consequently, the highest doses that did not exhibit toxic effects were selected in the subsequent experiments.

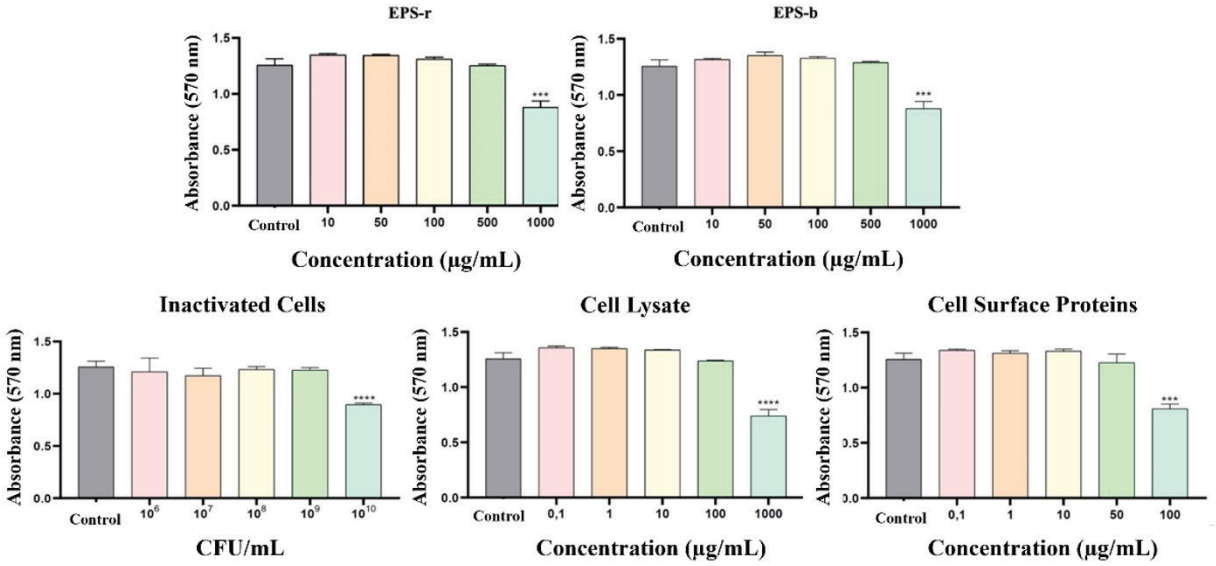

Figure 3. The effect of biotics derived from the *Lactiplantibacillus plantarum* EIR/IF-1 strain on the viability of hPDLF cells (***: $p<0.001$; ****: $p<0.0001$)

In order to determine the immunomodulatory role of biotics extracted from the EIR/IF-1 strain on hPDLF cells, an inflammation model was established in hPDLF cells. For this purpose, the effect of different concentrations of LPS from P. gingivalis on hPDLF cell viability was evaluated. The results indicated that LPS concentrations of 5 µg/mL ($p<0.05$) and 10 µg/mL ($p<0.001$) significantly reduced hPDLF cell viability. Based on these findings, a concentration of 1 µg/mL, which did not exhibit cytotoxic effects, was selected for cell stimulation assays (Figure 4).

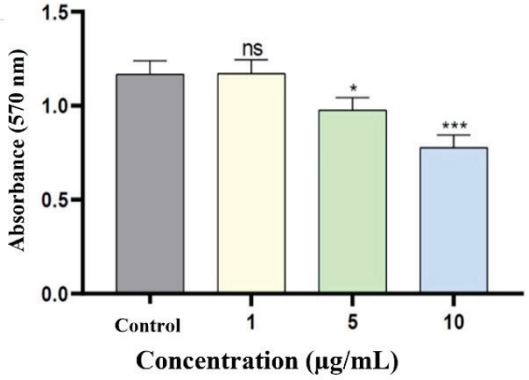

Figure 4. The effect of LPS derived from *Porphyromonas gingivalis* on the viability of hPDLF cells (ns: not significant; *: $p<0.05$; ***: $p<0.001$)

After co-incubating hPDLF cells with 1 µg/mL LPS and selected concentrations of the biotics derived from the EIR/IF-1 strain for 24 hours, the levels of IL-10, IL-8 and IFN-γ in the cell supernatants were determined using ELISA. The absorbance values obtained from the spectrophotometric measurements were evaluated using calibration curves of standards containing known amounts of recombinant cytokines. Regarding IL-8 production, a pro-inflammatory cytokine, the results indicated that LPS from P. gingivalis induced IL-8 production, while the biotics extracted from the EIR/IF-1 strain significantly reduced its production ($p<0.0001$). In contrast, when the results were evaluated in terms of the production of IL-10, an anti-inflammatory cytokine, it was found that biotics extracted from the EIR/IF-1 strain induced IL-10 production, with variations depending on the type of biotics (Figure 5). However, no signals were detected for IFN-γ production.

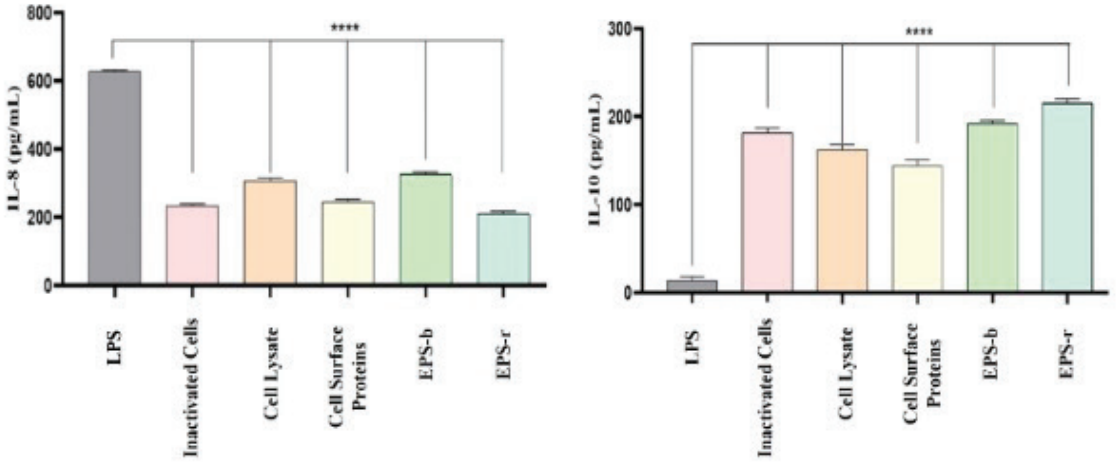

Figure 5. The effect of biotics derived from the *Lactiplantibacillus plantarum* EIR/IF-1 strain on IL-8 and IL-10 production in hPDLF cells induced by *P. gingivalis* LPS (****: $p<0.0001$)

Discussion

Microorganisms involved in the formation of dental plaque, which play a crucial role in the development of periodontal diseases, are considered important not only for their contribution to plaque formation through biofilm production but also for their ability to activate inflammatory responses.[27] Inflammation that occurs as a result of the host immune response ultimately leads to periodontal tissue destruction. During the progress of the disease, *Porphyromonas gingivalis* modulates the host's immune-inflammatory responses and contributes to periodontal tissue destruction by disrupting the homeostasis of the normal cell cycle. The LPS structure of *P. gingivalis* is chemically composed of multiple lipid A forms, including 3-hydroxy-15-methylhexadecanoic acid and

3-hexadecanoyloxy-15-methylhexadecanoic acid, acylated with a glucosamine beta-(1-6) disaccharide 1-monophosphate. This structure is recognized by the TLR-4 receptor on host cells, thereby triggering inflammation.[28] While inflammation initially serves a protective function for the host, if left unchecked, it can lead to tissue destruction.[29] The objective of this study was to examine the effects of postbiotics and paraprobiotics derived from *L. plantarum* EIR/IF-1 on the production of inflammatory cytokines in hPDLF cells stimulated by *P. gingivalis* LPS. We aimed to explore the potential of microbiota-derived biotics as adjunctive therapeutic agents for periodontal disease, a relatively underexplored area within contemporary periodontal research. This study is distinctive in its approach, as it investigates the capacity of postbiotics and paraprobiotics to modulate inflammatory responses in periodontal tissues, thereby offering novel insights into how microbiota-based interventions may provide therapeutic benefits for the management of periodontal disease. The results of this study contribute significantly to the expanding field of microbiota-based therapies, with potential implications for the development of innovative treatment strategies focused on mitigating periodontal inflammation.

Recent studies have indicated that bacteria possessing probiotic properties can effectively prevent inflammation associated with periodontal diseases through diverse immunological pathways including enhanced IgA production in the mucosa, increased macrophage activity, and augmented phagocytosis, all of which contribute to strengthening the immune response and preventing bacterial translocation in the mucosa.[30-32] Moreover, the ability of probiotics to inhibit the growth of major dental pathogens, such as *P. gingivalis*, reduce alveolar bone loss by modulating different signaling pathways, and exhibit immunomodulatory effects supports the hypothesis that probiotics may integrated into different therapeutic strategies for periodontal diseases.[33] However, challenges remain in the application of probiotics, as they require sustained colonization in the oral cavity, which can result in variability in their immunomodulatory effects. Additionally, probiotics can alter the host's microbial community, potentially leading to dysbiosis under certain conditions. The rapid colonization of exogenous probiotics within the established oral microbiota also presents a significant challenge. Furthermore, the use of live microorganisms in therapeutic applications carries risks, such as sepsis, and may present technical challenges related to cell viability, even if these risks are relatively low.[34] Therefore, the limitations associated with probiotics remain important challenges that need to be addressed. In this context, to overcome the disadvantages, an alternative approach has emerged that involves the use of probiotic-derived postbiotics or their inactive forms, such as paraprobiotics. These probiotic derived-mediators play key roles in the beneficial effects of live microorganisms and may offer potential for preventing or alleviating periodontal inflammation.[35] Current literature, however, indicates that the effects of postbiotics and paraprobiotics on inflammatory cytokine production in periodontal tissues remain inadequately explored highlighting a significant gap in the field. By investigating the impact of *L. plantarum*-derived postbiotics and paraprobiotics on inflammatory cytokine responses in hPDLFs exposed to *P. gingivalis* LPS, this study fills a critical gap in the literature. Our findings provide valuable insights into the potential application of microbiota-derived biotics for modulating inflammation in periodontal disease, paving the way for novel adjunctive therapies in clinical periodontal practice.

The mechanisms of action of postbiotics encompass modulation of the host cell-resident microbiota, regulation of systemic or local immune and metabolic responses, enhancement of epithelial barrier function, and signaling with the nervous system.[36] Immunmodulatory effects of postbiotics can be mediated by various mechanisms such as stimulating Th1 immune cells to increase cytokine production, while simultaneously reducing cytokine levels through Th2 cell stimulation.[37] Additionally, postbiotics interact with macrophages and inhibit the production of specific pro-inflammatory cytokines. A diverse range of metabolites within postbiotics act as mediators of these effects by

enhancing the production of anti-inflammatory cytokines and suppressing pro-inflammatory cytokines.[38,39] For instance, postbiotics derived from *Lactobacillus rhamnosus* GG have demonstrated anti-inflammatory properties by modulating the production cytokines such as IL-4, IL-5, and IL-10.[40] Similarly, other studies have shown that postbiotics influence the modulation of the anti-inflammatory cytokine IL-8 while affecting the production of IL-1β, IL-6, TNF-α, and IL-10 cytokines in macrophages.[41] Postbiotics derived from Bacillus coagulans have also been exhibite anti-inflammatory effects,[42] whereas those extracted from Bifidobacterium breve were shown to promote enteric cell maturation and viability, increase IL-10 production, and reduce TNF-α levels.[43] Considering that IL-1β, along with IL-6 and TNF-α, are critical mediators in periodontal tissue degeneration,[44-46] the ability of postbiotics to inhibit inflammation and promote angiogenesis in the epithelial tissues via the activation of α2β1 integrin collagen receptors holds significant therapeutic potential[47].

Bacterial EPS, one of the key component of postbiotics, are macromolecules known for their ability to facilitate interactions between bacteria and their environment, mediate adhesion properties, provide protection against pathogens, and exhibit anti-inflammatory effects.[48,49] Depending on the bacterial species, EPS can be classified as either homopolysaccharides or heteropolysaccharides.[50] Homopolysaccharides are composed of a single type of monosaccharide derivative and are synthesized within cells through glycosyltransferase activity.[51] In contrast, heteropolysaccharides consist of diverse monosaccharides, ranging from disaccharides to heptasaccharides.[52] Our findings in this study reveal that EPS-r derived from L. plantarum EIR/IF-1, which includes fractions with varying molecular weights (51 and 841 kDa) and contains glucose, galactose, and fructose monosaccharides,[17] exhibited more potent immunomodulatory effects compared to EPS-b.[53] Similarly, recent studies have also highlighted the capacity of EPS-r from various Lactobacillus spp. strains to modulate both systemic and mucosal immune responses. Purified EPS-r produced by *L.* rhamnosus RW-9595M has been reported to exert immunosuppressive effects on macrophages by inducing high levels of IL-10 (an anti-inflammatory cytokine) and low levels of TNF-α, IL-6, and IL-12 production.[54] Additionally, the acidic fraction of EPS-r produced by L. plantarum 14 was found to suppress the production of pro-inflammatory cytokines (IL-6, IL-8, and MCP-1) in porcine intestinal epithelial cells in response to enterotoxigenic E. coli.[55] *In vivo* studies corroborate these findings, demonstrating that administration of EPS-r produced by L. paraplantarum BGCG11 to mice led to reduced levels of IL-1β, TNF-α, and inducible nitric oxide synthase, alongside an increased production of IL-10.[49]

Paraprobiotics, a term encompassing inactive cells, cell lysates, and cell surface proteins, contain effector molecules that interact with host cells.[13] Inactive bacterial cells, rendered non-viable through methods such as heat treatment, chemical processing, sonication, or ultraviolet radiation, can exhibit immunomodulatory effects similar to those of probiotics or postbiotics. Among these inactivation techniques, heat treatment is widely regarded as the most common method.[15] In this study, microbial cells were fully inactivated using heat treatment. Our findings revealed that the inactive cells of the L. plantarum EIR/IF-1 strain significantly enhanced IL-10 synthesis.[53] Similar studies have demonstrated that inactivated cells of Lactobacillus spp. strains suppress the production of pro-inflammatory cytokines such as IL-6 and TNF-α while effectively promoting the production of anti-inflammatory cytokines like IL-10.[56] In another study, inactivation of *Lactobacillus* spp. strains via three different heat-treatment methods resulted in stimulation of dendritic and macrophage immune cells, leading to increased IL-12 production in mice.[57]

Bacterial lysates have been shown to exert modulatory effects on the host's immune mechanisms through TLR-mediated interactions with dendritic cells. Stimulation of dendritic cells with bacterial lysates leads to the release of chemokines and triggers the migration of polymorphonuclear neutrophils. Additionally, bacterial lysates play a key role in reducing

the levels of cytokines such as IL-4 and IL-13, which are released by Th2 cells, while increasing the levels of cytokines such as IFN-γ released by Th1 cells.[58] Our study demonstrated that the cell lysate from the L. plantarum EIR/IF-1 strain decreased IL-8 production while increasing IL-10 synthesis. Similar studies investigating the effects of bacterial cell lysates have reported that bacterial lysates stimulate the production of TNF-α, IL-1β, and IL-6 in the host. Furthermore, bacterial cell lysates interact with pattern recognition receptors (PRRs) in the host, playing a critical role in antibody production through their interaction with B cells.[59] Peptidoglycan structures from L. casei, L. johnsonii JCM 2012, and L. plantarum ATCC 14917 have been shown to suppress IL-12 production through the TLR-2 pathway.[60] Peptidoglycan purified from the L. salivarius Ls33 has been reported to exhibit anti-inflammatory properties by inducing IL-10 production.[61] Numerous studies have also demonstrated that teichoic acid derived from various Lactobacillus spp. strains reduced IL-8 expression and exhibited immunomodulatory properties by inducing anti-inflammatory effects on human intestinal epithelial cells.[62,63] Collectively, these findings highlight the importance of bacterial cell lysates in supporting host immunity.

Cell surface proteins are protein-based structures located on the outer membrane of cell, which regulate cellular material exchange, mediate various signaling pathways, and facilitate cell-cell interactions. Among the cell surface proteins, structures such as the S-layer protein, mucin-binding proteins, fibronectin-binding proteins, and collagen-binding proteins play essential roles in the mechanisms and actions of bacteria.[10] These cell surface proteins which enable contact with the host organism, thereby activating specific signal transduction pathways. Consequently, the activation of these pathways results in the secretion of chemokines and cytokines, which mediate the immunomodulatory effects of the cell surface proteins.[13,40] In line with the findings of our study, a similar investigation involving Lactobacillus spp. strains reported that cell surface proteins increased the production of the anti-inflammatory cytokine IL-10 in the host organism, while suppressing the production of the pro-inflammatory cytokine TNF-α. Furthermore, it was noted that cell surface proteins also reduced the expression of the pro-inflammatory cytokine IL-8.[64]

In this study, microbiota-derived biotics have demonstrated potential as adjunctive treatments for periodontal disease due to their ability to modulate inflammatory responses. The integration of probiotic-derived anti-inflammatory agents into various products and their eventual translation into clinical practice present a promising prospect. Although biotic-integrated products have not yet been widely implemented in clinical settings, numerous examples exist of probiotics as their natural producers, being successfully incorporated into clinical formulations. For instance, probiotic strains have been integrated into oral care products, including lozenges and mouthwashes, demonstrating their potential to reduce periodontal inflammation and support oral health.[65,66] Additionally, probiotic-based toothpaste has been shown to target local periodontal tissues during routine oral care, potentially reducing inflammation as reported by Amizic et al.[67] The short-term use of *Bifidobacterium animalis* subsp. *lactis* DN-173010 has a positive effect on plaque accumulation and gingival inflammatory parameters, even without oral hygiene measures.[68] However, challenges related to the viability and stability of probiotics in commercial formulations remain a significant concern.[34] In this regard, integrating biotics into oral healthcare products may offer a more stable and effective alternative for their translation into clinical practice. Despite our promising findings, the clinical relevance of our study is limited by its reliance on a restricted cytokine analysis and *in vitro* experimental conditions. While *in vitro* models are essential for preliminary investigations, they do not fully replicate the complexity of periodontal disease *in vivo*. Additionally, the limited cytokine panel analyzed constrains our understanding of the broader immune response involved in periodontal inflammation. Therefore, although our findings suggest the potential therapeutic effects of biotics, these effects must be validated through

preclinical studies before translation into clinical practice. To address these limitations, future research should focus on evaluating biotics in *in vivo* models that more accurately mimic the clinical environment. Conducting animal studies with a broader range of biomarkers will provide more comprehensive insights into the therapeutic potential of biotics in periodontal disease.

Conclusion

Understanding the importance of the oral microbiota in oral health has paved the way for the use of microbiota-derived biotics in the management of periodontal diseases. Although developments in this area are still emerging, current knowledge suggests that postbiotics and paraprobiotics may serve as potential candidates for controlling periodontal tissue inflammation. This study investigated the effects of EPS-b, EPS-r, cell lysates, cell surface proteins, and inactive cells derived from L. plantarum EIR/IF-1 on the inflammatory cytokine response induced by P. gingivalis infection in hPDLF cells. The results revealed that the active compounds extracted from the EIR/IF-1 strain, when applied at non-toxic doses, effectively reduced inflammation induced by P. gingivalis LPS. These findings suggest that biotics containing biologically active and effective components can be developed as a natural and reliable approach to mitigate and prevent periodontal inflammation. The integration of postbiotics, with their unique metabolite profiles, and paraprobiotics, with their excellent biological activities, into dental products holds promising potential for the treatment of periodontal diseases. In conclusion, this study highlights the potential of microbiota-derived biotics to make significant contributions to the management of periodontal diseases.

Ethical Approval

Ethical approval was not required for this study, as it does not involve human or animal subjects.

Conflict of interest

The authors have no conflict of interest to declare.

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Authorship Contributions

Idea/Concept: F.K. Design: F.K., H.K.D. Control/Supervision: F.K. Literature Review: H.K.D., E.O.O. Data Collection and/or Processing: H.C. Analysis and/or Interpretation: H.C., H.K.D., E.O.O. Writing the Article: F.K. Critical Review: F.K.

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Relationship Between Surface Roughness and Colour Stability of Alkasite, Dual-Cure and Bulk-Fill Composites

Alkasit, Dual-Cure ve Bulk-Fill Kompozitlerin Yüzey Pürüzlülüğü ile Renk Stabilitesi Arasındaki İlişki

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ABSTRACT

Objectives: This study aims to investigate the surface roughness of four different restorative materials on polished and non-polished surfaces and assess its impact on color stability.

Materials and Methods: For the study, we utilized four distinct restorative materials: an alkasite, a nanohybrid composite resin, a dual-cure bulk-fill composite resin, and a posterior bulk-fill composite resin. For each composite resin, polished and non-polished samples were prepared. Following immersion in a coffee solution for a duration of 28 days, the color changes of all samples were assessed with a portable spectrophotometer at days 1, 7, 14, 21 and 28. Surface roughness (Ra) was evaluated using a conventional profilometer. Additionally, surface analyses were conducted for one sample from each group utilizing Atomic Force Microscopy (AFM) and Scanning Electron Microscopy (SEM). Statistical analyses were performed using the Kruskal-Wallis test, the Mann-Whitney U test, Bonferroni-corrected ANOVA and Pearson correlation analysis.

Results: Upon examining the ΔE values at the conclusion of the 28-day period, significant differences among the groups were observed. Cention N exhibited the greatest color change, while Fill-Up demonstrated the least. Notably, the surface roughness values differed significantly among the groups ($p<0.05$). Within the polished groups, Cention N exhibited the highest Ra value, while Filtek One Bulk Fill presented the lowest Ra value. In the samples finished with Mylar strip, Fill-Up showed the highest Ra value and Z 550 showed the lowest Ra value. No linear correlation was identified between the surface roughness and the discoloration of the composite resins.

Conclusion: When using acid neutralising ion-releasing alkasite composite, their disadvantage in terms of colouration and surface roughness should be taken into account.

Keywords: *Composite resin, Discoloration, Surface properties*

ÖZET

Amaç: Bu araştırma, dört farklı restoratif materyalin polisajlı ve polisajsız yüzeylerde pürüzlülüğünü incelemeyi ve bu pürüzlülüğün renk stabilitesi üzerindeki etkilerini değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntemler: Çalışma için bir alkasit, bir nanohibrit kompozit rezin, bir dualcure bulk-fill kompozit rezin ve bir posterior bulk-fill kompozit rezin dahil olmak üzere dört farklı restoratif materyal kullanıldı. Her bir kompozit rezin için polisajlı ve polisajsız örnekler hazırlandı. Tüm örnekler 28 gün boyunca kahve çözeltisinde bekletildikten sonra, renk değişimi değerleri taşınabilir spektrofotometre ile 1, 7, 14, 21 ve 28. günlerde ölçüldü. Yüzey pürüzlülüğünü değerlendirmek için geleneksel bir profilometre kullanıldı (Ra). Yüzey analizleri, her gruptan bir örnek için Atomik Kuvvet Mikroskobu ve Tarama Elektron Mikroskobu kullanılarak yapıldı. İstatistiksel analizler, Kruskal-Wallis testi, Mann-Whitney U testi, Bonferroni düzeltmeli ANOVA ve Pearson korelasyon analizi kullanılarak gerçekleştirilmiştir.

Bulgular: 28. günün sonunda ΔE değerleri incelendiğinde gruplar arasındaki fark anlamlı bulundu ($p<0.05$). Cention N en büyük renk değişimini, Fill-Up ise en az renk değişimini gösterdi. Yüzey pürüzlülüğü değerleri gruplar arasında önemli ölçüde farklıydı ($p<0.05$). Polisaj uygulanmış gruplarda, Cention N en yüksek Ra değerini, Filtek One Bulk Fill ise en düşük Ra değerini gösterdi. Mylar bant ile bitirilen örneklerde ise Fill-Up en yüksek Ra değerini, FZ ise en düşük Ra değerini gösterdi. Kompozit rezinlerin yüzey pürüzlülüğü ile renk değişimi arasında doğrudan bir ilişki bulunmamıştır.

Sonuç: Asidleri nötralize edici iyon salan alkasit kompozitler kullanıldığında, renklenme ve yüzey pürüzlülüğü dezavantajları dikkate alınmalıdır.

Anahtar Kelimeler: *Kompozit rezin, Renklenme, Yüzey özellikleri*

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Introduction

Currently, various types of composite resins are available which are biocompatible, mechanically robust, offering easy and rapid application and high polishability as well as improved aesthetic features.[1,2] Although aesthetic expectations of patients have been fulfilled owing to technical developments in the composite resin structure, restorative dental materials have a number of drawbacks including the requirement for layered placement, bonding failure, risk of gap formation and extended restoration time. In an effort to mitigate these drawbacks, various strategies have been employed, such as incorporating new monomers, advancing filler technology, enhancing translucency, and altering photoinitiator systems.[3] Thanks to these innovations, manufacturers have introduced composite materials that allow the placement of composites up to 4-5 mm thick in a single step, replacing the current technique, in order to simplify the composite restoration procedure and save time.[4] Bulk-fill composites have higher polymerization depths and translucency compared to conventional composite resins.[5]

Dual-cure bulk-fill composites that combine both chemical and light-cure technology have been designed to improve polymerization of bulk-fill composites that can be placed in thick layers. Dual polymerization can eliminate the limitations of light-curing and the need for layered placement.[6] Furthermore, dual-cure resin restorations produce a deeper polymerization and a higher degree of conversion due to the continued reaction after photoactivation.[7] Although composite resins are stable materials, they are associated with a number of shortcomings that limit their use including microleakage caused by polymerization shrinkage/incomplete polymerization, adhesive applications that require extreme technical precision, and cytotoxic effects of degradation in the dynamic oral environment. In an attempt to resolve these problems, researchers have worked to develop composite materials that can provide chemical adhesion with dental hard tissues as well as stimulate remineralization and recently, Alkasite-based dual-cure bulk-fill composite materials have been formulated.[8] Alkaline fillers increasing the release of acid-neutralizing ions are used in these composites.[9,10] Diverse properties imparted to the composite materials may lead to variations in the surface structure of composite resins and in their responses to aging factors. Discoloration is one of the most visible reflections of aging factors and can occur for various reasons.[11] The reasons are related to the characteristics of the composite encompassing resin matrix structure, matrix-particle interface and particle size and volume. Extrinsic causes of discoloration are poor oral hygiene, food and beverages consumed, smoking and occupational factors.[12,13]

Apart from color change, surface roughness is another important parameter for assessing restorative materials.[14,15] It has been claimed that a smooth restoration surface reduces plaque accumulation and delays discoloration.[11] However, there are mixed results from the literature for this claim.[16-18] This study aimed to examine the surface roughness and coloration of four structurally different composite materials to assess the impact of surface roughness on color stability Accordingly, the study tested three hypotheses. The first null hypothesis ($H0_1$) was that there would be no difference among composite materials in terms of discoloration. The second null hypothesis ($H0_2$) was there would be no difference among composite materials in terms of roughness. The third null hypothesis ($H0_3$) was that there is no linear relationship between discoloration and surface roughness.

Materials and Methods

Ethical approval for the study was secured from the Sivas Cumhuriyet University Ethics Committee for Non-Interventional Clinical Studies (Ethical approval no: 2019-08/12). Four different composite resins were used in this in vitro study including an alkasite (Cention N (CN) Ivoclar Vivadent, Schaan, Liechtenstein), a nanohybrid composite resin (Filtek Z550 (FZ), 3M ESPE, St. Paul, MN, USA), a dual-cure bulk-fill composite resin (Fill-Up (FU), Coltene Whaledent, CH), and a posterior bulk-fill composite resin (Filtek One Bulk Fill (FOB), 3M ESPE, St. Paul, MN, USA) (Table 1).

Table 1. Restorative materials used in the study

Material	Type	Content	Manufacturer	Particle Ratio (w/v)
Cention N	Alkasite	Liquid: Dimethacrylates (UDMA, Aromatic aliphatic UDMA), initiators, stabilizers Powder: Calcium-barium-aluminum fluorosilicate glass, calcium fluorosilicate glass, isofillers, ytterbium trifluoride, initiators and pigments (particle size 0.1-7 μm)	Ivoclar Vivadent, Schaan, Liechtenstein	78.4%/5.6%
Filtek Z550	Nanohybrid Composite Resin	Bis-GMA, UDMA, Bis-EMA, PEGDMA, TEGDMA, Zirconia/ Silica (0,1-10 μm), Modified silica particles (20 nm)	3M ESPE, St. Paul, MN, USA	81.8%/67.8%
Fill-Up	Flowable Bulk-fill	TMPTMA, UDMA, Bis- GMA, TEGDMA, Dental glass, methacrylate, amorphous silica, zinc oxide (particle size 2 μm)	COLTENE, Whaledent, CH	65%/49%
Filtek One Bulk Fill	Bulk-fill	AUDMA, UDMA, AFM, diurethane-DMA, (1,12-dodecane-DMA), Ytterbium Fluoride, EDMAB non-agglomerated/non-aggregated silica (20 nm) non-agglomerated/non-aggregated zirconia (4-11 nm) non-aggregated zirconia /silica cluster filler (20 nm silica and 4-11 nm zirconia particles) agglomerated 100 nm particles	3MM ESPE, St Paul, MN, USA	76.5%/58.5%

Preparation of Samples

Teflon molds (8 mm in diameter, 4 mm in depth) were used to prepare samples in standard sizes. Teflon molds separated by Mylar strip were placed on a glass coverslip. After packing the composite resins into the molds, Mylar strip and glass coverslip were placed again sequentially. Then, polymerization was performed using a LED Curing Light (Elipar DeepCure-S, 3M ESPE, St. Paul, MN, ABD) with a wavelength of 430 nm–480 nm and light intensity of 1470 mW/cm^2 in accordance with the manufacturer's guidelines. While bulk fill composites were inserted at a 4 mm thickness in a single step, the conventional composite was placed in 2 mm increments by light-curing. A total of 40 specimens were prepared from each restorative material, 20 specimens (polished; non-polished) to evaluate the colour change and 20 specimens (polished; non-polished) to evaluate the surface roughness (n=10). For polished groups surface standardization was achieved using 1000-grit silicon carbide sandpaper. Then, samples were polished using gray, green and pink-colored Astropol (Ivoclar Vivadent, Schaan, Lihtenştayn) rubbers respectively. Each rubber was applied to one surface of the samples for 30 seconds with the help of a micromotor at an average pressure, 10,000 rpm using light rotational motion and water to avoid heat generation and groove formation. All samples were washed under distilled water for 1 minute and kept in an oven at

37°C for 24 hours. Samples finished with Mylar strip were stored at 37°C for 24 hours without any surface treatment. Randomly one sample from the samples whose surface roughness was evaluated was used for SEM and AFM analyses.

Assessment of Color Changes

The coffee solution was prepared by mixing 3.6 g of coffee (Nescafe Gold Classic, Nestle, Turkey) with 300 ml of boiled distilled water for 10 minutes. After storing the samples in distilled water for 24 hours, the initial color measurements were taken and recorded as baseline values. Subsequently, over a 28-day period, the samples were kept in an oven (FN 400, Nüve, Turkey) at 37°C for 3 hours a day in the coffee solution and for the remaining 21 hours in distilled water. During this period, the coffee solution was freshly prepared and renewed daily. Before taking color measurements at all observation times (days 1, 7, 14, 21, and 28), the samples were rinsed under running tap water for 10 seconds and dried with drying paper.

A portable spectrophotometer, Vita Easyshade Advance (Vita Zahnfabrik, Bad Sackingen, Germany), was used for color measurements. Measurements were conducted by placing the measuring tip of the device on the center of the sample, at the same time of the day and at the same place. Each sample underwent three repeated measurements, and the average values were documented as L0, a0, and b0*. The device was recalibrated after every three measurements." The following formula was used to calculate ΔE values between two measurements according to the CIELAB color system: ΔE*= [(L1*-L0*)2+(a0*-a1*)2+(b0*-b1*)2]½

Surface Roughness Measurement and SEM and AFM Examination

Surface roughness measurements of the samples were performed using a profilometer (Mitutoyo Surftest/ SJ-301, Tokyo, Japan). Each sample was placed on the profilometer platform ensuring a contact angle of 90º with the reader tip. The surface evaluation length of the surface profilometer was set at 4 mm and the surface cut-off length at 0.25 mm. The profilometer was recalibrated before and after measurements for each group. Measurements were taken from three points on each sample and the average surface roughness (Ra) was calculated from the arithmetic mean of three readings.

Following surface roughness measurements, one sample from each group was evaluated under AFM (Park System, XE-100 E, Korea) and SEM device (Tescan MIRA3, Czech Republic).

Statistical Analysis

The study data were analyzed using the SPSS statistical software program (22.0 Version, Armonk, NY: IBM Corp). The normality of data distribution was assessed using the Kolmogorov-Smirnov test. The ΔE values of the groups were compared using the Kruskal-Wallis and Mann-Whitney U tests, while the surface roughness values of the groups were analyzed using ANOVA with Bonferroni correction. Pearson correlation analysis was performed to examine the relationship between color change and surface roughness values. The Type I error rate was set at 0.05.

Results

Color Change

The results for color changes were expressed as ΔE1 for color change on Day 1, ΔE2 for color change on Day 7, ΔE3 for color change on Day 14, ΔE4 for color change on Day 21 and ΔE5 for color change on Day 28. Looking at the ΔE values at the end of 28 days, CN exhibited the greatest color change, while FU demonstrated the least (Table 2). Pairwise comparison of color change values from examination days 1, 7, 14, 21 and 28 among polished FOB, FZ, FU and CN restorative materials demonstrated a statistically significant difference among the composites at these timepoints ($p<0.05$) (Table 2).

