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ORIGINAL ARTICLE / ARAŞTIRMA MAKALESİ

A Novel Paraflash-Softbox Setup for Standardized Anterior and Posterior Intraoral Photography

Anterior ve Posterior Standardize İntraoral Fotoğraflama için Yeni Bir Paraflaş/Softbox Düzeneği

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ABSTRACT

Objective: The main limitation of intraoral dental photography is the standardization of the repetitive dental images. The parameters affecting the standardization can be divided into 3 groups such as; parameters related to the camera settings, parameters related to the flashlight, and parameters related to the shooting position. The parameters related to the camera settings are exposure [the combination of the lens aperture (f-stop) and the shutter speed], the sensitivity of the media (ISO), and white balance (WB), which may affect the brightness, sharpness, and depth of field of the dental image. The parameters related to the illumination are the power output of the light source, softboxes/diffusers, the distance of the light source, and the distance and angulation between the dual flashlights. The parameters related to the shooting position are the position of the dental unit and the clinician/camera which define the working distance. Among these, the clinician should standardize as many parameters as he/she can to provide accurate and precise repetitive intraoral dental images. This paper suggests two novel paraflash/softbox setups to provide the standardized intraoral photography of both anterior/posterior teeth and the occlusal surfaces at the same time, clinically.

Clinical Technique: The positions of dental unit and head support should be fixed. The first setup involves 3 paraflashes/softboxes fixed vertically and horizontally above the dental unit symmetrically at 45° of inclination. Two are positioned for introvert angulation and one should be placed right above the dental unit between the other two with a slight inclination towards the patient's head. The second setup involves only 2 paraflashes/softboxes fixed vertically at 45° of inclination above the dental unit and with the ability of horizontally re-positioning easily. Through these setups, the clinician can take both anterior and posterior repetitive intraoral dental photographs by minimizing the major parameters related to the camera settings, illumination, and shooting position.

Keywords: Dental photography, paraflash, softbox, occlusal photography, standardization

ÖZET

Amaç: Ağız içi dental fotoğrafçılıkta ana limitasyon tekrarlayan fotoğraflardaki standardizasyonun sağlanmasıdır. Standardizasyonu etkileyen parametreler temel olarak üç grupta incelenebilir. Bunlar kamera ayarları ile ilgili parametreler, flaş ışıkları ile ilgili parametrele ve çekim pozisyonu ile ilgili parametrelerdir. Kamera ayarları ile ilgili olanlar dental fotoğrafın alan deriniğini, keskinliğini ve aydınlığını etkileyebilen pozlama (objektif açıklığı ve deklanşör hızının birleşimi), ortam hassasiyeti (ISO) ve beyaz dengesi (WB) olarak sayılabilir. Flaş ışıkları ile ilgili olanlar ışık kaynağının çıkış gücü, softbox veya yansıtıcılar ve dual ışık kaynaklarının uzaklığı ve açılanmasıdır. Çekim pozisyonu ile ilgili olanlar ise çalışma uzaklığını belirleyen dental koltuğun ve klinisyenin/kameranın pozisyonudur. Tekraralayan intraoral dental fotoğraflarda kesin ve doğru çekimler için klinisyen bahsi geçen birçok parametreyi standardize ederek çekim yapmalıdır. Bu yayın anterior/posterior dişler ve okluzal yüzeylerden standardize intraoral fotoğraflar çekilebilmesi için iki yeni klinik paraflaş/softbox düzeneği önermektedir.

Klinik Teknik: Dental koltuk ve tetiyer pozisyonları sabitlenmiş olmalıdır. İlk düzenek dental koltuk üzerinde dikey ve yatay olarak 45° açı ile simetrik şekilde konumlandırılmış 3 adet paraflaş/softbox içermektedir. Flaşlardan iki tanesi içe doğru açılandırılmış şekilde ve bir tanesi koltuğun tam üzerinde, iki simetrik flaşın tam ortasında ve hasta başına hafifçe açılandırılmış olarak konumlandırılmaktadır. İkinci düzenek dental koltuk üzerinde dikey olarak 45° açı ile konumlandırılmış yalnızca iki adet paraflaş/softbox içermektedir. Bu düzenekteki iki flaş yatay düzlemde açıları değiştirilmeden kolayca yeniden pozisyonlandırılabilmektedir. Bu yeni düzenekler sayesinde klinisyen tekrar eden anterior ve posterior intraoral fotoğrafları kamera ayarları, aydınlatma ve çekim pozisyonları ile ilgili parametreleri minimalize ederek çekebilecektir.

Anahtar kelimeler: Dental fotoğrafçılık, paraflaş, softbox, okluzal fotoğraf, standardizasyon

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INTRODUCTION

Dental photography is not an option but a must for clinical practice today. Intra-oral and extra-oral dental records are essential for patient persuasion, digital treatment planning, provisional outcome simulations, restorative material shade selection, technician communication, and even legal issues (Korkut B, 2022; Hardan et al., 2022; Korkut et al., 2022). Regarding restorative dentistry, dental photography is a common diagnostic tool for dental conditions such as tooth decay, tooth wear, dental trauma, and for the evaluation of dental restorations (Signori et al., 2018). Also intraoral photography can be used to perform quantitative or qualitative scoring for purpose-made indices such as pink esthetic score white esthetic score, papilla index, etc.) (Bertl et al., 2019).

The follow-up records are important to assess the success rate of a restoration in terms of restorative dentistry. However, the main limitation is the standardization of the repetitive dental images Korkut B, 2022; Korkut et al., 2022; Jackson et al., 2019). There are several parameters affecting the standardization of dental photography (Snow, 2009). These parameters can be divided into 3 groups according to the major influencing factor such as; parameters related to the camera settings, parameters related to the illumination, and parameters related to the shooting position (Galdino et al., 2001).

Standardization parameters for intra-oral photography

1. Parameters related to the camera settings

Shooting parameters related to the selected camera are an important factor that may affect mainly the brightness, sharpness, and depth of field of the dental image. The major parameters are exposure, sensitivity of the media (ISO), and white balance (WB). The exposure is the combination of the lens aperture opening (f-stop) and the shutter speed and is influenced by the ISO and the distance of the camera to the subject (Korkut B, 2022; Snow, 2009).

The lens aperture determines the depth of field (focus range from front to back) and also the intensity of the light (Ahmad, 2009; Moussa et al., 2021). The aperture size is defined as the f-stop numbers at the camera settings (the larger the number is, the smaller the aperture will be) (Snow, 2009). In terms of intra-oral dental photography, to increase the depth of field, the lens aperture opening should be set as small as possible depending on the selected macro objective (the range is up to f18 – f64) (Terry & Snow, 2008). Once this parameter is set, it can be standardized that there will be no need to change it unless the camera and flashlight setups change. For better image quality with an acceptable depth of field, it is recommended to adjust the aperture between f22-f32. However, it is important to take into consideration that small aperture openings will lead to a decrease in the brightness of the images. If the aperture is smaller than f22, the depth of field and the image clarity may also be seriously diminished (Korkut B, 2022; Ahmad, 2009).

The duration of the light is guided by the shutter speed which is the length of time that the shutter remains open during the shooting (Snow, 2009). It is expressed in fractions of seconds such as 1/125s 1/250s (Korkut et al., 2022). In terms of intra-oral dental photography, the shutter speed can be set at 1/125 as a standard for both anterior and posterior/ occlusal shootings (Korkut B, 2022; Ahmad, 2020).

The ISO is a camera setting that determines the camera sensor sensitivity and therefore the image quality by providing or eliminating the unwanted speckled artifacts known as noise or grain on the dental image (Snow, 2009). ISO can be considered a stabilizer to the lens aperture in terms of the image brightness. If the ISO increases, the brightness increases. A constant ISO value of 200 is often ideal for intraoral purposes (Snow, 2009). However, the top limit should be ISO:400 to avoid noise regarding the cameras with the mirror (Korkut B, 2022). Whereas, the mirrorless cameras have the advantage of letting the ISO increase to 6400 without providing noise. Nevertheless, setting the ISO at a number in a range of 100-400 depending on the aperture setting can standardize the repetitive intra-oral photography unless the camera and flashlight setups change (Korkut B, 2022).

The WB is one of these parameters that should be calibrated to equalize the temperatures of the repetitive images (Snow, 2009). It can be performed either through the camera settings depending on the camera model or even by using a grey calibration card (%18) during the shooting (Snow, 2009; Ahmad, 2009).

Therefore, the parameters regarding the camera settings can be standardized for the selected dental photography kit, and once they are set there will be usually no need to change them if the parameters related to the illumination and the shooting position are also standardized.

2. Parameters related to the illumination

Illumination is the most important variable in dental photography which is provided particularly by the flash lights (Korkut B, 2022). The type of the flashlight (ring flash, dual flash, or paraflash), the power output of the selected light source, the use of softboxes/diffusers, the distance of the light source to the teeth, and the distance and angulation between the dual flashlights may influence the quality of illumination on the teeth to be captured. Additionally, the position of the patient's head may also affect the illumination and thereby the final outcome (Korkut B, 2022).

Many of these parameters can be calibrated for intraoral photography. The angulation of the twin flashes of paraflashes should be placed away from the objective at an angulation of approximately 45° for the anterior photography to obtain light refections at the transition lines (Hardan et al., 2022). But they should be placed very close to the objective for the posterior/occlusal photography to obtain good illumination. A mounting bracket such as the Owlbrckt (Torun & Torun Ağız ve Diş Sağlığı Hiz. Ltd. Şti., Ankara, Turkey) is very useful for the standardized placement of the dual flashes (Ahmad, 2009). Regarding the paraflash use, two paraflashes should be placed at an angulation of approximately 45° for the anterior photography.

The level of softness of the light also influences the quality of the photograph (Korkut B, 2022). Intraoral photography involves not only white teeth but also surrounding pink soft tissues like gingiva. Accordingly, soft illumination may provide better visuality, especially for soft tissues, which can be provided by using auxillary photography equipment such as diffusers, reflectors, or softboxes (Korkut B, 2022). Whereas, it is a well-known fact that the use of paraflashes / softboxes may be less informative in terms of the dental surface structures, compared to the battery-powered ring flashes and dual flashes (Korkut et al., 2022). The complications related to the restorations or the pathologies related to the natural dental tissues may not be visible through intraoral photography due to the highly diffuse paraflash illuminations, which may lead to clinical misinterpretations (Korkut et al., 2022). However, this issue usually depends on the brand and power output of the selected paraflashes. It is suggested to use 300-watt paraflashes at full power and 400-500-watt paraflashes at less than full power to avoid high light diffusion on the tooth surface for more informative intraoral photography. Some examples of such paraflashes in the market used for dental photography are VL 400 Plus Elfin (Visico, Zhejiang, China) and SK300 II (Godox, Shenzhen, China), and HiMax 500 (Hensel, Germany). However, using the HiMax 500 paraflashes / softboxes for intraoral dental photography may also inhibit the information on dental surface structures due to the high diffusion of the light depending on the flash power output and the camera settings (Korkut B, 2022). Therefore, it is very important to calibrate and standardize the parameters related to the illumination at maximum level to provide repetitive intraoral photographs.

In terms of the paraflash use, the size of the softbox is not an influencing factor for intraoral photography, due to the small size of the oral cavity. Therefore, the use of softboxes of 80x100, 60x90, or 50x70 are all considered indicated (Korkut B, 2022).

3. Parameters related to the shooting position

Taking photographs at different shooting angles bears a high risk of inconsistencies in the perception of reality due to potential distortions (Bertl et al., 2019). Positioning devices for intra-oral photography, pre-fabricated splints, and photography guides have been used previously to perform standardized intraoral anterior photography. However, such methods were considered quite complicated, and also their effectiveness has not been assessed (Bertl et al., 2019).

There are shooting parameters related to the position of the dental unit and the position of the clinician as well as the camera, which can alter the working distance (Snow, 2009). The angulation and height of the dental unit may affect not only the shooting distance but also the distance to the light source. This parameter can be standardized by setting the dental unit at a constant position for every kind of intraoral photography (anterior and posterior/occlusal) (Korkut B, 2022). The positioning of the clinician/camera is more complicated. Although the use of a mounting bracket can standardize the placement of the dual flashes, the position of the clinician is still an effective variable as the camera and the flashes are held by him/her. Therefore, to achieve a constant working distance, the objective should be set at manual focus mode and the clinician manually select a specific and consistent magnification ratio for each repetitive shooting (Snow, 2009; Ahmad, 2020). Whereas, using the constantly placed proper paraflashes / softboxes at 45° over the patient's head may also overcome almost all the standardization problems regarding the flashlights (Korkut B, 2022). The wall mounts can be effectively used with the paraflashes/softboxes in this regard clinically.

The paraflashes / softboxes have gained a wide range of use for anterior intraoral photography, besides the extraoral

portrait photography, due to the simplicity of the system and the effectiveness of the soft light illumination. Whereas, the paraflashes / softboxes have had a limited indication for the intraoral photography of the posterior dentition and the occlusal surfaces due to the insufficient illumination of the operating field. There must be an easy way to perform standard everyday clinical documentation by free-hand shooting, for the anterior and also the posterior dentition.

The suggested intraoral photography setups may provide the standardization in intraoral photography of both anterior/posterior dentition and the occlusal surfaces at the same time clinically. Two different paraflashes / softboxes placement options are recommended above the dental unit; (1) three paraflashes are placed constantly, (2) two paraflashes are placed with the ability of simple re-positioning (Fig. 1 and Fig. 2 a,b). Therefore, from now on the paraflashes softboxes can be considered indicated for also the posterior/occlusal intraoral photography through the suggested following simplified setups.

Figure 1: Recommended setup no 1 including 3 paraflashes at fixed positions above the dental unit.

Figure 2: Recommended setup no 2 including only 2 paraflashes above the dental unit with the ability of simple repositioning. (a) Placement for the paraflashes for the anterior photography. (b) Placement for the paraflashes for the posterior / occlusal photography.

Recommended clinical setup no 1 for anterior and posterior/occlusal intraoral photography

This setup involves 3 paraflashes with 50x70 softboxes which are vertically and horizontally fixed at approximately 2 meters above the dental unit. Two should be positioned symmetrically in 45° of introvert angulation and one should be placed right above the dental unit, between the other two, with a slight inclination towards the patient's head. The positions of the dental unit and head support should be fixed (Desai & Bumb, 2013).

Regarding the frontal photography of the anterior incisors and canines, only two symmetrical paraflashes should be operational and the one in the middle should be turned off. The clinician should stand at the 12 o'clock position. A direct photograph is taken by using two separate transparent lip retractors (Fig. 3 a-c).

Figures 3: (a) Standardized intraoral photography of anterior dentition with (3 paraflash setup / direct shooting). Only two symmetrical paraflashes are operational at 45° of angulation. The position of the dental unit and head support should be fixed. **(b)** Shooting should be performed at 12 o'clock position. The dental assistant is not required. **(c)** Intraoral frontal photography of anterior dentition.