Table 2. Comparison of ΔE values by examination days for polished Filtek One Bulk Fill, Z550, Fill-Up and Cention N composite samples immersed in coffee

	N	Mean	Median	Min.	Max.	Result
ΔE1 Filtek One Bulk-Fill	10	0.91 ± 0.29[a]	0.90	4.56	0.97	KW=13.60
Z550	10	1.20 ± 0.84[a]	0.97	0.97	3.44	P=0.004*
Fill-Up	10	1.06 ± 0.38[a]	1.03	0.57	1.65	
Cention N	10	3.73 ± 1.44[b]	3.88	1.58	6.82	
ΔE2 Filtek One Bulk-Fill	10	2.07 ± 0.52[a]	1.97	1.20	2.82	KW=20.80
Z550	10	2.11 ± 0.78[a]	2.14	0.98	3.67	P=0.000*
Fill-Up	10	1.47 ± 0.41[a]	1.62	0.82	2.02	
Cention N	10	7.77 ± 3.23[b]	7.80	3.80	14.71	
ΔE3 Filtek One Bulk-Fill	10	5.53 ± 0.82[a]	5.77	3.86	6.49	KW=32.80
Z550	10	7.50 ± 0.69[b]	7.50	5.92	8.51	P=0.000*
Fill-Up	10	2.12 ± 1.03[c]	1.92	0.73	4.71	
Cention N	10	14.55 ± 4.08[d]	14.22	8.75	20.55	
ΔE4 Filtek One Bulk-Fill	10	5.44 ± 1.28[a]	5.09	3.71	7.85	KW=32.80
Z550	10	8.63 ± 0.92[b]	8.54	7.33	10.35	P=0.000*
Fill-Up	10	2.54 ± 0.72[c]	2.55	1.45	4.24	
Cention N	10	15.17 ± 5.62[d]	15.41	2.98	23.05	
ΔE5 Filtek One Bulk-Fill	10	6.71 ± 1.05[a]	6.74	5.05	8.38	KW=40.00
Z550	10	10.44 ± 0.87[b]	10.40	9.55	12.50	P=0.000*
Fill-Up	10	3.66 ± 1.57[c]	3.34	1.87	6.83	
Cention N	10	20.08 ± 4.56[d]	20.59	12.46	25.99	

*Kruskal-Wallis test and Mann-Whitney U test: Different letters indicate statistically significant difference between the groups on the same day.

When the color measurements of the composite groups at days 1 and 7 were compared in pairs, the differences were found to be significant for FOB versus CN, FZ versus CN and FU versus CN ($p<0.05$) but the differences between other groups were non-significant ($p>0.05$). Significant differences in color change values were observed in pairwise comparisons among all groups on days 14, 21, and 28($p<0.05$). For the non-polished composite samples (those finished with Mylar strip), the difference in color change values was significant at days 7, 14, 21 and 28 when compared in pairs ($p<0.05$) (Table 3). On days 7, 14, 21 and 28, the difference was significant for the comparison between FU and FOB, between FU and FZ and between FU and CN N ($p<0.05$), with no substantial difference among other groups ($p>0.05$).

Table 3. Comparison of ΔE values by examination days for non-polished (finished with Mylar strip) composite groups immersed in coffee

	N	Mean	Median	Min.	Max.	Result
ΔE1 Filtek One Bulk-Fill	10	2.23 ± 0.96[a]	2.37	0.67	4.07	KW=2.40
Z550	10	2.34 ± 1.22[a]	2.28	0.84	4.98	P=0.494
Fill-Up	10	1.56 ± 0.70[a]	1.47	0.76	2.55	
Cention N	10	10.25 ± 5.66[a]	8.70	1.27	19.58	
ΔE2 Filtek One Bulk-Fill	10	5.21 ± 2.04[a]	5.03	2.86	9.82	KW=8.80
Z550	10	5.49 ± 2.43[a]	4.79	2.09	9.17	P=0.032*
Fill-Up	10	2.58 ± 0.69[b]	2.51	1.64	3.94	
Cention N	10	24.09 ± 9.21[a]	20.47	14.07	42.91	
ΔE3 Filtek One Bulk-Fill	10	8.87 ± 2.98[a]	8.86	3.65	15.32	KW=12.80
Z550	10	12.42 ± 2.19[a]	12.05	9.28	17.04	P=0.005*
Fill-Up	10	4.47 ± 0.754[b]	4.32	3.45	5.76	
Cention N	10	32.70 ± 7.38[a]	31.55	21.84	43.64	
ΔE4 Filtek One Bulk-Fill	10	10.94 ± 3,40[a]	9.49	7.98	18.45	KW=16.80
Z550	10	13.91 ± 2.19[a]	13.57	10.75	17.49	P=0.001*
Fill-Up	10	6.06 ± 1.15[b]	5.95	4.53	8.18	

Cention N	10	36.68±10.07[a]	35.21	24.01	57.54	
ΔE5 Filtek One Bulk-Fill	10	13.25 ± 4.40[a]	11.94	7.75	21.02	KW=13.60
Z550	10	15.69 ± 1.90[a]	15.19	12.98	19.30	P=0.004*
Fill-Up	10	7.40 ± 1.51[b]	7.21	5.59	10.28	
Cention N	10	42.50±11.35[a]	42.10	25.51	63.06	

*Kruskal-Wallis test and Mann-Whitney U test: Different letters indicate statistically significant difference between the groups on the same day.

Table 4. Surface roughness (Ra) values of polished and unpolished (Finished with Mylar strip) samples

		N	Mean	Median	Min.	Max.	Result
Polished	Filtek One Bulk-Fill	10	0.21 ±0.11[a]	0.18	0.12	0.52	P=0.001*
	Z550	10	0.23 ±0.10[ab]	0.21	0.12	0.51	
	Fill-Up	10	0.44 ±0.23[b]	0.19	0.13	0.84	
	Cention N	10	2.00 ±1.13[b]	0.38	0.16	3.86	
Non-polished (Mylar strip)	Filtek One Bulk-fill	10	0.34 ±0.24[cd]	0.24	0.14	0.93	P=0.000*
	Z550	10	0.14 ±0.02[c]	0.14	0.11	0.20	
	Fill-Up	10	0.76 ±0.73[d]	0.38	0.15	2.08	
	Cention N	10	0.48 ±0.18[d]	0.45	0.26	0.93	

* Analysis of Variance, Bonferroni Correction: Different letters indicate a statistically significant difference between the groups. The difference among the polished composite groups is indicated with the letters a and b and the difference among non-polished groups is indicated with the letters c and d.

Evaluation of surface roughness values for polished and non-polished samples of each restorative material showed a non-significant difference (p>0.05) except for FZ (p=0.006). Greater Ra values were found for polished FZ samples (Table 5).

Table 5. Surface roughness (Ra) values of polished and non-polished samples of the restorative materials

		N	Mean	Med.	Min.	Max.	Result
Filtek One Bulk Fill	Polished	10	0.21 ± 0.11[a]	0.18	0.12	0.52	P=0.139
	Mylar strip	10	0.34 ± 0.24[a]	0.24	0.14	0.93	
Z550	Polished	10	0.23 ± 0.10[a]	0.21	0.12	0.51	P=0.006*
	Mylar strip	10	0.14 ± 0.02[b]	0.14	0.11	0.20	
Fill-Up	Polished	10	0.29 ± 0.23[a]	0.19	0.13	0.84	P=0.096
	Mylar strip	10	0.76 ± 0.73[a]	0.38	0.15	2.08	
Cention N	Polished	10	0.85 ± 1.13[a]	0.38	0.16	3.86	P=0.762
	Mylar strip	10	0.48 ± 0.18[a]	0.45	0.26	0.93	

* Analysis of Variance, Bonferroni Correction: Different letters indicate a statistically significant difference between polished and non-polished subgroups of each composite group.

Pearson correlation test did not show a correlation between the surface roughness values and color change values of polished and non-polished groups (p>0.05) (Table 6).

Table 6. Correlation between surface roughness values and color change values of polished and finished with Mylar strip composite resins

Composite	Correlation	N	Mean	Result
Filtek One Bulk Fill	ΔE	10	6.71 ± 1.05	P=0.623
	Polished ΔRa	10	0.17 ± 0.02	
Z550	ΔE	10	10.44 ± 0.87	P=0.643
	Polished ΔRa	10	0.20 ± 0.08	
Fill-Up	ΔE	10	3.66 ± 1.57	P=0.120
	Polished ΔRa	10	0.42 ± 0.56	
Cention N	ΔE	10	0.08 ± 4.56	P=0.225
	Polished ΔRa	10	2.17 ± 4.39	
Filtek One Bulk Fill (Mylar strip)	ΔE	10	13.25 ± 4.40	P=.820
	Non-polished ΔRa	10	0.19 ± 0.06	
Z550 (Mylar strip)	ΔE	10	15.69 ± 1.90	P=.496
	Non-polished ΔRa	10	0.55 ± 0.67	
Fill-Up (Mylar strip)	ΔE	10	7.40 ± 1.51	P=.532
	Non-polished ΔRa	10	0.42 ± 0.12	
Cention N (Mylar strip)	ΔE	10	42.50 ±11.35	P=.991
	Non-polished ΔRa	10	0.68 ± 0.37	

* Pearson correlation test did not show a correlation

On AFM analysis, Average of Ra values (nm) obtained from three separate 10×10 µm scanning areas (Polished-Mylar Strip); FOB 19.228 – 18.348 nm, FZ 32.580 - 27,530 nm, FU 57,272 - 100,730 nm, CN 68,715 - 138,015 (Figure 2; A, B, C, D, E, F, G, H). For CN (Figure; G,H), deep grooves and irregularities were observed on the surface of non-polished groups and medium level surface irregularities were seen in polished groups. SEM images were in line with profilometer and AFM findings (Figure 1; A, B, C, D).

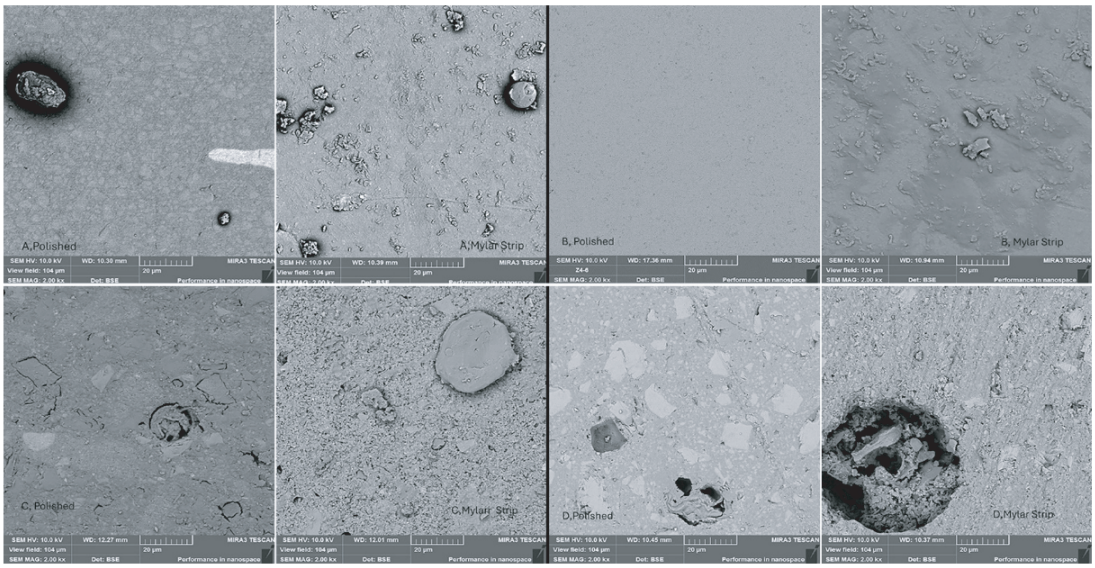

Figure 1, A: Filtek One Bulk-Fill polished and Mylar strip; B: Z550 polished and Mylar strip; C: Cention N polished and Mylar strip; D: Fill-Up polished and Mylar strip

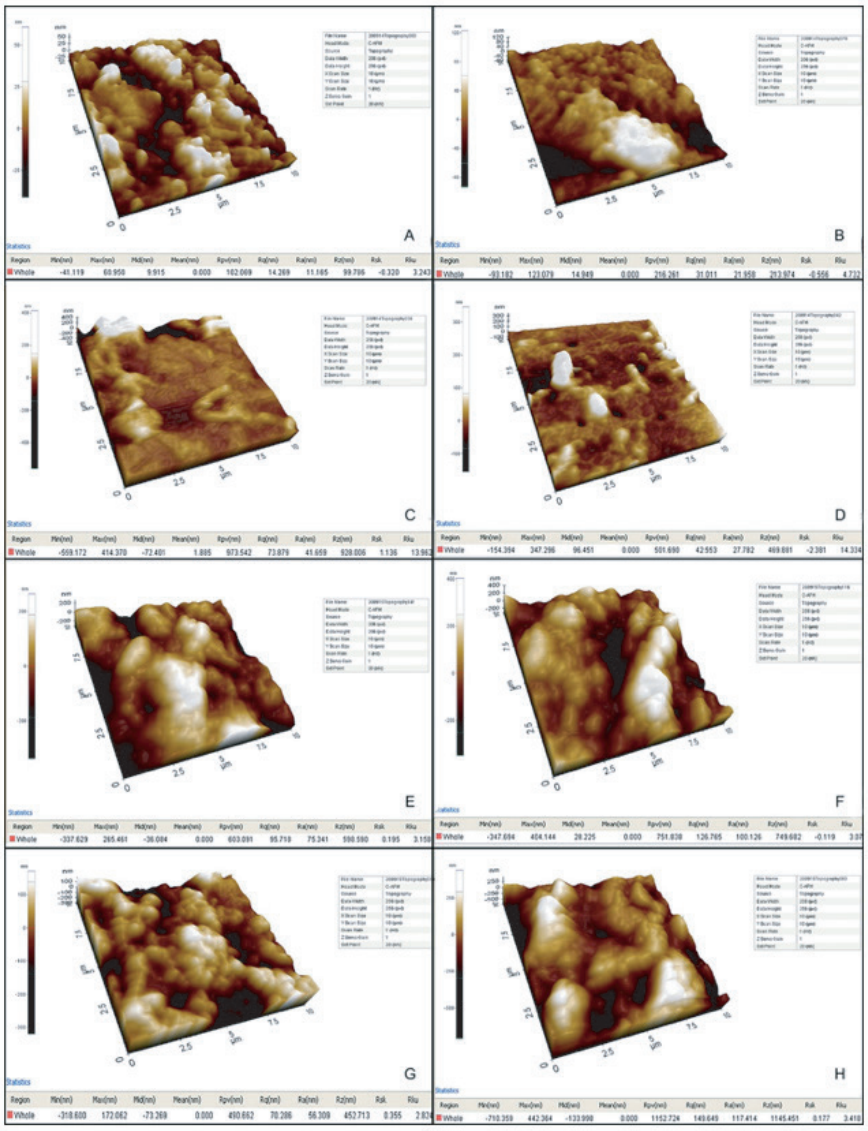

Figure2, A: Filtek One Bulk-Fill polished; B: Filtek One Bulk-Fill Mylar strip; C: Z 550 polished; D: Z 550 Mylar strip; E: Fill-UP polished; F: Fill-Up Mylar strip; G: Cention N polished; H: Cention N Mylar strip

Discussion

Discoloration that occurs in composite resin restorations over time is one of the primary causes for replacing dental restorations.[19] Many factors can affect the process of discoloration in composite materials, including resin matrix structure, incomplete polymerization, water absorption, foods and drinks, oral hygiene and surface roughness.[20]

Water absorption predominantly takes place directly within the resin matrix. In contrast, filler particles cannot absorb water but adsorb water on their surfaces. This causes more water absorption, resulting in a lower adhesion between the composite resin matrix and filler particles.[21] Water absorption by the resin matrix may lead to expansion and plasticization of the resin composition, hydrolysis of silane and microcrack formation. Penetration of coloring agents between the filler and matrix may cause discoloration.[22] Coffee contains water-soluble dyes, tannic acid, caffeine, phenolic acid and chlorogenic acid. The low polarity of the composite resin leads to increased adsorption and dye penetration by coffee pigments. Thus, coffee stains cannot be removed easily by brushing or polishing.[23]

There is no consensus on whether the resin structure or surface roughness accounts for discoloration of composite resins.[24,25] In our study, staining of composite resins, surface roughness and their correlation were investigated to find an answer to this question. Based on our findings, the first null hypothesis of our study "There would be no difference among composite materials in terms of discoloration" was rejected. According to the color changes of the polished and Mylar strip-finished groups immersed in the coffee solution, the materials were ranked in the greatest order and the lowest staining for all days: CN > FZ > FOB > FU.

CN was the only material that exceeded the clinically acceptable limit of 3.3 in ΔE values on Day 1[21]. It has been reported that the greatest color change observed in CN may be explained by the fact that 12-40% of the final matrix may show monomer leakage and also, fluoride release from the material may account for discoloration.[26,27] Günülol et al.[28] reported that a fluoride-releasing composite showed significantly higher water absorption and color change (ΔE) values compared to other materials. They stated that fluoride release from a restorative material depends on water diffusion capacity, which can result in degradation of the material's chemical structure and matrix bonds and matrix bonds of the material and the release of residual monomers. In a study by Park et al.[29] evaluating polymerization of fluoride-containing composites, it was suggested that dissociation of filler particles due to fluoride release may create gaps on the composite surface which may then cause a reduction in surface microhardness.

In line with our findings, some studies have reported a high level of staining for CN.[26,30] Amalavathy et al. suggested that this may be related to acidity of beverages or ion exchange activity on the sample surface.[31] Tannic acid found in coffee has phenolic hydroxy structures and the polyphenolic end groups of tannic acid are highly favorable for hydrogen bonding. [27] The highest ΔE value observed with CN can be ascribed to the formation of hydrogen bonds between tannic acid and the fluorosilicate compounds in CN.[32]

François et al.[30] reported a significant degradation in highly reactive calcium fluorosilicate glass fillers under acidic conditions due to acid attack. We think that the organic acids in coffee may cause degradation of filler glass particles[33, 34] and over time, cracks may occur at the resin-filler interface, weakening the material and further increasing surface roughness and discoloration.[35-37]

In our study, CN, FZ and FOB were the materials with the greatest color alteration. Analysis of the polished samples immersed in coffee solution showed a significant difference among the materials at day 14, which was also observed at other timepoints. At day 28, average ΔE values were 10.40 for FZ and 6.71 for FOB., Although the statistical analysis revealed no significant differences among the non-polished samples, FZ showed greater ΔE values than FOB at all examination days. Bis-GMA and TEGDMA monomers found in the resin matrix

are hydrophilic, whereas UDMA is hydrophobic. Therefore, the UDMA monomer is more resistant to color changes. Bis-GMA has a higher water absorption capacity compared to UDMA and Bis-EMA.[38] We posit that the monomer structure of FZ contributed to these observed findings.

In their study examining the long-term water absorption and solubility of composite resins with different structures, Alshabib et al.[39] reported that FOB showed low water absorption, which was attributed to UDMA found in the material.

In our study, FU, a medium-viscosity dual-cure bulk-fill composite showed the lowest ΔE values. It was also the only material that did not exceed the clinically acceptable ΔE limit at day 21. In contrast to our findings, the greatest staining was found in the FU group in a study by Freitas et al.[40] evaluating bulk-fill (Filtek Bulk Posteior, FU) and microhybrid (Filtek Z250) composites immersed in coffee solution after polishing; however, they did not observe a difference in discoloration among FU, Filtek Z250 and Filtek Bulk Fill Posterior with one of the polishing protocols they used.[18]

In a study by Monterubbianesi et al.[41] investigating the degree of monomer conversion of bulk-fill composites, they applied FU in one increment at a thickness of 4 mm, followed by light-curing with Elipar S10. Measurements taken from the bottom surface of the material after 24 hours showed that the extent of monomer conversion was 94.71% for this material. The high color stability of FU as observed in our study may be connected to the high extent of monomer conversion.

Surface roughness one of the key factors affecting the success of a restoration.[42,43] Surface roughness of the resin materials is affected by the type of monomers in their composition, the size and shape of fillers, the quality of adhesion to matrix and the depth of polymerization.[44] Based on our findings, the second null hypothesis of the study, "There would be no difference among composite materials in terms of roughness" was rejected. The rank order of surface roughness was CN > FU> FZ> FOB for the polished groups, whereas it was FU > CN> FOB> FZ for the non-polished groups.

The least surface roughness (Ra) values were observed in FOB and FZ. Consistently, low surface roughness was reported for FZ[45] and FOB[46,47] in three separate studies. However, the observation of the lowest Ra values in polished samples of FOB in contrast to non-polished samples of FZ in our study is noteworthy. These two composite resins have a similar inorganic structure but FZ is a nanohybrid material with a particle size ranging from 0.1 to 10 μm (mean 0.02 μm).[48] FOB contains 100 nm agglomerate ytterbium trifluoride to enhance the contrast of X-rays.[49] In addition to nanomer structures, FOB contains nanoclusters which are composed of loosely bound, nano-scale inorganic fillers and can be abraded without breaking off from the surface during polishing.[41,44] On the other hand, for FZ, larger particles may have detached from the surface during polishing and increased the Ra value. This may explain the small, non-significant difference in terms of surface roughness. Although both composite resins displayed a homogenous and smooth surface on SEM and AFM (Figure1;A,B. Figure 2;A,B,D,E) images, there were also scratches from the polishing process.

Greater surface roughness observed on both polished and non-polished composite surfaces of FU compared to the two a forementioned composites may be related to the larger particle size of fillers in FU. In order to achieve application of the composites in 4 mm thick layers, fillers with large particle size were used by increasing translucency.[50] Reduced size and increased volume of the particles result in less interparticle spacing, which protects the resin matrix during the polishing process and makes it difficult for the filler to detach from the surface.[51] FU (49%) has a lower filler volume compared to FZ and FOB (67.8% and 58.5% respectively) as well as larger filler particle size and irregular particle shape, all contributing to its higher roughness values.[52] On SEM images (Figure 1;D), traces of polishing rubbers and gaps created by the glass particles breaking off from the surface during polishing were observed.

AFM images (Figure2; E, F) showed deep slits and surface irregularities. FU cannot be applied as easily as light-cured composites and hardens without obtaining a perfectly smooth surface. We consider that the high surface roughness of FU is also associated with the difficulty of manipulation. While polishing after polymerization reduced the surface roughness of FU, it could not reach the Ra values of FOB and FZ. Paolone et al.[53] investigated surface roughness of four distinct bulk fill composites finished with different polishing systems and found that FU had the greatest surface roughness in each polishing group. The authors suggested that high Ra values of FU may be related to its large particle size (2 μm) and low filler content (65% by weight, 49% by volume).

CN was the other material showing a higher surface roughness in our study. Studies by Naz et al.[54] and Setty et al.[55] support our findings. This may have resulted from the large and irregularly shaped fillers of CN (0.1 to 7 μm) and the difficulty of inserting it into the cavity. On SEM images (Figure 1; C), non-polished samples of this composite showed an uneven surface appearance and small pits were observed in polished samples due to the particles detached from the surface.

With our findings, the third null hypothesis of our study "There is no linear relationship between discoloration and surface roughness" was accepted. Lu et al.[17] stated that surface roughness may not always be positively correlated with staining, and that surface roughness values below 0.1 μm (100 nm) have no effect on color stability. Öztürk et al.[25] did not find a correlation between color stability and 3D surface topography analysis and suggested that this may be related to the use of a different methodology and equipment.

Conclusions

In this in vitro study, based on the findings of high discoloration and roughness observed in alkasite samples, we conclude that these materials cannot be considered as viable alternatives to nano-filled composites. Considering the superior color stability of dual-cure composites, they are recommended for effective polymerization, particularly in the restoration of cavities where light penetration is challenging. However, the limited shade options and difficulties in cavity application are noted as significant disadvantages of these materials. In our study, no correlation was found between the surface roughness and discoloration of composite resins. The differences observed among the ΔE values of the materials may be attributed more to the composition of the resins rather than surface roughness.

Ethical Approval

Ethical approval for the study was obtained from the Sivas Cumhuriyet University Ethics Committee for Non-Interventional Clinical Studies. (Ethical approval no: 2019-08/12).

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Conflict of Interest Statement

The authors declare no conflicts of interest

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What Did We Learn About The Covid-19 Pandemic? Covid-19 Pandemisinden Neler Öğrendik?

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ABSTRACT

Objectives: This cross-sectional study aimed to assess the perception of COVID-19 and the awareness of necessary precautionary measures, including knowledge of symptoms, modes of transmission, preventive strategies, and methods of obtaining accurate, up-to-date information about these topics among Turkish dental staff.

Materials and Methods: An online survey consisting of 41 questions was conducted via Google Forms® from November 2, 2022, to January 10, 2023, targeting Turkish dental staff. The responses were entered into and analysed using SPSS version 22. The Chi-square test was applied, with a significance level set at $p<0.05$.

Results: A total of 448 dental workers participated, including 239 (53.3%) dentists and 209 (46.7%) auxiliary dental staff. Participants were asked about various precautionary measures against COVID-19, with the majority providing correct answers. However, only 31.5% of participants correctly identified the proper sequence for wearing Personal Protective Equipment (PPE) according to Centres for Disease Control and Prevention (CDC) guidelines, while 60.3% accurately described the sequence for removal. Among both professional and auxiliary staff, N95/FFP2 masks were considered the most protective, with 75.7% and 78.9% selecting them, respectively.

Conclusion: Dentists mainly reported gaining knowledge about COVID-19 through formal training provided by their institutions, whereas auxiliary staff tended to rely more on information from social media. In general, participants showed a good understanding of the required preventive measures. However, there is a need for more accurate and current institutional training to fill the gaps in knowledge regarding specific protocols.

Keywords: *Behavioral sciences, Dental staff, Educational measurement, Global health, Training support.*

ÖZET

Amaç: Bu kesitsel çalışmanın amacı, Türk diş hekimliği personeli arasında COVID-19 algısını ve COVID-19'a karşı gerekli önleyici tedbirlere ilişkin farkındalığı, semptomlara ilişkin bilgiyi, bulaşma yollarını, önleyici tedbirleri ve güncel doğru bilgi edinme yöntemini incelemektir.

Gereç ve Yöntemler: Google Forms Inc® üzerinden çevrimiçi bir anket (41 soru) yapıldı. Anket, 2 Kasım 2022 ile 10 Ocak 2023 tarihleri arasında Türk diş hekimliği personeli arasında gerçekleştirildi. Elde edilen yanıtlar SPSS 22 sürümüne girilerek ve analiz edilmiştir. Ki-kare testi uygulanarak $p<0,05$ olarak elde edilmiştir.

Bulgular: Çalışmamıza 239'u (%53,3) diş hekimi, 209'u (%46,7) diş hekimliği yardımcı personeli olmak üzere toplam 448 diş hekimliği personeli katılmıştır. Katılımcılara COVID-19'a karşı alınması gereken bazı önlemler sorulmuştur ve çoğunluğu doğru yanıtlar vermiştir. Ancak, Hastalık Kontrol ve Önleme Merkezi (CDC) yönergelerine göre Kişisel Koruyucu Ekipmanın (KKD) doğru takılma sırasını katılımcıların yalnızca %31,5'I doğru olarak bilirken, %60,3'ü çıkarma sırasını doğru bir şekilde bilmiştir. Diş hekimleri ve diş hekimliği yardımcı personeli arasında sırasıyla %75,7 ve %78,9 oranında N95/FFP2 maskenin en iyi koruyucu maske olduğu düşünülmüştür.

Sonuç: Diş hekimleri, COVID-19 hakkında çoğunlukla kurumsal eğitimlerden bilgi edindiklerini belirtirken, diş hekimliği yardımcı personeli bilgilerini genellikle sosyal medya üzerinden aldıklarını ifade etmiştir. Katılımcılar, COVID-19'a karşı alınması gereken önleyici tedbirler konusunda yeterli bir farkındalığa sahip olduklarını göstermiştir. Ancak, bazı protokollerdeki bilgi eksikliklerinin giderilmesi için kurumsal eğitimlerde daha doğru ve güncel bilgiler verilmesi gerektiği vurgulanmıştır.

Anahtar Kelimeler: *Davranış bilimleri, Diş hekimliği personeli, Eğitimsel ölçüm, Küresel sağlık, Alıştırma desteği.*

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Introduction

The dangerous and deadly disease known as the 2019 novel coronavirus (COVID-19), or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which emerged in December 2019 in Wuhan, China, has caused widespread confirmed cases worldwide and triggered a pandemic that has resulted in an international public health disaster.[1-3] This pandemic rapidly became a significant and challenging public health issue for countries around the world.3 On January 30, 2020, the World Health Organization (WHO) declared the outbreak a public health emergency of international concern, and on March 11, 2020, it officially declared the disease a pandemic.[4]

In dental hospitals, healthcare practitioners were considered to be at an elevated risk of cross-infection compared to other hospital staff and patients.[5] As a result, strict infection prevention measures for dental clinics and healthcare facilities in areas affected by COVID-19 were implemented to prevent cross-infection.[6] The goal was to control the spread of COVID-19 through guidelines set by international organizations such as the Centers for Disease Control and Prevention (CDC)[7] and the WHO.[8] Similar to other cross-infections, these guidelines include the use of personal protective equipment, hand hygiene, clinical disinfection, cleaning of contact surfaces, and thorough patient evaluation upon entering the clinic. Studies have emphasized that the transmission route of COVID-19 primarily occurs through aerosol particles in the air, making healthcare workers and hospital personnel particularly vulnerable to the virus.[9]

In this context, it is crucial for healthcare personnel working in dental hospitals to be well-informed about the infection control measures and to adhere to these protocols to control the transmission of the virus during the COVID-19 pandemic.[8,10]

The aim of this survey study was to assess the awareness of dentists and auxiliary dental staff—who have direct patient contact—regarding the precautions necessary to mitigate the risk of COVID-19 transmission. The null hypothesis posits that dentists have a greater awareness of precautions against virus transmission compared to auxiliary staff.

Materials and Methods

Ethical approval was obtained from the Ethical Committee of Yeni Yuzyil University (2021/01-563). The survey used for data collection in the present article, which evaluates the knowledge of the precautionary measures required to prevent the transmission of COVID-19 for the actively working dentists and dental staff working face to face with patients in the dental hospital, is composed of a total of 41 questions. Survey questions were prepared by conducting a systematic literature review on the clinical features, transmission routes and treatment methods of COVID-19 in online databases. In the first three questions in the first part of the questionnaire, demographic information including age, gender and educational level of the participants is questioned. The remaining 38 questions in our survey question the participants' information, attitude, and anxiety about COVID-19 and its means of transmission, and the practices they have taken to take precautions in this regard.

Table 1. Study groups used in the study

Group		n	Total n	Total %
Professional Dental Staff (Dentists)	Graduated	158	239	53.3
	Undergraduated	85		
Auxiliary Dental Staff (Dental Assistant, Dental Technician)	Graduated	104	209	46.7
	Undergraduated	105		

Survey participants were determined as professional dental staff and auxiliary dental staff. A percentage of 62.3 of the respondents were female and 37.7% were male. 58.7% of the participants were between 18-25, 24.3% were between 25-35, 10.7% were between 35-45, and 5.3% were over 45 years old. While 46.7% of the participants were composed of auxiliary dental staff, 53.3% were professional dental staff. A percentage of 23.5 of the participants consisted of undergraduate auxiliary dental staff, 23.2% were graduated auxiliary dental staff working in their field. While 16.1% of the participants were undergraduates of the faculty of dentistry, 37.3% consisted of graduated dentists. Both groups were divided into two subgroups as shown in Table 1. This survey study was conducted online between 02 November 2022 and 10 January 2023 via a link sent to the participants. Attention was paid to the fact that the participants in the survey were from various cities of Turkey. The answers to our questionnaire were collected by the transmission of data in online databases.

Statistical analysis

While evaluating the data gathered in the study, IBM SPSS Statistics Version 22.0 (IBM SPSS, Turkey) program was employed for statistical analysis. The study data were assessed using Chi-Square test was used to compare qualitative variables, alongside descriptive statistical methods (mean, standard deviation, frequency). Statistical significance was determined at the $p<0.05$ level. In addition, as a result of the pilot study, the reliability study of the questionnaire was executed, and the Cronbach alpha value was found to be 0.862. Thus, it has been observed that the study method is reliable.

Results

It has been observed that the rate of those who think that the main transmission route of Covid-19 is by droplet route ($p=0.001$) and sneezing ($p=0.005$) is statistically higher in the professional group than the auxiliary dental staff. It has been seen that both professional and auxiliary dental staff groups feel under high risk for COVID-19, however the rate of concern was found to be higher in the professional groups. Details about surface disinfection method preferences according to each group to be used after every dental patient are given in Table 2.

Table 2. Preferred effective disinfection method for the Coronavirus in the Auxiliary and Professional Dental Staff groups

	Auxiliary Dental Staff		Professional Dental Staff		Total		
	n	%	n	%	n	%	p
Using alcohol-based disinfectants	99	47.4%	100	41.8%	199	44.4%	0.049
No idea	12	5.7%	5	2.1%	17	3.8%	
None of them	0	0.0%	3	1.3%	3	0.7%	
Washing with soap	57	27.3%	68	28.5%	125	27.9%	
Disinfection with solutions containing sodium hypochlorite	41	19.6%	63	26.4%	104	23.2%	

All groups agreed that the combination of N95 + surgical mask + goggles + face shield + gloves was more effective against contamination of COVID-19. For patients exhibiting COVID-19 symptoms, most participants from both professional and auxiliary dental staff preferred to request a COVID-19 test and initiate treatment 14 days after receiving a negative result. Auxiliary dental staff were more confident than professional staff in the effectiveness of precautions taken to prevent cross-infection between treatment rooms and the laboratory in their institution (Table 3). Both auxiliary and professional dental staff believe that the

3-ply surgical mask is not enough for dental procedures while N95/FFP2 is more reliable. On the other hand, although the N99/FFP3 mask was another option in the same question, only a small percentage in both professional (36%) and auxiliary (24.4%) dental staff preferred this option (Table 4). The correct order for putting on and removing personal protective garments is given in Table 5 and 6 respectively.