Regarding the photography of the maxillary posterior dentition and occlusal surfaces, all three paraflashes should be operational. The clinician should stand at 12 o'clock position. An indirect photograph is taken by using an occlusal intraoral mirror and a C-shape transparent lip retractor (Fig. 4 a-c) (McLaren &Terry, 2001).

Figures 4: (a) Standardized intraoral photography of maxillary posterior dentition / occlusal surfaces (3 paraflash setup / indirect shooting by using an occlusal mirror). Third paraflash is turned on and all three paraflashes are operational. The position of the dental unit and head support should be fixed. **(b)** Shooting should be performed at 12 o'clock position. The dental assistant is required (Korkut B, 2022). **(c)** Intraoral occlusal photography of maxillary dentition.

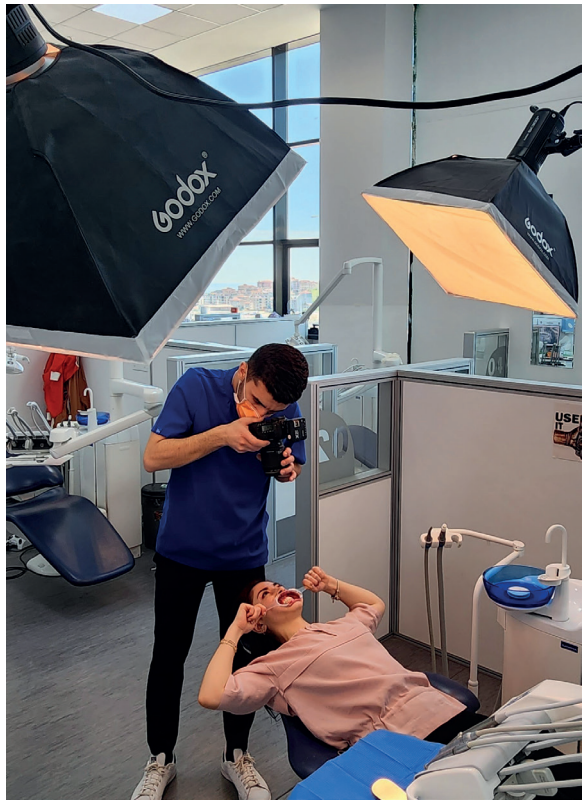
Regarding the photography of the mandibular posterior dentition and occlusal surfaces, all three paraflashes should be operational. The clinician should stand on one side of the patient. An indirect photograph is taken by using an occlusal intraoral mirror and a C-shape transparent lip retractor (Fig. 5 a-c).

Figures 5: (a) Standardized intraoral photography of mandibular posterior dentition / occlusal surfaces (3 paraflash setup / indirect shooting by using an occlusal mirror). The third paraflash is turned on and all three paraflashes are operational. **(b)** Shooting should be performed at the side of the patient. The position of the dental unit and head support should be fixed. The dental assistant is required. **(c)** Intraoral occlusal photography of mandibular dentition.

Recommended clinical setup no 2 for anterior and posterior/occlusal intraoral photography

This setup involves only 2 paraflashes with 50x70 softboxes which are fixed vertically at approximately 2 meters above the dental unit with symmetrically introvert angulation of 45°. However, the paraflashes can be repositioned horizontally, but not fixed in position. The ability of the horizontal movement is required for shooting both anterior and posterior intraoral photographs. The dental unit's and head support's positions should be fixed.

Regarding the frontal photography of the anterior incisors and canines. The two symmetrical paraflashes should be positioned apart from each other at approximately 1.5 m of distance on both sides. During the repositioning, the vertical height and the introvert angulation of the paraflashes should remain stable. The clinician should stand at the 12 o'clock position. A direct photograph is taken by using two separate transparent lip retractors (Fig. 6 a-c).

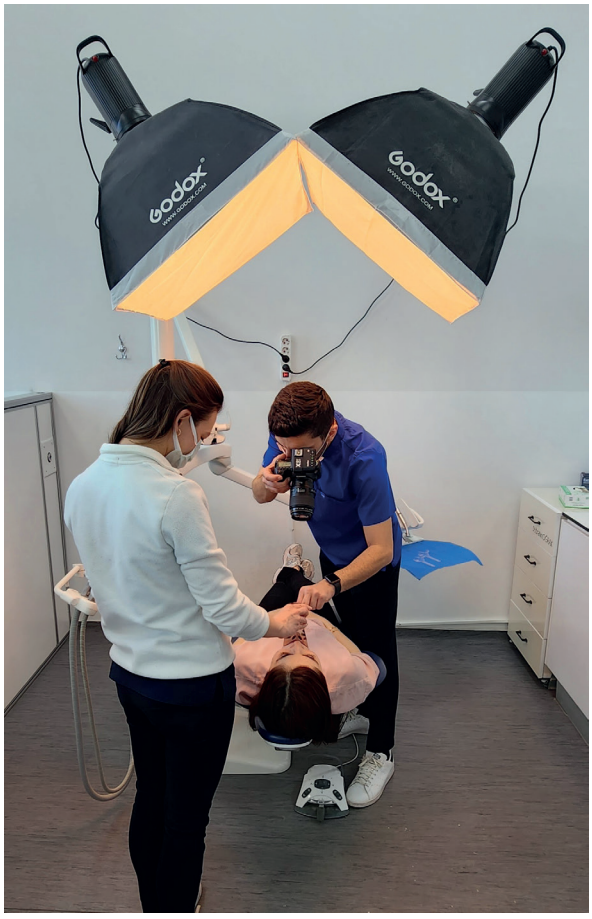


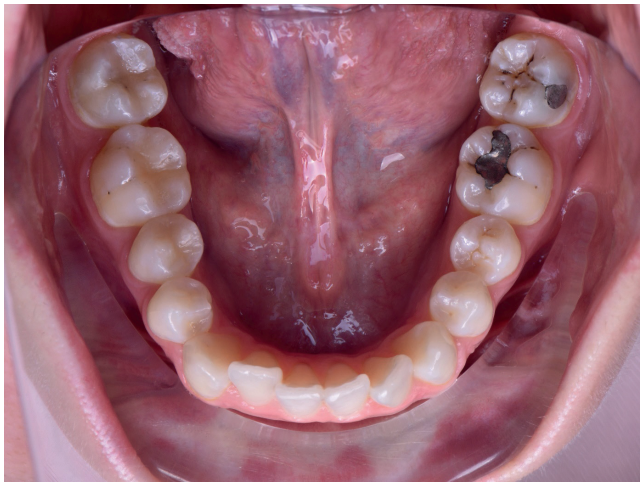
Figures 6: (a) Standardized intraoral photography of anterior dentition (2 paraflash setup / direct shooting). Both symmetrically positioned paraflashes are operational at 45° of introvert angulation. The position of the dental unit and head support should be fixed. **(b)** Shooting should be performed at 12 o'clock position. The dental assistant is not required. **(c)** Intraoral frontal photography of anterior dentition.

Regarding the photography of the maxillary posterior dentition and occlusal surfaces, the two symmetrical paraflashes should be transferred horizontally to the middle forming a tent-shape, right above the patient's head. During the repositioning, the vertical height of the paraflashes remains stable. The clinician should stand at the 12 o'clock position. An indirect photograph is taken by using an occlusal intraoral mirror and a C-shape transparent lip retractor (Fig. 7 a-c).

Figures 7: (a) Standardized intraoral photography of maxillary posterior dentition / occlusal surfaces (2 paraflash setup / indirect shooting by using an occlusal mirror). Both symmetrically positioned paraflashes are operational at 45° of introvert angulation. The position of the dental unit and head support should be fixed. **(b)** Shooting should be performed at 12 o'clock position. The dental assistant is required. **(c)** Intraoral occlusal photography of maxillary dentition.

Regarding the photography of the mandibular posterior dentition and occlusal surfaces, the two symmetrical paraflashes should be transferred horizontally to the middle forming a tent-shape, right above the patient's head. During the repositioning, the vertical height of the paraflashes remains stable. The clinician should stand on one side of the patient. An indirect photograph is taken by using an occlusal intraoral mirror and a C-shape transparent lip retractor (Fig. 8 a-c).





Figures 8: (a) Standardized intraoral photography of mandibular posterior dentition / occlusal surfaces (2 paraflash setup / indirect shooting by using an occlusal mirror). Both symmetrically positioned paraflashes are operational at 45° of introvert angulation. The position of the dental unit and head support should be fixed. **(b)** Shooting should be performed at the side of the patient. The dental assistant is required. **(c)** Intraoral occlusal photography of mandibular dentition.

CONCLUSION

This paper recommends contemporary, simplified clinical paraflash / softbox setups for both anterior and posterior intraoral photography for the first time. Standardization in intraoral dental photography for both anterior/posterior dentition and the occlusal surfaces can be enhanced by using one of the suggested setups for everyday clinical documentation.

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ORIGINAL ARTICLE / ARAŞTIRMA MAKALESİ

The Effect of Cavity Disinfectant on Microleakage of Self-adhesive Composite Restorations in Class V Cavities

Sınıf V Kavitelerde Kavite Dezenfektanlarının Self Adeziv Kompozit Restorasyonların Mikrosızıntısı Üzerine Etkisi

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ABSTRACT

Objectives: This *in vitro* study was aimed to evaluate the effect of chlorhexidine digluconate (CHX) containing cavity disinfectant on microleakage of Class V self-adhesive resin-based composite restorations.

Materials and Methods: Forty non-beveled Class V cavities (4 mm height x 2 mm width x 2mm depth) 1 mm above the cemento-enamel junction were prepared on lingual and buccal surfaces of 20 molar teeth. Samples were randomly divided into 4 groups (n=10); and lingual cavities were disinfected with 2% CHX (Bisco). Cavities were restored using 2 different self-adhesive composites: Vertise Flow (Kerr); Activa BioACTIVE (Pulpdent) according to manufacturer's instructions. Following 20 s polymerization with Valo (Ultradent) LED curing light, finishing and polishing were performed using Finishing Discs (Bisco). Teeth were coated with a nail polish excluding the restoration area and aged in distilled water at 24°C for 6 months. After immersion of the samples in 2% methylene blue solution, they were sectioned longitudinally in buccolingual direction with a diamond saw (Isomet 1000, Buehler). Microleakage on occlusal/gingival margins were scored under x8 and x20 magnification using a stereomicroscope (Leica MZ7.5). For statistical evaluation**,** Chi-square test was used. The significance level was set at $p < 0.05$.

Results: No statistically significant difference was detected between the total microleakage scores at occlusal and gingival margins (p=0.735; 0.944). Likewise, there was no significant difference between the gingival/occlusal margins of the restorations (p=0.216). CHX application did not show any statistically significance between microleakage values in Class V cavities restored with Vertise Flow or Activa BioACTIVE. (p=0.942; 0.577).

Conclusions: CHX cavity disinfectant did not prevent microleakage in Class V cavities restored with self-adhesive composites.

Keywords: Bioactive material, Cavity disinfectant, Class V cavity, Microleakage, Self-adhesive composite

ÖZ

Amaç: Bu *in vitro* çalışmanın amacı, klorheksidin diglukonat (CHX) içeren kavite dezenfektanının, sınıf V self-adeziv rezin bazlı kompozit restorasyonların mikrosızıntısı üzerindeki etkisini değerlendirmektir.

Gereç ve Yöntemler: 20 insan azı dişinin hem bukkal hem de lingual yüzeylerine mine-sement birleşiminin 1 mm üzerinde olan 40 adet standart sınıf V kavite (4 mm yükseklik x 2mm genişlik x 2mm derinlik) hazırlandı. Örnekler rastgele 4 gruba ayrıldı (n-10); tüm lingual kaviteler %2 CHX (Bisco) ile dezenfekte edildi. Kaviteler 2 farklı self-adeziv kompozit (Vertise Flow, Kerr; Activa BioACTIVE, Pulpdent) kullanılarak üretici talimatlarına göre restore edildi. Valo (Ultradent) LED ışıklı cihaz ile 20 sn polimerizasyon sonrası Finishing Discs (Bisco) kullanılarak bitim ve polisaj işlemleri yapıldı. Dişlerin restorasyon alanı dışında kalan yüzeyleri şeffaf oje ile kaplandı ve distile suda oda sıcaklığında (24°C) 6 ay yaşlandırıldı. Numuneler %2'lik metilen mavisi solüsyonuna bir saat daldırıldıktan sonra, hassas kesme cihazı (Isomet 1000, (Buehler)) ile bukkolingual yönde boylamasına kesitler alındı. Oklüzal/gingival mikrosızıntı stereomikroskop (Leica MZ7.5) kullanılarak x8 ve x20 büyütme altında skorlandı. İstatistiksel değerlendirme için, ki-kare testi kullanıldı ve anlamlılık düzeyi $p<0.05$ olarak belirlendi.

Bulgular: Kaviteye CHX uygulamasına göre restorasyonların oklüzal ve gingival mikrosızıntı değerlerinde istatistiksel olarak anlamlı fark bulunmadı (p=0.735; 0.944). Benzer şekilde, gingival ve oklüzal kenarlardaki mikrosızıntı seviyeleri arasında anlamlı fark saptanmadı (p=0.216). Vertise Flow veya Activa BioACTIVE

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ile restore edilen CHX ile muamele edilmiş ve edilmemiş sınıf V kavitelerde mikrosızıntı değerleri arasında istatistiksel açıdan anlamlı fark tespit edilmedi (p=0.942; 0.577).

Sonuç: CHX kavite dezenfektanı, self-adeziv kompozitlerle restore edilen sınıf V kavitelerde mikrosızıntıya engel olmamıştır.

Anahtar Kelimeler: Biyoaktif materyal, Kavite dezenfektanı, Mikrosızıntı, Self adeziv kompozit, Sınıf V Kavite

INTRODUCTION

Restorative materials in dentistry, re-establish functional, esthetic and biological properties of the teeth (Mishra et al., 2018). Resin-based composites are generally used for cervical lesions as these materials bond to the tooth structures and composite restorations are esthetically pleasing (Lokhande et al., 2014).