Table 3. Effectiveness of precautions taken to prevent cross-infections according to Auxiliary and Professional Dental Staff

	Auxiliary Dental Staff		Professional Dental Staff		Total		
	n	%	n	%	n	%	p
Definitely disagree	5	2.4%	13	5.4%	18	4.0%	0.007
Agree	10	4.8%	33	13.8%	43	9.6%	
Not sure	58	27.8%	57	23.8%	115	25.7%	
Agree	99	47.4%	103	43.1%	202	45.1%	
Definitely agree	37	17.7%	33	13.8%	70	15.6%	

Table 4. Most effective mask according to Auxiliary and Professional Dental Staff

	Auxiliary Dental Staff				Professional Dental Staff				
	No		Yes		No		Yes		
	n	%	n	%	n	%	n	%	p
N95 / FFP2	44	21.1%	165	78.9%	58	24.3%	181	75.7%	0.418
N99 / FFP3	158	75.6%	51	24.4%	153	64.0%	86	36.0%	0.008
Surgical Mask	187	89.5%	22	10.5%	227	95.0%	12	5.0%	0.044
Medical Mask	204	97.6%	5	2.4%	237	99.2%	2	0.8%	0.259
Cloth/Fabric Mask	208	99.5%	1	0.5%	236	98.7%	3	1.3%	0.627

Auxiliary dental staff believe that the strategies employed by the institution are sufficient to protect the professional and auxiliary dental staff, patients and institutional personnel (secretary/cleaning staff/security personnel), from COVID-19. However, the professional dental staff agreed only that themselves and their patients were adequately protected while they felt undecided about whether the institutional personnel, auxiliary dental staff were adequately protected. The data from this study demonstrated that dental professionals get information about COVID-19 from the institutional training courses while auxiliary dental staff prefer information social media.

Table 5. Correct order of wearing personel prootective equipment according to Auxiliary and Professional Dental Staff

	Auxiliary Dental Staff		Professional Dental Staff		Total		
	n	%	n	%	n	%	p
Gloves - Gown - Mask - Goggles/Face Shield	51	24.4%	43	18.0%	94	21.0%	0.370
Mask - Goggles/Face Shield - Gloves - Gown	27	12.9%	30	12.6%	57	12.7%	
Mask - Gown - Goggles/Face Shield - Gloves	67	32.1%	89	37.2%	156	34.8%	
Gown - Mask – Goggles/Face Shields - Gloves	64	30.6%	77	32.2%	141	31.5%	

Table 6. Correct order of removing personel protective equipment according to Auxiliary and Professional Dental Staff

	Auxiliary Dental Staff		Professional Dental Staff		Total		
	n	%	n	%	n	%	p
Gloves-Goggles/Face Shield-Gown-Mask	123	58.9%	147	61.5%	270	60.3%	0.023
Goggles/Face Shield-Gown-Mask-Gloves	27	12.9%	48	20.1%	75	16.7%	
Mask-Goggles/FaceShield-Gloves-Gown	21	10.0%	11	4.6%	32	7.1%	
Gown-Goggles/Face Shield-Mask-Gloves	38	18.2%	33	13.8%	71	15.8%	

Discussion

COVID-19 marks the first pandemic in history where technology and social media have been extensively utilized to ensure public safety and disseminate information. However, this widespread use has also contributed to the escalation of an infodemic. WHO refers to an infodemic as an excessive volume of information, which includes intentional efforts to spread misinformation that undermines public health responses.[11,12]

In the present study, 77.2% of the dental staff who participated in the survey reported that N95/FFP2 masks should be preferred for the use of masks related to COVID-19 precautions, while only 30.6% thought that N99/FFP3 masks should be preferred. It has been observed that a big percentage of the dental staff prefer to use N95 masks instead of N99 masks. However, as it is known, N99/FFP3 masks provide approximately 99% protection in terms of viral protection, while this rate is only around 95% for N95/FFP2 masks.[13] Although the 99% and 95% protection rates against COVID-19 are both high and similar, many people, including dental staff, believe that N95/FFP2 masks offer better protection due to a lack of information and unclear guidelines. This may be because the Ministry of Health's guidelines, as well as information in social media and the press, mainly mention N95 masks. As a result, dental staff may not have enough knowledge about N99 masks, especially if this information is not included in some institutional training programs. Although they provide a percentage of less protection than N99/FFP3 masks, the superiority of N95/FFP2 masks over surgical and fabric masks should not be overlooked. In a previous study it has been indicated that N95 masks had maximum efficacy, especially when used continuously[14]. According to the survey results, 7.6% of participants preferred surgical masks for professional dentistry approaches, while only 0.9% chose fabric masks. Almost all dental staff are aware that surgical and fabric masks provide less protection than N95 masks. According to the statements published by the CDC[15], the order of wearing personal protective equipment is specified as: Gown-Mask-Glasses/Face Shield-Gloves. In the present survey study, the results emphasized that 37.2% of

the professional dental staff and 32.1% of the auxiliary dental staff believe that the correct order of removal of protective equipment was Mask-Gown-Goggles/Face Shield-Gloves. However, the rate of knowing the correct order of wearing the protective equipment (Gown-Mask-Glasses/Face Shield-Gloves) was observed as only 32.2% in the professional dental staff group and 30.6% in the auxiliary dental staff group. Although the results are similar, both professional and auxiliary dental staff were found to lack accurate knowledge of the correct order for wearing personal protective equipment. This may be due to a misunderstanding, as masks have become a routine part of daily life, leading to less attention to proper usage. Again, according to the declarations published by CDC[15], the order of removing personal protective equipment is specified as Gloves-Goggles/Face Shield-Gown-Mask. As demonstrated by the current study, 61.5% of the professional dental staff and 58.9% of the auxiliary dental staff answered the question about the sequence of removal of the protective garments correctly. However, about 40% of both professional and auxiliary dental staff do not know the correct sequence for removing personal protective equipment. The findings suggest that the removal sequence is better understood than the wearing sequence. Although dental staff may sometimes overlook these procedures, following the correct order for putting on and taking off protective equipment plays a crucial role in preventing both direct and cross-contamination of COVID-19. For this reason, knowing the order of wearing and removing this equipment is a matter to be considered in the fight against COVID-19 infection. It is believed that healthcare professionals should receive more training and information on this topic. A previous study by Zaheer et al.[16] found that only 18.6% of healthcare professionals knew the correct order for wearing personal protective equipment, whereas this rate was 31.5% in the present study. This suggests that dental staff in Turkey follow the correct procedures for wearing personal protective equipment more accurately than healthcare professionals in Pakistan.[16] However, the present study was completed in January 2022, approximately 21 months later than the study of Zaheer et al. For this reason, higher results may have been obtained compared to the study of Zaheer et al, perhaps due to the increased knowledge of health personnel about the pandemic and the increased frequency of personal protective equipment use. In the same study by Zaheer et al, the correct application rate of personal protective equipment removal procedures was determined as 59%.[16] In the present study, a similar rate was found (60.3%). Surface contamination with the virus has been linked to the transmission of infection. Dental professionals, particularly those performing aerosol-generating procedures, are at high risk of exposure, and these procedures should be avoided whenever possible. For essential procedures, appropriate protective attire must be worn, high-volume evacuation suction and dental dams should be used, and thorough disinfection should follow.[17] Surface decontamination can be achieved with 0.1% sodium hypochlorite or 62%-71% ethanol for one minute.[17] The results of the current questionnaire showed that approximately 81.9% of respondents agreed that dental dams should be used during procedures. Additionally, participants agreed that disinfection after each patient should be performed using alcohol-based disinfectants (44.4%) or sodium hypochlorite solutions (23.2%).

In a survey study conducted by Quadri et al. and published in May 2020, it was found that 90.1% of respondents recognized sneezing as a symptom of COVID-19.[18] This supports the findings of our study, where 84.2% of participants identified sneezing as a sign of COVID-19. Findings of a previous survey study conducted by Khader et al.[5] on dentists, as the response to the question of what the symptoms of COVID-19 are, being fever (98.6%), cough (91.0%), shortness of breath (85.9%), were similar to the finding of the present study as fever (% 98) and cough (93.1%), etc. These rates are almost identical to the findings of the present study. In the same study by Khader et al. [5], coughing (90.5%) and hand contact (85.6%) were identified as the most common transmission routes of COVID-19, which aligns with the findings of the present study. Therefore, it can be concluded that certain COVID-19 symptoms are universally recognized due to the

increased awareness brought by the pandemic. In accordance with the collected data of the present study it can be advocated that dental staff generally seem to have sufficient knowledge about COVID-19 symptoms and transmission routes. While it is noticeable that there is no deficiency in general-valid information, it has been determined that there are deficiencies in some clinical applications.

Based on the results of this study, it can be inferred that nearly half of the dental staff believe that the precautions taken in Turkey are not the same as those in other parts of the world. They also feel that adequate measures have not been implemented to protect dentists, auxiliary dental staff, hospital staff, and patients, leading to fear and uncertainty about the pandemic.

Results of the present research demonstrated that the auxiliary dental staff mainly benefit from social media to obtain insights into COVID-19. This could serve as the reason for auxiliary dental staff to have adequate knowledge about the mode of transmission of COVID-19 but not all the preventive measures. Being dependent on social media may end up with incorrect or misleading information about COVID-19.[19] This is observed to cause more confidence in the auxiliary dental staff when compared to the professional dental staff. The higher confidence level and believe that they are protected against the virus in the auxiliary dental staff can be a result of deficient knowledge. Less to know is causing less stress in this case. This result is controversy to the result of a previous study in which it has been concluded that erroneous and deceptive information, coupled with a lack of knowledge, can contribute to increased anxiety and resistance to implemented measures.[19]
Prior investigations carried out in both the general population and among healthcare professionals have demonstrated that higher levels of training and work experience are correlated with increased knowledge of COVID-19.[20, 21] These observations may provide insight into our findings, as professional dental staff indicated that they obtained their knowledge through institutional training and informational sessions that offered current and relevant data. The association between knowledge and fear of COVID-19 has been minimally explored in research. A previous study demonstrated that, after controlling potential confounding variables, knowledge related to COVID-19 was independently associated with heightened fear of SARS-CoV-2 infection and severe manifestations of COVID-19.[21,22] Individuals with greater knowledge of the disease were more likely to fear contracting the virus compared to those with less knowledge. This finding may be influenced by the infodemic, particularly the spread of misinformation on social media platforms, which appears to impact non-professional healthcare workers more significantly than their professional counterparts.

In a previous study, it results showed that the time spent reading about COVID-19 was not significantly correlated with knowledge, whereas the level of scientific knowledge held by professional staff regarding COVID-19 was notably higher.[23]

Conclusion

It can be concluded that more awareness causes more concern about being in higher risk groups. Government authorities should not only disseminate timely, accurate, and up-to-date information but also implement national public health measures tailored to both the general population and specific subgroups. Such actions have the potential to enhance COVID-19-related knowledge, mitigate the impact of the infodemic, and alleviate associated fears. Since the dental staff working as being in the high-risk group, more frequent institutional training programs should be planned to spread accurate and up-to-date knowledge for all dental staff including auxiliary dental staff. Training programs for dental staff on epidemic protection, such as against COVID-19, are essential to ensure the safety of both healthcare workers and patients. These programs should cover key topics like proper use of personal protective equipment, sterilization protocols, patient screening procedures, and infection control measures. Training should be comprehensive, up-to-date with the latest public health guidelines, and regularly reinforced through both initial sessions and ongoing refresher courses. Ideally, dental staff should undergo training at least

quarterly, with additional sessions during peak times of health crises, to maintain high standards of safety and confidence in handling evolving health threats. It may also be concluded that a great amount of information has been gained due to the pandemic, but there is still more to be learned to be prepared for another pandemic that may occur in the future.

Ethical Approval
The ethical approval for this study was obtained from the Ethical Committee of Yeni Yuzyil University (2021/01-563).

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Conflict of Interest
None of the authors of this article have any affiliation, connection or financial interest regarding the subject or material mentioned in the article.

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Idea/Concept: S.O.Y, G.T Design: S.O.Y, G.T Control/Supervision: C.O Literature Review: S.O.Y Data Collection and/or Processing: S.O.Y Analysis and/or Interpretation: G.T Writing the Article: G.T Critical Review: S.O.Y, G.T.

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Comparison of Knowledge and Awareness Status of Senior Dental and Medical Students About MRONJ: A Cross-Sectional Study

Diş Hekimliği ve Tıp Fakültesi Öğrencilerinin MRONJ Hakkında Bilgi ve Farkındalık Durumlarının Karşılaştırılması: Kesitsel Çalışma

Selin Gaş[1*], Emine Öğüt[2], Erdinç Sulukan[3], Hümeyra Kocaelli Arıkan[4], Firdevs Şenel Veziroğlu[5]

ABSTRACT

Objective: Medication-related osteonecrosis of the jaw (MRONJ), a condition that can be managed and prevented through effective collaboration between dental and medical professionals, is a rare yet potentially serious disease. This study aimed to assess the knowledge and awareness of Turkish dental and medical school students regarding MRONJ.

Materials and Methods: A cross-sectional study was conducted among 254 dental and 234 medical students. Data were collected using an electronic and paper-based self-administered structured modified questionnaire consisting of five sections. SPSS Version 23 (IBM Corporation, Armonk, NY, USA) was utilized, with a significance level set at $p<0.05$.

Results: Both dental and medical students indicated that their curricula included courses on antiresorptive, antiangiogenic drugs, and the development of MRONJ associated with the use of these drugs. However, the level of knowledge and awareness among students in both groups regarding MRONJ was low. When comparing the awareness of MRONJ between medical and dental students, dental students (88.6%) exhibited a higher level than medical students (52.1%). Dental students also demonstrated greater awareness of the appropriate imaging techniques for diagnosing MRONJ compared to their medical counterparts ($p<0.05$). However, medical students' knowledge about dental approaches during bisphosphonate therapy was not as comprehensive as that of dental students.

Conclusion: Despite both dental and medical students having courses on MRONJ in their curriculum, their awareness and knowledge appear insufficient. This inadequacy may lead to misdiagnosis and inappropriate treatment modalities. Enhancing the quality and quantity of courses, with a focus on drugs inducing MRONJ and updated treatment protocols, could be proposed to address these issues.

Keywords: *Awareness, Dental Students, Knowledge, Medical Students, Osteonecrosis.*

ÖZET

Amaç: Antiresorptif, anti-anjiojenik ilaçların kullanımına bağlı gelişen çene kemik ölümü (MRONJ), diş ve tıp profesyonelleri arasındaki etkili işbirliği ile yönetilebilen ve önlenebilen nadir ancak potansiyel olarak ciddi bir durumdur. Bu çalışmanın amacı, Türk diş ve tıp fakültesi öğrencilerinin MRONJ hakkındaki bilgi düzeyini ve farkındalığını değerlendirmektir.

Gereç ve Yöntemler: 254 diş ve 234 tıp öğrencisi arasında kesitsel bir çalışma gerçekleştirildi. Veriler, beş bölümden oluşan bir elektronik ve kağıt tabanlı yapılandırılmış modifiye anket kullanılarak toplandı. Analizlerde SPSS Sürüm 23 (IBM Corporation, Armonk, NY, ABD) kullanıldı ve anlamlılık düzeyi $p<0.05$ olarak belirlendi.

Bulgular: Hem diş hem de tıp öğrencileri, müfredatlarının antiresorptif, anti-anjiojenik ilaçlar ve bu ilaçların kullanımına bağlı olarak gelişen MRONJ konulu dersleri içerdiğini belirtmişlerdir. Ancak, her iki grup öğrenci arasında MRONJ hakkındaki bilgi ve farkındalık düzeyi düşük bulunmuştur. Tıp ve diş hekimliği öğrencileri arasında MRONJ farkındalığı karşılaştırıldığında, diş hekimliği öğrencilerinin (%88,6), tıp öğrencilerine (%52,1) göre daha yüksek bir farkındalık düzeyine sahip olduğu gözlemlenmiştir. Diş hekimliği öğrencileri ayrıca, MRONJ teşhisi için uygun görüntüleme teknikleri konusunda tıp öğrencilerine göre daha fazla farkındalık göstermiştir ($p<0,05$). Tıp öğrencilerinin bifosfonat tedavisi almış veya almakta olan hastalarda diş tedavisi yaklaşımları konusundaki bilgisi, diş hekimliği öğrencilerinin bilgisi kadar kapsamlı bulunmamıştır.

Sonuç: Hem diş hem de tıp öğrencilerinin müfredatlarında MRONJ dersleri olmasına rağmen, farkındalık ve bilgilerinin yetersiz olduğu görülmektedir. Bu yetersizlik, yanlış teşhise ve uygun olmayan tedavi yöntemlerine yol açabilir. Bu sorunları ele almak için, MRONJ'a neden olan ilaçlar ve güncellenmiş tedavi protokollerine odaklanan derslerin kalitesini ve miktarını artırmak önerilebilir.

Anahtar Kelimeler: *Farkındalık, Diş hekimliği öğrencileri, Bilgi, Tıp öğrencileri, Osteonekroz.*

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Introduction

Bisphosphonate-Related Osteonecrosis of the Jaw (BRONJ) was initially described by Marx in 2003.[1] Bisphosphonates, commonly prescribed for conditions such as bone metastases from various cancers, multiple myeloma, osteoporosis, and metabolic bone diseases, have been subject to updates in 2007, 2009, and 2014.[2] AAOMS (American Association of Oral and Maxillofacial Surgeons) acknowledged in 2014 that various drugs, including denosumab, sunitinib, sorafenib, sirolimus, etc., can also induce osteonecrosis of the jaw, leading to the broadened term Medication-Related Osteonecrosis of the Jaw (MRONJ). The most recent position paper was published in 2022.[3] The treatment of Osteonecrosis of the Jaws (ONJs) poses a significant challenge for clinicians, lacking a universally accepted standard.[4-6] Consequently, prevention becomes a crucial focus. Effective preventive strategies can mitigate risk factors.[7-9] Therefore, it is imperative to possess sufficient information about MRONJ and collaborate closely with clinicians.

While numerous studies in the literature evaluate the knowledge of healthcare professionals, dental and medical students regarding MRONJ[10-12], none compare the awareness and understanding of MRONJ between medical and dental school students. Given the pivotal role of physicians in preventing MRONJ and ensuring the proper management of patients prescribed antiresorptive or antiangiogenic drugs, the study aims to evaluate, measure, and compare the knowledge of dental and medical school students regarding MRONJ.

Materials and Methods

A cross-sectional observational study was conducted by the attendance of senior dental and medical students in Istanbul, Turkey between January 2022 and April 2022. Ethical approval was obtained from the Ethic Comittee of Institutional Review Board at Istanbul Medipol University (Ethical Desicion Number: 1349). A total of 488 participants, 254 dental students and 234 medical students, applied for a modified survey- a validated self-administered questionnaire-, published by Rosella in 2017.[13] The survey was composed of five section (Table 1).The knowledge and awareness of the students by evaluating 1-General demographic data 2-General information about antiresorptive and antiangiogenic durgs 3- Theraupatic use of antiantiresorptive and antiangiogenic drugs 4- Diagnosing osteonecrosis of the jaws and risk factors 5- Dental management of patients receiving BP therapy were examined.

Table 1. Dental and Medical Students' Knowledge of MRONJ

Section 1: Demographic Profile	Age	…….
	Gender	Male Female
	Name of college	…….
Section 2: General Knowledge of Antiresorptive/ Antiangiogenic Medications	Have you encountered any antiresorptive medications such as bisphosphonate related information during your study years?	Yes No
	Have you encountered any antiangiogenic medications related information during your study years?	Yes No
	Where have you heard about anti-resorptive medications?	Never heard of it University Mass media Scientific journals Medical meetings Other (……)
	Where have you heard about antiangiogenic medications?	Never heard of it University Mass media Scientific journals Medical meetings Other (……)

	Do you think it is important to ask if patients are using anti-resorptive medications?	Yes No
	Do you think it is important to ask if patients are using antiangiogenic medications?	Yes No
Section 3: Knowledge of Therapeutic Uses of Antiresorptive/Antiangiogenic Medications	What diseases are targeted by antiresorptive therapy? (it is possible to mark more than one choice):	Bone metastases Osteomyelitis Multiple myeloma Osteopetrosis Chondroblastoma Osteogenesis imperfekta Paget's disease of bone Osteopenia and osteoporosis Hypercalcemia of malignancy I don't know
	What diseases are targeted by anti-angiogenic therapy? (it is possible to mark more than one choice):	Elastofibromas Metastatic colorectal cancer Leiomyomas renal cell cancer Neuroendocrine tumor of the pancreas Multiple myeloma Granular cell tumors I don't know
	Mark the name of the antiresorptive drugs you are familiar with	Alendronate (Fosamax) Risedronate (Actonel) Ibandronate (Boniva) Neridronate (Nerixia) Pamidronate (Aredia) Zolendronate (Zometa) Tiludronate (Skelid) Denosumab (Prolia) I don't know of any antiresorptive drug
	Mark the name of the antiangiogenic drugs you are familiar with (it is possible to mark more than one choice):	Sunitib (Sutent) Sorafenib (Nexavar) Bevacizumab (Avastin) Sirolimus (Rapamune) I don't know of any anti-angiogenic drugs
	In what ways is antiresorptive drug therapy administered?	Only oral Only parenteral Both oral ve parenteral I don't know
	Does the use of antiresorptive/antiangiogenic drugs lead osteonecrosis of the jaws?	Yes No I don't know

Section 4: Knowledge of Osteonecrosis of Jaw and Its Risk Factors	What is the correct definition of osteonecrosis of the jaw according to the American Association of Oral and Maxillofacial surgeons (AAOMS)?	a. Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region which has persisted for more than 8 weeks in patients in current or previous therapy with antiresorptive or antiangiogenic agents, and no history of radiation therapy to the jaws or obvious metastatic disease to the jaws.
		b. Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region which has persisted for more than 4 weeks in patients in current or previous therapy with antiresorptive or antiangiogenic agents, and no history of radiation therapy to the jaws or obvious metastatic disease to the jaws.
		c. Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region which has persisted for more than 8 weeks in patients in current or previous therapy with antiresorptive or antiangiogenic agents, and a medical history of radiation therapy to the jaws or obvious metastatic disease to the jaws.
		d. Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region which has persisted for more than 4 weeks in patients in current or previous therapy with antiresorptive or antiangiogenic agents and, a medical history of radiation therapy to the jaws or obvious metastatic disease to the jaws.
		e. I don’t know.
	Which imaging methods can be used in osteonecrosis of the jawbone? (You can mark more than one option.)	Scintigraphy Dental volumetric tomography Magnetic resonance imaging Panoramic radiography Periapical radiography No idea
	Which of the following are the risk factors related to osteonecrosis of the jaw? (You can mark more than one option.)	Tobacco Antibiotic therapy Alcohol Application way Hypertension Treatment time Hyperlipidemia Steroid therapy Total dose of drug administered Microtrauma No idea

Do you think patients should be checked by the dentist before starting an IV bisphosphonates treatment?	Yes No I don't know

Chi-Square Analysis: Comparison of dental and medical students`general knowledge about antiresorptive\antiangiogenic drugs, *p < 0.05

Statistical Analysis

A power analysis was performed and it was found that 340 samples produces a two-sided 95% confidence interval with a width equal to 0.220 when the sample correlation is 0.050. SPSS Version 23 (IBM Corporation, Armonk, NY, USA) was used for analysis. A Chi-square test was used to compare the categorical variables between groups. Probability of less than 0.05 (P < 0.05) was accepted as statistically significant.

Results

Among 254 dental students, 145 were females (57.1%) and 109 were males (42.9%); 234 medical students, 120 were females (51.9%) and 114 were males (48.7%). The general demographic characteristics of the students participating in the study were shown in Table 2 for the first section.

Table 2. General Demographic Characteristics of the Students

		Dental Students		Medical Students		p
		N	%	N	%	
Age	21-22	96	37.8	20	8.5	0.001
	23-24	131	51.6	126	53.8	
	>25	27	10.6	88	37.6	
	Total	254	100	234	100	
Gender	Male	109	42.9	114	48.7	0.116
	Female	145	57.1	120	51.3	
	Total	254	100	234	100	

Chi-Square Analysis: General Demographic Characteristics of the Students ,*p < 0.05

As shown in Table 3, while 95.3% of dental students and 76.1% of medical students stated that they had encountered antiresorptive drugs, it is observed that the number of students encountering antiangiogenic drugs has decreased statistically significantly (dental students: 76.7%; medical students: 68.3%). When both antiangiogenic and antiresorptive drugs were compared, the awareness of dental students was statistically higher than that of medical students (p<0.05). 92.9% of dental students reported that they first heard about drugs such as bisphosphonates in their curriculum, while this rate was 79.5% for medical students. 3.1% of dental students stated that they have never heard of antiresorptive drugs, whereas this rate was 17.9% for medical students (p<0.05). The majority of dental (82.3%) and medical (83.3%) students encountered information regarding antiangiogenic medications at the university. While the rate of dental students who have never heard of antiangiogenic drugs was 15.4%, this rate was 16.2% among medical students. The majority of medical (93.2%) and dental students (96.1%) reported that it is important to ask whether antiresorptive and antiangiogenic drugs are used in their patients.

Table 3. Comparison of General Knowledge About Antiresorptive/Antiangiogenic Drugs

		Dental Students	Medical Students		p
Have you encountered any antiresorptive medications such as bisphosphonate related information during your study years?	Yes	242 (95.3%)	178 (76.1%)	420 (86.1%)	0.001
Where have you heard about antiresorptive medications?	University	238 (93.7%)	186 (79.5%)	424 (86.9%)	0.001
	Never heard	8 (3.1%)	42 (17.9%)	50 (10.2%)	
	Scientific journals	5 (2.0%)	3 (1.3%)	8 (1.6%)	
	Scientific meetings	2 (0.8%)	2 (0.9%)	4 (0.8%)	
	Others	1 (0.4%)	0 (0.0%)	1 (0.2%)	
Have you encountered any antiangiogenic medications related information during your study years?	Yes	195 (76.7%)	160 (68.3%)	355 (71.2%)	0.001
Where have you heard about antiangiogenic medications?	University	210 (82.7%)	195 (83.3%)	404 (82.8%)	0.585
	Never heard	39 (15.4%)	38 (16.2%)	77 (15.8%)	
	Scientific meetings	1 (0.4%)	0 (0.0%)	1 (0.2%)	
	Media	3 (1.2%)	1 (0.4%)	4 (0.8%)	
	Others	1 (0.4%)	0 (0.0%)	1 (0.2%)	
Do you think it is important to ask if patients are using anti-resorptive medications?	Yes	244 (96.1%)	218 (93.2%)	462 (94.7%)	0.110
Do you think it is important to ask if patients are using antiangiogenic medications?	Yes	229 (90.2%)	212 (90.6%)	441 (90.4%)	0.496

Chi-Square Analysis: Comparison of General Knowledge About Antiresorptive/Antiangiogenic Drugs, *p < 0.05

The level of knowledge of the therapeutic usage of antiresorptive and antiangiogenic medications was demonstrated in Table 4 for the third section. Medical students were more familiar with all the mentioned antiresorptive drugs than dental students. While Zolendronate (Zometa) was the most heard antiresorptive drug, Tiludronate (Skelid) was the least heard antiresorptive drug for both groups. Similar to previous results, all antiangiogenic drugs were mostly known by medical students. Dental students knew less about antiresorptive and antiangiogenic drugs than medical students. Among the therapeutic uses of antiresorptive therapy, osteopenia and osteoporosis were the most commonly recognized among dental students (77.6%) and medical students (80.8%). The second most well-known disease was bone metastases (69.7% of dental students, 76.5% of medical students). None of the dental students were able to identify elastofibroma, metastatic colorectal cancer, leiomyoma, and renal cell cancer, while a few medical students (3.4%) identified these diseases ($p<0.05$). When the routes of administration were questioned, few dental students (20.5%) and medical students (19.2%) reported that they had no idea ($p>0.05$). The majority of dental students (73.6%) and medical students (78.2%) stated that these drugs are administered to patients by both oral and parenteral routes ($p>0.05$). Most dental students (88.6%) knew that antiresorptive/antiangiogenic drugs could cause osteonecrosis of the jaw. However, more than half of the medical students (52.1%) had no idea about this topic.

Table 4. Comparison of the therapeutic use of drugs

		FACULTY		Total	p
		Dental Faculty	Medical Faculty		
In which diseases is antiresorptive drug therapy indicated? (You can check multiple options.)	Elastofibroma	0 (0.00%)	8 (3.4%)	8 (1.6%)	0.843
	Bone metastases	177 (69.7%)	179 (76.5%)	356 (73.0%)	0.816
	Multiple myeloma	107 (42.1%)	158 (67.5%)	165 (33.8%)	0.002
	Osteogenesis imperfecta	136 (53.5%)	153 (65.4%)	289 (59.2%)	0.121
	Osteomyelitis	119 (46.9%)	48 (20.5%)	167 (34.2%)	0.001
	Osteopenia and osteoporosis	197 (77.6%)	189 (80.8%)	376 (77.0%)	0.964
	Osteopetrosis	69 (27.2%)	126 (53.8%)	195 (40.0%)	0.001
	Paget's disease	98 (38.6%)	82 (35.0%)	180 (36.9%)	0.910
	Chondroblastoma	42 (16.5%)	83 (35.5%)	125 (25.6%)	0.002
	Metastatic colorectal cancer	0 (0.0%)	8 (3.4%)	8 (1.6%)	0.132
	Leiomyoma	0 (0.0%)	8 (3.4%)	8 (1.6%)	0.132
	Renal cell carcinoma	0 (0.0%)	8 (3.4%)	8 (1.6%)	0.132
	No idea	23 (9.1%)	0 (0.0%)	25 (5.1%)	0.371
In which diseases is antiangiogenic drug therapy indicated? (You can check multiple options.)	Elastofibroma	53 (20.9%)	68 (29.1%)	121 (24.8%)	0.265
	Leiomyoma	52 (20.8%)	69 (29.5%)	121 (24.8%)	0.214
	Metastatic colorectal cancer	85 (33.5%)	136 (58.1%)	221 (45.3%)	0.001
	Multiple myeloma	81 (31.9%)	120 (51.3%)	201 (41.2%)	0.002
	Neuroendocrine tumor of the pancreas	65 (25.6%)	32 (13.7%)	97 (19.9%)	0.007
	Renal cell carcinoma	86 (33.9%)	116 (49.6%)	202 (41.4%)	0.009
	Granular cell tumor	59 (23.2%)	14 (6%)	73 (15%)	0.001
	No idea	124 (48.8%)	29 (12.4%)	153 (31.3%)	0.001
Please indicate the antiresorptive drugs that are actively prescribed today. (You can check multiple options.)	Alendronate (Fosamax)	92 (36.2%)	177 (75.6%)	269 (55.1%)	0.001
	Denosumab (Prolia)	80 (31.5%)	174 (74.4%)	254 (52.0%)	0.001
	Ibandronate (Boniva)	63 (24.8%)	89 (38.0%)	152 (31.1%)	0.283
	Neridronate (Nerixia)	23 (9.1%)	79 (33.8%)	102 (20.9%)	0.001
	Pamidronate (Aredia)	69 (27.2%)	152 (65.0%)	221 (45.3%)	0.001
	Risendronate (Actonel)	41 (16.1%)	123 (52.6%)	164 (33.6%)	0.001
	Tiludronate (Skelid)	31 (12.2%)	48 (20.5%)	79 (16.2%)	0.217
	Zolendronate (Zometa)	135 (53.1%)	188 (80.3%)	323 (66.2%)	0.135
	No idea	81 (31.9%)	18 (7.7%)	99 (20.3%)	0.001
	Sorafenib (Nexavar)	44 (17.3%)	144 (61.5%)	188 (38.5%)	0.001
	Sunitinib (Sutent)	40 (15.7%)	154 (65.8%)	194 (39.8%)	0.001
	No idea	182 (71.7%)	52 (22.2%)	234 (48.0%)	0.001
Please indicate the antiangiogenic drugs that are actively prescribed today. (You can check multiple options.)	No idea	52 (20.5%)	45 (19.2%)	97 (19.9%)	0.249
	Oral and parentheral	187 (73.6%)	183 (78.2%)	370 (75.8%)	
	Only oral	12 (4.7%)	4 (1.7%)	16 (3.3%)	
	Only parentheral	3 (1.2%)	2 (.9%)	5 (1.0%)	
Do the use of antiresorptive/antiangiogenic drugs cause osteonecrosis in the jaws?	Yes	225 (88.6%)	112 (47.9%)	337 (69.1%)	0.001
	No idea	23 (9.1%)	122 (52.1%)	145 (29.7%)	
	No	6 (2.4%)	0 (0.0%)	6 (1.2%)	

Chi-Square Analysis: Comparison of the therapeutic use of drugs *p < 0.05

In the fourth part of the survey, only half of the dental students (52%) and medical students (49.1%) chose the correct definition of MRONJ (Table 5). When asked about the appropriate imaging technique to diagnose MRONJ, the awareness of dental students was higher than that of medical students (77.6%-45.3%). Dental students were more familiar when panoramic and periapical radiography were of concern (77.6%, 45.3%). Among risk factors for MRONJ, the total dose of drug administered was the most recognized one by dental (77.6%) and medical (82.9%) students. This was followed by the duration of treatment and smoking, respectively (Table 5). Almost all dental students (95.7%) argued that patients should be checked by a dentist before starting iv bisphosphonate therapy, with a significantly higher rate compared to medical students (84.6%).

Table 5. Knowledge of Risk Factors Related to Osteonecrosis of the Jaw

		Dental Students	**Medical Students**		**p**
What is the correct definition of osteonecrosis of the jaw according to the American Association of Oral and Maxillofacial surgeons (AAOMS)?	Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region which has persisted for more than 8 weeks in patients in current or previous therapy with antiresorptive or antiangiogenic agents, and no history of radiation therapy to the jaws or obvious metastatic disease to the jaws.	35 (13.8%)	43 (18.4%)	78 (16.0%)	0,001
	Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region which has persisted for more than 4 weeks in patients in current or previous therapy with antiresorptive or antiangiogenic agents, and no history of radiation therapy to the jaws or obvious metastatic disease to the jaws.	132 (52.0%)	115 (49.1%)	247 (50.6%)	
	Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region which has persisted for more than 8 weeks in patients in current or previous therapy with antiresorptive or antiangiogenic agents, and a medical history of radiation therapy to the jaws or obvious metastatic disease to the jaws.	30 (11.8%)	23 (9.8%)	53 (10.9%)	
	Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region which has persisted for more than 4 weeks in patients in current or previous therapy with antiresorptive or antiangiogenic agents and, a medical history of radiation therapy to the jaws or obvious metastatic disease to the jaws.	27 (10.6%)	4 (1.7%)	31 (6.4%)	
	I don't know	30 (11.8%)	49 (20.9%)	79 (16.2%)	

Which imaging methods can be used in osteonecrosis of the jawbone? (You can mark more than one option.)	Dental volumetric tomography	187 (73.6%)	178 (76.1%)	365 (74.8%)	0.996
	Magnetic resonance imaging	110 (43.3%)	81 (34.6%)	191 (39.1%)	0.173
	Panoramic radiography	197 (77.6%)	94 (40.2%)	291 (59.6%)	0.001
	Scintigraphy	95 (37.4%)	110 (47.0%)	205 (42.0%)	0.114
	Periapical radiography	115 (45.3%)	39 (16.7%)	154 (31.6%)	0.001
	I don't know	16 (6.3%)	38 (16.2%)	54 (11.1%)	0.187
Which of the following are the risk factors related to osteonecrosis of the jaw? (You can mark more than one option.)	Alcohol	140 (55.1%)	132 (56.4%)	272 (55.7%)	0.962
	Microtrauma	137 (53.9%)	101 (43.2%)	238 (48.8%)	0.035
	Antibiotic therapy	56 (22.0%)	66 (28.2%)	122 (25.0%)	0.248
	Hypertension	57 (22.4%)	80 (34.2%)	137 (28.1%)	0.017
	Steroid therapy	137 (53.9%)	173 (73.9%)	310 (63.5%)	0.001
	Treatment time	182 (71.7%)	161 (68.8%)	343 (70.3%)	0.164
	Total dose of drug administered	197 (77.6%)	194 (82.9%)	391 (80.1%)	0.344
	Tobacco	168 (66.1%)	161 (68.8%)	329 (67.4%)	0.942
	Administration way	148 (58.3%)	82 (35.0%)	230 (47.1%)	0.001
	Hyperlipidemia	48 (18.9%)	79 (33.8%)	127 (26.0%)	0.001
	I don't know	23 (9.1%)	36 (15.4%)	59 (12.1%)	0.129
Do you think patients should be checked by the dentist before starting an IV bisphosphonates treatment?	Yes	243 (95.7%)	198 (84.6%)	441 (90.4%)	0.001
	No	2 (0.8%)	6 (2.6%)	8 (1.6%)	
	I don't know	9 (3.5%)	30 (12.8%)	39 (8.0%)	

Chi-Square Analysis: Knowledge of Risk Factors Related to Osteonecrosis of the Jaw,*$p < 0.05$

The fifth section of the survey, shown in Table 6, was about dental management of patients receiving bisphosphonate therapy. When the management of patients under iv BP therapy was of concern, 79.5% of dental students and 41.0% of medical students stated that invasive dental treatment is not safe and should not be performed ($p<0.05$). However, most medical students (56.4%) have no knowledge on the subject, which raises the suspicion of inadequacy of education. However, concerning the indication of invasive dental treatment for patients under oral BP therapy for less than 4 years without risk factors, 18.4% of dental students indicated it as unsafe, whereas the percentage was 9.4% for medical students ($p<0.05$). While 66.5% of dental students and 16.2% of medical students stated that being associated with a risk factor for less than 4 years made dental treatments unsafe in these patients ($p<0.05$), 60.2% of dental students and 16.7% of medical students argued that dental treatments could not be performed in patients who had been using oral bisphosphonates for more than 4 years ($p<0.05$).

Table 6. Knowledge of Dental Management in Patients Undergoing Bisphosphonate Therapy According to Dental and Medical Students

		Dental Students	Medical Students		p
Can invasive dental treatments be performed safely to patients during an intravenous bisphosphonate drug therapy?	Yes	29 (11.4%)	6 (2.6%)	35 (7.2%)	0.001
	No	202 (79.5%)	96 (41.0%)	298 (61.1%)	
	I don't know	23 (9.1%)	132 (56.4%)	155 (31.8%)	
Can invasive dental treatments be performed safely to patients using oral bisphosphonates for <4 years without risk factors?	Yes	164 (64.4%)	104 (44.4%)	268 (54.4%)	0.001
	No	46 (18.4%)	23 (9.4%)	69 (14.4%)	
	I don't know	44 (17.4%)	107 (45.4%)	151 (30.4%)	
Can invasive dental treatments be performed safely to patients using oral bisphosphonates for <4 years with risk factors?	Yes	45 (17.7%)	55 (23.5%)	100 (20.5%)	0.001
	No	169 (66.5%)	38 (16.2%)	207 (42.4%)	
	I don't know	40 (15.7%)	141 (60.3%)	181 (37.1%)	
Can invasive dental treatments be performed safely to patients using oral bisphosphonates for >4 years?	Yes	50 (19.7%)	30 (12.8%)	80 (16.4%)	0.001
	No	153 (60.2%)	39 (16.7%)	192 (39.3%)	
	I don't know	51 (20.1%)	165 (70.5%)	216 (44.3%)	
Would you like to know more about osteonecrosis of the jaws associated with the use of antiresorptive/antiangiogenic drugs?	Yes	242 (95.3%)	127 (54.3%)	369 (75.6%)	0.001
	No	12 (4.7%)	107 (45.7%)	119 (24.4%)	

Chi-Square Analysis: Knowledge of Dental Management in Patients Undergoing Bisphosphonate Therapy According to Dental and Medical Students,*$p < 0.05$

Discussion

In the literature, several studies regarding the knowledge of MRONJ by dentists and dental students can be found.[10,13,14] Nevertheless, the knowledge of osteonecrosis by medical students that are going to become doctors is crucial. There is only one study which reported the awareness about MRONJ among medical students.[15]

MRONJ is a potentially serious adverse event in patients with cancer and bone diseases who have been receiving antiresorptive or antiangiogenic drugs. It can cause painful bone exposure in maxilla and mandible. Having sufficient information about MRONJ is essential for improving treatment outcomes, reducing drug-related complications, and thus increasing the quality of life of patients. Although several studies in the literature have investigated MRONJ awareness in dentists and other healthcare professionals[16,17], few studies have evaluated the knowledge levels of dental and medical school students.[13,15] To the best of our knowledge, there has been no study comparing the knowledge levels of dental and medical school students. As a result of the study conducted by Almousa et al.[11] with the dental students, almost one third of the students stated that they did not receive any information about antiresorptive and antiangiogenic drugs during their undergraduate years. Unlike the previous study, in the current study, almost all of the dental students received information about antiresorptive drugs during their undergraduate years, while much less of the students in the medical school stated that they encountered this information compared to the dental students. In both groups, less of the participants in the study stated that they encountered information about antiangiogenic drugs. The difference between the knowledge levels of this drugs may be related to the subsequent reflection in the literature of antiangiogenic drugs causing osteonecrosis of the jaw. In Italy, Franchi et al.[15] measured the knowledge level of MRONJ in medical students and observed that they did not have sufficient knowledge. They reported that there was an increase in the knowledge awareness about MRONJ among the students who were in the 6th year of medical school compared to those in the 5th year, and they argued that the reason for this was the increase in the number of patients and practical experience in the last years of the students.

Due to the increasing incidence of MRONJ, there is a consensus among dentists to raise awareness of MRONJ and increase the training necessary to prevent it. However, the prescription of drugs that cause MRONJ by medical doctors necessitates the need for medical doctors to have sufficient knowledge about MRONJ.[18-21]

In their study, Escobeto et al.[14] found that senior dental students had a higher case resolution rate compared to dentists with private practice. López-Jornet et al.[22], compared the knowledge of BRONJs among students and dentists in Spain. Unlike with the previous study results, they reported that the dentists' knowledge of BRONJs was higher than that of the students. In the present study, it was observed that dental students had more knowledge about MRONJ than medical students.

In the current study, Turkish dental and medical students, with the majority of the participants could not recognize the generic and brand names of antiresorptive and antiangiogenic medication. Several studies in the literature have reported the similiar results with our study.[10,13,20] In the study of de Lima et al.[20], the majority of dentists and dental students could not classify these drugs and could not recognize their commercial brand names. This result made us think that the generic and brand names of MRONJ-related drugs were not emphasized enough during university years and were not included in the education curriculum. In the present study, Zolendronate (Zometa) was the most frequently known antiresorptive medication, followed by Alendronate (Fosamax) and Denosumab (Prolia) in both groups. Similiar to our study results, Almousa et al.[10] found that mentioned three medications were the most known ones. But in their study, Alendronate was the most recognized medication. S. Franchi et al.[15] reported that among Italian medical students which showed that the majority of the participants lacked knowledge regarding antiangiogenic medications caused MRONJ. Similiar findings were found in the current study. Medical students recognized both antiangiogenic drugs and antiresorptive drugs statistically less than the dental students. In both groups, antiangiogenic drugs were recognized less frequently than antiresorptive drugs. We hypothesize that this is due to the later realization that antiangiogenic drugs cause osteonecrosis of the jaw. When we investiagted the studies in the literature, including the present study, we observe that healthcare professionals do not have enough knowledge about antiresorptive and antiangiogenic drugs. In order to make the correct diagnosis of the disease and to reduce the possibility of getting osteonecrosis of the jaw, it is necessary to increase the relevant trainings in all health fields, especially in dentistry.

20% of the sample in both groups did not have any idea of the question, that is "In which ways is antiresorptive drug therapy administered?". Approximately 75% of both groups gave the response, oral and parenteral. This question was not included in any of the survey studies conducted in the literature. The purpose of measuring the answers given to this question is that the route of administration of the drug is also effective in the spread and speed of osteonecrosis of the jaw. The physician's knowledge of this situation will be an important factor in taking the necessary precautions.

Only half of the students who participated in the survey in both groups knew the definition of MRONJ correctly. While 20.9% of medical students declared that they had no idea, this rate was 11% among dental students. These results are alarming. Curriculum changes are required to increase awareness of MRONJ in both of the schools, especially in medical schools. In contrast, Rugieiro et al.[2] and Rosella et al.[13] observed that most of the dental students participating in the studies could not know the correct definition of MRONJ. Lack of information on the definition of MRONJ may lead to delayed diagnosis in people who may develop MRONJ and, accordingly, to an increased risk of other complications that may affect quality of life.

When asked about the imaging methods that can be used in the diagnosis of MRONJ, the majority of dental students answered panoramic radiography (77.6%) and dental volumetric tomography (73.6%), while the majority of medical students (76.1%) answered dental volumetric tomography. However, medical school students thought that MRONJ could be diagnosed with panoramic and periapical radiography at a lower rate compared to dental school students. This results make us think that there are deficiencies in our health education system. Courses in medical and dental faculties should be coordinated and joint courses should be available when necessary. Radiological

imaging methods are very important in the early diagnosis of MRONJ.[23,24] In many cases, early diagnosis can be determined only by radiological evaluation. However, imaging methods have not been questioned in any study evaluating MRONJ awareness in the literature. For this reason, we wanted to measure the knowledge level of students in dentistry and medical faculties in Turkey about imaging methods. As a result, we observed that the students did not have sufficient knowledge level.

When the question about possible risk factors for MRONJ was evaluated, the most of the participants in our study stated that the total dose of drug was risk factor, while more than 50% stated that alcohol, steroid treatment, tobacco use and duration of treatment were risk factors. It is a known fact that the increase in the dose of drug administered and the duration of treatment also increase the risk of osteonecrosis.[25] The answers of the participants in our study were insufficient. However, compared to the study by Almousa et al.[10], the participants in the present study were found to more knowledgable about risk factors. The majority of the participants, especially almost all of the dental students, asked, "Should patients be checked by dentists before starting iv bisphosphonate therapy?" when asked the question, answered yes. Similarly, Almousa et al.[10] stated that the dentists and dental students participating in the study answered yes to this question. Franchi et al.[15], in their study, similar to the present study, medical students are aware that patients should go to a dentist before starting bisphosphonate therpy. Another common point in the mentioned three studies is that the iv route of administration carries a greater risk for MRONJ than the oral route.

It is known that the risk of developing osteonecrosis is minimal if bisphosphonates are used orally for less than 4 years.[2] Administration of the drug intravenously or subcutaneously increases the risk of osteonecrosis. In our study, while 79.5% of dental students stated that invasive dental treatments could not be performed while using iv bisphosphonates, less than half of the medical school students stated the same answer. Unfortunately, 56.4% of the medical students stated that they did not have any idea about this subject. These results are worrying. Some precautions should be taken. Especially in medical faculties, more documents on the subject should be presented to students. "Can invasive dental treatments be performed in individuals who have been using oral bisphosphonates for less than 4 years and have no risk factors?" While only 64.4% of dental students answered yes to the question, the rate of the medical school students was 44.4%. Almost half of the medical students declared that they had no idea about this subject. However, there are few students who declare that they have no idea about the subject among the students of the dental school. Almousa et al.[10] reported similar results in their study. These results suggest that the participants in both studies did not have enough knowledge about MRONJ and the disease could not be managed properly.

"Can invasive dental treatments be performed safely to patients using oral bisphosphonates for <4 years without risk factors, and in patients who have used oral bisphosphonates for more than 4 years?" The answers given to the questions are not satisfactory for both groups. Especially the majority of medical students stated that they had no idea about this issue. Similarly, Almousa et al.[10] and López-Jornet et al.[22] in their study, they observed that both dentists and dental students did not have a good command of the dental treatment approach in patients who used or were using bisphosphonates. The present study results showed that despite the existence of guidelines both groups (students and practising dentists) had confused ideas as to how to carry out invasive dental treatment (extraction of teeth) in cases of patients taking bisphosphonates.[22]

A clinician should know the drugs associated with MRONJ, have knowledge of the risk factors and dental approach when MRONJ occurs. It is also important that medical doctors and dentists cooperate in order to manage MRONJ and improve patients' quality of life. Almost all of the dental students participating in our study stated that they were willing to learn more about MRONJ regarding the use of antiresorptive and antiangiogenic drugs. Unfortunately, only 54.3% of medical school students were found to be eager

to gain knowledge. For the ideal maintenance of MRONJ in the future, due attention should be paid to the issue in all fields of health, especially in medical faculties today. Necessary training should be provided.

Conclusion

For all the sections in the survey, the level of knowledge is insufficient in dental students, especially medical students. Although medical students have more incomplete information, they are also not willing to have more information. This situation is threatening. Based on our study results, we can say that some courses should be common in medical and dental schools, the importance of consultation should be emphasized and it should be taught that working in cooperation is important. Necessary seminars should be given, case reports should be presented and workshops should be organized to correct the lack of knowledge about MRONJ.

Ethical Approval

The necessary ethical approval for this study was obtained from Istanbul Medipol University Institutional Review Board and Ethics Committee (Ethical approval no: 1349).

Conflict of interest

The authors have no conflict of interest to declare.

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Author Contributions

Idea/Concept: S.G, E.Ö, E.S, H.K.A, F.Ş.V Design: S.G, E.S, H.K.A, F.Ş.V Control/ Supervision: S.G, H.K.A, F.Ş.V Literature Review: S.G, E.Ö, E.S., H.K.A, F.Ş.V Data Collection and/or Processing: S.G, E.Ö, E.S, F.Ş.V Analysis and/or Interpretation: S.G, E.Ö, E.S, H.K.A, F.Ş.V Writing the Article: S.G, E.Ö, E.S, H.K.A, F.Ş.V Critical Review: S.G, E.Ö, E.S, H.K.A, F.Ş.V.

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Evaluating In Vitro Performances of Various Pit and Fissure Sealing Materials

Farklı Pit ve Fissür Örtücülerin In Vitro Performansının Değerlendirilmesi

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ABSTRACT

Objectives: The aim of the study was to evaluate the penetration depth and microleakage of a resin infiltrant (Icon, DMG), and two fissure sealants (Glass Carbomer, GCP Dental; Teethmate F-1, Kuraray) applied to fissures and pits on the enamel surface in vitro.

Materials and Methods: For the penetration test, 90 human molars were kept in 0.1% ethanolic tetramethyl rhodamine isothiocyanate 24 hours to label all accessible pores. Prior to application, materials were labeled with a 0.1% rhodamine isothiocyanate. A confocal microscope was used to analyze slices of teeth that were perpendicular (n=20). The maximum percent penetration (maxPDY) was computed by measuring the maximum depth of penetration (maxPD) and the maximum depth of lesion (maxLD). For the microleakage test, 30 human molars were preserved in basic fuchsin dye. Teeth were divided in the mesiodistal direction, pieces were examined with a stereomicroscope and scored (n=10). Kruskal-Wallis and Mann-Whitney U tests were used for the statistical analysis (p=0.05).

Results: The maxPD values of the Icon group was statistically higher than the Glass Carbomer and the Teethmate F-1 groups ($p<0.05$). The maxPD values of Glass Carbomer and the Teethmate F-1 groups were similar ($p>0.05$). Glass Carbomer group showed severe microleakage values and internal cracks. There was no difference between Icon and Teethmate F-1 groups statistically ($p>0.05$).

Conclusion: Icon and Teethmate F-1 groups displayed favorable performance. Although the penetration depth of the Glass Carbomer is similar to Teethmate F-1 group, further research on the clinical performance of this material is needed due to its excess microleakage.

Keywords: *Dental resins, Fissure sealants, Minimally invasive surgical procedures*

ÖZET

Amaç: Bu çalışmanın amacı, mine yüzeyindeki pitlere ve fissürlere uygulanan bir infiltrantın (Icon, DMG) ve iki fissür örtücünün (Glass Carbomer, GCP Dental; F1-Teethmate, Kuraray) penetrasyon derinliğini ve mikrosızıntısını in vitro olarak değerlendirmektir.

Gereç ve Yöntemler: Penetrasyon testi için, 90 adet insan azı dişi kullanıldı. Erişilebilir tüm gözenekleri işaretlemek için dişler 24 saat boyunca %0,1 etanolik tetrametil rodamin isotiyosiyanat'da bekletildi. Materyaller uygulanmadan önce %0,1 rodamin isotiyosiyanat ile işaretlendi. Dik diş kesitleri konfokal mikroskopta incelendi (n=20). Maksimum penetrasyon derinliği (maxPD) ve lezyon derinliği (maxLD) ölçüldü ve maksimum penetrasyon yüzdesi hesaplandı (maxPDY).

Mikrosızıntı testi için, 30 adet insan molar dişi kullanıldı (n=10). Dişler 24 saat bazik fuksin boyasında bekletildi. Dişlerden meziodistal yönde kesitler alınarak stereomikroskopta incelendi ve skorlandı (n=10). İstatistiksel analizde Kruskal-Wallis ve Mann-Whitney U testleri kullanıldı (p=0.05).

Bulgular: Icon grubunun maxPD değerleri Glass Carbomer ve Teethmate F-1 gruplarına göre istatistiksel olarak daha yüksekti($p<0.05$). Glass Carbomer ve Teethmate F-1 gruplarının maxPD değerleri benzerdi ($p>0.05$). Glass Carbomer grubu ciddi mikrosızıntı değerleri ve içsel çatlaklar gösterdi. Icon ve Teethmate F-1 grupları arasında istatistiksel olarak anlamlı fark yoktu ($p>0.05$).

Sonuç: Icon ve Teethmate F-1 grupları istenen performansı göstermiştir. Glass Carbomer'in penetrasyon derinliği Teethmate F-1 grubuna benzer olsa da mikrosızıntısının fazla olması nedeniyle bu materyalin klinik performansı konusunda daha fazla araştırmaya ihtiyaç vardır.

Anahtar Kelimeler: *Dental rezinler, Fissür örtücüler, Minimal invaziv cerrahi işlemler*

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Introduction

Minimal intervention concept is relied on all the factors that included progression of disease and thus completes concepts of prevention, control and treatment. Detection of lesions early as possible, risk assessment and practice of preventive strategies is the most important stages for the patient. Therefore, patient education is also important. If the disease are present, other therapeutic strategies is required. For example demineralization, therapeutic sealants and restorative care such that minimal loss of tissue.[1] Pits and fissures of occlusal surfaces are the most important locations for dental caries risk, because of its unfavorable morphology. Even in individuals with good oral hygiene, the presence of caries in pits and fissures makes the situation more remarkable and important.[2] Although fissure sealant application is an effective method for preventing fissure caries, the cariostatic effects of fissure sealants depend on the physical closure of pits and grooves.[3] Fissure sealants isolate the lesion from the oral environment and can prevent the progression of the caries process by inhibiting the glycolytic activity of bacteria.[4] The protective effect of fissure sealants varies from 87% in the first year to approximately 60% after 4-5 years depending on the permanence of the restoration.[5,6] Nevertheless, they penetrate only to the upper layers of caries lesions.[7] Although authors allegation that sealing caries provides the occasion arrest the decay process but, caries progression can be prevented by covering the enamel initial lesions before they become cavitated. [2,8,9]

Caries infiltration is a minimally invasive dentistry approach used to treat incipient caries lesions on the proximal and flat surfaces of teeth. Resin infiltration aims to seal the demineralized enamel lesion body in incipient caries with light-cured low-viscosity resins.[10]

Various fissure sealants have been used from past to present. These; cyanoacrylates, polyurethanes, polycarboxylate cements, composite resins, polyacid modified composite resins, resin modified glass ionomer cements, glass ionomer cements, ormocers (organic modified ceramics), glass carbomer and resin infiltration systems. Resin-based and glass ionomer-based materials are the most commonly used fissure sealants.[11,12] The aim of the study was to evaluate the penetration depth and microleakage of a resin infiltrant (Icon, DMG), and two fissure sealants (Glass Carbomer, GCP Dental; Teethmate F-1, Kuraray) applied to fissures and pits on the enamel surface in vitro. The tested null hypothesis is that there were no statistically significant differences in the penetration depth and microleakage of different fissure sealing materials.

Materials and Methods

The Selçuk University Faculty of Dentistry Non-Interventional Clinical Research Evaluation Committee ethically approved the study (2014/03).

Penetration test and image analysis

According to the results of the Power analysis (G*Power software v3.1.10), a requirement of at least 18 samples in each group was determined with 95% confidence (0.05-α) and f=0.5 effect size for penetration test; a requirement of at least 10 samples in each group was determined with 95% confidence (0.05-α), 90% test power (1-β) and f=0.3 effect size for microlekage test. The number of samples was considered to be 20 for the penetration test (n=20) and 10 for the microleakage test (n=10).

Icon etch resin infiltrant (DMG, Hamburg, Germany), Glass Carbomer sealant (GCP Dental, Germany) and Teethmate F-1 sealant (Kuraray Medical, Okoyama, Japan) fissure sealing materials are used in this study.

Ninety non-carious third human molars extracted in the last 6 months were included. Sixty samples used for penetration test. The samples were randomly divided into three groups (n=20) then stored in 0.1% thymol solution. Fissures scored as according to ICCMS[13] (International Caries Classification and Management System) codes 0 and 1 independently.

Teeth were cleaned and stored in 0.1% ethanolic tetramethyl rhodamine isothiocyanate (TRITC, Sigma-Aldrich, Steinheim, Germany) for 24 hours to label all reachable pores in pre-staining for penetration test. Fissure sealing materials were labeled with 0.1% rhodamine isothiocyanate

(RITC, Sigma-Aldrich, Steinheim, Germany) before applying fissures.[14] HCl-gel was applied to teeth where Icon infiltrant would be applied for 120 seconds, and 37% phosphoric acid was applied to teeth where Glass Carbomer and Teethmate F-1 sealants would be applied for 40 s.

Firstly, for Group 1, RITC labeled Icon infiltrant was applied for 180 s entire deepest surface area of fissures. After, fissures were filled with resin infiltration material from beginning to end, light curing was performed with Monitex Blue Lex GT-1200 (Monitex Industrial Co., Taiwan) for 60 s.

Group 2 RITC labeled Glass Carbomer sealant capsule was activated by mixing for 15 s and applied onto the fissures in 60 s working time. Glass Carbomer surface gloss (GCP Dental, Germany) was applied and polymerized 60 s with Carbo-Led (GCP Dental, Germany).

Group 3 RITC labeled Teethmate F-1 sealant was applied for 60 s onto fissures and were polymerized for 20 s Monitex Blue Lex GT-1200.

The roots of the teeth were cut and the crown parts were embedded in acrylic. Three pieces of approximately 1200 µm thickness were obtained from each tooth perpendicular to the lesion surface (Isomet Buehler, Illinois, USA). Each piece of sample was fixed on a microscope slide. Samples polished with 1200, 2400, 4000 abrasive sandpaper and then were kept in 30% hydrogen peroxide for 12 s to remove free red fluorophore. After washing with water, the samples were kept in 100 µm sodium fluorescein in 50% ethanol solution (NaFI-Aldrich, Steinheim) for 3 minutes to stain the dentin and the porous structure where the fissure sealant was not infiltrated.[14] Finally, the samples were washed with deionized water for 10 s and dried with air-water spray.

Evaluation of samples with microscope was imaged at Selcuk University Advanced Technology Application and Research Center. Samples were examined at 10X magnification in a confocal laser scanning microscope (Nikon A1R-A1Confocal Microscope, Japan). Depth of penetration and depth of lesion were evaluated and compared using a confocal microscope images.

In dual fluorescence mode, images were acquired simultaneously in samples stained with RITC and NaFl. Images were recorded at 1024x1024 pixels and 2606 µm x 2606 µm. It allows the separation of the red (RITC) dye in the infiltrant part, the green (NaFI) dye in the non-infiltrating part and the porous part in dual flourescence mode technique.[14] Sections with the deepest fissure from each tooth sample were selected and used for analysis (n=20).

Microleakage test and image analysis

Thirty non-carious third human molars were used for mikroleakage test (n=10). Nail polish was applied 1 mm outside the fissure borders of the teeth and materials applied onto the fissures. The teeth were kept in 0.5% basic fuchsin (VWR Prolabo Chemicals, USA) solution at 37 °C for 24 h and then washed with water.

The teeth were cut in the mesio-distal direction using a water-cool bidirectional diamond-coated separator (Isomet Buehler, Illinois, USA). One side of the cut teeth samples were examined with stereomicroscope (Olympus, Tokyo, Japan). The dye penetration of the samples was assessed under top illumination with a stereomicroscope at 40X magnification. Microleakage values were evaluated using with the data obtained in the previous study of Pardi et al.[15]

The ranked scale used to score dye penetration was 0= no dye penetration; 1= dye penetration limited to the outer half of the sealant; 2= dye penetration extending to the inner half of the sealant; 3= dye penetration extending to the underlying fissure. The flow chart figure of the study is shown below (Fig. 1).

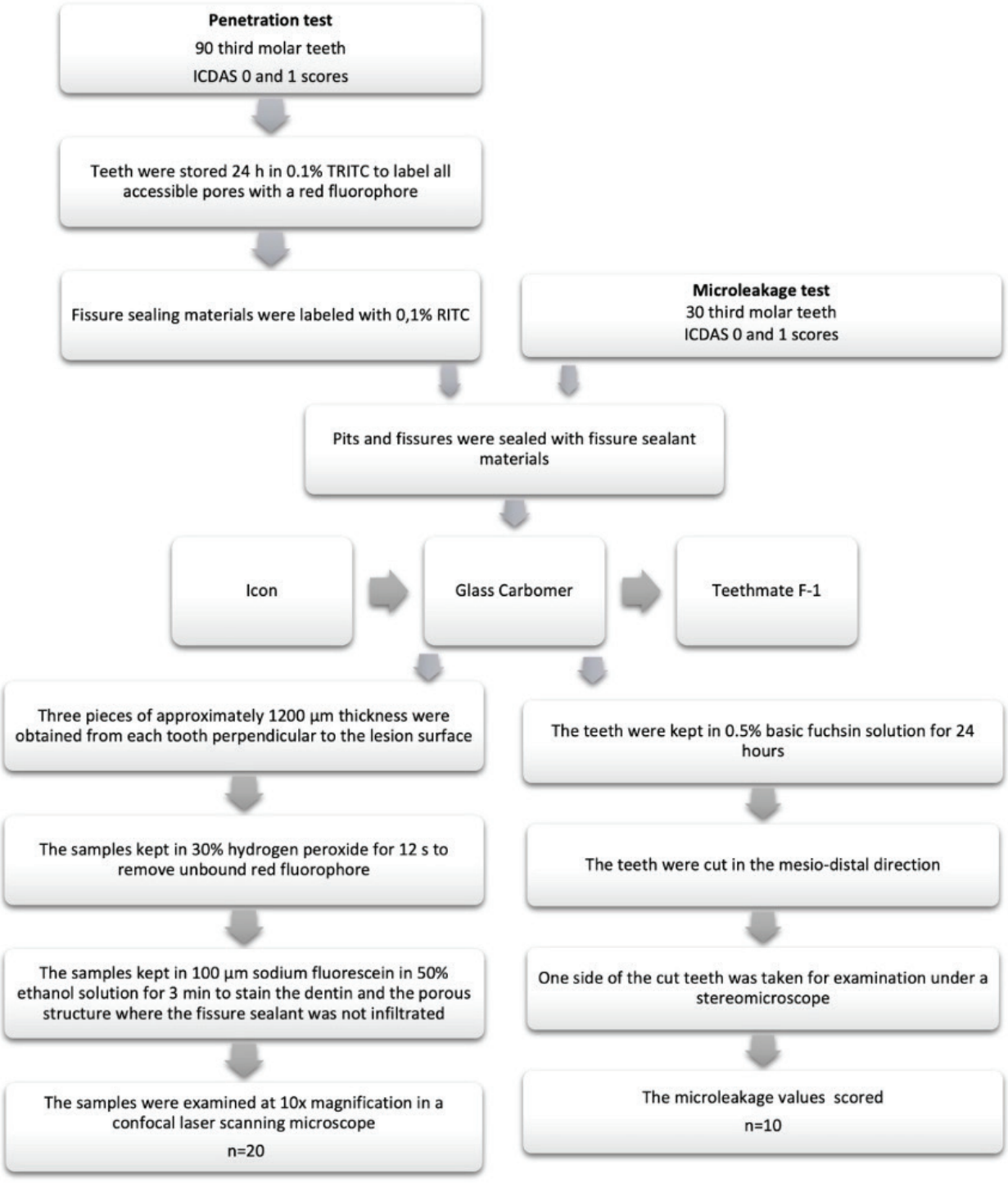

Figure 1. Flowchart of the study.

Statistical analyzes

Statistical analyzes were made using IBM SPSS Statistic 20 and MS Excel 2007 programs. The depth of penetration (maxPD) and the depth of the lesion (maxLD) were analyzed, and the percent penetration was calculated as the outcome variable.

(max)PDY = (max PD)/ (max)LDx100.

The normal distribution of the data was controlled with the Shapiro-Wilk test. Differences between groups were evaluated with the One-way ANOVA test ($p<0.05$).

Differences between microleakage scores were evaluated statistically by Kruskal Wallis and Mann-Whitney U-test ($p<0.05$).

Results

It was observed that the maxPD values different from each other according to the viscosity of the applied materials, the presence of air bubbles, organic deposits at the base of the fissure and the shape of the fissures (Figure 2). There was no statistically significant difference between the group 1 and 3 ($p>0.05$). All materials showed almost full penetration in V-type and U-type fissures (Fig. 2).

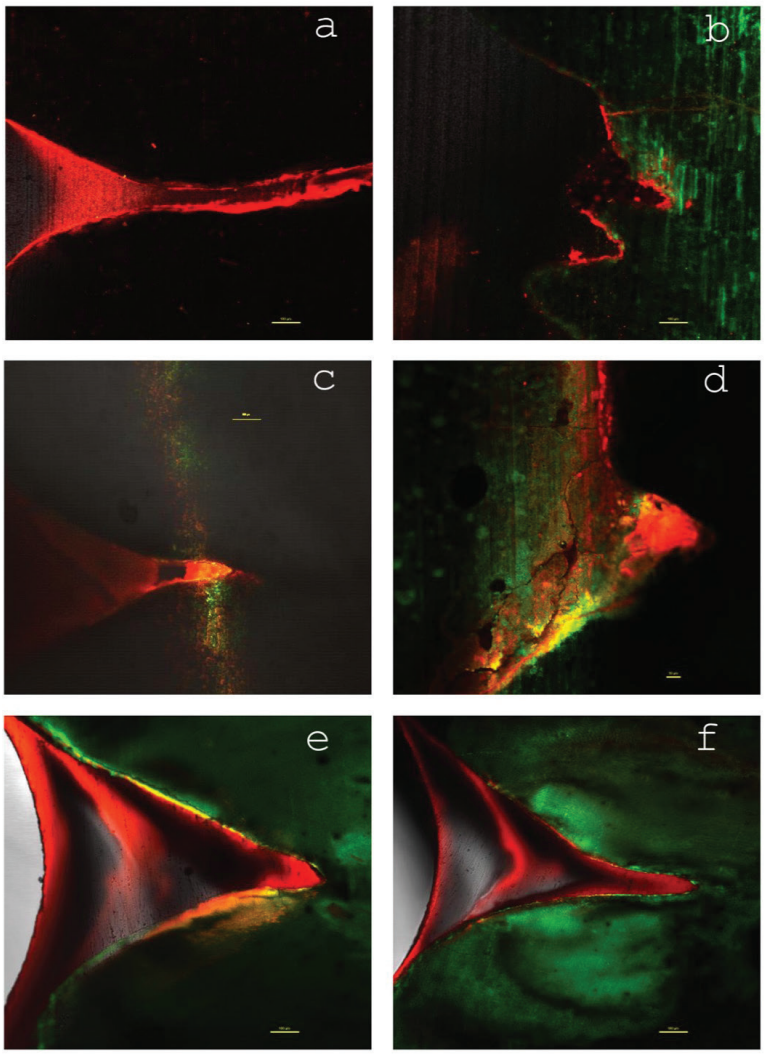

Figure 2. Penetration depth image of Group 1(a,b); Group 2(c,d) and Group 3(e,f).