The longevity of composites depends on microleakage and resistance to masticatory forces (Mishra et al., 2018). Microleakage is one of the critical factors causing failure of resin-based restorations (Guo et al., 2016). Shrinkage can occur during the polymerization of resin-based restorative materials, if the adhesion force is not strong enough to resist the effects of the shrinkage, gap formation will occur between the tooth and the restoration. Microorganisms and oral fluids leak into the cavity from this gap (Nilgun Ozturk et al., 2004; Kleverlaan & Feilzer, 2005). Deeper invasion of microorganisms in the tooth structure may cause secondary caries, post operative sensitivity and inflammatory changes in the pulp (Silveira de Araújo et al., 2006). Marginal sealing depends on many factors such as: restoration technique, mechanical and physical properties of the material, etc (Van Ende et al., 2017). Recently, self-adhesive and flowable composites have been advanced as a new category. According to the manufacturer's instructions, these composites do not require prior etching or bonding. (Rahimian-Imam et al., 2015). They contain acidic monomers and manufacturer's claim these products provide marginal sealing and prevent overwetting, overdrying, and overetching (Autio-Gold, 2002). Activa BioACTIVE-Restorative is a resin-based flowable composite containing glass ionomer and resin composite components. An acid-base setting reaction occurs between the fluoroaluminum silicate particles and the polyacid components (Sauro et al., 2019). Activa has the ability to release and replenish calcium, phosphate and fluoride from saliva, thus stimulating the formation of apatite. This is effective against discoloration and microleakage, and improves mechanical properties (Gjorgievska et al., 2008; Firouzmandi et al., 2020). One of the most preferred methods for measuring microleakage is dye penetration with methylene blue due to ease of application and fair price. Methylene blue has a role in tracing the degree of infiltration and has lower molecular weight even smaller than bacteria thus detecting leakage where bacteria could not penetrate (Patel et al., 2015).

After the cavity preparation, the smear layer formed on the cavity and enamel-dentin border, and the microorganisms in the dentinal tubules cannot be eliminated completely (Akturk et al., 2019; Attiguppe et al., 2019; Cellik & Bahsi, 2019). For restorations longevity, the presence of bacteria plays a significant role in success of the treatment (Imazato et al., 2001). It has been shown that, various cariogenic microorganisms survive more than a year under restorative materials (Sharma et al., 2011). Cavity disinfection is an acceptable procedure that can prevent the risks resulting from the microorganisms in the tooth structure (Elkassas et al., 2014). One of the most common broad-spectrum antibacterial cavity disinfectant solutions, clorhedixine digluconate (CHX) (Varoni et al., 2012) is considered as the gold standard due to its potential to eliminate a wide range of gram-positive and gram-negative bacteria (Balagopal & Arjunkumar, 2013).

The purpose of this study was to evaluate the effect of CHX containing cavity disinfectant on microleakage of Class V self-adhesive resin-based composite restorations. The null hypothesis (H0) of the study is that there is no significant difference in microleakage amount between applications with or without cavity disinfectant.

MATERIALS AND METHODS

Ethics committee approval of this *in vitro* study was received by Ethics Committee of Marmara University Faculty of Dentistry with the number 2021-21 on the date of 07/10/2021. Forty non-beveled Class V cavities (4 mm height x 2 mm width x 2mm depth) 1 mm above the cemento-enamel junction were prepared on lingual and buccal surfaces of 20 molar teeth. were prepared on lingual and buccal surfaces of 20 molar teeth. In this study, 20 non-carious human molar teeth extracted for periodontal or orthodontic reasons were used and disinfected with 0.1% thymol solution. After disinfection protocol, all teeth were immersed in distilled water for 24 h. A total of 40 non-beveled Class V cavities (with dimensions of 4x2x2 mm) were prepared on both the buccal and lingual surfaces. The occlusal and gingival margins of the cavities

were located on the enamel. Samples were randomly divided into 4 groups (Fig. 1).

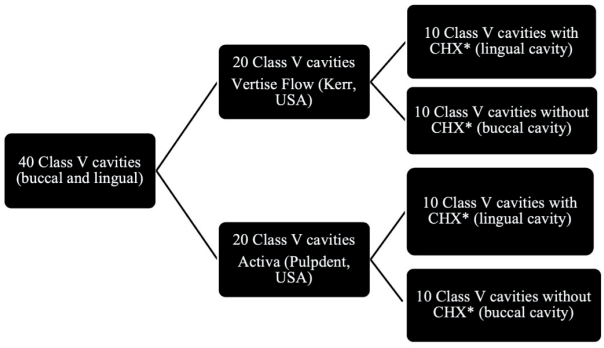

Figure 1: Study plan and groups. (% 2 CHX).

Following 37% orthophosphoric acid (Etching Gel, President, GERMANY) application to enamel for 15 s, each cavity was rinsed for 20 s and air-dried for 2 s avoiding excessive pressure. All the lingual cavities were disinfected by 2% CHX (Cavity Cleanser, BISCO, USA) application according to manufacturer's instructions. Buccal and lingual cavities were restored using 2 different self-adhesive composites (Vertise Flow, Kerr, USA; Activa BioACTIVE, Pulpdent, USA) as recommended by the manufacturers (Table 1). After 20 s polymerization with Valo Cordless (Ultradent, USA) LED curing light (power output: 1000 mW/cm2), finishing and polishing procedures of the restorations were performed using 4-step grinding (coarse, medium, fine, and ultrafine) aluminum oxide-coated discs (Finishing Discs, Bisco, USA) and polishing rubber (Enhance Pogo, Dentsply Sirona, USA). Each disc was used for only 5 samples, and the polishing time was 15 s for each disc for all the samples. The teeth were coated with a clear nail polish excluding the restoration surface area and aged in distilled water at room temperature (24°C) for 6 months. Samples were immersed in 2% methylene blue solution for one hour. Each tooth was then sectioned longitudinally in buccolingual direction with a diamond saw (Isomet 1000, Buehler, USA). Occlusal and gingival margin microleakage amounts were scored under x8 and x20 magnification using a stereomicroscope (Leica MZ7.5, Leica Microsystems, Germany) (Fig. 2). Scoring criteria for dye penetration indicating microleakage are listed in Table 2.

Table 1. The self-adhesive composites and cavity disinfectant, their compositions and manufacturer's instructions for use.

Product Name	Manufacture	Composition	Instructions for Use
Vertise flow	Kerr, USA	GPDM adhesive monomer, Prepolymerized filler containing barium glass filler, nano-sized colloidal silica, nano-sized ytterbium fluoride	Vertise flow composite is self-adhesive and therefore does not require etching or bonding protocol prior to placement. Wash thoroughly with water spray and air dry at maximum air pressure for 5 s. Select the desired shade. Dispense Vertise flow onto prep with provided dispensing tip. Use provided brush to apply Vertise flow to the entire cavity wall and beveled area with moderate pressure for 15-20 s to obtain a thin layer (<0.5mm). Remove excess material around margins with the brush if necessary. Light cure for 20 s. For A3.5 and Universal Opaque shades, light cure each increment for 40 s.
Activa BioACTIVE	Pulpdent, USA	Bioactive glass, silica, diurethane modified with hydrogenated polybutadiene, methacrylate monomers, modified polyacrylic acid, sodiumfluoride, camphorquinone (photoinitiator)	Isolate and prepare tooth to receive a restoration. Ideal margin preparations are rounded with no sharp angles. Etch prepared surface for 10-15 s with 37% phosphoric acid etching gel, or selective etch enamel for 15 s, rinse and lightly dry, removing all excess moisture with high volume evacuation, compressed air, and/or a cotton pellet, but do not desiccate the tooth. Place mix tip at cavity floor. Apply ACTIVA in increments of up to 4 mm, keeping mix tip submerged in the material. Light cure for 20 s (with low intensity setting) between each layer.
Cavity Cleanser	BISCO, EUA	2% CHX	Apply acid according to your choice of adhesive. A dry, but non-desiccated, surface is ideal before applying. Moisten dentin surface with CAVITY CLEANSER using a brush or absorbent pellet. Remove puddled solution with a new absorbent pellet, leaving site moist. Do not dry. Continue with adhesive and direct composite technique.
Etching Gel	President, GERMANY	37% Phosphoric acid – Purified water – Thickener – Colorant	Isolate tooth and prepare the cavity in a conservative manner. Equip the disposable tip after removing the cap. Etch enamel and dentin with etching agent for 15 s. Rinse gel thoroughly and remove excess water from the preparation with a gentle stream of air for 1-2 s.

Table 2. Occlusal and gingival margin microleakage scores.

Score	Scoring criteria for dye penetration indicating microleakage (occlusal margin)	Scoring criteria for dye penetration indicating microleakage (gingival margin)
0	No dye penetration	No dye penetration
1	Dye penetration limited to ½ or less of the occlusal wall	Dye penetration up to ½ of the gingival wall
2	Dye penetration exceeding ½ of the occlusal wall	Dye penetration along the gingival wall
3	Dye penetration limited to ½ of the cavity base	Dye penetration up to ½ of the cavity base
4	Dye penetration exceeding ½ of the cavity base	Dye penetration exceeding ½ of the cavity base

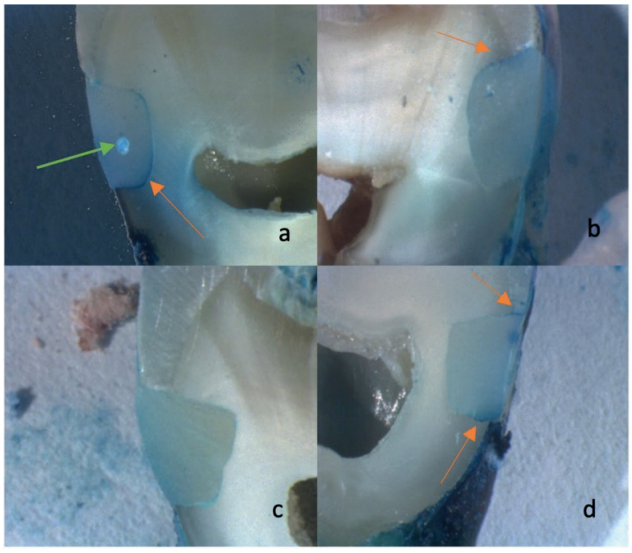

Figure 2: Microleakage evaluation of the restorations under the stereomicroscope. a – Gap in composite (green arrow) and gingival margin score as 3 (orange arrow), b – Occlusal margin score as 2, c – Occlusal and gingival margin scores as 0, d – Occlusal margin and gingival margin scores as 1.

The obtained data were analyzed using IBM SPSS V23 (IBM Corp, USA). Analysis results are presented as frequency (percentage) for categorical data. Chi-square test was used to compare microleakage amounts according to different restorative materials and CHX application. The significance level was set at $p<0.05$.

RESULTS

The microleakage scores obtained using stereomicroscope are presented in Table 3 and 4. No statistically significant difference was detected between the microleakage amounts of the restorations regarding CHX application ($p>0.05$). Composite type did not have any statistically significant effect between the microleakage amounts in CHX applied groups. Similarly, CHX application did not have any significant effect between the microleakage amounts in the restorations (Table 3).

Table 3. Comparison of microleakage in Class V cavities compared to CHX application.

Cavity	Composite	Microleakage Score	CHX (-)	CHX (+)	Total	p*
Oclusal	Vertise Flow	Score 0	2(20)	1(10)	3(15)	0.819
		Score 1	7(70)	8(80)	15(75)	
		Score 2	1(10)	1(10)	2(10)	
		Score 4	0(0)	0(0)	0(0)	
	Activa BioActive	Score 0	2(20)	2(20)	4(20)	0.587
		Score 1	7(70)	8(80)	15(75)	
		Score 2	0(0)	0(0)	0(0)	
		Score 4	1(10)	0(0)	1(5)	
	Total	Score 0	4(20)	3(15)	7(17.5)	0.735
		Score 1	14(70)	16(80)	30(75)	
		Score 2	1(5)	1(5)	2(5)	
		Score 4	1(5)	0(0)	1(2.5)	
Gingival	Vertise Flow	Score 0	4(40)	6(60)	10(50)	0.638
		Score 1	5(50	3(30)	8(40)	
		Score 2	1(10)	1(10)	2(10)	
		Score 4	0(0)	0(0)	0(0)	
	Activa BioActive	Score 0	3(30)	1(10)	4(20)	0.557
		Score 1	6(60)	7(70)	13(65)	
		Score 2	0(0)	1(10)	1(5)	
		Score 4	1(10)	1(10)	2(10)	
	Total	Score 0	7(35)	7(35)	14(35)	0.944
		Score 1	11(55)	10(50)	21(52.5)	
		Score 2	1(5)	2(10)	3(7.5)	
		Score 4	1(5)	1(5)	2(5)	
Total	Vertise Flow	Score 0	6(30)	7(35)	13(32.5)	0.942
		Score 1	12(60)	11(55)	23(57.5)	
		Score 2	2(10)	2(10)	4(10)	
		Score 4	0(0)	0(0)	0(0)	
	Activa BioActive	Score 0	5(25)	3(15)	8(20)	0.577
		Score 1	13(65)	15(75)	28(70)	
		Score 2	0(0)	1(5)	1(2.5)	
		Score 4	2(10)	1(5)	3(7.5)	
	Total	Score 0	11(27.5)	10(25)	21(26.3)	0.896
		Score 1	25(62.5)	26(65)	51(63.7)	
		Score 2	2(5)	3(7.5)	5(6.3)	
		Score 4	2(5)	1(2.5)	3(3.8)	

There was no statistically significant difference between the distribution of microleakage scores of the restorations considering different brands of self-adhesive composites. Likewise, there was no statistically significant difference between the distributions of microleakage occurring in the restoration according to the use of different brands

of self-adhesive composites (Table 4). The amount of microleakage has not been scored as 3 in any of the groups. There is no statistically significant difference between the distributions of microleakage scores of the occlusal and gingival margins (Table 5).

Table 4. Comparison of microleakage in restoration according to the use of different brands of self-adhesive composites in class V cavities.

Cavity	Microleakage Score	Vertise Flow	Activa BioActive	Total	p*
Occlusal	Score 0	3 (15)	4 (20)	7 (17.5)	0.37
	Score 1	15 (75)	15 (75)	30 (75)	
	Score 2	2 (10)	0 (0)	2 (5)	
	Score 4	0 (0)	1 (5)	1 (2.5)	
Gingival	Score 0	10 (50)	4 (20)	14 (35)	0.107
	Score 1	8 (40)	13 (65)	21 (52.5)	
	Score 2	2 (10)	1 (5)	3 (7.5)	
	Score 4	0 (0)	2 (10)	2 (5)	
Total	Score 0	23 (57.5)	28 (70)	51 (63.7)	0.09
	Score 1	13 (32.5)	8 (20)	21 (26.3)	
	Score 2	4 (10)	1 (2.5)	5 (6.3)	
	Score 4	0 (0)	3 (7.5)	3 (3.8)	

Table 5. Comparison of microleakage with respect to the occlusal and gingival margins.

Microleakage score	Occlusal	Gingival	Total	p*
Score 0	7 (17.5)	14 (35)	21 (26.3)	0.216
Score 1	30 (75)	21 (52.5)	51 (63.7)	
Score 2	2 (5)	3 (7.5)	5 (6.3)	
Score 4	1 (2.5)	2 (5)	3 (3.8)	

DISCUSSION

Microleakage has been defined as one of the important factors causing failure of resin-based composite restorations (Guo et al., 2016). The ability of a composite to reduce the amount of microleakage at tooth-restoration interface is also a basic factor in estimating its clinical success (Siso et al., 2009). This study was designed to compare the microleakage properties of CHX containing cavity disinfectant and self-adhesive flowable composite to analyze the relationship between resin-dental tissue and microleakage.

Siso et al. evaluated microleakage in composite resin restorations following antimicrobial pretreatments such as laser, CHX, adhesive agent, and scores were lower at enamel margins than gingival margins (Siso et al., 2009). In the present study, there was no statistically significant difference between the occlusal and gingival microleakage scores. This result may be due to the fact that the occlusal and gingival margins of the cavities were located 1 mm above the cemento-enamel junction. Low ow surface energy, high organic components, tubular structure, and dentinal fluid pressure make bonding to dentin more difficult than enamel (Van Ende et al., 2017).

In their study based on a 6 to 12 months evaluation, Angeloni et al. showed that CHX had no effect on bonding to dentin in a self-adhesive restoration (Araujo et al., 2001). In the current study, CHX application had no effect on microleakage at the cavity margins at the enamel level. However, they said that there was a significant difference in the storage time for bond strength. In the present study, there was only 6 months of storage time, which can be considered a limitation

CHX application did not have any significant effect on the adhesion of the restorative material to the dental tissues. In Activa BioActive and Vertise Flow self-adhesive flowable composites, no significant difference was found between the microleakage values regardless of CHX application. There are studies reporting that self-adhesive flowable composites have similar properties such as fracture strength when compared with each other (Firouzmandi et al., 2020). Only microleakage was evaluated in the present study and selective etching was performed for both composites and no significant difference was observed.

An ideal disinfectant should have an effective antimicrobial role and should not inhibit the adhesion of the restorative material (Elkassas et al., 2014). The results of this *in vitro* study showed that the use of a 2% CHX-containing cavity cleaning solution before application of self-adhesive composites had no effect on the sealing ability. There was no statistically significant difference for any group in the microleakage assessment for the restorations preconditioned with CHX.

The results of this *in vitro* study support the null hypothesis that microleakage is not affected by disinfectant use. Further studies with standardized protocols are required to allow robust conclusions regarding microleakage and biocompatible restorations. The effect of cavity disinfectant on self-adhesive flowable composite should also be evaluated since they can reduce the clinical steps of great importance in restorative dentistry.

Correlating the results of this study with the available literature revealed that CHX application for cavity disinfection had no effect on the bonding ability of self-adhesive flowable composite restorations. In addition, further *in vitro* and *in vivo* studies are required to assess the interaction and long-term clinical success of CHX with other self-etch adhesive systems.

CONCLUSION

Within the limitations of this *in vitro* study:

1. CHX pretreatment had no effect on microleakage in Class V cavities restored with self-adhesive flowable composite resins.

2. Self-adhesive flowable composites showed no difference in microleakage.

3. Microleakage amount at the occlusal and gingival margins of the cavities was similar.

Conflict of Interests

N/A.

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ORIGINAL ARTICLE / ARAŞTIRMA MAKALESİ

Assessment of Brainstem Reflexes with Transcranial Magnetic Stimulation in Bruxism: The Role of Central Mechanisms in Pathophysiology

Bruksizmde Beyin Sapı Reflekslerinin Transraniyal Manyetik Stimülasyon ile Değerlendirilmesi: Merkezi Mekanizmaların Patofizyolojideki Rolü

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ABSTRACT

Objectives: We aim to prove the central etiology hypothesis for bruxism, we plan to examine the structural components that contribute to the occurance of RMMA/Bruxism such as cortical, subcortical structures and as a key roleplaying component, the brainstem structures by investigating the MEP, CSP, MIR (SP1 and SP2) and the blink reflex (R1 and R2) and central conduction time.

Materials and Methods: In this study, a total of 77 subjects investigated to find any difference between the two groups. The MIR and blink reflexes studied by transcranial magnetic stimulation (TMS) and electric stimulation. The cortical silent period (CSP) evoked in contralateral masseter muscle by TMS. Central motor conducting times were evaluated.

Results: The absence of SP2 (component of MIR), R2 (component of blink reflex) latency and left APB (abductor pollicis brevis) muscle F wave latency are found to be significantly different between two groups.

Conclusions: As a result of our study, the loss of the SP2 component and the prolongation of the latency of the R2 component, and the localization of reflex circuits in the brainstem, although their pathways are separate, bruxer suggested that the pathophysiology may have a central origin in most of the bruxers.

Keywords: Bruxism, Transcranial Magnetic Stimulation, Masseter Inhibitory Reflex

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ÖZ

Amaç: Bu çalışmada bruksizmin merkezi mekanizmalarla ilgili olabileceği hipotezini kanıtlamak için MEP, CSP, MIR (SP1 and SP2), göz kırpma refleksi (R1 and R2) ve merkezi iletim zamanını inceleyerek RMMA/Bruksizm oluşumuna katkıda bulunan kortikal, subkortikal yapılar ve anahtar rol oynayan beyin sapı yapıları gibi yapısal bileşenlerin incelenmesi amaçlanmaktadır.

Gereç ve Yöntemler: Bu çalışmada, iki grup arasında herhangi bir fark olup olmadığını bulmak için toplam 77 kişi ile çalışılmıştır. MIR ve göz kırpma refleksleri, transkraniyal manyetik stimülasyon (TMS) ve elektrik stimülasyonu ile incelenmiştir. Kortikal sessiz periyot (CSP) kontralateral masseter kasta TMS ile uyarılmıştır. Merkezi motor iletim süreleri değerlendirilmiştir.

Bulgular: SP2 (MIR komponenti)'nin olmayışı, R2 (blink refleks komponenti)'nin latansı ve sol APB (Abdüktör pollisis brevis) kastan ölçülen F dalgası latansı incelendiğinde iki grup arasında istatistiksel olarak anlamlı şekilde fark bulunmuştur.

Sonuç: Çalışmamız sonucunda SP2 bileşeninin kaybolması ve R2 bileşeninin gecikme süresinin uzaması ve beyin sapındaki refleks devrelerinin lokalizasyonu, yolları ayrı olmasına rağmen, patofizyoloji bruksistlerin çoğunda merkezi bir kökene sahip olabileceğini desteklemektedir.

Anahtar Kelimeler: Bruksizm, Transkraniyal Manyetik Stimülasyon, Masseter Inhibitor Reflex

INTRODUCTION

Bruxism may be classified as noctrunal or diurnal bruxism according to circadian manifestations, as primary (idiopathic) and secondary (iatrogenic) according to the presence of underlying neurological or psychiatric disease and drug use (Guaita & Högl, 2016).

According to the updated concensus, the definition of bruxism is explained with repetative masticatory muscle activity characterized by clenching or grinding of the teeth and by bracing or thrusting of the mandibula involuntarily. In healthy indiviuals bruxism shouldn't be considered as a

disorder. The absence of tooth contact supports that it is a central movement. In the concensus a grading system as has been proposed for possible, probable and definitive bruxism (Lobbezoo et al., 2018).

It can also be defined as the involuntary, unconscious, and excessive grinding of teeth (Lal & Weber, 2022).

High-level activities of the chewing muscles have negative oral consequences such as chewing muscle pain, temporomandibular joint pain, periodontal problems, tooth wear, prosthodontic problems (Raphael et al., 2016).

Its etiology is multifactorial, both peripheral (morphological) and central (pathophysiological and psychological) factors play a role. While it was thought to be caused by defects in the occlusal and orofacial region structures in the past, the findings from the recent studies gradually raise the importance of central factors in the pathogenesis (Winocur et al., 2007; Nélio et al., 2015; Manfredini et al., 2017).

Understanding "chewing automatism" defined as rhythmic masticatory muscle activity (RMMA) without tooth-grinding is important to understanding the pathogenesis of bruxism. This activity is observed in 60% of healthy people (Lavigne et al.,1996), it is 3 times more common in bruxers (Lavigne et al., 2003) and is usually associated with sleep arousals (unconscious and transient changes in brain electroencephalography (EEG) activity, lasting 10-15 seconds, with or without changes in cardiac rate and muscle tone).

Brainstem structures play a particularly key role in the genesis and control of rhythmic jaw movements and RMMA. Numerous nuclei in the brain stem (nucleus reticularis pontis oralis, pontis caudalis and parvocellularis) and neurotransmitters (serotonin, dopamine, GABA, and noradrenaline) regulate the tone of the muscles in the formation of the chewing movement (Lavigne et al., 2003). Studies have demonstrated that dopamine reduction in the mesocortical and nigrostriatal pathways causes disinhibition in the frontal cortex, resulting in increased RMMA and bruxism.

As we aim to prove the central etiology hypothesis for bruxism, we plan to examine the structural components that contribute to the occurance of RMMA/bruxism such as cortical, subcortical structures and as a key roleplaying component, the brainstem structures by investigating the MEP, CSP, MIR (SP1 and SP2) and the blink reflex (R1 and R2) and central conduction time.

MATERIALS AND METHODS

Our study was conducted in the Neurophysiology Laboratory of Dokuz Eylül University and Ethics Committee approval was obtained from Dokuz Eylül University. Forty bruxers (25 females and 15 males) and 37 normal subjects (17 females and 20 males) aged between 16-73 years were included in the study. Participants were selected from volunteers who were admitted to the Neurology Department Sleep Disorders Center of Dokuz Eylül University with various complaints and met bruxism diagnosis criteria after the examination.

All participants provided an informed written consent form.

Inclusion criteria were determined based on the moderate and severe chronic bruxism criteria set by the American Sleep Disorders Association (Table 1) (Koyano et al., 2008).

Cortical motor evoked potentials (c-MEP), CSP, MIR (Silent periods 1 and 2 (SP1 and SP2)), and central conduction time (CMCT) were measured using the TMS method by recording from both masseter muscles. The blink reflex (R1 and R2) was studied by the electrical stimulation method.

Our study was approved by Dokuz Eylul University Non-Interventional Research Ethics Committee with protocol number 3155-GOA and decision number 2017/06-34.

Table 1. Inclusion and exclusion criterias of the study

Inclusion Criteria	Exclusion Criteria
• The patient's awareness about bruxism •Awarness of grinding sounds or clenching at sleep •If one or more of the followings presents additionally • Tooth ware • Jaw muscle fatigue, pain • Masseter muscle hypertrophy	• Known neurological disease • History of epilepsy • Craniofacial pain • Temporomandibular joint disorder • Chronic headache • Missing more than 2 molar teeth, except wisdom tooth • Use of removable dentures • Pregnancy • Cardiac Pacemaker • Cochlear implant • Metal-containing implant • Menstrual period for female patients

Neurophysiological Examination:

Transcranial Magnetic Stimulation (TMS) patient selection questionnaire was applied to all subjects; eligible subjects were included in the study. Before the examination, a demographic data form consisting of age, height, weight,

body mass index (BMI), and neck circumference was completed.

TMS is a method of generating an electrical field in the brain by means of electromagnetics and may be used for neuromodulation and neurostimulation when applied sufficiently to depolarize neurons (Rossi et al., 2009; Herrero et al., 2018).

Cortical Motor Evoked Potential (c-MEP) and Cortical Silent Period (CSP):

C-MEP recording was performed from the contralateral masseter muscle by performing 6-8 single stimulations. Optimal MEP responses for the masseter muscle were obtained by performing a stimulation at a magnitude of 40% of the maximum device output (Pauletti et al., 1993).

The CSP refers to an interruption in electromyographic activity when cortical magnetic stimulation is applied while the target muscle is in voluntary contraction (Rossini & Rossi, 2007), and the duration of the activity increases as the magnetic stimulation intensity is increased (Cantello et al., 1992). The silent period elicited by transcranial stimulation is generated by intracortical inhibition systems (Cohen et al., 1992).

Masseter inhibitory reflex (MIR):

MIR is a reflex inhibition that occurs in the muscles that close the jaw as a result of mechanical, electrical, or magnetic stimulation of the mouth or face area and can only be demonstrated by electrophysiological methods. It is a protective reflex related to mandibular movements during mastication and articulation (Huang et al., 2014). It is generated by stimulation of the mental nerve, and consists of two silent periods that occur as an interruption in the electromyography (EMG) recording performed while the ipsilateral and contralateral masticatory muscles are in voluntary contraction: silent period 1(SP1) and silent period 2(SP2). The afferent stimuli of SP1 are connected to an inhibitory interneuron which is located in the H region surrounding the ipsilateral trigeminal motor nucleus and directly reaches the motor nucleus, and they cross at the motor nucleus level. SP2 is a polysynaptic reflex with a latency of 45-50 seconds (Cruccu et al., 1991). Interneurons responsible for SP2 are located in the bulbar reticular formation near the trigeminal nucleus caudalis (Huang et al., 2014). It is thought that SP2 is probably conveyed to the spinal trigeminal tract by A-beta fibers, and occurs by interacting polysynaptically with ipsilateral and contralateral interneurons and inhibiting masseteric motor neurons (Cruccu et al., 1984).

For MIR recording, patients were asked to perform voluntary contraction at 30% of their maximum contraction, and this level was determined by audiovisual feedback. The responses were superimposed while establishing the duration, the time from the onset of the MEP response to the point at which basal activity reappears was marked and recorded.

Central Motor Conduction Time:

It was calculated using the F wave latency method. Ag-Ag surface cup electrodes were placed on the left abductor pollicis brevis (APB) muscle using the belly-tendon method. The cortical stimulation point was designated by using similar studies in the literature as references to obtain cortical evoked potential. The latency of the motor response (M response) obtained by performing supramaximal electrical stimulation of the median nerve at the wrist level was recorded. Among the F waves obtained after 10 consecutive supramaximal stimulation, the one with the shortest latency was chosen.

Peripheral conduction time was calculated by the formula of ((F latency + M latency) – 1) x0.5 (Hallet, 2007).

Central Conduction time was calculated according to the formula of the (Udupa & Chen, 2013); left APB MEP latency – peripheral conduction time.

Blink Reflex:

Medelec EMG device was used. The active electrode of Ag-Ag surface cup electrodes was placed lateral to the lateral epicanthus and the reference electrode was placed 2 cm lateral to the active electrode. Stimulation intensity was increased at 10-second intervals until stable responses were recorded. Latencies of ipsilateral R1 and contralateral R2 responses were recorded.

Statistical Analysis:

The samples were normally distributed according to Kolmogorov Smirnov test and parametric statistics were used. In this study we investigated whether central factors

affect bruxism or not as has been done in previous studies (Galloway et al., 2013; Huang et al., 2014). We didn't assess the amount of correlation between central factors with bruxism.