The number of samples with 100% maxPD value were determined as 13 in the Group 1, 6 in the Group 2 and 10 in the Group 3. The maxPD values of the group 1 was statistically higher than the group 2 and the group 3 ($p<0.05$). The maxPD values of group 2 and 3 were similar ($p>0.05$) (Table 1).

Table 1. Mikroleakage scores of materials.

SCORES OF MICROLEAKAGE	Group 1 (Icon)	Group 2 (Glass Carbomer)	Group 3 (Teethmate-F1)
0	7	-	8
1	3	1	2
2	-	2	-
3	-	7	-

Group 2 showed significantly higher microleakage values than group 1 and 3 ($p < 0.05$). Group 2 showed severe microleakage values and internal cracks. There was no statistically significant difference between group 1 and 3 ($p>0.05$). Low microleakage values were observed in group 1 and 3 ($p > 0.05$). Microleakage values was determined as group 2>1>3 respectively (Table 2).

Table 2. Penetration depth of materials.

MATERIALS	PD_{mean}± SD	PD_{min}-PD_{max}
Group 1 (Icon)	90,54 ± 14,30[a]	61,64 -100
Group 2 (Glass Carbomer)	77.30 ± 16,01[b]	44,74 - 100
Group 3 (Teethmate-F1)	85,11 ± 21,07[ab]	45,32 -100

*PD_{mean}: Penatration depth mean, SD: Standart deviation. **Small letters show the statistical differences. There is no statistical difference between the average values with the same letter according to the One-Way Anova test.

Discussion

Minimally invasive approaches aimed at protecting healthy tooth tissues as much as possible have become remarkable in dental applications in recent years. As a result of this approach, the use of adhesive restorative materials has increased. The performance of a restoration is closely related to the material selection. For this reason, penetration depth and microleakage characteristics of different pit and fissure sealant materials were investigated in this study. Considering the results obtained from the study, the null hypothesis was rejected. Both the penetration depth and the microleakage of the Glass Carbomer sealant group were found to be different from the other groups.

Clinical studies ensure that all properties of the materials are determined in the most realistic conditions.[16] However, in vivo studies, it cannot be determined which properties of the materials cause success and which properties cause failure. In vivo conditions, it is impossible to determine the effect of physical and mechanical stresses that occur during function in the oral environment on the failure of the material. In vitro tests have advantages such as being easy to apply, fast and cheaper.[17] Therefore, penetration and microleakage properties, which are important in the clinical success of the materials, were evaluated in our study.[2]

From past to present, the most preferred fissure sealants have been glass ionomer-based and

resin-based materials. However, resin-based fissure sealants are considered to be the most successful materials in terms of their high retention rates and effectiveness. Viscosity is another factor for the ideal penetration, sealing and ideal marginal adaptation of the fissure sealant material.[18,19] Irinoda et al.[20] evaluating the effect of viscosity reported that low viscosity fissure sealant penetrates better into enamel than high viscosity ones. On the other hand, Barnes et al.[21] stated that viscosity does not affect the sealing properties of fissure sealants, so clinical success can be affected by changing the surface energy of enamel rather than making modifications in fissure sealants. In this study, the confocal laser microscope analysis method, which is used by many researchers was used to evaluate the penetration depth.[7,22]

Simultaneous images were obtained by staining the healthy enamel surface, porous tissue and fissure sealant with fluorescent dyes. Using more than one fluorescent dye separates images of different materials in studies. The fluorescent dye should be easily soluble and a good stimulant in the emission wavelength range.[23] Rodamin and fluorescein derivatives display these characteristics. Therefore, fluorophores are most commonly used materials in dental research. Fluorophores usually dissolve in non-polimerized monomers when marked with fluorescent resin dye. Chemical combination of fluorescent dyes with TEGDMA, HEMA or BIS-GMA-based resin bonding groups is not possible. For this reason, the dye is thrown out of the resin matrix and penetrates into the surrounding structures .[17,23]

Researchers have shown that fissure sealants penetrate the V and U shaped fissures the most; and penetrates the I and IK shaped fissures the least.[24-28] Although the fissure sealant has low viscosity, it cannot penetrate well and the fissure sealant becomes more difficult as the viscosity increases in I and IK shaped deep fissures. Our study supports previous studies. In our study, the penetration of Glass Carbomer sealant group which is the highest viscosity was found to be lower than other materials. The penetration depth of Icon Infiltrant and Teethmate F-1 sealant, both with low viscosity, was not statistically different from each other ($p>0.05$). These results show that viscosity of the sealant influences the penetration ability. Unlike other studies found that there was no difference in penetration between materials of different viscosity.[25,29]

Icon infiltrant contains TEGDMA that is a methacrylate-based resin matrix.[30]Also, before the Icon infiltrant is implemented, 99% ethanol is applied to the enamel surface to evaporate the remaining water. This application reduces viscosity and contact angle of the material, thus increasing the penetration of the material to the surface.[30,31] In some studies, TEGDMA containing infiltrants in two different forms with and without solvent was applied to the enamel lesions to compare the penetration ability and the effect of stopping progress of lesion, so infiltrants containing TEGDMA and ethanol solvent were found to be more effective.[32]

Paris et al.[7] compared infiltration abilities of fissure sealants and resin infiltrants in non-cavitated enamel fissure caries. The penetration of fissure caries treated with resin infiltrants was found to be significantly better compared to fissure sealants or soft etch infiltrants. However, no significant difference was observed in the penetration of resin sealants and resin infiltration in shallow lesions (ICDAS-code 0 and 1). Again, to this study, the hydrochloric acid used for infiltration provides deeper penetration in the enamel than phosphoric acid used in fissure sealants. In recent study, fissure morphology is another parameter that affects penetration depth. The effectiveness of the penetration depends on the wettability of the infiltrant and this is related to the complete accession of the acid to the fissures. Paris et al.[33] revealed that the most important step before caries infiltration was a complete drying. Clean surfaces with high free energy increase wettability compared to lower free energy surfaces coated with organic biofilm. Furthermore, thanks to the lower contact angle between the liquid and the solids, liquids penetrate easier to the porous solid structure. Presence of biofilm on the surface also changes the surface features, increases the contact angle between solids and liquids and possibly reduces the wettability of infiltrant.[34] In addition, Paris et al.[33] revealed that air bubbles remained in the

lesion when infiltrant was penetrating and air gap obstructs the infiltrant flow, especially on the fissure base. In our study, air bubbles were also observed into the fissure.

Fissure sealants that are the low viscous materials easily penetrate the pores formed by acids on the enamel surface. However, despite the improvement of their physical properties, polymerization shrinkage has not been prevented. The fissure sealants shrink by volume 1,5-4% during their polymerization with visible light which causes marginal gap formation. Marginal gaps are habitat for bacteria, causing microleakage and thus cause failure of restoration.[35,36] For this reason, another important factor affecting the efficacy and success of the fissure sealants is the adaptation performance to enamel. The ability to reduce the microleakage of the fissure sealent is achieved by a good marginal adaptation.[37,38] In our study, Icon infiltrant and Teethmate F-1 sealant revealed successful results with favorable adaptation and microleakage values.

Paris et al.[10] investigated the penetration potential of caries infiltration system in proximal lesions of different ICDAS (2,3,4,5) codes. Resin-based materials penetrate into the micropores formed by acidification, thus resin tags varying from 25 to 100 microns in length are formed, thus providing a mechanical lock between the resin and the enamel surface.[2,39] Resin tags not only contribute to the mechanical retention of the sealer but also surround the enamel crystals, reducing the effect of microorganism-derived acids.[40] In the resin infiltrant, these extensions are generated up to 800 microns thanks to hydrochloric acid. Contrary to this, glass ionomer-based fissure sealants are chemically bonded to enamel and dentine. Using relatively high molecular weight, acidic, polycarboxylic-based polymers in its own structure, glass ionomers roughened the tooth structure due to its low pH (self-etch). However, this structure is weaker.[41] For this reason, the microleakage of Glass Carbomer sealant that is the glass ionomer-based fissure sealant was found to be higher than other materials in the present study. Glass Carbomer sealant could not penetrate up to the fissure depths. In the confocal microscope analysis, we observed adaptation losses with wide and long intervals in the material and enamel interface which support our detections. Possible causes of differences in microleakage values are thought to be the content and percentage of fillers, the concentration of light-sensitive agents and the intensity of the polymerization light.[42] Microleakage for fissure sealants is an important indicator of adaptation and hiding power of the material to the dental tissue.[43]

Microleakage becomes more important issue because there is no cavity preparation in fissure sealants. Long-term adaptation of fissure sealants are weaker than composite restorations.[42] Today, it is reported that the most important reasons for replacing or repairing of restorative materials are marginal leakage and related complications. Therefore, it is important firstly to determine the marginal leakage and adaptation of temporary materials.[17]

The advantages of using glass ionomer-based materials can be determined in long-term use. For this reason, these materials tested in vitro must be tested in oral applications with clinical trials. More in vivo and in vitro studies will be useful to assess the efficacy of novel fissure sealant materials resulted from rapid developments and increased demand for minimal intervention.

Conclusion

Resin-based fissure sealants have been found to be more successful. In vitro penetration depths and internal fractures were observed in glass ionomer-based material. Although the penetration depth of glass ionomer-containing materials is deemed insufficient according to the results of this study, there will be indications for the use of different materials in different clinical situations due to the need to use them. Regular restoration checks will overcome this problem.

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Ethical Approval
The necessary ethical approval for this study was obtained from The Selçuk University Faculty of Dentistry Non-Interventional Clinical Research Evaluation Committee (2014/03).

Conflict of interest
None of the authors of this article has any relationship, connection or financial interest in the subject matter or material discussed in the article.

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Silikon Esaslı Self Retantif Parmak Protezi: Olgu Sunumu

Rehabilitation of a Patient with Partial Finger Amputation with Silicone Prosthesis: Case Report

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ÖZET

Amaç: Bu vaka raporunun amacı tek parmağında kısmi eksiklik bulunan hastanın, vakum yöntemiyle kendinden retansiyonlu bir silikon protez ile rehabilitasyonunu anlatmaktır.

Olgu sunumu: Tek parmağında kısmi eksiklik bulunan 42 yaşında bayan hasta protez gereksinimi ile başvurdu. Alınan anamnez sonrası özellikle görsel olarak rahatsız olduğunu sosyal hayatında sıkıntı çektiği için protez istediğini belirtti. Gerekli planlama ve hazırlık aşamasından sonra konvansiyonel yöntemlerle ölçü alındı ve silikon protez hazırlandı. Hastanın eksik parmağına adapte edildi.
Sonuç: Silikon parmak protezi ile geri bildirimin değerlendirildiği bu olgu sunumunda, hastanın yaşam kalitesi ve psikososyal uyumunu iyileştirdiği gözlemlenmiştir. Fonksiyon açısından kısıtlı etkisi olsa da estetik görünüm açısından tatmin edici sonuçlar elde edilmiştir.

Silikon, Parmak, Amputasyon, Maksillofasiyal Protez

Anahtar kelimeler: *Silikon, Parmak, Amputasyon, Maksillofasiyal Protez*

ABSTRACT

Objectives: The aim of this case report is to describe the rehabilitation of a patient with partial finger amputation using a self-retaining silicone prosthesis by the vacuum method.

Case report: A 42-year-old female patient with a partial amputation of one finger reffered for non-functional prosthesis. After clinical examination, non-functional, self-retantive- silicon based somatoprosthesis was planned to increas the quality of life. And then standard conventional methods was started like as maxillofacial prosthesis. Measurements were taken by and a silicone prosthesis was prepared. It was adapted to the patient's missing finger.

Conclusion: This case report evaluating feedback with a silicone finger prosthesis found that it improved the patient's quality of life and psychosocial adjustment. Although the effect was limited in terms of function, satisfactory results were obtained in terms of aesthetic appearance.

Keywords: *Silicone, Finger, Amputation, Maxillofacial Prosthesis*

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Giriş

Protetik diş tedavisi Sabit Kron – Köprü Protezleri, Hareketli Total ve Parsiyel Protezler ve Çene Yüz Protezleri olarak 3 temel alandan oluşmaktadır. Amerikan maksillofasiyal protez akademisine göre çene yüz protezleri Protetik Diş Tedavisinin bir yan dalı olarak kabul edilirken ülkemizde Protetik Diş tedavisi temel alanı içinde yer almaktadır. Protetik diş tedavisi çalışma alanı şu şekilde sınıflandırılabilmektedir: **Çeneyüz Protezleri, Extraoral protezler** (1. Oküler - Sadece Göz kısmını içeren protezler 2. Orbital Protezler Göz ve göz çevresini içeren protezler 3. Aurikular Protezler Kulak Protezleri 4. Nazal Protezler 5. Orta yüz Protezleri Yüzün bir bölümünü oluşturan protezler 6. Somatik Protezler-Somatoprotezler-Vücudun el, **parmak vb.** gibi bir bölümünü oluşturan protezler 7. Radyasyon koruyucu protezler radyoterapi sırasında kullanılan protezler) **İntraoral Protezler** (1. Cerrahi obturatörler - Maksillanın (üst çene) kısmen veya tamamen kaybından sonra cerrahi alanı kapatan protezler 2. Geçici ve Daimi Obtüratörler 3. Palatal Lift Protezleri 4. Palatal ogmentasyon protezleri 5. Mandibular rezeksiyon protezleri 6. Florür uygulama protezleri). Silikon parmak protezleri parmak ampütasyonlarında yapılmaktadır. Parmak amputasyonları, parmağın bir kısmının veya tamamının konjenital hastalıklar veya travma nedeniyle kaybedilmesidir. Latince 'amputate' kelimesi deri ile çevrili bir vücut parçasının bir kısmının veya tamamının çıkarılması' olarak tanımlanmıştır.[1] Parmak ve kısmi parmak amputasyonları, kavrama ve güç kaybına ek olarak önemli fonksiyonel eksikliklerle sonuçlanan en sık karşılaşılan kısmi el kayıplarındandır. Parmak eksikliği, hastaların hem fiziksel hem sosyal yaşamını ciddi oranda olumsuz etkilemektedir. Tek parmakta mevcut kısmi amputasyon fonksiyonel hareketlerde kısıtlılığa neden olurken estetik açıdan da yaşam kalitesini tamamıyla düşüren bir durumdur. Parmak amputasyonunun psikolojik etkileri daha fazla olabilmektedir dolayısıyla bu hastalarda yapılan parmak protezi, minimal düzeyde işleve katkıda bulunurken kozmetik ve psikolojik açıdan daha etkili olmaktadır.[2,3] Parmak protezleriyle eksik dokunun rekonstrüksiyonu yapıldığında hastalara estetik görüntü ve fonksiyon yeniden kazandırılabilmektedir.[4] Estetik bir parmak protezinin doku ile birleşimi belirgin olmamalı, renk ve yüzey özellikleri doğal dokularla uyumlu olmalı, kırışıklıklar ve tırnaklar gibi karakteristik özelliklere sahip olmalıdır. Amputasyon sonrası kalan parmak dokusu protezin tutuculuğunu, estetiğini ve dokuyla uyumunu belirleyeceğinden oldukça önemlidir.[5,6]

Çene yüz protezleri kapsamında extraoral sınıflamada yer alan parmak, göz, kulak, burun, el vb. dahil olmak üzere herhangi bir organın yapay olarak yeniden yapılandırma sürecine somatoprotezler denir.[7] Ekstra oral protezlerde tutuculuk çeşitli yöntemlerle sağlanabilir. Parmak protezlerinde tutuculuk çeşidine karar verirken, tutulan doku miktarına, kemik tutulumuna (distal falanks), amputasyon açılarına ve seviyelerine, diğer parmakların tutulumuna göre değerlendirme yapılır. Parmak protezlerinde dört tip tutuculuk vardır. Silikon proteze negatif basınç sağlayacak kadar doku bulunan hastalarda vakum yöntemiyle tutuculuk sağlanabilir. Silikon protez ve doku ile uyumlu tıbbi yapıştırıcılar uygulanabilir ancak burada önemli olan kaybedilen doku miktarıdır. Kayıp doku alanı çok fazla ise tutuculuk tamamıyla azalacağı için daha girişimsel uygulamalar da tercih edilebilmektedir. Komşu iki parmağa halkalarla mekanik sabitleme yapılabilen yöntemlerden olduğu gibi, dental implantların dokuya yerleştirilmesiyle protez ile implant arasında mekanik olarak da tutuculuk sağlanabilmektedir.[8] İmplant destekli parmak protezlerinin, kemikte oluşan basınç ve titreşim sayesinde bir miktar dokunma hissi ve bir takım fonksiyonel hareketleri kazandırdığı bildirilmiştir.[9,10] Bu açıdan değerlendirildiğinde implantlar ile sağlanan tutuculuk diğer tutuculuk çeşitlerine göre daha üstün sayılabilir ancak her durumda uygulanması mümkün olmayabilir.[11,12] Mevcut kemik miktarı yeterli değilse veya hasta cerrahi müdahaleye uygun değilse diğer protez ve tutucu şekilleri değerlendirilmelidir. Cerrahi endikasyonu olmayan hastalarda en sık uygulanan süspansiyon yöntemi ise vakum ile tutuculuktur.[13] Vakum ile tutuculukta silikon malzeme esnek olduğu için ve protezin uyumu doğru yapıldıysa çıkarma işlemi sırasında

negatif bir basınç oluşur ve çok kısa dokularda bile çıkarmak çok zor olmaktadır.[14]

Parmak protezlerinin işlevsellik açısından çeşitleri mevcuttur. Pasif silikon protezler, vücuttan güç alan protezler, total parmak amputasyonu için dışarıdan güç alan protezler veya göreve özel protezler şeklinde ayrılır.[8] Fonksiyonel protezlerin üretimi için kullanılan teknik ve malzemeler açısından özel ekipmanlara ihtiyaç vardır. Fonksiyonel protezler ile anatomik bir parmak gibi fleksiyon ve ekstansiyonu taklit edebilen protezler üretilebilmektedir ancak bu protezlerin tasarlanması ve üretimi için profesyonel merkezlere ihtiyaç vardır.[7] Hastaların sosyal yaşama daha rahat adapte olmalarını sağlamak ve estetik açıdan daha iyi görüntü elde edebilmek amacıyla pasif silikon protezler tercih edilebilir. Hastanın fiziksel özelliklerine uygun karşıt parmak ile uyumlu ve konforlu bir protez hem psikolojik hem kozmetik açıdan memnun edici olacaktır. Silikon protezler estetik açıdan olumlu sonuçlar sağlar, ancak işlevselliği de iyileştirdiklerine dair kanıtlar kesin değildir.[15] Silikon protezlerin birçok avantajı bulunmaktadır. Kullanılan silikon malzeme tahriş edici değildir. Silikon protezler ile tutuculuk rahat, güvenli ve basit bir şekilde sağlanır, kişiye özel tasarlanır ve renklendirmeler ile birebir uyum sağlanabilir. Bu sayede kaybedilen dokuya doğal ve estetik görünümü geri kazandırılarak psikolojik travma ortadan kaldırılmış olur. Silikon parmak protezinin başarısı, doğru tanı ve tedavi planlaması, protezin üretiminde kullanılan malzeme ve teknikler, hekimin bilgi ve becerisi, hastanın kullanım şekli gibi çeşitli faktörlere bağlıdır.[16]

Bu olgu sunumu, kısmi parmak amputasyonu geçiren hastanın silikon protez ile rehabilitasyonu ve yapılan protezde uygulanan retansiyon yöntemi ile protetik sonuçlarını bildirmeyi amaçlamaktadır.

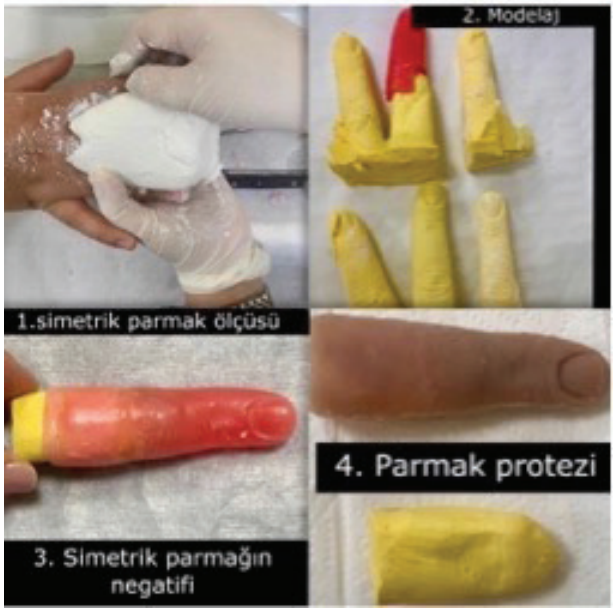
Olgu Sunumu

Tek parmak ampütasyonu olan bayan hasta, ampütasyonu gerçekleştiren Ortopedi Travmatoloji- El Cerrahisi Uzmanı tarafından operasyonları yapılıp iyileşme sürecinin tamamlanıp, girişimsel olmayan protetik tedavi için hazır olduğu kanısına varılan hasta tarafımıza yönlendirildi. Gaziantep Üniversitesi Diş Hekimliği Fakültesi Protetik Diş Tedavisi Anabilim Dalı kliniğinde hastanın muayenesi yapıldı. Sağ elin 3. parmağının distal falanksında kayıp olduğu tespit edildi (Resim 1). Tedavi süreciyle ilgili hasta onamı alındı ve retansiyonun rahatlıkla sağlanabileceği bir protez planlandı.

Resim 1. Amputasyon sonrası kalan parmak dokusu

Ampute edilen alanın fotoğraf kayıtları alındıktan sonra hastanın her iki eline sıvı vazelin uygulandı. Her iki elin aljinat ölçü maddesi ile ölçüsü alındı (Resim 2). Ampute parmağın bulunduğu elin ölçüsünden alçı model elde edildi. Simetrik elin ölçüsü izole edildi. Simetrik parmağın ölçü boşluğuna mum eritilip döküldü, eritilen mum kabul edilir soğuklukta iken ampute parmak, içinde akışkan mum bulunan simetrik parmağın ölçü boşluğuna yerleştirildi ve soğuması beklendi. Simetrik parmağın mum materyalden bir kopyası elde edildi. Daha sonra bu mum materyal ampute parmağın üzerinde uyumlandı retantif alana kadar uzatıldı, polisajı yapıldı ve mum modelaj geleneksel yöntemlerle muflaya alındı. Silikon materyal (Technovent UK, Med Dent, Türkiye) üretici firma talimatına göre karıştırıldı. Renklendiriciler manuel olarak ilave edildi, karışım sağlandı ve üretici firma talimatına göre polimerizasyon sağlandı (Resim 3).

Resim 2. Aljinat ölçü maddesi ile ölçü alımı



Resim 3. Ölçü, modelaj ve bitim aşaması

Silikon esaslı parmak protezi mufladan çıkarıldı ve parmağa adapte edildi (Resim 4). Çapaklar temizlendi ve hastamıza teslim edildi. Parmak protezlerin yapımı geleneksel çene yüz protezlerinin yapım aşamalarıyla aynı şekilde olmaktadır. Ancak dokuya tam uyumlu rengin ayarlanabilmesi teknolojik alt yapı yada klinik tecrübe gerektirmektedir. Vakada rengin dokuyla aynı tonda bitirilebilmesi için multidisipliner bir çalışma gerçekleştirilmiş, protezin bir kısım aşamaları Gaziantep Üniversitesi'nde, bir kısım aşamaları ise Gazi Üniversitesi ile ortak çalışılarak planlanmış ve bitirilmiştir.

Resim 4. Mufla aşaması sonrası hastaya teslim edilen parmak protezi

Tartışma

Kaybedilen dokunun yerine konulmasında kullanılan protezlerin yapımında tercih edilen materyallerin sahip olması gereken birçok özellik vardır. Materyalim biyouyumlu olması, yeterli fiziksel, kimyasal ve mekanik özelliklere sahip olması gibi pek çok özelik sayılabilir. Maksillofasiyal protetik materyaller içinde bugün en popüler olan materyal silikonlardır. Maksillofasiyal Protezlerin yapımında kullanılan materyallerdeki gelişmeler sahip oldukları elastikiyet, biyouyumluluk ve kullanım kolaylığı nedeniyle geniş bir kullanım alanına sahiptir ve birçok avantajından dolayı parmak protezlerinin yapımında da oldukça sık tercih edilmektedir.[17] Literatürle uyumlu olacak şekilde olgumuzda silikon esaslı dokuyu oldukça net taklit edebilen bir materyal kullanılmıştır.

Parmak ampütasyonları travma, tümör, diyabet, ateroskleroz gibi vasküler hastalıklar ve konjenital nedenlerle gerçekeleşebilmektedir. Parmak ampütasyonlarının tedavisi cerrahi aya da konservatif olarak yapılabilmektedir. Parmak protezleri medikal yapıştırıcılar, mekanik tutuculuk ya da dental implant osseosintegrasyonu gibi çeşitli tekniklerle yapılabilmektedir. Estetik dikkate alınarak yapıldığında kaliteli silikon materyallerin kullanımıyla cilt tonu ile optimal uyumlu protezler üretilebilmektedir.[18-21]

Nemli ve ark.[22], implant destekli parmak protezlerinde kullanılan sürtünme ile tutuculuk

sağlayan döküm metal teleskobik tutucu, sürtünme ile tutuculuk sağlayan zirkonya tutucu, sürgü tipi hassas tutucu ve manyetik tutuculardan oluşan dört farklı tutucu sistemi karşılaştırılmış ve bu tutucu sistemlerinin farklı düzeylerde tutuculuk sağladığı, ancak her birinde yeterli retansiyon elde edildiğini gözlemlenmiştir. Ayrıca, tüm tutucu türlerinin proteze rijit bir destek sağladığı ve böylece hastalara kavrama fonksiyonunu kazandırdığını da bildirmektedirler. Rapor edilen bu sonuç vaka raporumuzun sonucunu desteklemektedir.

Yapılan bir araştırmada, parmak amputasyonu geçirmiş 42 hasta (tek veya çoklu parmakları kısmi veya tam olarak kesilmiş) değerlendirilmiştir. Hastaların çoğu vakum süspansiyonu kullanmakta olup, kısa güdüklerin nadir olduğu durumlarda tıbbi yapıştırıcı tercih edilmiştir . Araştırmada, amputelerin silikon parmak protezine uyumu ve rehabilitasyon sürecindeki adaptasyonları, Trinity Amputasyon ve Protez Deneyimi Ölçekleri (TAPES) kullanılarak değerlendirilmiştir. Sonuçlar, silikon parmak protezlerinin amputasyon sonrası adaptasyon sürecinde önemli bir rol oynadığını göstermektedir. Protezlerin el fonksiyonlarına etkisi optimum düzeyde olmasa da amputelerin yaşam kalitesini iyileştirebileceği sonucu rapor edilmektedir.[23]

Literatürdeki bir başka vaka raporunda, implant destekli parmak protezi planlanan bir hastaya ön hazırlık ve değerlendirme amacıyla doku yapıştırıcısı kullanılarak tutuculuk sağlanan bir silikon protez hazırlanmıştır. Hasta, protezin estetik görünümü, tutuculuğu, kullanımı ve temizleme kolaylığından memnun kalmış ve bu memnuniyet sonucunda implant destekli protez yapılmasından vazgeçtiği bildirlmiştir.[24] Olgumuzda ampute parmağın tutuculuğu protez stabilite ve retansiyonuna yeterli katkıyı sağlayacak durumdaydı ve herhangi bir tutucu faktöre ihtiyaç duyulmadı. Silikon materyalin parmağa sıkıca oturuyor olması istenen retansiyonu sağladı.

Literatürde self retantif silikon parmak protezlerinin yapılan çalışmalarla motor gelişime katkı sağladığı, kavrama gücü, kozmetik faktör, yaşam kalitesi üzerinde olumlu etkiler ortaya koyduğu gösterilmektedir[3]. Silikon parmak protezleri estetik ve psikolojik açıdan hastalara büyük avantaj sağlamaktadır. Günümüzde teknolojinin hızla gelişmesi ile malzeme ve üretim yöntemi açısından gelişmeler yaşanmaktadır. CAD/CAM (Bilgisayar destekli tasarım/Bilgisayar destekli üretim) ve 3 boyutlu yazıcı yöntemi ile hem fonksiyonel hem pasif silikon protezler üretilebilmektedir ancak şu anda sadece sınırlı sayıda merkez, hastalar için bu tür protezleri özel olarak üretebilecek uzmanlığa sahiptir. Konvansiyonel yöntemle üretilen silikon protezlerde en zor ve en kritik aşamalardan bir tanesi hastanın cildi ile renk uyumunu yakalamaktır. Estetik bir parmak protezi üretimi için renk eşleştirme yöntemleri vardır. Yayınlanmış bir vaka raporunda, katmanlı renk eşleştirme tekniği ile hazırlanan protezlerde gerçeğe yakın bir renk elde edilmiş ve olumlu sonuçlar alınmıştır.[25]

Aynı zamanda dijital olarak spektrokolorimetre ile renk eşleştirme yapılabilmektedir. Bu sistem, maksillofasiyal protezlerde kullanılmak üzere cilt tonlarının doğru eşleştirilmesini kolaylaştırmak için büyük bir kolaylık sağlamaktadır.[26] Estetik ve tutucu bir protez, bir parmağın başarılı protez restorasyonunda temel belirleyici faktörlerdir.

Tercih edilen silikon esaslı materyaller de kullanıma bağlı olarak uzun dönemde renk değişikliği görülebilmektedir. Bu renk değişikliklerindeki temel etkenler şu şekilde açıklanabilmektedir: Güneş ışığının sahip olduğu ultraviyole ışınları, kullanılan takma tırnak yüzük gibi kozmetik ürünlerin takılıp çıkarılması esnasında oluşan aşınma ve kimyasal abrazyonu, elastomerik yapının sürekli maruz kaldığı ıslanma ve kuruma döngüsü.[27]

Zamanla renk değişikliğiyle beraber fiziksel ve mekanik özelliklerin kaybı da meydana gelebilmekte ve en fazla bozulma protezlerin kenarlarında görülebilmektedir. Bu değişiklikler protezin ömrünü belirleyen önemli parametrelerdir. Kullanım ve temizliğe bağlı oluşabilecek yırtılmalar konusunda hastalar bilgilendirmeli farkındalıkları artırılmalıdır.

Estetik ve tutucu bir protez, bir parmağın başarılı protez restorasyonunda temel belirleyici faktörlerdir.

Sonuç

Bu vaka raporunda herhangi bir invaziv tutucuya ihtiyaç duyulmadan kendinden retansiyonlu hazırlanan silikon parmak protezi hem retansiyon hem de hasta memnuniyeti açısından oldukça başarılı bulunmuş, 1 yıllık klinik takipte self retantif parmak protezi renk stabilitesini korumuştur.

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CASE REPORT

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Fusion In Primary Teeth: Report of Three Cases

Süt Dişlerinde Füzyon: Üç Farklı Olgu

Ceren Kaplan[1*], Tuğçe Akçora[2], Özlem Martı Akgün[3]

ABSTRACT

Objective: Fusion is a developmental dental anomaly resulting from the union of two adjacent teeth. The etiology of fusion is not definitively known. This developmental anomaly can lead to functional and aesthetic problems in individuals' lives. Furthermore, in the majority of cases with fusion in primary teeth, a lack of permanent teeth is identified. The aim of this case report is to present three patients diagnosed with fusion in primary dentition.

Case Report: The first patient, a 4-year-old child, presented to our clinic for routine examination. Clinical and radiological assessments revealed fusion in the mandibular anterior region, as well as the absence of one primary lateral tooth and a permanent lateral tooth. The second patient, a 6-year-old, visited our clinic due to dental pain. Oral and radiographic findings indicated fusion in the mandibular anterior region and the absence of a lateral permanent tooth. The last patient was a 5-year-old who presented with dental pain. Radiographic findings showed fusion in the mandibular region. The guardians of the patients were informed about the relevant anomalies. Written and verbal consent was obtained from the legal guardians prior to the necessary treatments. The patients whose treatments were completed are being monitored regularly for potential complications arising from their anomalies.

Conclusion: Fusion in primary teeth represents a rare dental anomaly with significant clinical implications. Early diagnosis, preventive interventions like fluoride applications, and a multidisciplinary approach are essential to addressing potential complications effectively. Additionally, the long-term follow-up of these patients is critical to monitor developmental changes and ensure optimal outcomes. This study underscores the importance of collaborative efforts between pediatric dentists, orthodontists, and restorative specialists in formulating individualized treatment plans for such anomalies.

Keywords: *Fused Teeth, Pediatric Dentistry, Tooth Abnormalities*

ÖZET

Amaç: Füzyon, birbiriyle komşu olan iki dişin birleşimden kaynaklı gelişimsel bir dental anomalidir. Füzyonun etyolojisi kesin bir şekilde bilinmemektedir. Bu gelişimsel anomali bireylerin yaşamında fonksiyonel ve estetik açıdan problemlere sebep olabilir. Bununla birlikte, süt dişlerinde füzyon görülen vakaların çoğunluğunda sürekli diş eksikliği tespit edilmektedir. Bu olgu raporunun amacı süt dentisyonda füzyon tespit edilmiş üç hastanın sunumu amaçlanmıştır.

Olgu sunumu: 4 yaşında kontrol amacıyla kliniğimize başvurmuş hastanın klinik ve radyolojik incelemelerinde mandibular anterior bölgede füzyon, tek süt lateral ve daimi lateral dişlerin eksik olduğu saptanmıştır. İkinci hasta ise; 6 yaşında olup, diş ağrısı dolayısıyla kliniğimize gelmiştir. Hastanın oral ve radyografik bulgularında mandibular anteriorda füzyon ve lateral daimi diş eksikliği saptanmıştır. Son hastamız ise; 5 yaşında olup diş ağrısı kaynaklı kliniğe başvuruda bulunmuştur. Hastanın oral radyolojik bulgularında mandibular bölgedeki dişlerinde füzyon olgusuna rastlanılmıştır. Hastaların velileri ilgili anomali hakkında bilgilendirilmiştir. Gerekli tedaviler öncesinde yasal vasilerinden yazılı ve sözlü onamları alınmıştır. Tedavileri tamamlanan hastaların anomali kaynakları olası durumlar için düzenli takipleri gerçekleştirilmektedir.