Data were assessed by SPSS 18 program. In addition to descriptive statistics, chi-square for categorical variables from hypothesis tests, t-test for continuous variables were used. A $p<0.05$ value was considered statistically significant.

RESULTS

Demographic Data:

There was no significant difference between the groups in terms of age (p=0.334), in terms of BMI (p=0.617), in terms of neck circumference (p=0.631) (Table 2).

Table 2. Demographic data

	Normal(n=37)	Bruxer(n=40)	P<0.05
Age	41.49±12,355	44.45±14.22	0.334
Body Mass Index	25.85±4.3752	25.33±4.212	0.617
Neck Circumference (cm)	36.32±4.3	35.85±4.165	0.631

Neurophysiological Parameters:

1) Motor-evoked potentials in masseter muscle (c-MEP): c-MEP obtained from the left masseter muscle with stimulation from the right hemisphere was found to be mildly longer in the bruxer group compared to the control group (6.21±1.15/6.14±0.912 ms). There was no statistically significant difference between the groups. (p right=0.757, p left=0.336) (Table 3).

2) Cortical silent period (CSP): There was no statistically significant difference between the groups for CSP durations obtained with right and left stimulation (p right stimulation=0.757, p left stimulation=0.991) (Table 3).

3) Central Motor Conduction Time: There is no significant difference between the groups in terms of central motor conduction time (NK:7.75 ± 2.993 and B:7.75 ± 2.12 ms) (p=0.998) (Table 3).

4) Masseter Inhibitory Reflex (SP1 and SP2): While SP1 was detected both in the normal control (NC) and bruxer (B) groups, the absence of SP2 was prominent in the bruxer group and was statistically significant (**p=0.00**). (Table 4), (Fig. 1) (Fig. 2)

Table 3) Latency of motor evoked potentials (c-MEP), durations of cortical silent period (CSP) obtained from both masseter muscles with stimulation from the right and left hemispheres time

	Normal		Bruxer		P<0.05 (R/L)
	R hemisphere stimulation	**L hemisphere stimulation**	**R hemisphere stimulation**	**L hemisphere stimulation**	
c-MEP latency	6.14±0.912	6.098±0.81	6.21±1.15	6.3±0.954	0.757/0.336
CSP (ms)	50.95±25.746	50,42±26.41	54.021±24.92	50.5±24.22	0.757/0.991
CMCT(ms)	7.75 ± 2.993		7,75± 2.993		0.998

CSP: Cortical silent period **L**: Left **R**: Right **CMCT**: Central motor conduction

Table 4. MIR SP1 and SP2 components

	Normal	Bruxer	P<0.05
Duration of SP1 (ms)	24.17±5.64	29.07±22.17	0.196
Duration of SP2 (ms)	36.22±7.8	35.1±9.02	0.678
Presence of SP1 %	100	100	
Presence of SP2 %	**84**	**35**	**0.00**

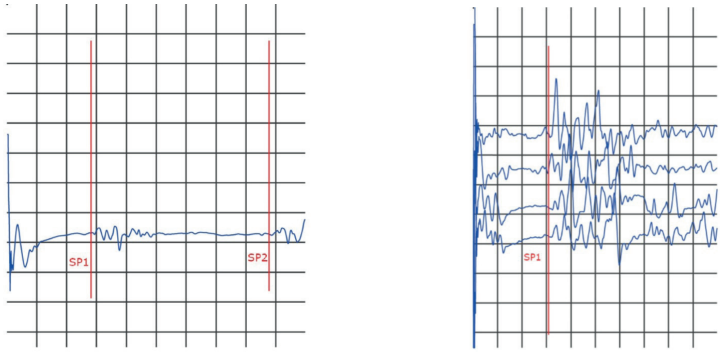

Figure 1: Masseter Inhibitory Reflex

5) APB muscle cortical MEP, M response, and F latency: No significant difference was found between the normal control and the bruxwe group in terms of cortical MEP latency (21.26 ± 2.75/20.57. D2.04 ms) and M response latency (2.94 ± 0.37/ 3.01 ± 0.46 ms) obtained by recording from the APB muscle (MEP latency p=0.216 and M latency p=0.472).

F wave latency was found to be significantly shorter (23.6 ± 2.51 /25.07 42.34 ms) in the bruxer group, and this difference was statistically significant (**p=0.01**). As the mean age of the groups is similar, this difference may be explained by the variation in the limb length of the subjects as well as the involvement of the lower brainstem upper spinal region when interpreted in conjunction with the impact on the R2 response of the blink reflex. (Malick et al., 2000).

6) Blink reflex: While R1 latency was similar in both groups (N: 11.28 ± 1.313 and B: 11.27 ± 1.314 ms) (p = 0.982), R2 latency was significantly prolonged in the bruxer group (35.08±4.445 /32.755±4.613 ms) and this difference was statistically significant (**p=0.027**) (table 5).

Table 5. Blink reflex (R1 and R2) and F wave latency recorded from the left median nerve

	Normal	Bruxer	P<0.05
R1 latency (ms)	11.28 ± 1.313	11.27± 1.314	0.982
R2 latency (ms)	**32.755±4.613**	**35.08±4.445**	**0.027**
F wave latency (ms)	25.07±2.34	**23.6±2.51**	**0.01**

DISCUSSION

Demographic Data:

Studies have reported that bruxism is more common in females and similarly, the number of females in the bruxer group selected was also found to be higher in our study (Melis &Abou-Atme, 2003). However, no statistically significant difference was observed.

Neurophysiological Parameters:

About Neurophysiological parameters, there was no statistically significant difference between the groups in terms of MEP latency, CSP durations obtained with right and left stimulation, MIR, APB muscle cortical MEP, M response latency, but the absence of SP2 was prominent in the bruxer group and statistically significant (p=0.00). F wave latency was found to be significantly shorter in the bruxer group and the difference is statistically significant (p=0.01). Lastly R2 latency was significantly prolonged in the bruxer group and the difference is statistically significant (p=0.027).

In this study there was no significant difference between two groups in terms of age, BMI and neck circumference.

Neurophysiological Assessment:

In our study, no difference between the groups in terms of MEP latency and central motor conduction time was observed, however in the literature, MEP latency, amplitude, and central motor conduction time were also found to be similar to normal controls (Gastaldo at al., 2006; Huang et al., 2014). This similarity between the groups can be considered as that corticobulbar tract functions are also normal in bruxers and there is no change in cortical motor system excitability (Gastaldo et al., 2006).

In a study of Parkinson's patients, while MEP latencies and amplitudes remained the same, the duration of the CSP was prolonged after Levodopa treatment. The dopamine reduction in the basal ganglia and the nigrostriatal pathway has been proposed to lead to abnormal silent periods may be as a result of reduced facilitation of the motor cortex leading to excitation of the cortical inhibitory interneurons (Priori et al., 1994; Inghilleri et al., 1996). In our study, CSP, CCT, and MEP latencies for both cortical hemisphers were found to be similar. This conclusion indicated no significant excitability differences between cortexes in both hemispheres among two groups.

In a previous study aiming to understand the abnormal networks related to the excitability of masticatory pathways in patients with sleep bruxism the MIR after electrical stimulation and auditory startle reaction (ASR) were examined in sleep bruxers and control groups. The duration of SP1 and SP2 components of MIR was found to be shorter in sleep bruxers than controls means a lower suppression of SP's in sleep bruxer group. The ASR responses including masseter muscle found to be similar in both groups meaning the integrity of brainstem pathways mediating ASR are intact in sleep bruxers unlike dopamine related pathophysiology like dystonia, restless leg syndrome in which exaggerated ASR responses were observed as an indicator of disinhibition of reticulospinal pathways (İnan et al., 2017).

Plamen Tzvetanov 2009, found S2 in MIR reduced in intensity and duration or absent in 66.7 % of the individuals with episodic TTH (Tansion Type Headache). The changes

observed in TTH were claimed to be due to hyperexcitability of the raticular nuclei, that has inhibitor effect on the medullar inhibitor interneurons (Tzvetanov et al., 2009).

It has been claimed that SP1 and SP2 disappeared in mid-pontin lesions, only one of the SP1 and SP2 components were affected in isolated lesions of different regions, and therefore these pathways are independent from each other (Ongerboer et al.,1990). Stimulation of the bulbar reticular formation located in the pontomedullary junction area caused an inhibitory effect on bilateral trigeminal motor nuclei. (Takatori et al. 1981).

In our study, the most remarkable finding is that while SP1 is obtained in both healthy subjects and bruxers (Figure 1, SP2 is significantly absent in bruxers (Figure 2). The absence of SP2 in bruxers was found to be insignificant in one of two previous studies (p=0.053) (Gastaldo et al. 2006) and the absence of SP2 in bruxers was found to be significant in the other study (p=0.041) (Huang et al., 2014).

The inhibitory effect conveyed to the trigeminal motor nucleus is considered to originate from the ventral nucleus pontis caudalis and has a role in the SP2 mechanism (Tanaka et al., 1999; Lund & Kolta, 2005; Lund & Kolta, 2006; Kolta et al., 2010). While SP1 is not affected, the loss of only SP2 in bruxers may be the result of a pathology involving the brain stem region especially lower ponds and medulla similar as R2 component.

Other remarkable findings in our study are also associated with the blink reflex. The blink reflex is the response of contraction of the orbicularis oculi muscle to the stimulation of the supraorbital nerve. It has two components of R1 and R2. R1 has a short latency (13 ms) and the response is ipsilateral. The R2 component has a long latency (40 ms) and the response is bilateral. R1 is an oligosynaptic response and its circuit is located in the pons like SP1. The afferent fibers of R2 descend from the pons to the most caudal part of the spinal trigeminal nucleus in the spinal trigeminal area in the lateral medulla. R2 ascends bilaterally and polysynaptically, medial to the spinal trigeminal nucleus and in the lateral medullary reticular area, and reaches the facial nerve (Scott et al., 2003).

In a study examining blink and MIR together in individuals with dystonia and blepharospasm, no significant abnormality was found in R1 and R2 (Ongerboer De Visser & Kuypers, 1978; Pauletti et al., 1993). However, a significant shortening was observed in the recovery times of SP2 and R2. This condition has been regarded as a decrease in the control of the basal ganglia over the brainstem reflex networks (Aramideh & Ongerboer de Visser, 2002).

On the other hand neuroplastic changes occurs as a result of periferal changes in the oral-facial and mastication systems also indicates the affect and relation of central mechanism involving masticatory activity and bruxism.

A study hypothesised that bidirectional or multidisectional motor movements may differentially alter excitability of the tongue and first dorsal interosseous (FDI) muscle groups, found significant neuroplastic changes in the tongue motor cortex area (MI) as a result of bidirectional and multidirectional training of the tongue. Multidirectional training results in a great number of motor map sites that show a significant increase in excitability (Boudreau et al., 2013).

Previous TMS studies in healty subjects support the idea that repeated standardized jaw movements can result in neuroplastic changes centrally. These changes include chorticomotor control of jaw closing muscles (Lida et al., 2014).

A significant increase in the amplitude of the masseter muscle MEP's (p=0,036) after four weeks of altering the occlusal vertical dimension (OVD) and a significant increase in numerical rating scale scores of masticatory ability after four weeks may indicate an adaption of the masticatory systems to the altered oral conditions (Deng et al., 2018).

Such results also indicates the importance of periferal affects on masticatory system and also strenght the affect of periferal factors on bruxism.

In summary, since it is considered that the R2 response is polysynaptic response and is predominantly originated from synaptic connections in the medullary region, the absence of SP2 and the prolonged R2 latency which were statistically significant in bruxers as a result of our study can be considered to be an indicator of medullar involvement (Scott et al., 2003). Although the R2 circuit is also polysynaptic like SP2, it descends to more caudal than SP2 and is conveyed via different pathways. Although it is conveyed via different pathways, the fact that both responses were affected together in our study strengthens our hypothesis of the central origin of bruxism. Also significantly shorter latency of F. Waves of the bruxer group than the control group may be a sign of the lower brainstem where the late blink reflex component R2 traces were found and the upper cervical area interaction (Malick et al., 2000). However, more comprehensive studies with larger numbers of patients are warranted.

Limitations of The Study:

The main limitation of this study is that the cases were selected by dental examination and patient reports. Polysomnographic examination was not performed.

The second limitation is this study is an open study not blind. Also bruxer group wasn't classified as sleep, awake and both.

Another limitation is that SP1 and SP2 were assessed while bruxers were awake. As voluntary contraction is required when evaluating MIR, it is impossible to evaluate it during sleep. The effect of wakefulness and awareness on reticular formation structures and brainstem reflex circuits is unknown.

While assessing the MIR, it is necessary to have a voluntary contraction, but as the masticatory force increases, SP2 decreases, and as the stimulation intensity increases, it increases (Gastaldo et al., 2006). In order to minimize this condition, the bite level was monitored audiovisually on the monitor, and each individual was ensured to have the same intensity of stimulation. Since conditions such as sense of discomfort, pain, irritability, and anxiety can affect inhibitory trigeminal reflex circuits, efforts have been made to make people as calm and neutral as possible (Gastaldo et al., 2006). Although both cases were tried to be minimized, they may have influenced reflex responses.

Our examinations were done in a separate room in which the TMS device and EMG device were found in the neurology department.

This study cannot be generalized due to the number of participants.

CONCLUSION

The pathophysiology of bruxism has not been elucidated yet. Both central and peripheral causes are considered to be factors. As a result of our study, the loss of the SP2 component and the prolongation of the latency of the R2 component, and the localization of reflex circuits in the brainstem, although their pathways are separate, bruxer suggested that the pathophysiology may have a central origin in most of the bruxers.

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CONFLICTS OF INTEREST STATEMENT

There is no conflicts of interest in this study.

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ORIGINAL ARTICLE / ARAŞTIRMA MAKALESİ

Evaluation of 4% Mangosteen (MG) Gel as a Local Drug Delivery in adjunct to Scaling and Root planing on Clinical Parameters and GCF MMP-9 levels in Chronic Periodontitis Patients – A Split Mouth Randomized Controlled Trial

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ABSTRACT

Objective: The current study was conducted to assess the efficacy of 4% Mangosteen (MG) gel in adjunct to scaling and root planing (SRP) on clinical parameters and gingival crevicular fluid (GCF) matrix metalloproteinase 9 (MMP-9) levels in the management of patients with chronic periodontitis.

Materials and Methods: This double blinded, randomized, placebo-controlled, split mouth, clinico-biochemical study was carried out on 13 patients (26 experimental sites) with Stage II and Grade B periodontitis. Following subgingival SRP, the 13 control sites were treated with LDD of placebo gel and the 13 test sites with 4% MG gel. Clinical parameters including plaque index (PI), gingival bleeding index (GBI), probing depth (PD) and relative attachment level (RAL) were recorded and GCF was collected from all the experimental sites for MMP-9 analysis, using Enzyme Linked Immunosorbent Assay (ELISA); at baseline and 3 months post treatment.

Results: Both, control and test sites, demonstrated improvement in the clinical parameters and reduction in GCF MMP-9 levels during the study period. Test sites exhibited a statistically significant reduction (P <0.05) in PD and RAL (gain in clinical attachment level; CAL) and GCF MMP-9 levels than the control sites. All the clinical parameters showed a positive correlation with the GCF MMP-9 levels.

Conclusions: Within the limitations of this study, 4% MG gel proves to be an efficacious adjunctive agent to SRP, for management of chronic periodontitis.

Keywords: *Garcinia mangostana*, GCF, Local drug delivery, MMP-9, Periodontitis, Scaling and root planing.

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INTRODUCTION

Periodontitis is a multifaceted inflammatory disease that results in the breakdown of tooth supporting apparatus. It occurs as a consequence of interplay between the host and pathogenic bacteria present in the biofilm and if left untreated, ultimately results in tooth loss (Singh et al., 2018). The host-immune interactions produce several inflammatory molecules locally such as cytokines, matrix metalloproteinases (MMPs), their inhibitors and regulators making them some of the important indicators of the disease (Checchi et al., 2020).

The main goal of periodontal therapy is to diminish the pathogenic microflora, thereby reducing the production of the inflammatory molecules. Scaling and root planing (SRP) are the foundation of periodontal therapy that aim at removal of the biofilm thus delaying the microbial repopulation (Singh et al., 2018; Wei et al., 2021) which reduces the inflammatory burden and provides a biocompatible root surface. The anatomical complexity of the tooth and the inadequate access to the pathogens deep within the pockets, limit the efficacy of SRP alone to entirely eradicate the infections. Combining SRP with various antimicrobial and anti-inflammatory agents, that improve tissue regeneration, has been shown to enhance its therapeutic effect (Goodson et al., 1985; Pradeep et al., 2013). These agents can be administered systemically as well as locally. Owing to several unintended effects of the systemic antimicrobials such as gastro-intestinal intolerance, development of resistance and requirement of large doses for administration, utilization of local drug delivery (LDD) has been amplified in periodontics (Drisko, 1996; Wei et al., 2021). LDD improves patient compliance, pharmacokinetics, & lowers the total drug dosage requirement. Herein, the drug is directly administered at the intended site with a sustained release,

and can be formulated as gels, chips, fibres, microparticles and nano systems (HR et al., 2019).

Even though numerous materials are being used as LDD, the necessity for effective, safe and affordable alternatives has continually driven researchers to explore natural products. *Garcinia mangostana* Linn., commonly known as Mangosteen (MG), is a popular fruit in the tropical Southeast Asia especially in Malaysia, Indonesia, and Thailand. MG rind contains multiple bioactive compounds that promote its therapeutic effects including xanthones, flavonoids, saponins, tannins, phenols, gartanines, and garcinones amongst several others (Aljuanid et al., 2022). Xanthones are polyphenols and are the major biomolecules that exhibit antioxidant, antiproliferative, antibacterial, and anti-inflammatory properties (Widyarman et al., 2019; Tangsuksan et al., 2022).

MMPs are protein molecules which breakdown the extracellular matrix (ECM) during the disease progression (Checchi et al., 2020). MMP-9 (Gelatinase B) is a 92 kilo Dalton (kDa) enzyme that primarily degrades type IV collagen of the basement membrane. Significantly higher level of gingival crevicular fluid (GCF) MMP-9 has been observed in periodontitis patients in contrast to healthy counterparts (Rai et al., 2010). The greater reduction of MMP-9 levels in GCF post-SRP in periodontal patients, deem it an important biomarker of periodontal disease (Luchian et al., 2022). MMP-9 is also expressed by osteoclasts, that are responsible for alveolar bone loss due to periodontal inflammation (Luchian et al., 2022). A xanthone of MG, α-mangostin, has demonstrated inhibition of the mRNA levels and promoter activity of MMP-9 in vitro on human renal carcinoma cells (Chen et al., 2017).

MG extract has been found to be bactericidal against periodontal pathogens including *P. gingivalis* and *A. actinomycetemcomitans* (Hendiani et al., 2016). Subgingival LDD of 4% MG gel, adjunctive to SRP, has demonstrated a significant reduction in pockets depth, gingival bleeding index values and improvement of clinical attachment levels along with antimicrobial and antioxidant effect in chronic periodontitis patients (Rassameemasmaung et al., 2008; Mahendra et al., 2017; Manjunatha et al., 2022).

To the best of our knowledge there is a paucity of trials that evaluated the efficacy of MG gel as a LDD agent and its effect on GCF MMP-9. Therefore, the present study intended to assess and compare the efficacy of 4% MG gel as a LDD, adjunctive to SRP on clinical parameters & GCF MMP-9 levels in the management of chronic periodontitis.

MATERIALS AND METHODS

The study was authorized by the Institutional Review Board (Ref. No. BDCH / Exam 574 / 2020 – 2021); Clinical Trials Registry – India Identifier: CTRI/2021/12/038758 and abided to the principles in the Helsinki Declaration (revised 2008).

Patients with chronic periodontitis, aged 30-65 years of either sex, who were systemically healthy, with minimum of 2 sites in different quadrants with probing depths ≥ 5 mm, loss of clinical attachment ≤ 3-4 mm i.e., Stage II and Grade B periodontitis, and who did not use chemotherapeutic mouth rinses or any other agents were included in the study. Patients with an identified or supposed allergy to MG, history of chronic smoking and alcohol consumption, having undergone systemic &/or topical antibiotic &/or anti-inflammatory therapy in last 3 months, who were treated for periodontitis in the past 6 months, pregnant and lactating mothers, those with systemic conditions affecting treatment outcomes, individuals who were unable to maintain the oral hygiene or come for the recall visits were excluded from the study.

This randomized, double blinded, placebo controlled, prospective, split mouth, clinico-biochemical study was conducted on 13 patients (26 experimental sites) fulfilling the aforementioned criteria. They were recruited from the Department of Periodontics, Bapuji Dental College and Hospital, Davangere, Karnataka, India. A thorough verbal and printed description regarding the study was given to all the patients and a signed consent to partake was obtained from them prior to the commencement. At screening, case history was taken followed by clinical examination and recording of the parameters. Full mouth supragingival scaling was done and oral hygiene instructions (OHIS) were given to them. Alginate impressions were made and casts poured for the preparation of acrylic stents. After 2 weeks, patients with full mouth PI and GBI scores ≤25% were chosen for the study. The selected sites were randomized (by computer generated random number sequence) equally into the following experimental groups:

Control Group – 13 Sites to be treated with subgingival SRP and placebo gel delivery.

Test Group – 13 Sites to be treated with subgingival SRP and 4% MG gel delivery.

Collection of GCF

At baseline, under adequate isolation, the supragingival plaque was debrided gently from the selected experimental sites to avoid contamination and blocking of the micro capillary pipette. A standardized volume of 3µl GCF was collected in 1-5µl calibrated and color-coded micropipettes (Sigma-Aldrich, USA) with extra-crevicular method (Fig. 1) and was transferred into sterile Eppendorf tubes (Flex-Tube® – Microtube, Eppendorf, North America) containing 50µl of 0.9% phosphate buffered saline (GibcoTM, Thermo Fisher Scientific, USA). All the collected samples were sent to the research laboratory, and were stored at – 80 °C until their analysis. Visibly contaminated samples were discarded. GCF samples were collected similarly at 3 months post-treatment from all the experimental sites.

Figure 1: GCF collection by using a microcapillary pipette.

Clinical Measurements

A blinded periodontist (M.K.) examined and recorded the parameters, who was calibrated by a senior clinical investigator (G.G.V.) prior to the study. At baseline and 3 months post-treatment, the i) Plaque index (PI) (Silness and Loe,1964); ii) Gingival Bleeding Index (GBI) (Ainamo and Bay, 1975); iii) Probing Depth (PD) and iv) Relative Attachment Level (RAL) were recorded. The customized acrylic stents and UNC-12 Periodontal probe (HuFreidy®, USA) were used to record PD and RAL (in mm), with apical border of the stent as a fixed reference point.

Treatment protocol

All the selected patients were subjected to complete subgingival scaling with ultrasonic scalers (Woodpecker® India) and, root planing was carried out with Columbia universal 4R-4L, 2R-2L curettes (HuFreidy®, USA) at the selected experimental sites. The 4% MG gel was formulated according to Rassameemasmaung et al., (2008) and the placebo gel was similarly formulated, without the active ingredient i.e., MG. The prepared gels were packaged into similar tubes, and the demarcation for their identification was blinded from the administrator. The tubes were UV sterilized and stored at 4°C throughout the study period. In test group 4% MG gel (Fig. 2) while in control group placebo gel respectively were delivered in the designated sites with a 10cc syringe and a 21-gauge blunted tip needle (Unolok, Dispovan, HMD, Faridabad, Haryana, India), gently until it spilled over from the marginal gingiva and was allowed to settle inside the pocket. A periodontal pack (Coe-PakTM, GC America Inc., Illinois, USA) was placed up to a week, to prevent the delivered gel from flowing out, the ingress of oral fluids and the cross-over effect. OHIS were given.

Figure 2: Subgingival LDD OF 4% MG gel.

Biochemical analysis of GCF MMP-9 with ELISA

GCF MMP-9 levels were determined using EliKine™ Human MMP 9 ELISA Kit (Abbkine, Delhi, India), conferring to the instructions given by the manufacturer. The kit utilized the sandwich technique of double antibody type, to determine the Human MMP-9 concentrations in GCF samples. A microplate pre-coated with antibody specific to Human MMP-9 was employed. Standards and GCF samples were added to the microplate wells and the Human MMP-9 in the sample was bound by the immobilized antibody. Post removal of any unbound elements, an antibody specific for Human MMP-9 conjugated with biotin, was pipetted into the microplate wells. After washing, streptavidin-horseradish peroxidase (HRP) conjugates were added. Washing was repeated to eliminate any unbound streptavidin-enzyme reagent, which was followed by the addition of transparent HRP substrate (TMB). TMB turned blue by the breakdown of HRP, and further to yellow after the stop solution was added. The optical density (OD) value was determined

using an ELISA reader (iMark™ Microplate Absorbance Reader), measured at 450 nm wavelength (OD 450nm). The MMP-9 level was determined in picograms/microlitre (pg/µl), and was directly proportional to the OD 450nm value.

Statistical Analysis

The documented clinical and biochemical results were tabulated and statistically analysed by an expert. The data was presented as mean ± standard deviation. For the intragroup and intergroup comparisons, the Welch's paired-t test was applied to determine if significant changes occurred in the parameters at baseline and 3 months post treatment in both the groups. Pearson's correlation coefficient analysis was employed to check the linear correlation and strength of the relationship between two sets of data variables i.e., the clinical and biochemical (GCF MMP-9 levels) parameters. The *P* value < 0.001 was set as statistically highly significant (HS**); < 0.05 as significant (S*) and > 0.05 as non-significant (NS). GraphPad Software, Boston was used to carry out the statistical analysis.

RESULTS

Both control and test group sites demonstrated a significant reduction in the mean PI, GBI, PD (Figure 3A), RAL [gain in CAL] (Figure 3B) scores & in mean GCF MMP-9 levels (Figure 3C) from baseline to 3 months (Table 1). Comparison of mean PI, GBI, PD, RAL values and GCF MMP-9 levels in the test group sites demonstrated a significant decrease in contrast to the control sites at 3 months post treatment (Table 2). The clinical parameters and GCF MMP-9 levels demonstrated a positive correlation at 3 months post treatment, which was statistically not significant in both the groups (Table 3).

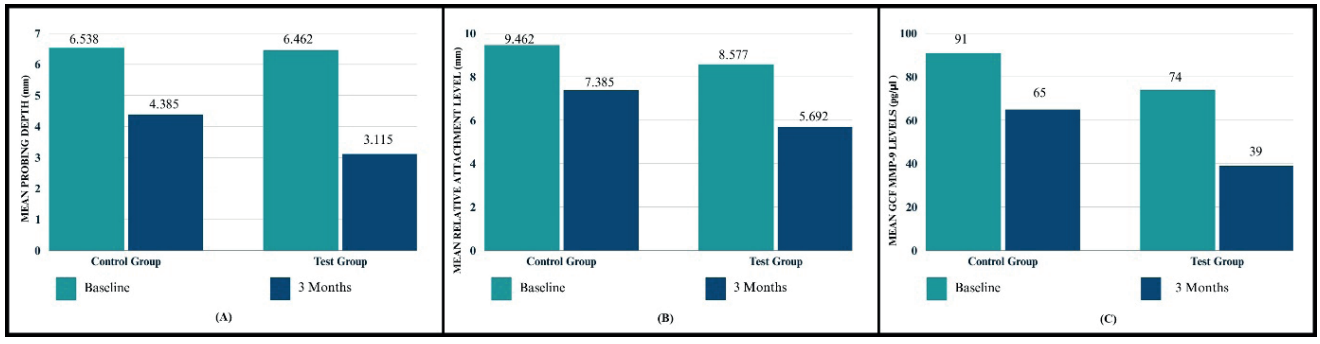

Figure 3: (a) Comparison of mean PD scores at baseline and 3 months post-treatment in control and test groups. (b) Comparison of mean RAL scores at baseline and 3 months post-treatment in control and test groups. (c) Comparison of mean GCF MMP-9 levels at baseline and 3 months post-treatment in control and test groups.