Sonuç: Süt dişlerinde füzyon, klinik uygulamada benzersiz zorluklar oluşturan nadir bir dental anomalidir. Erken teşhis, olası komplikasyonların yönetiminde kritik bir rol oynar. Çürük riskini ve diğer ilişkili sorunları en aza indirmek için flor uygulamaları gibi koruyucu önlemler önemlidir. Etkilenen hastaların bireysel ihtiyaçlarını karşılayan tedavi planları geliştirmek için pedodontistler, ortodontistler ve restoratif uzmanların yer aldığı multidisipliner bir yaklaşım gereklidir. Gelişimsel değişikliklerin izlenmesi ve olumlu sonuçların sağlanması için uzun vadeli takip kritik öneme sahiptir. Bu çalışma, bu tür vakalarda kapsamlı bakım sağlamak için diş hekimleri arasındaki iş birliğinin önemini vurgulamaktadır.

Anahtar Kelimeler*: Füzyon Dişler, Pedodonti, Diş Anomalileri*

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Introduction

Dental Anomalies are defined as irregularities observed in the number, volume, shape, tissue, and eruption status of teeth during their development. These anomalies can manifest in both primary and permanent dentition. While the precise etiology of dental anomalies remains unclear, environmental and genetic factors are known to play significant roles in their emergence.[1] Dental anomalies can be classified into several categories: structural anomalies (such as amelogenesis imperfecta, dentinogenesis imperfecta, and enamel hypoplasia), number anomalies (including hypodontia and hyperdontia), size anomalies (like microdontia and macrodontia), eruption anomalies (such as transposition and delayed eruption), and shape anomalies (including fusion and gemination).[1,2]

Fusion is a specific developmental anomaly characterized by the union of at least two independently developing primary or permanent teeth. Abnormalities occurring during the morphodifferentiation stage of tooth development can lead to variations in tooth form and size. Fusion represents the merging of two distinct tooth germs and may also be referred to as a double tooth or conjoined tooth.[2,3] Clinically, the appearance of fused teeth can vary, appearing normal or larger depending on the embryological stage at which the fusion occurs. Fusion is believed to result from physical forces acting between two or more tooth germs before calcification, leading to the fusion of the inner enamel epithelium and adjacent dental papillae while keeping the pulp chamber and roots separate.4,5 Racial and genetic factors can influence the occurrence of fusion, which is particularly prevalent in primary dentition and often observed in the lower anterior region. While fusion in the posterior region of permanent dentition is rare, it can occur in both types of dentition, with a higher prevalence in primary dentition (approximately 0.5%) compared to permanent dentition (about 0.1%).[6-8] Accurate diagnosis of fusion necessitates radiographic imaging.[8]

Fusion can occur between teeth of the same or different dentitions, as well as between normal and supernumerary teeth. Depending on the stage of fusion, it may result in a complete fusion, which creates a wide tooth crown, or an incomplete fusion, which involves root merging. Complete fusion is characterized by a single pulp chamber and root canal, while incomplete fusion may present as one pulp chamber with two separate roots or two pulp chambers with two root canals.[9,10]

The exact causes of fused teeth are not fully understood, but potential contributing factors include pressure, trauma, physical stress, or contact between developing teeth, which may lead to necrosis of the epithelial tissue.[8] Environmental factors such as fetal exposure to alcohol, hypervitaminosis, and thalidomide embryopathy have also been suggested as possible influences.[9,11,12] Given that thalidomide has not been used for routine medical conditions for decades and women prescribed thalidomide for specific indications today are required to adhere to strict contraceptive protocols, its relevance as an etiological factor is considerably limited. Additionally, some researchers propose that autosomal inheritance may play a role in the etiology of fusion.[8,10,13]

This study presents the clinical and radiographic findings of fusion observed in three patients who visited a pediatric dental clinic for various dental needs. Fused teeth are considered a rare dental anomaly, and this study aims to highlight the potential complications associated with fusion and raise awareness among dental professionals regarding this condition.

Case Reports

Case I

A 4-year-old healthy male patient presented to our clinic for a routine check-up. The patient's anamnesis revealed no systemic health problems. It was learned that the patient had undergone dental treatments at another healthcare facility under general anesthesia due to severe decay and material loss in the upper jaw. Consequently, all teeth in the maxilla were extracted. A dental prosthesis was fabricated for the upper jaw; however, the patient refused to use it due to difficulties in adaptation and discomfort, resulting in non-compliance with

its usage. The parents were informed about the importance of prosthesis use, and strategies to encourage adaptation were discussed.

Clinical and radiographic findings revealed fusion in teeth 82 and 83, unilateral absence of primary lateral incisors, and bilateral absence of permanent lateral incisors (Figure 1 and Figure 2). In this case, initial caries were detected in the fused teeth, but no significant material loss was observed. As a preventive measure, the patient was subjected to regular fluoride applications, and the fused teeth were closely monitored over time. Additionally, a root fragment of a tooth was detected in the upper jaw. Initially, the parent was informed about the relevant anomalies. Following this, written informed consent was obtained from the patient's parents. Subsequently, the root fragment in the upper jaw was surgically removed.

The systemic health of the patient in this case was unremarkable, with no reported medical conditions or developmental disorders. Such information underscores the nonsyndromic nature of the observed fusion anomaly. Nonetheless, future studies should consider evaluating systemic influences, such as nutritional deficiencies, metabolic disorders, or environmental exposures, as potential contributing factors to similar cases.

The use of dental prostheses in children presents unique challenges compared to adults due to ongoing growth and developmental changes. Children often experience discomfort and resistance to prosthesis use, particularly in the early stages.[14] Adaptation difficulties are commonly associated with the sensation of a foreign object in the mouth, which can interfere with daily activities like eating and speaking. Families play a crucial role in providing encouragement and support during this adjustment period.[14,15]

Proper maintenance and hygiene are critical for the success of pediatric prostheses. However, ensuring consistent cleaning practices can be challenging for young patients. Parental involvement in maintaining prosthesis hygiene is essential to prevent complications such as plaque accumulation and associated oral health issues.[15]

Psychological factors also influence prosthesis acceptance. Children may feel self-conscious about wearing a prosthesis, which could affect their social interactions and self-esteem. Open communication with both the child and the family, along with emphasizing the health benefits of prosthesis use, can help mitigate these concerns.[15,16]

In this case, the patient's upper teeth had been completely extracted, and a removable dental prosthesis was fabricated. However, the child declined to use it, reportedly due to discomfort and an inability to adapt to the prosthesis. Psychological factors, such as anxiety or unfamiliarity, may have contributed to this refusal.[16] Further evaluation by a pediatric psychologist or prosthodontist could provide deeper insights into the reasons behind the non-use and potentially improve compliance in future similar cases.

The patient was encouraged to use the prosthesis, and the family was advised on ways to promote its use. The parents were informed about the importance of maintaining oral hygiene, and regular follow-ups were conducted to ensure the condition remained stable. Finally, the patient was placed on regular follow-up schedules to be referred to the orthodontics clinic.

Figure 1. Fusion of teeth 82 and 83 in the panoramic radiograph of a 4-year-old male patient.

Figure 2. The intraoral appearance of the patient.

Case II

A 6-year-old male patient presented to our clinic with a complaint of pain. Radiographic and clinical examinations revealed deep dentin caries, and the source of the pain was identified. Additionally, fusion was detected in teeth 82 and 83, along with the absence of permanent lateral incisors in the same area (Figure 3 and Figure 4). The medical history obtained from the patient's parents indicated that the patient had no systemic diseases and was not taking any regular medications. Furthermore, there was no history of trauma in the head and neck region. In this case, initial caries were detected in the fused teeth, but no significant material loss was observed. As a preventive measure, the patient was subjected to regular fluoride applications, and the fused teeth were closely monitored over time. The parents were informed about the importance of maintaining oral hygiene, and regular follow-ups were conducted to ensure the condition remained stable.

Initially, the family was informed about dental anomalies and the potential complications that could arise. Subsequently, verbal and written informed consents were obtained from the patient's parents for the necessary dental treatments, and appropriate information was provided. After addressing the relevant dental treatment needs, oral hygiene motivation was provided, and the patient was referred to the orthodontics clinic for further management and placed on regular follow-up.

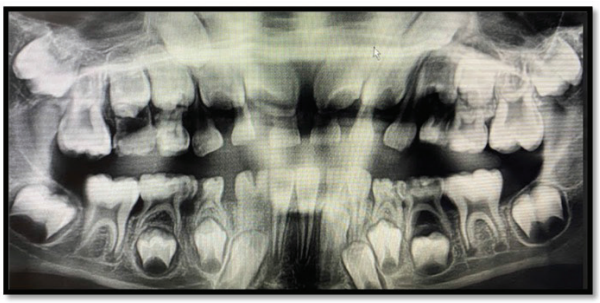

Figure 3. Fusion of teeth 82 and 83 was observed in the panoramic radiograph of a 6-year-old male patient.

Figure 4. The intraoral appearance of the patient.

Case III

A 5-year-old healthy male patient presented to our clinic with a complaint of pain. Clinical and radiographic findings revealed deep dentin caries and fusion in teeth 71 and 72 (Figure 5 and Figure 6). No absence of permanent teeth was observed. The medical history obtained from the patient's guardian indicated that the patient had no systemic conditions and had not experienced any trauma to the head and neck region.

The necessary verbal and written informed consents were obtained from the patient's parents prior to initiating dental treatment. After addressing the relevant dental treatment needs, oral hygiene motivation was provided. The patient's parents were informed about the detected dental anomaly, and the patient was placed on regular follow-up to monitor for any potential complications.

Figure 5. Fusion of teeth 71 and 72 was observed in the panoramic radiograph of a 5-year-old male patient.

Figure 6. The intraoral appearance of the patient.

Discussion

Fusion in primary teeth can lead to complex clinical scenarios, including the potential for delayed eruption of permanent teeth due to altered resorption patterns. Studies indicate that hypodontia in permanent teeth often accompanies fusion in primary teeth, with reported incidences ranging from 20% to 37.5%.[17] Mechanistically, the absence of a permanent tooth following primary tooth agenesis is attributed to disruptions during odontogenesis, suggesting a developmental linkage rather than a general rule. Genetic loci, such as MSX1 and PAX9, have been implicated in nonsyndromic tooth agenesis and may also influence fusion anomalies, though definitive evidence is limited.[18] These genetic markers are associated with various patterns of tooth development and anomalies, highlighting the need for further research in this area. Relevant studies provide valuable insights into the genetic predispositions that may underlie such conditions.[1] While MSX1 and PAX9 mutations are well-documented contributors to nonsyndromic tooth agenesis, their role in dental fusion remains less clear. Theoretically, disruptions in genes regulating dental development could contribute to anomalies such as fusion by altering the timing and spatial organization of tooth bud formation.[17,18] However, direct evidence linking these loci to fusion anomalies is scarce.[1,18] Genetic studies involving next-generation sequencing could provide valuable insights into potential associations and mechanisms underlying these conditions.[17]

Fusion teeth and the complications they may create necessitate multidisciplinary treatment approaches. Collaboration between pediatric dentistry and orthodontics is crucial for identifying dental anomalies and achieving more effective prognoses in treatment during both primary and mixed dentition. Fusion is a dental anomaly that is more frequently observed in primary dentition.[2,3] Which is why pediatric dentists typically diagnose most cases. Furthermore, cooperation between orthodontics and pediatric dentistry is essential to prevent potential complications that may arise in the future. In such cases, it is vital for pediatric dentists to be aware of other anomalies that may occur alongside fusion. Additionally, various imaging methods are helpful in diagnosing complex cases. The literature suggests that the use of computed tomography is also recommended for complicated cases.[19,20] In this context, oral radiologists play a significant role in the diagnostic process.

Fusion in primary teeth can lead to increased root volume or a wider root surface area compared to the crown size of the permanent tooth, potentially resulting in delayed root resorption.[1] This can cause delays in the eruption of the permanent tooth or even ectopic eruption. Numerous studies have shown that the fusion of primary teeth can influence various anomalies in permanent dentition, such as hypodontia, fusion, supernumerary teeth, and microdontia.[2,8] Nik Hussein and Abdul Majid noted that the presence of fusion in primary dentition is associated with findings in approximately 60% of permanent dentition cases.[21] While many studies report no impact on permanent teeth when fusion occurs between primary incisors, some have indicated a prevalence of hypodontia

in permanent dentition ranging from 20% to 37.5%.[11,13,22] Gellin's investigations revealed that when fusion is observed in primary anterior teeth, 100% of cases showed hypodontia of the permanent lateral teeth.[23] Over half of our cases exhibited hypodontia, a rate that is similar to some studies in the literature, although further research is warranted.

The occurrence of fusion in primary teeth is infrequent, and the treatment approach should be customized for each individual case. The aesthetic consequences of fusion in primary dentition can result in various forms of malocclusion.[24] The precise etiology of these anomalies remains unclear, although existing literature indicates a potential interplay of genetic and environmental influences.[25] Upon examining the clinical cases, it was observed that there was no reported family history of fusion or congenital tooth absence among the patients' families. Similar findings in other studies have also shown a lack of correlation between genetic and environmental factors in instances of dental fusion.[22,26,27] Fusion takes place during the morphodifferentiation phase of tooth development, and the proximity of two tooth germs may generate pressure or physical forces that could contribute to the occurrence of fusion.[9] Nonetheless, additional evidence and epidemiological research are necessary to better elucidate the causes of this developmental anomaly.

Dental fusion can often be mistaken for gemination, which is identified by an increased bifid crown and sulcus due to the invagination of a single tooth germ.[9] Differentiating between a fused tooth and a geminated tooth can be accomplished through both clinical assessments and radiographic evaluations. A frequently encountered differential diagnosis highlights that geminated teeth may cause crowding, whereas fusion typically leads to the ectopic eruption of the permanent tooth because of the larger root area associated with the fused tooth.[6] In a standard clinical evaluation, this abnormality may manifest as a broad tooth with the appearance of having two crowns separated by a groove. An extensive patient history, in conjunction with radiographic and clinical assessments, is essential for accurate diagnosis and formulating an effective treatment plan. Both periapical and panoramic radiographs are required to identify fused teeth.[4,6]

In some cases of fused teeth, visible labial and lingual grooves extend to the root surface. This can lead to plaque accumulation, caries, and various periodontal and endodontic issues.[25,27,28] The morphological differences of primary teeth and the presence of anomalies can complicate the implementation of endodontic treatment due to reasons such as deep dentin caries and excessive root resorption. However, such situations have not been encountered in our cases. [25,28-30]

Fused teeth are often asymptomatic; however, they can lead to orthodontic problems. When two teeth are fused, they occupy less space in the dental arch, potentially leading to orthodontic issues such as diastema and similar problems. The fusion of a normal tooth with a supernumerary tooth can also result in orthodontic complications such as crowding and space issues.[25,27] In our cases, no orthodontic problems such as diastema or crowding have been observed yet, likely due to the young age of the diagnosed patients, who are still in their growth and development stages. Future monitoring of these patients is essential to assess potential complications arising from this anomaly.

Morphological anomalies in primary dentition are a significant concern for pediatric dentists due to the potential for associated clinical problems, such as dental caries, delayed eruption, and anomalies in permanent dentition (including crowding, supernumerary teeth, or hypodontia).[8,25] Early diagnosis of such anomalies facilitates a more comprehensive, long-term treatment plan, leading to a more favorable prognosis and reducing the need for complex orthodontic interventions. Each patient-specific treatment plan should be formulated as a protocol addressing their specific needs. It is crucial to identify this anomaly early and conduct a detailed analysis of potential problems in each case, thereby enabling the initiation of a conservative, individualized treatment plan.

Concrescence is a dental anomaly characterized by the union of two adjacent teeth at the root level, often due to the deposition of cementum. While it shares similarities with fusion, concrescence is distinct in that it typically occurs after root formation is complete and involves cementum rather than dentin. Understanding these distinctions is crucial for accurate diagnosis and appropriate treatment planning.[31] Additionally, studies indicate that fusion in primary teeth may lead to delayed eruption of permanent successors.[32,33] This delayed eruption is likely due to the altered resorption patterns and increased root volume associated with fused teeth. In contrast, concrescence does not directly affect eruption but may complicate dental extractions and other procedures due to the shared cementum layer. Both conditions require a detailed clinical and radiographic evaluation to differentiate and manage effectively.[31-33]

Fusion and concrescence are developmental anomalies often conflated due to their similarities. Fusion involves the union of two tooth germs during the developmental stage, leading to shared dentin and enamel structures.[34,35] In contrast, concrescence is a post-developmental anomaly characterized by the fusion of tooth roots through cementum deposition, typically caused by external factors such as trauma or localized inflammation. Unlike fusion, concrescence does not impact the crown morphology significantly.[36,37] A clear understanding of these anomalies is crucial for accurate diagnosis and appropriate management strategies.

Concrescence, a related anomaly characterized by cementum fusion post-root formation, should be differentiated from fusion, which involves dentin and occurs during development. This distinction is critical for diagnosis and treatment planning.[37] While it shares similarities with fusion, concrescence is distinct in that it typically occurs after root formation is complete and involves cementum rather than dentin. Understanding these distinctions is crucial for accurate diagnosis and appropriate treatment planning.[35-37] Recent literature highlights the importance of understanding these associations to improve treatment outcomes.

Fusion anomalies in primary teeth are frequently associated with delayed eruption of their permanent successors.[33] This delay is hypothesized to result from altered eruption pathways and abnormal root morphology in fused teeth, which may interfere with the resorption process necessary for normal eruption. Studies have documented prolonged eruption times, particularly in cases where fusion involves the incisor and canine regions.[33-35] Clinical monitoring and radiographic follow-ups are essential to anticipate and address such delays effectively. Moreover, the clinical implications of fusion extend beyond eruption delays, as fused teeth often present with larger-than-normal crowns, irregular shapes, or complex root canal systems, which can complicate restorative and endodontic treatments.[38,39]

Fusion may also predispose teeth to an increased risk of caries and periodontal issues due to the presence of irregular contact points and grooves at the fusion site.[38,40] Recent literature underscores the importance of identifying these challenges early and adopting a multidisciplinary approach that involves pediatric dentists, orthodontists, and restorative specialists to formulate individualized treatment plans. A comprehensive understanding of the long-term developmental changes in both fused and concrescent teeth is crucial to improving patient outcomes and avoiding complications.[9,31-34]

Fusion teeth and the complications they may create necessitate multidisciplinary treatment approaches. And achieving more effective prognoses in treatment during both primary and mixed dentition. Fusion is a dental anomaly that is more frequently observed in primary dentition, which is why pediatric dentists typically diagnose most cases.[12,19] Furthermore, cooperation between orthodontics and pediatric dentistry is essential to prevent potential complications that may arise in the future. In such cases, it is vital for pediatric dentists to be aware of other anomalies that may occur alongside fusion. Additionally, various imaging methods are helpful in diagnosing complex cases. The literature suggests that the use of computed tomography is also recommended for

complicated cases on text; oral radiologists play a significant role in the diagnostic process.[33,40]

Conclusion

Fusion in primary teeth represents a rare dental anomaly with significant clinical implications. Early diagnosis, preventive interventions like fluoride applications, and a multidisciplinary approach are essential to addressing potential complications effectively. Additionally, the long-term follow-up of these patients is critical to monitor developmental changes and ensure optimal outcomes. This study underscores the importance of collaborative efforts between pediatric dentists, orthodontists, and restorative specialists in formulating individualized treatment plans for such anomalies.

Dental fusion is one of the more common dental anomalies observed in primary dentition compared to permanent dentition. Dental fusion may be associated with a genetic predisposition and permanent tooth hypodontia. Comprehensive clinical and radiographic evaluations are crucial for the early detection of developmental dental anomalies. The diagnosis and treatment of fusion teeth in young children have always been challenging. The most appropriate dental intervention is conducted through a multidisciplinary approach involving pediatric dentists, orthodontists, and restorative specialists, taking into account the child's condition, expectations, and level of cooperation with dental treatment. Dentists need to be aware of the various complications caused by fusion. In cases of fused teeth, preventive procedures and close monitoring are critical, even in the absence of signs and symptoms. Furthermore, the frequency of fusion teeth occurring in similar areas supports evidence of shared genetic control over developmental dental disorders among individuals with a positive family history.

Early diagnosis and a multidisciplinary approach are vital in managing fusion anomalies. Clinicians should maintain vigilance for complications, provide preventive care, and coordinate with specialists for comprehensive management. This study emphasizes the importance of early diagnosis, preventive care, and a multidisciplinary approach in managing fusion anomalies in primary teeth. Clinicians should adopt individualized treatment plans that consider both functional and aesthetic needs, including regular fluoride applications, orthodontic evaluations, and restorative procedures as necessary. Furthermore, the inclusion of genetic counseling and psychological support for patients and families may improve overall outcomes. Regular follow-ups are critical to monitor eruption patterns, ensure proper occlusion, and address complications proactively.

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Conflicts of Interest

None of the authors of this article has any relationship, connection, or financial interest in the subject matter or material discussed in the article.

Authors' Contribution

Idea/Concept: C.K Design: C.K, T.A Control/ Supervision: Ö.M.A Literature Review: C.K, T.A Data Collection and/or Processing: C.K, T.A Analysis and/or Interpretation: Ö.M.A, C.K Writing the Article: C.K, T.A, Ö.M.A Critical Review: Ö.M.A.

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CASE REPORT

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Candidiasis in Oral Lichen Planus: Complication of Topical Corticosteroid Overuse

Oral Liken Planusta Kandidiazis: Aşırı Topikal Kortikosteroid Kullanımına Bağlı Komplikasyon

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ABSTRACT

Objectives: Topical steroids represent the mainstay of management for symptomatic oral lichen planus (OLP), owing to their effectiveness in alleviating pain and inflammation. However, their use may result in adverse effects, such as secondary oral candidiasis (OC), influenced by factors such as potency, duration and frequency of use, and site of application. This study presents a case of OC following topical steroid therapy for OLP, emphasizing the importance of patient compliance in treatment.

Case report: A 78-year-old woman diagnosed with cutaneous lichen planus four months prior was referred to our clinic for evaluation of new oral lesions. Erosive OLP lesions on the buccal and labial mucosa and tongue were noted upon intraoral examination. The patient was prescribed mometasone furoate 0.05% spray to be used twice daily. As a result of the patient using the medication at a higher dose and frequency than recommended, pseudomembranous OC was observed on the buccal mucosa and soft palate at the follow-up appointment two weeks later. The patient was prescribed an oral suspension of nystatin (100,000 IU) for gargling four times a day, and complete resolution of the OC was achieved within a period of 14 days. Subsequently, the OLP lesions reverted to a reticular form with appropriate use of the topical steroid. The patient remains under regular follow-up at our clinic.

Conclusion: Secondary OC may obscure and/or aggravate the clinical features and symptoms of OLP, potentially hindering effective management. Close monitoring of pharmacological therapy and timely intervention for secondary OC are crucial for achieving optimal treatment outcomes.

Keywords: *Adverse effect, Corticosteroid, Oral candidiasis, Oral lichen planus.*

ÖZET

Amaç: Topikal kortikosteroidler, ağrı ve enflamasyonu hafifletme konusundaki etkinlikleri nedeniyle semptomatik oral liken planusun (OLP) temel tedavi seçeneğidir. Ancak ilaçların etkinlik gücü, kullanım süresi, sıklığı ve uygulanma bölgesi gibi faktörlere bağlı olarak sekonder oral kandidiazis (OK) gibi yan etkilere yol açabilirler. Bu çalışmada, OLP tedavisinde topikal steroid kullanımına bağlı olarak gelişen bir OK olgusu sunulmakta ve hasta uyumunun tedavi sürecindeki önemi vurgulanmaktadır.

Olgu sunumu: Dört ay önce kutanöz liken planus tanısı konmuş olan 78 yaşındaki kadın hasta, yeni ortaya çıkan oral lezyonların değerlendirilmesi amacıyla kliniğimize sevk edilmiştir. İntraoral muayenede bukkal ve labial mukozada, ayrıca dilde eroziv OLP lezyonları tespit edilmiştir. Hastaya, günde iki kez kullanılmak üzere mometazon furoat %0,05 sprey reçete edilmiştir. İlacın önerilenden daha yüksek dozda ve daha sık kullanılması sonucunda, iki hafta sonraki kontrol randevusunda bukkal mukozada ve yumuşak damakta psödomembranöz OK geliştiği gözlenmiştir. Hastaya günde dört kez gargara yapması için nystatin oral süspansiyon (100.000 IU) reçete edilmiş ve 14 gün içinde OK tamamen ortadan kalkmıştır. Sonraki süreçte, topikal steroidlerin uygun kullanımıyla OLP lezyonları retiküler forma gerilemiştir. Hasta, kliniğimizde düzenli takip edilmektedir.

Sonuç: Sekonder OK, OLP'nin klinik belirtilerini ve semptomlarını gizleyerek ve/veya şiddetlendirerek tedavi sürecini olumsuz etkileyebilir. Bu nedenle, farmakoterapinin dikkatle izlenmesi ve sekonder OK gelişmesi durumunda erken müdahale edilmesi, optimal tedavi sonuçlarının elde edilmesinde kritik öneme sahiptir.

Anahtar kelimeler: *Yan etki, Kortikosteroid, Oral kandidiazis, Oral liken planus.*

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Introduction

Lichen planus (LP) is a common T-cell-mediated chronic inflammatory mucocutaneous condition of unknown aetiology that affects the skin, scalp, nails, and the mucous membranes of the oral cavity, oesophagus, and genitals. Oral mucosal lesions may manifest independently or in association with cutaneous lesions.[1-4] Oral lichen planus (OLP) is predominantly observed among middle-aged women over the age of 40, with a reported female-to-male ratio of approximately 3–4:1. The worldwide prevalence of OLP varies between 0.5% and 2.2%.[1,4-6]

OLP manifests clinically with a wide spectrum of intraoral findings, including reticular, papular, atrophic, erosive/ulcerative, plaque-like, and bullous forms, or a combination of two or more of these.[2-5] A common feature of all clinical variants of OLP is the presence of white lines, known as "Wickham's striae." The reticular variant, which appears as asymptomatic reticular white striations, is the most prevalent clinical form of OLP. The atrophic, erosive/ulcerative, and bullous variants are typically symptomatic, presenting as erythematous-ulcerated areas surrounded by white striae at the periphery.[4] OLP lesions characteristically exhibit bilateral and symmetrical distribution, with the most frequently affected sites being the buccal mucosa, tongue, and gingiva.[1,4-8] Patients with OLP commonly report complaints ranging from a sensation of roughness to burning, pain or discomfort in the affected areas. These symptoms are aggravated by thermal, chemical, or mechanical irritation of the affected tissue during activities such as consumption of hot, spicy, and acidic foods, use of oral hygiene products, brushing, flossing, or periodontal procedures such as scaling and root planing and may have a detrimental effect on the patients' life quality and limit their ability to maintain proper oral hygiene.[1,8,9]

Given the uncertain aetiology of OLP, current treatment strategies primarily aim to provide symptomatic relief.[9] The chronic clinical course of OLP, with fluctuations in disease activity characterised by recurrent episodes of exacerbation and remission, varies significantly both between patients and within individual patients over time, posing a management challenge for clinicians.[4,8,10] A number of treatment options are available for OLP, including topical and systemic corticosteroids, topical and systemic retinoids, azathioprine, calcineurin inhibitors (e.g. cyclosporine, pimecrolimus, tacrolimus), dapsone, griseofulvin, hydroquinone, laser therapy, mycophenolate, phototherapy, and thalidomide.[11] The selection of the most appropriate treatment plan is dependent on many factors, including the general health status of the patient, the presence of underlying psychological factors that may trigger the condition, the location and extent of oral lesions, the severity of symptoms, the degree of patient compliance with the treatment plan, potential drug interactions, and the cost-effectiveness of the selected treatment modalities.[12]

Topical corticosteroids are considered the most effective and reliable treatment option to alleviate the signs and symptoms of OLP, owing to their capacity to modulate the local immune response and are recommended as the first-line therapy for long-term symptomatic management of OLP.[2,3,9] However, a significant challenge in the management of OLP with corticosteroids is the risk of developing secondary oral candidiasis (OC), which is a frequent consequence of long-term corticosteroid therapy. The risk is dependent on numerous factors, such as the potency of the corticosteroid, the duration and frequency of use, and the site of application, and requires antimycotic therapy.[1,13-17]

In this study, a case who developed OC during topical steroid treatment for OLP is presented and the importance of patient compliance in treatment is emphasised.

Case Report

A 78-year-old woman, diagnosed with cutaneous LP four months earlier, was referred by her dermatologist to the dental outpatient clinic of the Faculty of Dentistry, Marmara University, Oral and Maxillofacial Radiology Department, for dental consultation due to oral lesions that had appeared two weeks prior. The patient had a medical history of hypertension, arrhythmia, angina pectoris, nephritis, and asthma and

was taking valsartan and hydrochlorothiazide (80 mg/12.5 mg), apixaban (5 mg), sotalol hydrochloride (80 mg), trimetazidine dihydrochloride (20 mg), allopurinol (300 mg), and spironolactone (25 mg). She had no smoking history and no known allergies. Informed consent for the case presentation was obtained from the patient.

Extraoral examination revealed the presence of polygonal, flat-topped papular lesions with symmetrical distribution on the hands and feet. The skin was observed to be dry and scaly. The patient reported using topical corticosteroids for the treatment of these lesions, which had been previously confirmed to be LP by histopathological examination, as per the instructions provided by her dermatologist.

A thorough intraoral examination revealed painful erosive-ulcerative lesions accompanied by radiating white striae on bilateral buccal mucosa, labial mucosa, and tongue (Figure 1A-C). Following an evaluation of the patient's clinical history and the observation of the lesions, a diagnosis of "erosive-ulcerative OLP" was established. The patient was informed about general precautions to be taken in the management of OLP, including the importance of stress management, maintaining meticulous oral hygiene, and avoiding thermal, chemical, or physical trauma to the oral mucosa. She was prescribed mometasone furoate 0.05% spray, to be applied 1 puff twice daily (50 micrograms per puff) for two weeks.

Figure 1A-C. Erosive-ulcerative oral lichen planus lesions with radiating white striae on (A&C) bilateral buccal mucosa and (B) tongue.

At the subsequent follow-up appointment, two weeks later, pseudomembranous OC was observed on the buccal mucosa and soft palate (Figure 2A-C). Further questioning revealed that the patient had been using the mometasone furoate 0.05% spray, which had been highly effective in relieving her symptoms. However, she had been applying the spray at a higher dose and frequency than prescribed – specifically, using 2 puffs four times per day (400 micrograms), instead of the recommended 1 puff twice daily (100 micrograms). The patient was instructed to gargle with an oral suspension of nystatin (100,000 IU) four times daily, which resulted in the complete resolution of OC within 14 days (Figure 3A-C).

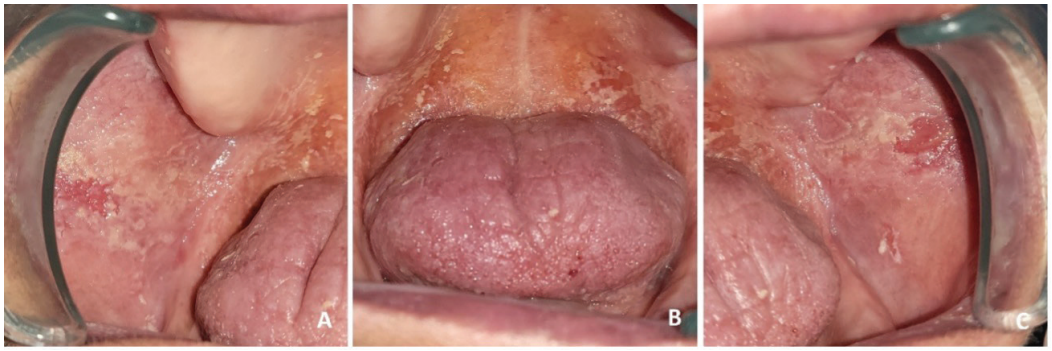

Figure 2A-C. Pseudomembranous oral candidiasis on (A&C) bilateral buccal mucosa and (B) soft palate due to overuse of mometasone furoate 0.05% spray at the follow-up visit two weeks later.

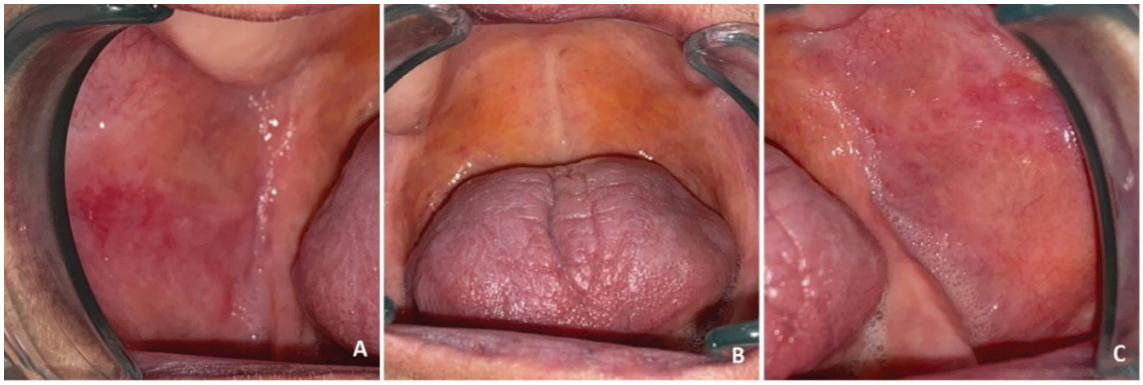

Figure 3A-C. Complete resolution of oral candidiasis on (A&C) bilateral buccal mucosa and (B) soft palate within 14 days with nystatin oral suspension (100,000 IU) use four times daily.