Table 1. Intragroup comparison of the clinical and biochemical parameters in control and test groups at baseline and 3-months post treatment

Parameters	CONTROL GROUP (n=13)			TEST GROUP (n=13)		
	Baseline (C0)	3-months (C3)	P-Value #	Baseline (T0)	3-months (T3)	P-Value #
PI	1.423 ± 0.277	0.634 ± 0.299	<0.001**	1.308 ± 0.355	0.076 ± 0.120	<0.001**
GBI	1.084 ± 0.229	0.472 ± 0.128	<0.001**	1.042 ± 0.170	0.265 ± 0.274	<0.001**
PD (mm)	6.538 ± 0.720	4.385 ± 0.982	<0.001**	6.462 ± 0.557	3.115 ± 0.711	<0.001**
RAL (mm)	9.462 ± 1.898	7.385 ± 0.869	<0.05*	8.577 ± 0.909	5.692 ± 1.974	<0.001**
GCF MMP-9 (pg/µl)	91 ± 7.2	65 ± 24	<0.05*	74 ± 25	39 ± 25	<0.05*

Values are presented as mean ± standard deviation.
PI: Plaque Index; GBI: Gingival Bleeding Index; PD: Probing Depth; RAL: Relative Attachment Level; GCF MMP-9: Gingival Crevicular Fluid Matrix Metalloproteinase – 9
*# Welch's paired t – test. **HS: highly significant (P<0.001) *S: significant (P<0.05)*

Table 2. Intergroup comparison of the clinical and biochemical parameters between control and test groups at baseline and 3-months post treatment

Parameters	BASELINE			3 MONTHS			Mean difference ± SEM at 3 months (T3-C3)	P-Value #
	Control (n=13)	Test (n=13)	P-Value #	Control (n=13)	Test (n=13)	P-Value #		
PI	1.423 ± 0.277	1.308 ± 0.355	>0.05 NS	0.634 ± 0.299	0.076 ± 0.120	<0.001**	-0.557 ± 0.089	<0.001**
GBI	1.084 ± 0.229	1.042 ± 0.170	>0.05 NS	0.472 ± 0.128	0.265 ± 0.274	<0.05*	-0.206 ± 0.084	<0.05*
PD (mm)	6.538 ± 0.720	6.462 ± 0.557	>0.05 NS	4.385 ± 0.982	3.115 ± 0.711	<0.001**	-1.269 ± 0.336	<0.001**
RAL (mm)	9.462 ± 1.898	8.577 ± 0.909	>0.05 NS	7.385 ± 0.869	5.692 ± 1.974	<0.05*	-1.692 ± 0.598	<0.05*
GCF MMP-9 (pg/µl)	91 ± 7.2	74 ± 25	<0.05*	65 ± 24	39 ± 25	<0.05*	-25.66 ± 9.675	<0.05*

Values are presented as mean ± standard deviation and mean difference ± standard error of mean (SEM).
PI: Plaque Index; GBI: Gingival Bleeding Index; PD: Probing Depth; RAL: Relative Attachment Level; GCF MMP-9: Gingival Crevicular Fluid Matrix Metalloproteinase – 9
*# Welch's paired t – test. **HS: highly significant (P<0.001) *S: significant (P<0.05) NS: non-significant (P>0.05)*

Table 3. Correlation of GCF MMP-9 levels with clinical parameters at 3 months post-operatively

Parameters	GCF MMP-9 levels at 3 months			
	Control group		Test group	
	Correlation coefficient (r)	P-value #	Correlation coefficient (r)	P-value #
PI	0.475	> 0.05 NS	0.045	> 0.05 NS
GBI	0.209	> 0.05 NS	0.097	> 0.05 NS
PD	0.483	> 0.05 NS	0.132	> 0.05 NS
RAL	0.009	> 0.05 NS	0.056	> 0.05 NS

PI: Plaque Index; GBI: Gingival Bleeding Index; PD: Probing Depth; RAL: Relative Attachment Level; GCF MMP-9: Gingival Crevicular Fluid Matrix Metalloproteinase – 9
 # Pearson's Correlation Coefficient Analysis r : correlation coefficient NS: non-significant (P>0.05)

DISCUSSION

Herbal agents have been employed in the field of medicine for treatment of several diseases (Aljuanid et al., 2022). MG is one such source of herbal medicine, originating from the tropical Southeast Asia. The significant biomolecules in MG pericarp are the xanthones like α – and γ-mangostin that have antioxidant (Manjunatha et al., 2022), anti-inflammatory (Hendiani et al., 2017; Putri et al., 2017; Lim et al., 2019; Ridwan et al., 2021), antibacterial (Rassameemasmaung et al., 2008; Mahendra et al., 2017; Widyarman et al., 2019; Tangsuksan et al., 2022) and antitumorigenic (Chen et al., 2017; Xu et al., 2017) properties.

Xanthones of MG can substantially regulate and minimalize oxidative damage due to the reactive oxygen species, thus inhibiting the degeneration of cells (Manjunatha et al., 2022). They also inhibit the inflammation by suppressing the lipoxygenase (LOX) and cyclooxygenase (COX) production, which are responsible for the release of prostaglandins (PGs) that further induce MMPs and result in osteoclastic bone resorption. Kresnoadi et al., (2017) in their study demonstrated a substantial reduction in the expression of nuclear factor kappa B (NF-kB) and receptor activator of NF-kB ligand (RANKL), which are essential for osteoclast development and progression of periodontitis, when MG was used along with a xenograft for preservation of extraction sockets. α-mangostin has demonstrated inhibitory effect on interleukin 1β (IL-1β) induced expression of COX-2, PGs, inducible nitric oxide synthase (iNOS), nitric oxide (NO), in

chondrocytes, indicative of its anti-inflammatory and anti-oxidant effects on the chief inflammatory mediators (Pan et al., 2017).

The xanthones present in MG pericarp, also destroy bacterial adhesins to inhibit the attachment of bacteria to the tissue, result in coagulation of bacterial cells, eliminate bacterial virulence factors and interfere with bacterial metabolism thus demonstrating its anti-bacterial properties on periodontal pathogens (Widjaja et al., 2019; Ridwan et al., 2021). MG pericarp extract has shown bactericidal activity against *P.gingivalis, T.denticola, S.aureus* at a minimum inhibitory concentration (MIC) range of 3.12 – 4 µg/ml (Phongpaichit et al., 1994; Rassameemasmaung et al., 2008; Mahendra et al., 2017).

LDD in the form of gels have been widely used as an adjunct to SRP and have demonstrated their potential role in improving the periodontal clinical parameters (Pradeep et al., 2013). Gels are easy to prepare, administer and they offer a sustained release of the drug with minimum dose frequency and toxicity (Bural et al., 2018). Subgingival LDD of 4% MG gel following SRP has shown a significant reduction in PD, PI, BI values and improvement in CAL gain in chronic periodontitis patients (Rassameemasmaung et al., 2008; Hendiani et al., 2017; Mahendra et al., 2017; Manjunatha et al., 2022). Hence in the present study a 4% concentration i.e., 4 µg/ml of the MG gel was considered as LDD in adjunct to SRP.

MMP-9 is a catabolic enzyme mainly involved in the degradation of collagen type IV, the fundamental constituent of the basement membrane (Luchian et al., 2022). It also degrades collagen type V & XI, proteoglycans, and elastin present in the connective tissue (Bildt et al., 2008). Neutrophils are the chief source of MMP-9, with increased concentrations being produced by the inflamed junctional epithelial cells in advanced periodontal disease (Yabluchanskiy et al., 2013). Other cells such as macrophages, keratinocytes, fibroblasts, osteoclasts and eosinophils in periodontitis are also responsible for expression of the MMP-9 gene (Franco et al., 2017). MMP-9 has been found to regulate IL-1, – 6, – 8, and PGs during various stages of inflammation in periodontitis (Franco et al., 2017). Hence, it can be assumed that increased MMP-9 concentrations may precisely indicate the inflammatory status of periodontitis in patients, and be a valuable biomarker for diagnosis and prognosis following periodontal therapy.

GCF originates from and is specific to the periodontium, constituting numerous reaction products associated with periodontal inflammation, analysis of which can indicate the changes in the tissues with progression of the disease. A thorough literature search revealed that the elevation in GCF MMP-9 levels is associated with chronic periodontitis (Rai et al., 2010; Han et al., 2012; Yakob et al., 2013). Non-surgical management of localized aggressive periodontitis, involving SRP and systemic antimicrobial therapy, has demonstrated a reduction in the levels of MMPs locally and a positive correlation with the clinical periodontal parameters (Gonçalves et al., 2013). But there is a paucity of evidence on the effect of LDD, particularly of MG, on GCF MMP-9 levels and the clinical parameters when used as an adjunct to SRP. Hence, we carried out this study to assess and compare the effect of 4% MG gel as an LDD, on clinical parameters and GCF MMP-9 levels in chronic periodontitis, as an adjunct to SRP.

There were no dropouts during the entire study period. All the patients tolerated the MG gel without any adverse reactions. All the clinical parameters demonstrated a non-significant difference in the mean baseline values of both groups, indicative of uniformity in the selection of experimental sites (Table 2). At 3 months post treatment, the mean PI scores of the test sites were reduced significantly ($P < 0.001$) than the control sites, which can be attributed to the antibacterial effect of the MG gel against the plaque microorganisms (Mahendra et al., 2017). These findings were similar to the trials carried out by Mahendra et al., (2017) and Manjunatha et al., (2022). Removal of the biofilm, reinforcement of oral hygiene instructions at screening and baseline visits, in addition to the "Hawthorne effect" could have improved the hygiene maintenance and treatment outcomes in the patients.

Similarly, the mean GBI scores showed a significant reduction ($P < 0.05$) in test sites than the control sites at 3 months post treatment. Our results were in congruence with the findings of Rassameemasmaung et al., (2008), Mahendra et al., (2017) and Manjunatha et al., (2022). The local vasoconstrictive and strong anti-inflammatory effect of MG mediated via inhibition of PGs, ILs and MMPs (Pan et al., 2017; Lim et al., 2019; Aljuanid et al., 2022; Luchian et al., 2022) could be responsible for the reduced ulceration of the gingiva and thus its tendency of bleeding on probing.

Increase in the probing depth and loss of clinical attachment are salient features of periodontitis. We observed a highly significant mean PD reduction ($P < 0.001$) in the test sites than the control sites at 3 months post operatively. Although shrinkage of gingival tissues naturally occurs

after SRP (Goodson et al., 1985) resulting in the PD reduction, the additional reduction in inflammation by 4% MG gel application, could have enabled the reconstruction of connective tissue fibres thereby improving the resistance to penetration by the probe. Recording of RAL is a clinical method to determine disease severity and progression of disease activity. RAL denotes the extent of the periodontal support that is present around a tooth. Post treatment, at the end of 3 months the test group sites showed a significant decline ($P < 0.05$) in the mean RAL scores i.e., betterment in the attachment levels, than the control sites which may be substantiated by synergistic effects of mechanical debridement and LDD of the MG gel. SRP reduces gingival inflammation, which results in tissue contraction & better gingival tissue adaptation. Root planing also aids in increasing the clinical attachment either via generation of new periodontal ligament fibres (new attachment) or via establishment of long junctional epithelium (repair) (Greenstein, 2000). In adjunct to SRP, the anti-inflammatory (Hendiani et al., 2017; Putri et al., 2017; Lim et al., 2019; Ridwan et al., 2021), antioxidant (Manjunatha et al., 2022), anti-bacterial properties (Rassameemasmaung et al., 2008; Mahendra et al., 2017; Widyarman et al., 2019; Tangsuksan et al., 2022) of the 4% MG gel might have brought out better results in the test group. Studies have also revealed an analogous reduction in PD and increase in the clinical attachment levels (CAL) with the sub gingival delivery of MG gel (Rassameemasmaung et al., 2008; Mahendra et al., 2017; Hendiani et al., 2017; Manjunatha et al., 2022).

The analysis of GCF is amongst the least invasive methods which can provide information about the current and future disease outcomes after treatment, in contrast to the measurement of clinical parameters which are comparatively invasive and only indicative of the periodontal destruction that has occurred in the past (Qasim et al., 2020). It helps in improving the accuracy of diagnosis for better management of the periodontal disease. Pre-treatment mean GCF MMP-9 levels were greater in the control group (91±7.2 pg/µl) than test group (75±25 pg/µl) with a significant difference ($P < 0.05$), though the mean values of all four clinical parameters had a non-significant difference (Table 2). This highlights the importance and precision of biochemical analysis in determining the disease severity at specific diseased sites when compared to clinical parameters alone. At 3 months, a statistically significant reduction ($P < 0.05$) was observed in the mean GCF MMP-9 levels of the test group sites than those of control group. Study results of Marcaccini et al., (2010) revealed elevated GCF MMP-9 concentrations in patients with stage II grade B periodontitis compared to the healthy patients, which were lowered when re-evaluated at 3 months after SRP, similar to our results. Our results are also analogous to those of Rai et al., (2010) who reported increased levels of GCF MMP-9 concentrations in periodontal patients compared to healthy patients.

Xanthones of MG have shown downregulation of MMP-9 and upregulation of tissue inhibitors of metalloproteinase (TIMP-1 and 2) in ovarian cancer cells (Xu et al., 2017). α-mangostin has also exhibited a reversal in the expression MMP-3, – 9 and – 13 levels (Pan et al., 2017). It is effective in increasing IL-10 levels, an anti-inflammatory cytokine, which can downregulate the production of NO, collagenase, and gelatinase (MMP-9) thereby regulating inflammation and maintaining homeostasis (Ridwan et al., 2021). Thus, the adjunctive use of MG in our study might have reversed and/or indirectly decreased the MMP-9 concentrations via the aforementioned mechanisms. Hence the potent anti-inflammatory effect of MG against MMP-9 can be credited for reduction in the GCF MMP-9 levels, which was also evident after 3 months of LDD.

In our study, the clinical parameters along with GCF MMP-9 levels presented a non-significant positive correlation in both the groups signifying a possible role of MMP-9 in the periodontal inflammatory process. Our results are comparable to those of Preshaw (Preshaw et al., 2020) wherein GCF MMP-9 levels post non-surgical periodontal therapy, demonstrated a reduction along with an improvement in the clinical status in Type 2 diabetics with moderate periodontitis. In contrast, study by Peniche (Peniche et al., 2019) demonstrated highest levels of GCF MMP-9 levels in healthy subjects compared to subjects having periodontitis with Type 2 diabetes. They attributed this disparity to limitations of the ELISA test kit and its variations, which cannot quantify active forms. The difference observed in our results compared to Peniche et al. can be credited to the changes in the study design, groups employed for comparison, duration of follow-up, methods of GCF sampling and statistical analysis.

CONCLUSIONS

From the present study we can conclude that following SRP, the sub gingival LDD of 4% MG gel effectively controlled the periodontal disease progression as observed by the improved clinical parameters and decreased GCF MMP-9 levels in the test group. This substantiates the

synergistic anti-inflammatory activity of MG gel and that it can be used adjunctively with SRP for better clinical results in the treatment of chronic periodontitis patients. The GCF concentrations of MMP-9 were correlated positively with the four clinical parameters, though they were not statistically significant. Thus, it can be postulated that the presence of MMP-9 locally influences the periodontal status and can be considered as a promising biomarker for the disease.

Conducting the study with a bigger sample size, an extended follow up period with a positive control and multiple applications of the MG gel are needed for further validation of its efficacy as a LDD agent. Evaluation and comparison among variants of MG LDD in the form of chip, micro & nanoparticle systems, electro spun fibres etc. can shed more light on Mangosteen's potential as a targeted therapeutic modality against MMP-9, in the management of chronic periodontitis.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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ORIGINAL ARTICLE / ARAŞTIRMA MAKALESİ

Interprofessional Approaches in Research Planning Training: Multidisciplinary Perspective in Oral and Dental Health

Araştırma Planlama Eğitiminde Meslekleraras Yaklaşımlar: Ağız ve Diş Sağlığına Multidisipliner Yaklaşım

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ABSTRACT

Objectives: This study evaluates the effectiveness of an interdisciplinary educational intervention in improving the perceptions of interdisciplinary education, research competency, and research anxiety among postgraduate students in various health disciplines.