Following the appropriate use of the prescribed topical steroid, the erosive-ulcerative OLP lesions underwent a complete transformation into reticular form after a period of six weeks, resulting in a substantial reduction in the symptoms and signs of oral lesions, as well as a significant improvement in the patient's quality of life (Figure 4A&B). The patient continues to attend regular follow-ups at our clinic, monthly for the first three months, followed by every six months to monitor the course of the disease, control oral hygiene, and evaluate treatment compliance.

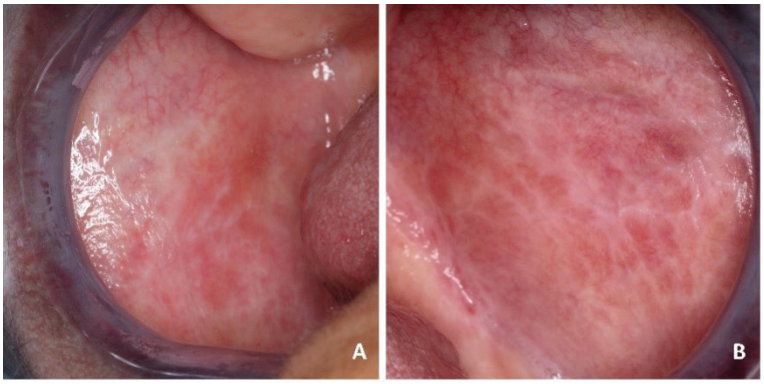

Figure 4A&B. Following the appropriate use of the prescribed topical steroid, the erosive-ulcerative oral lichen planus lesions underwent a complete transformation into the reticular form after six weeks.

Discussion

Although asymptomatic OLP does not require treatment, it is recommended that irritation caused by sharp tooth cusps, fractured restorations, and unopposed teeth should be eliminated and monitored. Oral hygiene control has been shown to be beneficial in OLP management.[18] Most patients with erosive OLP are symptomatic and approximately 90.9% have involvement of multiple oral sites. The erosive form is characterized by a longer duration, involvement of a greater number of sites (oral, oesophageal, and genital), and a higher prevalence in elderly patients compared to the reticular or atrophic forms, as observed in the present case.[19]

Topical corticosteroid treatment, whether as a standalone modality or in conjunction with systemic steroids, is recommended as the primary therapeutic approach for symptomatic OLP cases due to minimal side effect profile and cost-effectiveness in long-term management.[1,18] Many studies have demonstrated the efficacy of adhesive base, aqueous solution, spray, mouthwash, microemulsion, soluble tablet, and intralesional injection forms of various topical corticosteroids including fluocinonide, betamethasone, mometasone furoate, clobetasol propionate, triamcinolone acetonide, fluocinolone acetonide, fluticasone propionate, prednisolone, and dexamethasone.[7,10] Since it is

important that the mucosal surface remains in contact with the steroids for a period of minutes, formulations including mouthwashes or adhesive pastes are widely recommended.[2]

A review of the literature indicates that mometasone furoate is a viable treatment option for erosive-ulcerative OLP, with statistically significant reductions in pain and erythema/ulceration surface area, and no serious side effects reported.[20] Considering its efficacy and proven safety in the management of erosive-ulcerative OLP symptoms, mometasone furoate - routinely used in the management of symptomatic OLP cases in our clinic - was selected as the most appropriate treatment for the patient presented.

The most frequently observed adverse effect associated with topical corticosteroid therapy is OC, caused by the overgrowth of candida in the oral flora.[10] It has been demonstrated that a variety of yeast species, especially *Candida albicans*, can be isolated from the oral cavity of individuals who do not present any clinical symptoms of OC.[4] However, it is believed that systemic and local factors that decrease the resistance of the individual facilitate the transition of yeasts from a commensal to a parasitic state. Systemic factors predisposing to OC include nutritional deficiencies, endocrine disorders, steroid/antibiotic/immunosuppressive/cytostatic treatment, smoking, malignancies, and immunopathies. Local factors include mechanical trauma, epithelial changes resulting from other oral mucosal diseases, denture use, low salivary flow rate and pH.[4,13-16,21,22]

Some of these factors have been identified in patients suffering from OLP. It has long been recognized that epithelial cell defects are present in OLP lesions. Moreover, a significant body of studies has demonstrated that the LP reaction is the consequence of a cell-mediated immunological response to antigenic alterations in the basal cell layer.[21] In addition to allergic reactions, xerostomia, and sensitivity to mechanical irritants, a relatively high incidence of endocrine disorders, such as diabetes mellitus, has been observed in patients diagnosed with OLP.[14,21] The presence of hyperkeratosis, a histopathological feature of OLP, creates favourable conditions for candida adhesion, colonisation, and infection.[21,23] Similarly, clinically observed erythema or superficial erosion in OLP lesions may be indicative of the disease itself or of superimposed candidiasis. Both conditions have the potential to cause mucosal soreness and pain.[23] Previous studies have reported that disruption of mucosal integrity and changes in composition of the oral microenvironment promote and facilitate candida species colonization and subsequent invasion in erosive OLP patients.[4,24] Long-term corticosteroid treatment in OLP patients may also facilitate the growth of candida and the transition from commensalism to parasitism, impair host resistance and immune responses to candida species, and induce OC by modulating inflammatory processes and cell-mediated immunity.[4,13-16] Secondary OC is more common in patients with OLP undergoing topical steroid therapy, with documented incidences ranging from 11.4% to 76.7%.[4,8,10,14,17,21,25] In particular, the atrophic, erosive-ulcerative, and bullous OLP variants are erythematous, symptomatic, and frequently associated with OC.[4,17,24,25] The reticular form, on the other hand, typically manifests asymptomatically and is not associated with candidal infection. Therefore, the majority of studies on OC in OLP patients have focused on the erosive type of OLP, as in our case.

The development of secondary OC may complicate the management of atrophic and erosive-ulcerative OLP forms in particular, as it often obscures and/or exacerbates clinical signs and symptoms, causes burning, soreness, discomfort, and pain, and requires antifungal treatment.[4,8,14,21,24-26] Nystatin, fluconazole, miconazole, ketoconazole, and amphotericin B are the most commonly prescribed antifungal agents for the therapeutic management of OC. Alternative therapeutic agents such as chlorhexidine have also been shown to have both antibacterial and antimycotic properties.[15,23] Despite the uncertain relationship between candida colonization and OLP, it has been frequently observed that antimycotic treatment of erosive lesions with secondary OC results in clinical improvement and symptom relief, with OLP lesions transforming to reticular

form.[4,21,26] Nystatin suspension, which is routinely prescribed for the treatment of OC cases in our clinic, was used in the treatment of OC in the presented patient and it was observed that OC disappeared completely and OLP lesions transformed into a reticular form after antifungal treatment. One of the most controversial issues is whether antifungal agents should be used as a standard protocol for secondary OC prophylaxis when treating OLP with corticosteroids.[18] Clinical experience and training in the management of such cases depend on the implementation of a carefully selected protocol, which may vary from one clinician to another. It is important to emphasise that failure to consider the possibility of a candidal infection may lead to ineffective treatment of OLP. It is strongly advised that patients diagnosed with OLP should be monitored closely in terms of fungal infections for the initial 2 months. In the erosive-ulcerative OLP subtype, where topical steroids are frequently administered, the risk of candida superinfection is significantly higher, and these potential prognostic indicators may assist clinicians in identifying such OLP patients as being at risk of candida superinfection.[17]

Furthermore, the possibility of malignant transformation of OLP due to hyphal invasion by candida species has also been suggested, and this has been attributed to the production of carcinogenic candida metabolites, including nitrosamine and acetaldehyde.[27,28] The use of antifungal agents in selected OLP cases may reduce the capacity of *Candida albicans* to synthesise carcinogenic compounds such as N-nitrosobenzylmethylamine.[26] OLP lesions with known risk factors for oral malignancy, including tobacco use, alcohol consumption, or candidal superinfection, require careful follow-up due to the increased possibility of malignant transformation.[29]

Conclusion

In conclusion, topical corticosteroids represent a highly effective and safe treatment option for symptomatic OLP and are therefore recommended as the first-line therapy. Due to its chronic nature, complete clinical remission remains difficult to achieve in most OLP cases, even with appropriate treatment. No single management approach is universally applicable and the optimal strategy varies between patients. The choice of the potency, formulation and dosage of the topical steroid to be used, which affects the response to treatment, depends on professional judgement. It is important to tailor the frequency of topical steroid application, duration of treatment, and concomitant antifungal use for each patient, taking into account the patient's overall health status, severity of OLP lesions and compliance with the treatment plan. Appropriate management of OLP will have a significant impact on reducing pain and therefore enhancing the quality of life for a significant number of patients.

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Conflicts of interest

The authors declare that they have no conflict of interest.

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Author contributions

Idea/Concept: B.G Design: B.G Control/ Supervision: B.G, S.Y, B.A Literature Review: BG, ŞEY, SY, BA Data Collection and/ or Processing: B.G, Ş.E.Y Analysis and/or Interpretation: B.G, Ş.E.Y Writing the Article: B.G, Ş.E.Y, S.Y, BA. Critical Review: B.G, Ş.E.Y, S.Y, B.A

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Rejeneratif Endodontik Tedavide Yeni Bir Yaklaşım Olarak Pulpa Transplantasyonları

A New Approach to Regenerative Endodontic Treatment: Pulp Transplantations

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ÖZET

Günümüzde rejeneratif endodontik tedavi immatür nektrotik dişlerin endodontik tedavisinde ilk seçeneklerden biri olarak önerilmektedir. Bu tedavinin diş sağkalımı üzerinde yüksek başarı oranlarına sahip olduğu kanıtlanmış olsa da rejeneratif endodontik tedavinin asıl hedefi olan organize pulpa dokusunun oluşumu kanıtlanamamıştır. Geleneksel rejeneratif endodontik tedavileri izleyen çalışmalardan elde edilen histolojik veriler, rejenere edilmiş bir pulpa-dentin kompleksinin yerine bir onarım dokusunun oluştuğunu kanıtlamıştır. Asıl hedef olan pulpa dokusunun tüm tabakaları ile beraber yeniden oluşmasını sağlamak için doku mühendisliği teknolojilerinde hızla ilerleyen gelişmelerin de katkısıyla yeni rejenerasyon teknikleri üzerinde çalışılmaktadır. Modern doku mühendisliğinin üç temel kavramı olan kök hücreler, büyüme faktörleri ve doku iskelesini içermekte olan ve geliştirilmekte olan bu teknikler "hücre bazlı rejeneratif endodontik tedavi" şeklinde tanımlanmaktadır. Dental pulpa kök hücrelerinin ve diğer dental mezenkimal kök hücrelerin başarılı bir şekilde izolasyonundan bu yana ise kök hücre transplantasyonu ve kök hücre aracılı pulpa rejenerasyonunun klinik öncesi araştırmaları önemli ölçüde ilgi görmektedir. Bu çabalar ise yakın zamanda süt dişi pulpa dokusunun daimi dişe transplantasyonu gibi klinik uygulamalara dönüşerek endodonti ve pedodonti alanlarında büyük ses ve yeni bir bakış açısı getirmiştir. Bu derlemede geleneksel rejeneratif endodonti tekniği ile ilgili başarı tartışmalarına yer verilmiş ve geliştirilmekte olan yeni rejeneratif endodonti teknikleri incelenmiş ve bu tekniklerin kullanıldığı olgu raporları incelenmiştir.

Anahtar kelimeler: *Diş pulpası; Doku mühendisliği; Rejeneratif endodonti; Transplantasyon*

ABSTRACT

Today, regenerative endodontic treatment is recommended as one of the first options in the endodontic treatment of immature nectrotic teeth. Although this treatment has been proven to have high success rates on tooth survival, the formation of organized pulp tissue, which is the main goal of regenerative endodontic treatment, has not been proven. Histological data from studies following conventional regenerative endodontic treatments have proven that a repair tissue is formed in place of a regenerated pulp-dentin complex. In order to ensure the regeneration of the pulp tissue with all its layers new regeneration techniques are being studied with the contribution of rapidly advancing developments in tissue engineering technologies. These techniques, which include stem cells, growth factors and tissue scaffolding, which are the three basic concepts of modern tissue engineering, are defined as "cell-based regenerative endodontic treatment". Since the successful isolation of dental pulp stem cells and other dental mesenchymal stem cells, preclinical research on stem cell transplantation and stem cell-mediated pulp regeneration has attracted significant attention. These efforts have recently turned into clinical applications such as the transplantation of the pulp tissue of a primary tooth to a permanent tooth, bringing a great impact and a new perspective in the fields of endodontics and pedodontics. In this review, discussions on the success of traditional regenerative endodontics techniques are included, new regenerative endodontic techniques that are being developed are examined, and case reports in which these techniques are used are examined.

***Keywords*:** *Dental pulp; Regenerative endodontics; Tissue engineering; Transplantation*

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Giriş

Rejeneratif tıp ve doku mühendisliği gibi bilim dallarının öneminin farkına varılması ve yapılan çalışmaların son yıllarda hızla artması, tıbbın her alanında olduğu gibi, diş hekimliği alanında da rejeneratif uygulamaların önem kazanmasına neden olmuştur.[1]

Rejenerasyon kelime anlamı olarak zarar görmüş hücrenin, dokunun veya organın kendini yenileyebilme kapasitesidir. Rejeneratif endodontik tedavinin asıl amacı pulpa dokusunu tüm tabakaları ile beraber yeniden oluşturmaktır. Geleneksel rejeneratif endodontik tedavileri (RET) izleyen hem hayvan çalışmalarından hem de insan dişlerinden elde edilen histolojik veriler, rejenere edilmiş bir pulpa-dentin kompleksinden ziyade yeni bir onarım dokusunun oluştuğunu histolojik olarak kanıtlamıştır.[2,3] Bu onarım dokusunun esas olarak kemik, sement ve fibröz dokulardan oluştuğu ortaya koyulmuştur.[4] Geleneksel rejeneratif endodonti tekniklerinin pulpa rejenerasyonunu gerçek anlamda gerçekleştirememesi ve kök hücre tabanlı doku mühendisliği teknolojilerindeki son gelişmeler, pulpa/dentin kompleksi için yeni bir rejeneratif yaklaşıma doğru eğilimi artırmıştır.[5]

Klinik olarak başarılı bir pulpa rejenerasyonu elde etmek için yeni bir yöntem olarak kök kanalı tedavisi gerektiren dişlere, hastanın çekilmiş başka bir dişinden alınan diş pulpası kök hücrelerinin transplantasyonu fikri ortaya atılmıştır.[6,7] Daha yakın zamanda ise pulpa kök hücre transplantasyonundan ziyade tüm pulpanın transplantasyonunun, kök hücrelerin doğal ortamlarında farklılaşması için daha uygun bir "doku iskelesi" oluşturabileceği fikri gündeme gelmiştir.[5] Bu sayede çoğu sinir ve kan damarının zaten oluşmuş olması, nakledilen pulpanın revaskülarizasyonu ve bağlantı sürecini kolaylaştıracağı düşünülmektedir. Ayrıca, pulpa rejenerasyon tekniğinin bu yöntemi, kök hücrelerin in vitro olarak laboratuvar ortamında genişletilmesine ihtiyaç duyulmadan sadece klinik prosedürlerle elde edilebilmesine olanak tanımaktadır.[5,8]

Rejeneratif Endodontik Tedavi Tarihçesi ve Tanımlamaları

Rejeneratif endodonti, pulpa-dentin kompleksindeki hücreler ile birlikte dentin ve kök yapısını da içeren zarar görmüş dokuları yenisi ile değiştirmek için tasarlanmış biyolojik temelli prosedürler olarak tanımlanmaktadır.[9]

Geçmişten bu yana bu tedavi prosedürünün tanımlanması ile ilgili farklı görüşler oluşmuştur. Yeni oluşan dokunun içeriğinin tam olarak bilinmediği ve kesin olan tek şeyin kan desteği olduğunu savunanlar "revaskülarizasyon" tanımını desteklemişlerdir. Öte yandan Huang ve Lin[10] revaskülarizasyon terimi yerine "indüklenmiş veya yönlendirilmiş doku jenerasyonu veya rejenerasyonu" terimlerini önermiştir. Lenzi ve Trope[11] kök kanalı içerisinde spesifik olmayan canlı dokuları tarif ettiği için ve kök kanal boşluğunda yeniden oluşan dokuların sadece kan damarları değil aynı zamanda sert ve yumuşak dokular da olduğunu vurgulayarak "revaskülarizasyon" yerine daha uygun bir terim olarak "revitalizasyon"u önermişlerdir. Weisleder ve Benitez[12] ise kök gelişiminin devam etmesinin sadece basit bir apikal kapanma olmadığını ve bu durumun fizyolojik kök gelişimi ile eşit olduğundan bahsetmiş ve "maturogenezis" teriminin uygun olduğunu düşünmüşlerdir. Hargreaves ve ark.[13] bu tedavi protokolünü indüklenmiş veya yönlendirilmiş doku rejenerasyonu ile ilişkilendirdikleri için "rejeneratif endodontik terapi" terimini tercih etmişlerdir. Diogenes ve ark.[14] yaptıkları çalışmada geleneksel RET sonucu oluşan dokunun onarım dokusu olduğunu vurgulamış ve "rehberli endodontik onarım" terimini önermiştir. Ardından Lin ve ark.[15] geleneksel RET'nin hücre temelli bir yaklaşım olmadığını ve modern doku müdendisliği kavram ve yöntemlerinin kullanılmadığının altını çizerek "hücresiz RET" (CF-RET) ve doku mühendisliği kavramlarına uyan ve kök hücre temelli tekniğe ise "hücre bazlı RET" (CB-RET) terimini uygun görmüştür. Hücresiz yaklaşım (CF-RET), kök apeksinin çevresinde bulunan kök hücrelerin proliferasyonunu, göçünü ve farklılaşmasını artırarak yenilenmeyi amaçlamaktadır. Hücre bazlı yaklaşım ise temel olarak çoklu doku iskelesi sistemleri ve büyüme faktörleri ile birlikte çeşitli

kök/progenitör hücre kaynaklarının kullanımına dayanmaktadır.[16] CB-RET, American Association of Endodontists (AAE) ve European Society of Endodontology (ESE) tarafından henüz önerilmememektedir ve üzerinde yapılan çalışamalar hala devam etmektedir. Günümüzde literatürde revaskülarizasyon, revitalizasyon ve rejeneratif endodonti benzer anlamlı olarak ve birbirinin yerine kullanılmakla birlikte en çok tercih edilen terim RET terimidir.[17]

Rejeneratif Endodonti Tekniği İle İlgili Başarı Tartışması

RET sonrası başarısızlığı belirten net bir fikir birliği literatürde tanımlanmamıştır.[18] Ağrı, sinüs yolu, mobilite, şişlik, perküsyon hassasiyeti gibi semptomların tedavi bitiminde devam etmesi başarısızlığın bir işareti olarak nitelendirilmiştir.[19] Ancak bazı çalışmalarda renklenme, kök oluşumunun devam etmemesi, kanal içerisine kanın dolmaması, koronal sızıntı, dişte kırık oluşması, kısmi kanal obliterasyonu gibi bulgular başarısızlık olarak gösterilmiştir.[20-22] AAE 2021 yılında RET için klinik uygulamalarda kullanılmak üzere tedavi prosedürü oluşturmuştur. Bu rehberde RET sonrasında ulaşılması beklenen hedefler belirlenmiştir.[23]

Tedavi hedefleri

1. Primer hedef: Semptomların eliminasyonu ve kemik dokusunda iyileşme
2. Sekonder hedef: Kök duvarlarının kalınlığında ve/veya boyunda artma (arzu edilir ancak şart değil)
3. Tersiyer hedef: Vitalite testine pozitif yanıt alınması[24]

RET'nin primer hedefi olan enfeksiyonun bulgu ve semptomlarının elimine edilip kemik iyileşmesinin gerçekleşmesinin genel olarak ulaşılabilir bir hedef olduğu ve bu hedefe çok yüksek oranlarda ulaşıldığı gösterilmiştir.[24] Tong ve ark.[24] ve Torabinejad ve ark.[25] yaptıkları iki sistematik incelemede RET'nin primer hedefine yüksek olasılıklarla (%91-94 oranında periapikal iyileşme) ulaşılabilineceğini göstermişlerdir. RET'nin sekonder hedefi olan kök kanalı duvarlarının kalınlığında artış ve/veya boyunda artma, çalışmalarda değişik oranlarda görülmüştür.[24,26] Diogenes ve ark.[27] gerçekleştirdikleri çalışmada, RET sonrası nekrotik pulpalı genç sürekli dişlerde tersiyer hedef olan vitalite testine pozitif yanıt alınmasının yayınlanan olguların %50-60'ında görüldüğünü belirtmişlerdir. Ayrıca kök kanalı boşluğunda oluşan dokunun histolojik değerlendirmesi sonucu duvarların kalınlaşmasından sorumlu olan dokunun sement, kemik ve periodontal ligament benzeri doku olduğu ortaya konmuştur.[20] Bu durum kök kanalı boşluğunda oluşan farklı karakterdeki dokunun uzun vadede nasıl bir davranış göstereceği sorusunu gündeme getirmiştir.[28] Özellikle doku iskelesi olarak kan pıhtısı kullanan geleneksel RET'leri izleyen hem hayvan çalışmalarından hem de insan dişlerinden elde edilen histolojik veriler, yeni rejenere edilmiş bir pulpa-dentin kompleksinden ziyade yeni bir onarım dokusunun oluştuğunun histolojik kanıtını göstermiştir.[28]

RET ile ilişkili kanal içi kalsifikasyonun %62,1 oranında görülen bir bulgu olduğu da Song ve ark.'nın[29] yaptıkları çalışmada gösterilmiştir. Bunun sebebi ise kök kanalı boşluğunda oluşan pıhtının içerdiği büyüme faktörlerinin periapikal dokulardaki istenmeyen diğer kök hücreleri çekmesi ve mineralize dokuların (kemik, sement vb.) kök kanalı içinde ektopik birikimini başlatabilmesidir. Kök kanalı boşluğunda oluşan progresif daralma ise eğer ileride gerekli görülürse yapılacak olan endodontik tedaviyi zorlaştırmaktadır.[30,31]

Biyolojik doku iskelesi olarak kan pıhtısı kullanımın oluşturduğu sorunları ortadan kaldırmak için trombosit açısından zengin plazma (TZP) ve trombosit açısından zengin fibrin (TZF) gibi otolog trombosit konsantreleri kullanılan nispeten daha yeni RET teknikleri tanıtılmıştır. Ancak bu trombosit konsantrelerinin doku iskelesi olarak kullanımı çocuk hastalarda kan alımı sırasında koopeerasyon sorunu yaşanabileceği için sınırlıdır ve klinik kullanımları için ek ekipman ve laboratuvar süreci gerektirmektedirler.[17] Ayrıca maaliyetlerin yüksek olması, santrifüj işlemlerinin zorluğu gibi dezavantajlara da sahiptirler.[32,33] Bununla beraber Kim ve ark.[34] yaptıkları çalışmada TZP ve TZF iskelelerinin kan pıhtısına üstünlüğünün kanıtlanmadığını vurgulamışlardır. Bunlara ek

olarak TZP ve TZF kullanılan çalışmalarda elde edilen sonuçlar yine, rejenere bir pulpa yerine mineralize ve fibröz bağ dokuları içeren onarım dokusuna ilişkin benzer histolojik bulguları göstermiştir.[3]

Geleneksel RET'de dentin, EDTA kullanımı sonrası serbest kalan büyüme faktörlerinin içsel bir kaynağı olarak kullanılmıştır, ancak bu uygulama, in vivo deneylerde primer dentinin veya gerçek pulpa dokusunun histolojik olarak gösterilmesine yol açmamıştır[5]. Benzer şekilde daha önce RET ile tedavi edilen ancak daha sonra sekonder travma ve kırıklar nedeniyle çekilen dişlerin histolojik değerlendirmesi, yeni oluşan dokunun kaybedilen diş pulpasına benzemediğini düşündürmektedir.[14]
Ayrıca yeni oluşan vaskülarize iyileşme dokusunun sürekli kök gelişimini teşvik etme potansiyelinin apikal papilla ve Hertwig epitelyal kök kınının travma veya apikal periodontitis sonucu aldığı hasarın boyutuyla sınırlı olduğu ve öngörülemeyen tedavi sonuçlarına yol açtığı bilgisi unutulmamalıdır.[15,35,36] Geleneksel RET'de kök gelişiminin devam etmesi kök kanalının apikal üçte birlik kısmındaki artık kök hücrelere bağlı olduğu ve bu hücrelerin de sınırlı bir kısmının kök kanalına ulaşabildiği düşünüldüğünde, bu tekniği kullanarak tüm pulpa dokusunu yenilemenin oldukça güç olduğu düşünülmektedir.[2]

Bu sonuçlar, bu geleneksel tedavi yaklaşımının "rehberli endodontik onarım"[14] veya "CF-RET"[15] olarak tanımlanmasına yol açmıştır. Geleneksel RET'lerin (CF-RET) pulpa rejenerasyonunu gerçek anlamda sağlayamadığı kanıtlanmış olsa da oluşan sement, kemik ve periodontal ligament benzeri dokunun klinik olarak başarısızlık sayılmadığı vurgulanmalıdır. Gerçek anlamda pulpa rejenerasyonu görülmese de oluşan onarım dokuları diş sağkalımını devam ettirebilmektedir.[34] Bunun yanında kök kanalında kaybedilen dokunun canlılığını ve kısmen savunma mekanizmasını biyolojik olarak geri kazandırmakta, nekroz/apikal periodontitisin semptom ve bulgularının eliminasyonunu sağlamakta, böylece hasta ve klinisyen merkezli başarılı sonuçlara ulaşabilmektedir.[14] Hasta merkezli başarı, şişlik ve ağrı gibi hastalık semptomlarının kaybolması ve dişin sağkalımının devam etmesi ile elde edilmektedir. Klinisyen merkezli başarı ise hasta merkezli başarı kriterlerine ek olarak radyografik olarak iyileşmenin görülmesi, kök kanal gelişiminin devam etmesi ve vitalite sonuçlarına pozitif yanıt alınması ile elde edilmektedir. Bilim insanı merkezli başarı ise ancak pulpa rejenerasyonun histolojik olarak gerçekleşmesi ile elde edilebilmektedir.[14]

Sürekli Diş ve Süt Dişi Pulpa Kök Hücreleri
Kök hücreler, bazı dokularda bulunan ve ihtiyaç halinde birçok hücreyi oluşturma potansiyeline sahip, sürekli olarak çoğalabilen, çeşitli dokulara dönüşebilen ve kendi kendini yenileyebilen ana hücreler olarak tanımlanmaktadır.[37]

Kök hücreler farklı hücrelere dönüşüm potansiyellerinin farklı olmasından dolayı ikiye ayrılırlar: embriyonik kök hücreler ve erişkin kök hücreler. Embriyonik kök hücreler çok daha yüksek farklılaşma potansiyeline sahiptirler.[38] Göbek kordonu, kemik iliği, yağ dokusu, ve diş pulpası erişkin kök hücrelerin vücudumuzda bulundukları dokulara örnektir.[39] Embriyonik kök hücrelerle kıyaslandığında farklılaşma potansiyelleri daha zayıf olmasına rağmen çok daha kolay elde edilebilmeleri, erişkin kök hücrelerin son yıllarda popülerlik kazanmasını sağlamıştır.[9] Ayrıca erişkin kök hücreler, hastaların kendileri tarafından üretilebildikleri için rejenerasyonun gerçekleştirilmesinde RET için de umut vadetmektedirler.[40]

Diş çevresindeki dokularda birçok erişkin kök hücre bulunmasına rağmen RET, kök hücre olarak en çok apikal papilla kök hücreleri (SCAP), periodontal ligament kök hücreleri (PDLSC), dental pulpa kök hücreleri (DPSC) ve dental folikül kök hücreleri (DFSC) gibi apikal dokularda canlı kalmış hücrelerden yardım almaktadır.[41,42] Bunların dışında RET için kulllanılan dental olmayan kök hücreler ise kemik iliği kök hücreleri (BMMSC), yağ dokusu kaynaklı kök hücreler (ADSC), embriyonik kök hücreler (ESC) ve indüklenmiş pluripotent kök hücrelerdir (iPSC).[43] Dental kök hücreler, pulpa rejenerasyonu için tercih edilen ana hücrelerdir çünkü mükemmel proliferatif aktiviteye, nöral ve vasküler farklılaşma yeteneğine sahiptirler ve özellikle ESC'ler ile kaşılaştırıldığında dental

kök hücreler daha az etik sorun teşkil etmektedir.[44] Ayrıca, dental pulpa kök hücrelerinin, hayat boyu erişimlerinin ve elde edilmelerinin kolaylığından dolayı en uygun kök hücre kaynaklarından biri olabileceği belirtilmektedir.[45]

Gronthos ve ark.[46] ilk olarak insan DPSC'lerini insan üçüncü azı dişlerinden izole etmiş ve tanımlamıştır. DPSC'ler esas olarak üçüncü azı dişlerinden veya ortodontik olarak çekimi gereken dişlerden elde edilebilirler. Son yıllarda, çekilmiş süt dişlerinden de multipotent kök hücreler izole edilmeye başlanmıştır ve bu hücrelerin onarım potansiyelleri de incelenmektedir.[47] Stem cells from human exfoliated deciduous teeth (SHED) veya human deciduous pulp stem cells (hDPSC) erişkin kök hücrelerden daha hızlı çoğalır, daha az olgunlaşmıştır ve bu nedenle daha çeşitli hücre tipine dönüşme potansiyeline sahiptirler.[47] Bu farklılık sayesinde birden çok terapi amaçlı uygulamaya olanak sağlamaktadırlar. hDPSClerin ayrıntılı biyolojisi belirsizliğini korusa da bu hücrelerin pulpa rejenerasyonu yanında kemik oluşumunu indükleyebileceği, dentini oluşturabileceği ve implantasyondan sonra da hayatta kalabileceği gösterilmiştir.[48] Bu nedenle, süt dişlerinin, otolog kök hücre transplantasyonu ve doku mühendisliği dahil olmak üzere kök hücre tedavileri için bir kaynak olabileceği düşünülmektedir.[48] Rosa ve ark.'nın[49] 2013 yılında yaptıkları hayvan çalışmalarında hDPSC'ler, diş pulpası rejenerasyonu için başarıyla kullanılmıştır.

Sonuç olarak süt dişleri, üçüncü büyük azı dişleri ve ortodontik sebeplerle çekilen dişler gelecekte rejeneratif tedaviler için önemli bir kaynak olarak değerlendirilmektedir. Ayrıca, kişinin kendi hücrelerinin depolanması ve kullanılması; allojenik hücrelerin kullanılmasında yaşanabilecek immunolojik ve etik zorlukların üstesinden gelmeyi sağlayacaktır.[50] Kök hücre tedavileri, geniş kapsamlı tıbbi faydaları ile hastalıkları ve defektleri tedavi etmede devrim yaratan bir tedavi modeli olarak hızla ilerlerken süt dişi pulpası kök hücreleri de bu çalışmalarda kullanılacak ideal bir kaynak olarak görülmektedir.[48]

Pulpa Transplantasyonları İle İlgili Çalışmalar

1. Daimi Dişe hDPSC Ototransplantasyonu

Xuan ve ark.[6] ilk olarak yaptıkları hayvan deneylerinde otolog süt dişi kök hücrelerinin implantasyonunun, odontoblast tabakası, kan damarları ve sinirleri içeren rejenere diş pulpasını oluşturduğunu göstermişlerdir. Yaşları 7 ile 12 arasında olan, sürekli kesici dişleri travma görmüş ve apikal periodontitis teşhisi konan hastalar rastgele bir şekilde iki gruba ayrılmıştır: kök hücre implantasyon grubu (deney grubu) ve geleneksel apeksifikasyon grubu (kontrol grubu). Deney grubundaki hastaların, travma görmüş kesici dişine, otolog süt kanin dişi pulpasından elde edilen hDPSC agregatları implante edilmiştir. Kontrol grubunda travma görmüş kesici diş, kalsiyum hidroksit kullanılarak apeksifikasyon yöntemi ile tedavi edilmiştir. hDPSC implantasyonunun güvenliğini değerlendirmek için, hDPSC implante edilmiş 20 hastayı 24 ay boyunca takip etmişler ve herhangi bir yan etki gözlemlememişlerdir.[6] Otolog hDPSC'ler hastanın maksiller süt kanin dişinden elde edilmiştir. Süt dişi pulpa dokusu enzimler yardımı ile hDPSClerine ayrıştırılmıştır. Hücreler, kültürde 2 hafta boyunca genişletilmiş ve normal mezenkimal kök hücre (MSC) morfolojisi göstermiştir. Bir hastanın dişi, hDPSC implantasyonundan 12 ay sonra yeniden diş travması alması nedeniyle çalışma dışı bırakılmıştır. Diş çekilmiştir ve dişte yeni oluşan pulpa benzeri doku pulpektomi ile çıkarılarak histolojik olarak incelenmiştir. Histolojik boyama, hDPSC implantasyonunun, normal diş pulpasına benzer şekilde odontoblast tabakası, bağ dokusu ve kan damarları içeren 3 boyutlu bir pulpa dokusu rejenerasyonuna yol açtığını göstermiştir. Bu çalışma ile hDPSC'lerin bir doku iskelesi olmadan travma görmüş kesici dişlere implante edildiğinde pulpa dokusunun üç boyutlu olarak rejenere edilebileceğini destekleyen ilk deneysel ve klinik kanıtları sağlamaktadır. Otolog hDPSC implantasyonunun 24 aya kadar güvenli bir yaklaşım olduğu gösterilse de tam güvenlik ve etkinliği gözlemlemek için daha uzun süreli takip gerekmektedir.[6]

Liang ve ark.[51] 2018 yılında yaptıkları bir çalışmada in vitro kök hücre kültürüne ihtiyaç olmadan pulpa-dentin kompleksinin rejenere edilebilirliğini araştırmış ve bu amaçla, pulpal MSC'lerin kaynağı olarak hücre kültürü olmadan ufaltılmış pulpanın (minced pulp, MP) doğrudan naklini kullanan yeni bir protokol önermiştir. Yaptıkları in vitro deneylerden elde ettikleri veriler, MSC'lerin MP dokularından doku iskelesine göç ettiğini ve MP'nin pulpa rejenerasyonu için bir MSC kaynağı olarak kullanılmasına izin verdiğini ve böylece hücre nakli için DPSC'lerin in vitro kültürüne olan ihtiyacı ortadan kaldırdığını göstermiştir. Bu çalışmanın ardından pulpa rejenerasyonu için pulpanın bütün olarak transplante edilmesi ile ilgili araştırmalar artış göstermiştir. 2019 yılına gelindiğinde Huang ve ark.[52] RET için biyolojik doku iskelesi olarak otolog süt dişi pulpası kullanmanın uygulanabilirliğini hayvanlar üzerinde yaptıkları çalışmalarda göstermiştir.

2. Daimi Dişe Pulpa Otoransplantasyonu

Yapılan bu çalışmaların ardından Feitosa ve ark.[5] pulpa-dentin kompleksinin rejenerasyonu için otolog pulpa transplantasyonun insanlar üzerindeki uygunluğunu araştırmış ve "diş pulpası ototransplantasyonu" olarak adlandırdıkları yeni bir RET yöntemi ileri sürmüşlerdir. Tüm pulpanın naklinin, DPSC'lerin doğal ortamlarında farklılaşması için en uygun "iskeleyi" vereceğini düşünmüşlerdir. Çünkü pulpanın içinde çoğu sinir ve kan damarının var olmasının transplante edilen pulpanın revaskülarizasyonunu ve bağlantı sürecini kolaylaştırabileceği ileri sürülmüştür. Bununla beraber pulpa ototransplantının içinde barındırdığı büyüme faktörlerinin dentinogenezi teşvik etme, odontoblast progenitörlerinin fenotipik ekspresyonuna rehberlik etme ve farklılaşmayı kolaylaştırma potansiyeli yüksektir, ayrıca iyileşmenin ilk aşamalarında anjiyogenezi teşvik ederek kök hücre çoğalmasını teşvik edebilmektedir.[53] Feitosa ve ark.[5] hazırladıkları olgu serisinde diş pulpası ototransplantasyonu için klinik prosedürleri tanımlamayı ve bu RET yöntemiyle tedavi edilen 3 hastanın en az 9 aylık klinik takibini gerçekleştirmeyi amaçlamışlardır.

Çalışmaları için kök kanalı tedavisine ihtiyaç duyan tek köklü bir küçük azı ve çekimi gereken üçüncü büyük azı dişine sahip üç hasta seçilmiştir. Kanal enstrümantasyonunda döner eğeler ve irrigasyon için de triantibiyotik solüsyon (siprofloksasin, minosiklin ve metronidazol) kullanılmıştır. Klinik protokol revaskülarizasyona benzer olmadığı için apikal kanama indüklenmemiştir. Çekilen üçüncü büyük azı dişine önce bir çentik atılmış ardından oluşturulan çentiğe keskin ve düz bir cerrahi elevatör ile bastırılmış ve pulpa küçük bir presel ile dikkatli bir şekilde çıkarılmıştır. Pulpa dokusu donör dişten reseptör dişin kök kanalına dezenfekte edilmiş gütaperka konları yardımıyla yerleştirilmiştir.[5] Pulpa ototransplantasyon prosedürüne tabi tutulan her bir dişe birinci yılın sonunda apikal revaskülarizasyonu doğrulamak için ultrasonik değerlendirme yapılmış ve revaskülarizasyon kanıtlanmıştır. 1 yıllık takipte tüm hastalarda endodontik/periodontal komplikasyon belirtileri gözlenmemiştir.[5] Sonuç olarak pulpa dokusu ototransplantasyonunun, transplant reddinin olmaması, tüm hücrelerin aynı DNA ve RNA'yı içermesi, tamamen olgun bağ dokusu içermesi, oluşturulmuş bir nöronal ağ ve önceden oluşturulmuş vaskülarizasyon gibi çeşitli avantajlara sahip olduğu ve bu faktörlerin pulpa rejenerasyon tedavilerinin başarısını arttıracağı düşünülmektedir.[5]

Bu çalışmanın ardından rejeneratif tedavilerde pulpa transplantasyonu ile ilgili yapılan araştırmaların sayısı artmıştır. Pulpa kaynağı olarak üçüncü büyük azı dişleri dışında mesiodenslerin kullanımı ve süt dişlerinden elde edilecek pulpanın tranplatasyonu fikri ortaya atılmıştır.[28,45] Transplante edilen pulpa, fizibilitesi ve hücre büyümesi, farklılaşması ve konak reddi riski olmaması nedeni ile optimal bir doku iskelesi görevi görebilir.[5] Aynı potansiyel, kök hücrelerin ve büyüme faktörlerinin zengin bir kaynağı olan süt dişi pulpası için de geçerlidir.[54]

3. Daimi Dişe Süt Dişi Pulpası Ototransplantasyonu

Çehreli ve ark.[28] süt dişi pulpasının, nekrotik pulpalı ve apikal periodontitisli genç sürekli dişlerin RET'leri için doğal ve biyolojik bir doku iskelesi olarak kullanılacağı bir olgu serisi planlamıştır. Tüm dişlere ortak, iki seanslık RET protokolü uygulanmıştır. İkinci (ototransplantasyon) seansta, diş kuronları

dezenfekte edilmiş sonra sürekli kesici dişlerin giriş kaviteleri tekrar açılmıştır. Ototransplantasyondan önce apikal kanama indüklenmemiştir. Ardından donör süt maksiller kanin diş kuronu üzerinde bir endodontik giriş kavitesi açılmıştır. Tüm pulpayı (koronal ve radiküler pulpa) çıkarmak için önceden sterilize edilmiş tirnerf kullanılmıştır. Daha sonra, tüm pulpa steril bir presel kullanılarak trirnerften ayrılmış ve süt kanin sterilize edilmiş gütaperka konları kullanılarak alıcı dişin kök kanalına nazikçe yerleştirilmiştir. Süt kanin dişinin kök kanalı, iyodoform içerikli kalsiyum hidroksit patı ile doldurulmuştur.[28] Sonuç olarak, tüm dişler klinik semptomların yokluğunda tam periradiküler iyileşme göstermiştir. Kök duvar kalınlığında hafif bir artış göstermiştir. Kök kanal daralması veya obliterasyonuna dair görünür bir işaret olmamıştır. Donör süt kanin dişlerinde klinik semptomlar görülmemiş ve radyografik olarak kalsiyum hidroksit-iyodoform patının rezorpsiyonu ile fizyolojik kök rezorpsiyonunun kanıtını göstermiştir.[28]

Çehreli ve ark.[28] hazırladıkları olgu serisinde, kök duvarı kalınlığındaki artışın 1 ve 2 yıllık radyografik gözlemi, tipik olarak daha progresif ve kontrolsüz kök duvarı kalınlaşması potansiyeli olan rutin bir geleneksel revaskülarizasyon olgusuna kıyasla belirgin şekilde yavaş ve kontrollü olarak bulunmuştur. Süt dişi pulpasının kalsifikasyon için düşük eğilime sahip olması, indüklenmiş apikal kanamanın olmaması ile birleştiğinde agresif mineralize edici özelliklere sahip SCAP olmayan hücrelerin kök kanalına akışını önlemiş olabileceği varsayılmıştır.[55] Bu sayede zaman içinde kontrolsüz ve progresif kalsifik doku birikimini olumlu bir şekilde sınırlamış olabileceği düşünülmüştür.[28]

Bu çalışma ile, hasta dostu, komplike olmayan bir ototransplantasyon protokolü kullanılarak, nekrotik, açık apeksli genç sürekli dişlerin RET'lerinde süt dişi pulpasının biyolojik bir doku iskelesi olarak kullanım potansiyeline sahip olabileceği gösterilmiştir.[28]

Yapılan son çalışmalar sonucunda tüm pulpa dokusunun transplantasyonun, rejenerasyon için optimal bir "iskele" oluşturabileceği düşünülmektedir. Aynı hastadaki bir dişe, çekimi gereken üçüncü büyük azı dişinin pulpa ototransplantasyonunun, vücut reddi ve inflamasyon riski olmaksızın gerçek pulpa rejenerasyonu için klinik olarak uygulanabilir bir prosedür olduğu gösterilmiştir.[5] Bununla birlikte, iki farklı kişi arasında diş pulpası transplantasyonu araştırmaya açık bir prosedürdür. Allojenik transplantasyonun bu klinik prosedürün başarısını değerlendirmek için bir sonraki adım olabileceğini düşünen Feitosa ve ark.[8] bu konu üzerinde bir olgu sunumu yapmışlardır.

4. Daimi Dişe Allojenik Pulpa Transplantasyonu

Feitosa ve ark.[8] diş pulpası allojenik transplantasyonu için klinik prosedürleri tanımlamayı amaçlayan ve böyle bir RET prosedürü ile tedavi edilen üç hasta için en az 24 aylık bir klinik takip gerçekleştirmştir. Çalışmalarına üçüncü azı dişinin veya süt dişinin çekimine ihtiyaç duyan oğulları/kızları olan ve kendi tek köklü küçük azı dişlerine kök kanalı tedavisi gereken üç hasta dahil edilmiştir.[8] Çalışmanın sonunda üç aylık kontrole kadar dişlerde elektrikli pulpa testine yanıt saptanmamıştır. Hastaların altıncı ay takiplerinde reseptör dişlerin periapikal radyolsüensileri, bilgisayarlı tomografi görüntülerinde hafifçe artmış olarak bulunmuştur. Ancak ikinci yıl takibinde bu radyolüsensinin tamamen yok olduğu görülmüştür. Sonuç olarak 24 aylık takip aşamasında hiçbir olguda endodontik/periodontal komplikasyon/radyolüsensi belirtisi gözlenmemiştir. Olgu serisindeki tüm dişler, 6-12 ay sonra elektrikli pulpa testine pozitif yanıt vererek pulpa canlılığı göstermiştir. Her bir dişin periapikal bölgesinde ultrasonik görüntüleme ile karakteristik nabız görüntüleri alınmış, kan perfüzyonu doğrulanmış ve böylece üç hasta için revaskülarizasyon kanıtlanmıştır.[8]

Mevcut çalışmada periapikal radyolüsensilerin ilk 6 aylık süreçte hafif artış göstermesi, allojenik hücrelerin varlığına bağlı olarak bazı enflamatuar mediatörlerin bölgeye gelmesi sonucu daha düşük kanlanmanın bir sonucu olabileceği düşünülmüştür.[8]

Feitosa ve ark.'nın[8] çalışması anne-baba ve çocuklar gibi yakın akrabalar arasında ve

belki de diğer aile üyeleri arasında pulpa transplantasyonunun mümkün olabileceğini gösteren ilk girişimdir. Bunun bir sonraki aşaması uzak aile üyeleri ve aile dışı donörler/reseptörler arasında pulpa transplantlarının uygunluğunu araştırmak için olası kan testlerine odaklanmak olabilir.

Sonuç

Endodontik rejenerasyon adına apikal kanamanın indüklenmesi dışında kök kanalına transplante etmek için trombositten zengin fibrin, lökositten zengin fibrin, trombositten zengin plazma, ekstrakte edilip kültür ortamında genişletilmiş diş pulpası kök hücreleri, ufaltılmış pulpa gibi çeşitli otolog karışımlar önerilmiştir. Bu tedaviler, trombosit konsantrelerinin hazırlanması veya kök hücre genişletilmesi için laboratuvar işlemleri gerektirmektedir. Pulpa transplantasyonları ise önceki klinik stratejilere kıyasla herhangi bir laboratuvar müdahalesi gerektirmeme gibi önemli bir avantaja sahiptir. Başka bir deyişle, pulpa transplantasyonu, klinik ortamı dışında başka ortam ve ekipmana gerek olmaksızın tamamen bir klinik diş hekimi muayenehanesinde gerçekleştirilebilmektedir. Bununla beraber hücreleri, doku iskelelesini ve büyüme faktörlerini ayrı ayrı kullanan teknikler ile karşılaştırıldığında tüm bu bileşenleri doğal olarak içeren bir ototransplant ile daha hızlı bir doku rejenerasyonu gözlemlemek mümkün olabilir. Ancak pulpa transplantasyonlarının rutin olarak uygulanması savunulmadan önce uygulamanın klinik prosedürünü ve prognozunu belirlemek adına daha fazla çalışma yapılması gerekmektedir.

Etik Kurul Onayı

Makalemiz derleme türünde olduğu için etik kurul onayı gerekmemektedir.

Çıkar Çatışması

Bu makale yazarlarından hiçbirinin makalede bahsi geçen konu veya malzemeyle ilgili herhangi bir ilişkisi, bağlantısı veya parasal çıkar durumu söz konusu değildir.

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Bilgisayarli Oklüzal Analiz Sistemleri

Computerized Occlusal Analysis Systems

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ÖZET

Diş hekimliğinde oklüzyon; artikülasyon, temaslar ve zamanlama açısından değerlendirilmesi gereken bir faktördür. Doğru belirlenmesi için standart bir yöntem yoktur, çeşitli alternatifler kullanılabilir. Geleneksel yöntemlere ek olarak dijital analiz yöntemleri bunlara örnektir. Dijital oklüzal analizin kullanıldığı çalışmalar, bu sistemlerin daha kısa sürede, daha doğru oklüzal temas tespitinde bulunduğunu göstermiştir. Teknolojinin gelişimiyle de kullanımı yaygınlaşmıştır.

Klinik ortamda dijital olmayan yöntemler hatalı yorumlanabilir. Temasları belirlemek için kullanılan ısırma kağıtları oklüzal yükü ölçemez. Kağıt kalınlığı, kalitesi gibi özellikler bile temas alanları üzerinde etkilidir. Bu sebeple bu yöntemlere ek olarak objektif yorumlamaya dayalı sistemler gereklidir.

Bu makalenin amacı kullanılan güncel dinamik oklüzal analiz sistemlerini, bu sistemlerin avantajlarını ve sınırlamalarını açıklamaktır.

Anahtar Kelimeler: *Analiz, Bilgisayarlı Oklüzal Analiz, Dijital, Oklüzyon*

ABSTRACT

Occlusion in dentistry; articulation is a factor that needs to be evaluated in terms of contacts and timing. There is no standard method for accurate determination, various alternatives can be used. In addition to traditional methods, digital analysis methods are examples of these. Studies using digital occlusal analysis have shown that these systems detect more accurate occlusal contact in a shorter time. Its use has become widespread with the development of technology.

In the clinical setting, non-digital methods may be misinterpreted. Bite papers used to determine contacts cannot measure occlusal load. Even features such as paper thickness and quality have an impact on the contact areas. For this reason, in addition to these methods, systems based on objective interpretation are required.

The purpose of our study is to touch upon information about traditional methods and digital systems. It aims to examine the studies and systems in this field.

Key words: *Analysis, Computerized Occlusal Analysis, Digital, Occlusion*

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Giriş

Oklüzyon, 2017 yılında yayınlanan Prostodonti Terimleri Sözlüğü'ne göre maksiller ve mandibular dişlerin çiğneme yüzeyleri arasındaki statik ilişki olarak tanımlanmıştır. Dişler oklüzyona geldiğinde kuvvet dengeli olmalıdır.[1] Çiğneme fonksiyonunun düzgün olabilmesi için, oklüzal temasların uygun şekilde oluşturulması gerekmektedir. Oklüzyon, sadece dişler arasındaki karşılıklı temastan ibaret değildir. Çiğneme sistemini oluşturan tüm bileşenlerin birbiriyle uyumlu çalışmasını da içermektedir.[2] Bu bileşenlere dişler, periodontal dokular, nöromüsküler sistem, kaslar, temporomandibular eklem ve kraniyofasiyal kemikler de dahildir. Oklüzal kuvvetin uygun şekilde dağılması diş hekimliğinin pek çok alanı için kritik bir faktördür.[3]

Günümüze kadar oklüzyonu belirlemek için birçok farklı kayıt yöntemi kullanılmıştır. [4] Bunlar; aljinat, şeffaf asetat levhalar, mylar kağıt şeridi, balmumu, artikülasyon kağıtları, polieter, balmumu artikülasyon kağıdı, oklüzal spreyler, silikon, ipek şeritler, fotoğraf karşılaştırma yöntemi, folyolar, oklüzal sonografi, basınca duyarlı filmler, dijital-bilgisayarlı oklüzal analiz sistemleridir (BOA).

Daha önce yapılan tanımlamalara göre ideal oklüzyon kayıt malzemesi bir takım özellikler barındırmalıdır; [5]

- Kemik seviyesi yetersiz olan ve mobiliteye sahip dişlerin teması sırasında doğru oklüzyonu göstermek;
- Kabul edilebilir boyutsal stabilite;
- Polimerizasyondan sonra kuvvetlere karşı yüksek direnç;
- Kullanım ve kontrol kolaylığı;
- Kayıt sırasında bölgedeki dokularda zararlı etkinin olmaması;
- Dişlerin temas bölgelerinin olduğu gibi kaydedilmesi;
- Kayıtların doğru şekilde tekrarlanabilir olmasıdır.

Ancak bu özelliklerin hepsini bir arada bulunduran ideal bir kayıt malzemesi bulunmamaktadır.

Geleneksel Yöntemler ve Bilgisayarlı Oklüzal Analiz Yöntemi

Yeni yöntemlerin arayışı sonrası teknoloji yardımıyla dijital sistemler kullanıma başlanmıştır. Çoğu meslek grubundaki gibi diş hekimliğinde de dijital sistemlerin kullanımı son yıllarda önemli gelişmelere yol açmaktadır. Gelişimlerin avantajlarını değerlendirmek için geleneksel yöntemlerle kıyaslamak gerekmektedir.[6]

Dijitalin dışında geçmişten günümüze kadar artikülasyon kağıtları da kullanılmaktadır. Artikülasyon kağıtları dişler arası temasları belirlemek için en sık kullanılan yöntemdir. Bu yöntemde hastalar, diş yüzeyinde çeşitli mürekkep izleri bırakan kağıt parçalarını ısırır.[7] Artikülasyon kağıtlarının sınırlamalarından biri, tükürük tarafından kolayca şeklini kaybedebilir. Kalın (25-350μ)[8] ve nispeten esnek olmayan bir yapıda olması da dezavantaj sayılabilmektedir. Bundan dolayı artikülasyon kağıtlarının kullanımı daha fazla ve istenmeyen işaretlemeler ile sonuçlanabilmektedir.[9,10] Ayrıca rengin doygun olması ile işaret, büyüklüğü, kuvvet miktarı veya ortaya çıkan temas zamanlaması arasında bir ilişki olmadığı için kağıtlar oklüzal yükü ölçemez.[11] En önemli kısıtlaması ise, oklüzal analiz büyük ölçüde öznel yorumlamaya bağlı kalır. Hekimler arasında yorumlamada farklılıklar gözlenir.[12,13] Buna karşı bilgisayarlı oklüzal analiz (BOA) ise tekrarlı ölçülebilme, zaman tasarrufu, kuvvet ve doğru kapanış ilişkisini sağlar. Mandibulanın üç boyutlu hareketlerinde oluşan dişsel temasları doğru olarak gösterir ve bu sayede ölçüm hassasiyetini artırır.[14,15]

Teknolojik cihazlar sayesinde teşhis ve tedavinin doğruluğu artmıştır. Buna ek olarak birçok işlem için harcanan süreyi de kısaltmaktadır.[16] Bu cihazlar daimi restorasyonların daha doğru şekilde yapılmasını sağlar. Restorasyonlar için tasarım süreci daha yakından izlenebilir ve hastanın esas ihtiyacına göre doğru oklüzal ayarlamalar yapılabilir.[17]

Dijital Oklüzyon dönemi, 1984 yılında T-Scan (Tekscan Incorporation, Boston, USA) teknolojisinin, subjektif olarak oklüzyonu tespit etmesi ve günlük klinik kullanımda hassasiyet

sağlaması ile gelişmeye başlamıştır.[18] Oklüzal temasların doğru bir şekilde belirtilmesi söz konusu olduğunda, BOA'nın, dijital olmayan yöntemlere göre etkinlik açısından üstün veya benzer olduğu rapor edilmiştir.[19,20] Oklüzal analiz sisteminin kullanıcıları, bu teknolojinin oklüzal kuvvet ve doğru temas noktalarını belirlemede klinisyenlere birçok yarar sağladığını belirtmektedirler. Gelişmiş bilgiler ve kişisel yorumlamayı gerektiren geleneksel yöntemlerle karşılaştırıldığında daha avantajlı ve doğru görünmektedir.[21–24] Geleneksel olarak oklüzyon değerlendiren yöntemler objektif değerlendirme sunamamaktadır.[25] Dijital cihazlarda ise temas noktaları hastanın ısırma yoğunluğunu objektif şekilde yansıtmaktadır .[26]

Accura (Parkell Inc., Farmingdale, NY, ABD), OccluSense (Dr. Jean Bausch GmbH & Co. KG, Köln, Almanya) ve T-Scan Novus (Tekscan, Inc., S. Boston, MA, ABD) gibi cihazlar oklüzal analizi dijitale dökmek için geliştirilmiştir ve oklüzal temasları belirlemek için en yaygın olarak bilinen dijital sistemlerdir.[27–29]

Accura Sistemi

2017 yılında üretilen, düşük maliyet ve rahat kullanım rahatlığı sağladığı iddiasıyla Accura sistemi oklüzal kuvvet değişimini ölçüm sırasında gösterebilen BOA sistemi olarak piyasaya sunuldu. Accura film 256 farklı seviyede oklüzal kuvveti ölçebilmektedir. 160 mikron kalınlığındaki sensör filmi poliamid esaslıdır. Veri bilgilerini Wireless Fidelity (Wi-Fi) ile bilgisayara aktarır. Film sensörünün teknik özellikleri T-Scan'e benzerdir.[30]

Sensörlerin teknik özellikleri benzer olsa da T-scan Novus sensöründeki algılama bölgesi sayısı, film boyutuna göre 1122 ile 1370 arasında değişir. Accura sisteminde ise algılama bölgesi sayısı 1172 ila 1390 arasında değişmektedir. Ortak özellikleri ise çiğneme kuvvetini kaydeden 256 seviyesi vardır.[31] 24 kişi üzerinde yapılan bir çalışmada Accura ve T-scan arasında belirgin bir fark bulunamamıştır.[32]

OccluSense Sistemi

OccluSense sistemi, 2019 yılında tanıtılan yeni BOA sistemidir. OccluSense, kablosuz bir cihazdır. Analizleri Wi-Fi yoluyla bir bir yazılıma ileten ektra kayıt koluna sahiptir. Sensör ile bu bilgiler görüntülenir.[33] OccluSense tarayıcısında iki adet kontrol düğmesi (yeşil ve pembe), şarj olup olmadığını gösteren kırmızı LED ışık, bir LED ekran ve kullanım sırasında sensörler ile ekranı sabit tutmak için mandallar bulunmaktadır. Kullanılmadan önce şarj edilmelidir. Dört dakika kullanılmadığında kapanmaktadır. Occlusense sensörü 60 mikron kalınlığındadır.[34]

Hasta üzerinde yapılan çalışmada maksimum oklüzal kuvvet ve lateral hareketlere tespit edilmiştir. T-Scan ile karşılaştırılmıştır. Benzer sonuçlar elde edilse de T-Scan noktasal alanlarda daha iyi sonuç vermiştir. Occusense ise belirli yerlerin dışında daha geniş oklüzal kuvvet alanlarını gösterir. Ayrıca bu çalışmada hiçbir T-Scan sensörü delinmemişken Occlusense sensörü üç kullanımdan sonra delinmiştir. Ayrıca çalışma yapan hekim Occlusense'in belirli aralıklarla Wi-Fi bağını kopardığı ve bu sebeple kayıt süresinin çok arttıpını rapor etmiştir. [35]

T-Scan Sistemi

T-scan sistemi oklüzal analiz cihazları arasında en sık kullanılan sistemler arasındadır.[36] Sistem 1987 yılında William L. Maness tarafından geliştirilmiştir.[37] Oklüzal analize özel basınca duyarlı sensör teknolojisinin kullanımı T-Scan ile başlamıştır.[38]

T-Scan III sistemi, USB ile bilgisayara bağlanan bir el cihazından oluşur; el ile tutulan kısmı ise, çene kavsine uygun U şekilli bir basınç ölçüm sensörlü plakadan oluşur. Sensör 60 μm (0.06 mm) kalınlığında ve iletken mürekkepli 1500 hassas alıcı noktasına sahiptir. Isırma kuvveti ile sensöre giden elektrik azalır, bu objektif ölçüm kaydedilir[37] Yazılım mevcut verileri işleyerek renkli üç boyutlu ve iki boyutlu grafikler haline getirir. Diş yapısı mezio-distal olarak ikiye bölünerek veya dört parçaya bölünerek analiz edilebilir. Üç boyutlu grafiklerde oklüzal temasların yoğunluğuna göre renkler değişir. Oklüzal temasın maksimum olduğu bölgeler pembe ile gösterilirken, minimum temas alanları mavi ile gösterilir.[39]

T-scan sistemi sayesinde dişlerin her segmenti için dengesiz kuvvetlerin çoklu düzeltmeleri

gerçekleştirilebilir.[40] Bu sistemde basınç değişiklikleri elektrik yüküne dönüşerek oklüzal kuvvet ölçümleri yapılabilmektedir. Kuvvetin konumu sensör üzerindeki hassas alıcıların yerleri ile tespit edilebilir. [41] T-scan sistemi sayesinde implant destekli ve diğer protetik restorasyonlardaki kırık oluşma riski azalır. Bunun yanı sıra teşhis ve hasta eğitimi daha olumlu hale gelir ve oklüzyon ile ilgili sonuçlar dijital ortamda belgelenip kayıt altına alınabilir.[42] T-Scan III sistemi ile yapılan çalışmada oklüzyon bozukluklarının TME rahatsızlıklarına sebep olacağı kanıtlanmıştır. Oklüzyonun düzeltildiği vakalarda baş ağrısı, eklem ağrısı, fonksiyon bozuklukları gibi şikayetlerin azaldığı bildirilmiştir.[43]

T-Scan Novus Sistemi (T-Scan 10)

T-Scan Novus sistemi ince, daha esnek, basınca duyarlı, yüksek çözünürlüğe sahip sensör ile [38] 256 farklı oklüzal kuvveti ölçer ve aynı anda görüntüleyebilir. Bu sistemde kayıt kolu, iki farklı boyutta sensör ve daha yüksek çözünürlüğe sahip olan iki sensör bulundurur.[44] Sensörü 100 mikron kalınlıktadır.[45]

Yapılan bir çalışmada bruksizme sahip hastalarda oklüzal splint ile yapılacak tedavilerde oklüzyonu doğru şekilde ayarlamak için T-Scan Novus sistemini önermişlerdir.[46] Aynı şekilde bruksizme sahip hastalarda yapılan bir diğer çalışmada da T-Scan Novus sisteminin oklüzal splint tasarımı ve dişe uygulanması açısından daha hassas olduğu, optimal ve uyumlu temas oranlarına ulaşmayı sağladığı belirtilmektedir.[47] T-Scan Novus hekimin belirlediği kadranların oklüzal yüklerini gösterebilir. Yükün nerede daha fazla olduğunu grafiklerle sunar. Ayrıca bu sistemde implantlara fazla oklüzal yük gelmesine karşı alarm sistemi bulunur. T-Scan Novus sistemi sekiz farklı kasın aktivitesini ölçen elektromyografi (EMG) cihazları ile koordine kullanılıp oklüzyon-kas ilişkisinin teşhisine izin vermektedir.[33] T-Scan Novus sensörleri 24 defa değiştirilmeden kullanılabilir ve 60-80 mikrona kadar sıkıştırılabilir.[48] Occulusense sensörünün ise steril edilemediği için bir defa kullanılması önerilir. Klinik kullanımda Occlusense'in maliyeti daha yüksek olmaktadır. Ayrıca T-Scan kayıt sırasında önizleme yapmayı ve bunları kaydetmeyi sağlarken Occlusense böyle bir avantaj sağlamaz, verilerin canlı olarak izlenmesine ve kaydına izin vermez.[33]

BOA Sistemlerinin Avantajları

BOA, oklüzal sensörün ısırıldığı ilk andan maksimum ısırmaya kadar ölçüm yapabilir. Kuvvet değişimini algılarken, ısırmanın kuvvet miktarını ölçme özelliği bulunmamaktadır. Sensörün kalınlığı 100 mm'dir (0,1 mm), ısırma kuvveti ile bu kalınlık 60mm'ye kadar düşer. Sensörün sıkışabilme özelliğiyle çift taraflı girişim sağlarken artikülasyon kağıtlarının ise tek taraflı girişimi ile karşılaştırıldığında ona göre gelişmiş okluzal kuvvet verileri sağladığını iddia edilmektedir.[30] BOA nispeten maliyet açısından kabul edilebilir, tekrarlı kullanılabilir ve çok sayıda görsel değerlendirmeye imkan sağlayabilir. Sistemin bruksizmli hastalarda avantajlı olduğu bilimsel olarak kanıtlanmıştır. Dijital sistemlerin rutin olarak klinikte kullanılması oklüzyon sorunlarının ve ağız hastalıklarının daha kesin tedavisini sağlayacaktır. Oklüzyon ile birçok diş hastalığının arasındaki yakın ilişkiyi daha net ispat edecektir.[49]

T-scan sistemi, restorasyonunun tamamlanmasının ardından dinamik oklüzal analiz yapılarak dişsel çatışmaların daha doğru düzeltilmesi için tutarlı, kullanışlı ve tekrarlanabilen bir yöntemdir.[50] Artikülasyon kağıdı ve mumlar gibi geleneksel oklüzal göstergeler yalnızca temas alanı ve bulunduğu konumu gösterebilirken, T-Scan oklüzal temas zamanı ve basınç oranlarını dijitalize etmek ve kaydetmek gibi ek özelliklere sahiptir.[51]

İki farklı teknolojinin birleştirildiği başka bir çalışmada bilgisayarlı EMG, BOA ile birlikte kullanılmıştır. Oklüzyonun doğruluğunu kontrol edebilmesine ek olarak kas aktivitesini de değerlendirilmiştir. Aynı zamanda bu yöntemle analizin kayıt altına alınıp belgelenmesi sağlanmaktadır.[52]

15'i sağlıklı ve 15'i tedavi gören toplam 30 travma hastasının oklüzal analizinin yapıldığı bir çalışmada T-Scan sisteminin oklüzyon belirleme kağıtları ile uyumlu sonuçlar verdiği gösterilmiştir.[53]

Bu dijital teşhis yöntemi, oklüzal analiz verilerinin kişiden kişiye farklı yorumlanmasının önüne geçer, dinamik oklüzyonun doğru kaydını sağlar.[54] T-Scan sistemi kullanılarak gerçekleştirilen BOA, protetik tedavi kalitesini ve doğruluğunu artırır.[55]

BOA Sistemlerinin Dezavantajları

BOA kullanımı bir dizi beceri gerektirdiğinden hekimlerin karşılaştığı zorluk, cihazın prosedürleriyle geçen sürenin artmasıdır. Doğru tespit, uygun ayarlamaları doğru şekilde yapmayı, hastaya gerekli çene hareketleri sırasında sözlü şekilde yol göstermeyi, aynı anda ekranı takip etmeyi ve kayıtta neler olup bittiğini anlamayı gerektirir.[30] Bundan dolayı, BOA teknolojisinin geleneksel göstergelere kıyasla daha avantajlı olduğunu kanıtlamak için daha fazla çalışma önerilmektedir.[56]

T-Scan sistemi 0.06 mm'yi geçmeyen temasları algılayamamaktadır.[57] BOA cihazlarının sensörleri ince (0,1 mm) yapılmıştır, ancak artikülasyon kağıtlarına kıyasla daha kalındır. Bu durum sadece oklüzyonu değil aynı zamanda çiğneme kaslarının aktivitesini de değiştirmektedir.[58] Ayrıca, kuvvetler keskin tüberküllerin olduğu bölgelerde küçük bir alanda yoğunlaştığından dolayı sensörler zarar görebilir. Bu sebeple bazı araştırmacılara göre BOA cihazların kullanımının sınırlı olacağı kabul edilmektedir. BOA cihazlarının sensörlerinin hassasiyetinin, sensörlerin birçok kez kullanılmasıyla azalacağı ve hassasiyetinde kayıp olacağı bildirilmiştir.[60,61] Maksimum çiğneme gibi yüksek etkili kuvvetler, ince sensörlerin hassas algılama bölgerine zarar verebilir, bu da kaydedilen toplam kuvvet miktarında ek hatalara neden olabilir. Oklüzyon esnasındaki karşılıklı temas alanları sensördeki katlantılar görüntüde artefakt oluşturabilir.[62] Geleneksel yöntemlerden daha pahalıdır.[63]

Sonuç

Dijital oklüzal analiz sistemleri klinisyenlere daha doğru tedavi gerçekleştirmelerini sağlar. Oklüzyon üzerinde yapılan düzeltmelerde zaman kaybının ve yanlış tedavilerin önüne geçilir. Oklüzal temasların objektif bir şekilde grafiksel gösterilmesi gibi avantajları sayesinde geleneksel yöntemlere kıyasla daha doğru sonuçlar sağlamaktadır. Hasta-hekim ilişkisini iyileştirir ve öngörülebilir bir tedavi akışı sağlar. Dijital sistemlerin amacı geleneksel yöntemlerin olumsuzluklarını ve eksikliklerini gidermektir. Klinik ortamında doğru bir tedavi yaklaşımı için geleneksel ve dijital yöntemlerin birbirini tamamlaması ve birlikte kullanılması daha doğrudur. Sistemlerin eksik yönleri teknolojinin zamanla gelişmesiyle giderilebilecektir.

Etik Kurul Onayı

Makalemiz derleme türünde olduğu için etik kurul onayı gerekmemektedir.

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