Materials and Methods: This prospective cohort study was conducted at Marmara University during November 2023. A two-day training program, "Multidisciplinary Approach to Oral and Dental Health" was conducted, involving educators and postgraduate students from dentistry, speech and language therapy, nutrition and dietetics. The program consisted of four modules, combining didactic training and workshops. Data were collected pre-post-intervention using validated scales: Interdisciplinary Education Perception Scale (IEPS), Research Competency Scale (RCS), and Research Anxiety Scale (RAS). Scores were analyzed using a t-test for pre-test and post-test calculations. In the findings, a p-value of <0.05 was considered statistically significant.

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Results: Initially, 30 participants were registered for the study, but the final analysis was conducted on 26 participants. The statistical analysis indicated significant improvements in the post-intervention scores for both the IEPS and the RCS. The average score for IEPS increased from 86.65 before the intervention to 91.04 after (p=.028), and for RCS, it rose from 25.92 to 28.08 (p=.010). However, RAS showed no significant change, with scores averaging 30.85 before and 30.65 after the intervention (p=.710).

Conclusions: The intervention effectively enhanced interdisciplinary education perception and research competency among participants, emphasizing the potential of short-term, structured multidisciplinary programs in postgraduate dental education.

Keywords: Interprofessional relations, dentistry, speech therapy, dietetics, research

ÖZ

Amaç: Bu çalışma, çeşitli sağlık disiplinlerinde lisansüstü eğitim alan öğrencilerin disiplinlerarası eğitim algılarını, araştırma yetkinliklerini ve araştırma kaygılarını iyileştirmede disiplinlerarası bir eğitim müdahalesinin etkinliğini değerlendirmektedir.

Gereç ve Yöntemler: Bu prospektif kohort çalışma, 2023 Kasım ayında Marmara Üniversitesi Diş Hekimliği Fakültesi'nde gerçekleştirilmiştir. Diş hekimliği, dil ve konuşma terapisi, beslenme ve diyetetik alanlarından eğitimcilerin ve lisansüstü öğrencilerin katıldığı "Ağız ve Diş Sağlığına Multidisipliner Yaklaşım" başlıklı iki günlük bir eğitim programı yürütülmüştür. Program didaktik eğitim ve atölye çalışmalarını birleştiren dört modülden oluşmuştur. Veriler müdahale öncesi ve sonrasında onaylanmış ölçekler kullanılarak toplanmıştır: Disiplinlerarası Eğitim Algısı Ölçeği (IEPS), Araştırma Yetkinliği Ölçeği (RCS) ve Araştırma Kaygısı Ölçeği (RAS). Toplanan skorlar pre-test post-test kıyaslamaları t-test kullanılarak analiz edilmiştir. İstatistiksel anlamlılık değeri olarak p<0.05 kabul edilmiştir.

Bulgular: Başlangıçta çalışma için 30 katılımcı kaydedilmiş, ancak nihai analiz 26 katılımcı üzerinde gerçekleştirilmiştir. İstatistiksel analiz, hem IEPS hem de RCS için müdahale sonrası puanlarda önemli gelişmeler olduğunu göstermiştir. Özellikle, IEPS için ortalama puan müdahale öncesinde 86.65 iken müdahale sonrasında 91.04'e (p =.028) ve RCS için 25.92'dan 28.08'ye (p

=.010) yükselmiştir. Bununla birlikte, RAS, müdahale öncesinde 30.85 ve müdahale sonrasında 30.65 puan ortalamasıyla önemli bir değişiklik göstermemiştir (p = .710).

Sonuç: Müdahale, katılımcılar arasında disiplinler arası eğitim algısını ve araştırma yetkinliğini etkili bir şekilde geliştirmiş ve mezuniyet sonrası diş hekimliği eğitiminde kısa süreli, yapılandırılmış multidisipliner programların potansiyelini vurgulamıştır.

Anahtar Kelimeler: Disiplinlerarası iletişim, diş hekimliği, konuşma terapisi, dietetik, araştırma

INTRODUCTION

The World Health Organization's (WHO) definition of oral health encompasses the basic functions and psychosocial effects of oral structure, which can change throughout life and are closely related to overall health (WHO, 2022). The Food and Drug Administration's (FDA) definition, on the other hand, links oral health to the presence or absence of diseases, comfort in social interactions due to teeth, and physiological functions like chewing and speaking (Glick et al., 2016). In light of these definitions, while the traditional roles of dentists have focused on assessing and managing oral cavity diseases, education and continuous professional development programs have not sufficiently emphasized other important aspects like physiological functions and psychosocial states (Glick et al., 2016). Considering the impact of oral health on an individual's overall health status, psychological well-being, and essential functions like speaking and eating, it becomes evident that health and social care sectors need to adopt an interdisciplinary educational approach that includes non-dental clinicians in oral health (Fisher et al., 2023). This approach is essential as no single discipline possesses all the knowledge required for patient care (Matziou et al., 2014), highlighting the necessity for integrated and person-centered oral health services that include non-dentist members as essential components of the healthcare team (Zaher et al., 2022).

Despite numerous calls to action, limited success has been reported in integrating oral health and its connection to general health into the education of healthcare professionals and in primary care practices, as well as in establishing collaborations (Goodell et al., 2019). Recent literature has reported on the outcomes of interprofessional education (IPE) initiatives, involving students from various health fields including dentistry, medicine, nursing, pharmacy, optometry, occupational therapy, physiotherapy, social work, and dental hygiene (Coan et al., 2019; Hartnett et al., 2019; Janotha et al., 2019). However, is a notable scarcity of studies conducted in conjunction with disciplines directly related to oral health, such as speech and language therapy or nutrition and dietetics. Increasing such studies could benefit health workers by fostering mutual recognition of roles and expertise, building trust and validation, and enhancing participants' willingness to contribute to the team (Stadick, 2020).

Alongside education and patient care, intraprofessional collaborations, long considered a core value in dentistry, are also crucial for research and innovation (Feinberg et al., 2015; Polverini, 2013). In recent years a growing recognition of the importance of interdisciplinary and transdisciplinary team-based collaborative research has been seen (Bennett & Gadlin, 2012; Buscemi et al., 2012; Wuchty et al., 2007). Larger teams, intentionally assembled to tackle a common hypothesis or objective across various research and educational fields, can help overcome these concerns (Waite et al., 2023). Such teams not only collaborate effectively but also integrate knowledge from different perspectives (Pelfrey et al., 2021), enhancing their capacity to address solution-focused research questions and overcome challenges (Conn et al., 2019; Thompson et al., 2021).

Our study aims to address a gap in the literature by evaluating the impact of a training program, which includes didactic education and workshops, involving educators from dentistry, speech and language therapy, and nutrition and dietetics, as well as postgraduate students from these disciplines. The program's objective is to assess its effect on participants' perception of IPE, their perceived research competence, and their levels of research anxiety.

MATERIALS AND METHODS

Ethics approval

Ethical approval for the study was obtained from the Non-Interventional Clinical Studies Ethics Committee of Marmara University, Faculty of Health Sciences (IRB Approval number: 26.10.2023/103).

Study design

In this study, a single-arm pre-post intervention quantitative research design was conducted to evaluate the effectiveness of the educational intervention in enhancing

interprofessional discipline perception and research anxiety among postgraduate student participants.

This prospective cohort study was conducted at Marmara University during November 2023. A two-day training program titled "Multidisciplinary Approach to Oral and Dental Health" was organized for this study. Educators from three disciplines (dentistry, speech and language therapy, nutrition and dietetics) were selected for the program. The criterion for educator selection was having previously conducted scientific research with the event coordinator (F.B.), who then invited them to participate as trainers. The program was promoted through the deanship of the faculties or professional organizations' social media accounts and WhatsApp groups, using educators from all three disciplines. The training was open to postgraduate students who had reached the thesis stage but had not yet determined their thesis topics.

While implementing targeted team training, learning objectives and inclusive goals were clearly communicated to participants beforehand. These objectives were succinctly set as enabling postgraduate students to plan multidisciplinary work. Participants were encouraged to think beyond their professional boundaries and engage in discussions that included other disciplines. The event comprised a total of four modules, each incorporating didactic trainings and workshops relevant to all three disciplines: 1=Research Planning, 2=Orthognathic Surgery, 3=Cleft Lip and Palate, 4=Workshop Activities. The Research Planning module covered identifying research questions, literature review, basic statistics, and ethical considerations. The Orthognathic Surgery and Cleft Lip and Palate modules included experiences and case studies from the educators of oral and maxillofacial surgery, orthodontics, speech and language therapy, nutrition and dietetics, and gastronomy. Practical applications were conducted for the final component of the course. During the workshop component, students jointly discussed research scenarios that could encompass all three disciplines. These scenarios were designed to facilitate: 1=Learning multidisciplinary work as health professionals, 2=Gaining fundamental literature search skills, and 3=Recognizing the need for interdisciplinary communication and teamwork in conducting research.

Sample size

Although the optimal size for multidisciplinary student groups remains undefined (Keijsers et al., 2016), it is recommended that each group should have no more than 10 members (Thompson et al., 2020). Consequently, a limit of 10 participants per discipline was set. For the workshops, groups of six were formed, comprising two individuals from each discipline, resulting in five groups in total.

In this study, a structured randomization method was used to evenly distribute participants across groups based on their disciplines. Initially, participants were listed in Microsoft Excel according to their respective disciplines, and a random number between 0 and 1 was assigned to each using Excel's "RAND( )" function. These numbers were used to randomly order participants within each discipline. Subsequently, groups containing an equal number of participants from each discipline were formed. This was done by allocating the first two participants from each ordered list to the first group, the next two to the second group, and so on until all groups were formed. This method ensured an equal representation of each discipline in every group.

Outcome variables

Before the event commenced and after its conclusion, data were collected from postgraduate students using validated and adapted instruments: the Interdisciplinary Education Perception Scale (IEPS), the Research Competency Scale (RCS), and the Research Anxiety Scale (RAS). These tools were employed to assess changes in participants' perceptions of interdisciplinary education, their research competencies, and levels of research anxieIEPS, developed in 1990(Luecht et al., 1990) and validated in Turkish in 2019(Terzioğlu et al., 2019). The in-class reliability coefficient of the IEPS was found to be r=0.920 and the internal consistency coefficient of Cronbach's alpha was α=0.926 and the scale was found to be highly reliable. It has 17-items, 3-subdimensions tool used to assess health care students' perceptions of IPE. The sub-dimensions are Competence and Autonomy (CA) which is measured with 1-3-5-7th items its sub-scale Cronbach's alpha value is α=0,823. Perceived Need for Collaboration (PNC) which is measured with 2-6-8th items and Cronbach's alpha value is 0.563. The Perception of Actual Cooperation (PAC) which is measured with the rest and alpha value is α=0.543. It's a 6-point Likert scale ranging from 1=strongly disagree to 6=strongly agree, with possible scores between 17-102. High total score and high sub-dimension scores indicate that the perception of interdisciplinary education is positive (Terzioğlu et al., 2019). To determine the research competencies of the participants, Büyüköztürk's one-factor 7-item RCS

was used.(Büyüköztürk, 1999) The items in the scale can be answered with "not at all", "a little", "moderately", "quite" and "completely" options. The highest score that can be obtained from this scale is 35 and the lowest score is 7. A high score on the scale indicates high anxiety and a low score indicates low anxiety. In the original form of the scale, Cronbach's alpha reliability coefficient was calculated as α=0.89. The RAS was developed by Büyüköztürk and it aims to determine participants' attitudes towards scientific research with 12 items under a single factor (Büyüköztürk, 1997). The scale has a five-point Likert scale ("strongly disagree", "disagree", "undecided", "agree", "agree" and "strongly agree"), with 7 items reflecting anxiety and 5 items not reflecting anxiety. The statements reflecting the anxiety state were coded as 5 for "completely agree" and 1 for "strongly disagree". ". As a result of this coding, there is a linear relationship between the scores obtained from the scale and the anxiety level and the lowest anxiety score is 12 and the highest anxiety score is 60. It's Cronbach's alpha value α=0.87

Statistics

For the age variable, mean and standard deviation values were calculated. Frequency values were computed for categorical variables such as gender, discipline, previous multidisciplinary training, research project experience, and the university. The survey values were analyzed using a t-test for pre-test and post-test calculations. In the findings, a p-value of <0.05 was considered statistically significant. Graphpad software was used for statistical analyses.

RESULTS

The study initially included 30 registered participants and conducted with 26 graduate students who participated in the "Multidisciplinary Approach to Oral and Dental Health" training at Marmara University Faculty of Dentistry. Two participants did not come to the event despite registering, and 2 participants were excluded from the study and not included in the final analysis because they did not attend the workshops on the last day and did not complete the post-test questionnaires. The study sample included young adults with a mean age of 25.12 ± 2.10 years ranging from 22 to 32 years. The gender distribution was heavily skewed towards females (n = 23) as compared to males (n = 3). Participants came from three academic disciplines, with the majority from nutrition and dietetics (n = 10) and dentistry (n = 10), followed by speech and language therapy (n = 6). Regarding previous education, 22 participants reported no prior education in the multidisciplinary area, while 4 had some previous education. In terms of project experience, 15 participants had no prior experience, while 8 had some experience. The participants were primarily from Marmara University (n = 15), with others coming from various universities. including Uskudar University, Istanbul Medipol University, Istinye University, Istanbul Aydin University, Atlas University, and Istanbul University (Table 1).

Table 1. Demographic and Academic Characteristics of Study Participants

Parametres	Mean (SD)	n
Age	25.12 (2.10)	
Gender		
Female		23
Male		3
Disciplines		
Dentist		10
Speech and Language Therapist		6
Dietitian		10
Previous education		
Yes		4
No		22
Previous project		
Yes		9
No		17
Educators		
Dentist		8
Speech and Language Therapist		2
Dietitian		5

Statistical analysis revealed significant differences between pre – and post-intervention measurements in two of the three scale. The IEPS-pre measurement showed significantly lower values (86.65 ± 12.20) compared to the IEPS-post measurement (91.04 ± 12.40), with a t-test yielding a p-value of .028 (Figure 1). The IEPS-pre CA measurement showed higher values (20.27 ± 3.58) compared to the post measurement (21.12 ± 3.41), with a Wilcoxon test yielding a p-value of .099. The IEPS-pre PNC subscale measurement showed lower values (16.65 ± 2.04) compared to the post measurement (17.27 ± 1.12), with a Wilcoxon test yielding a p-value of .368. The IEPS-pre PAC measurement showed significantly lower values (49.85 ± 8.02) compared to the post measurement (53.54 ± 8.44), with a Wilcoxon test yielding a p-value of .004 (Figure 2).

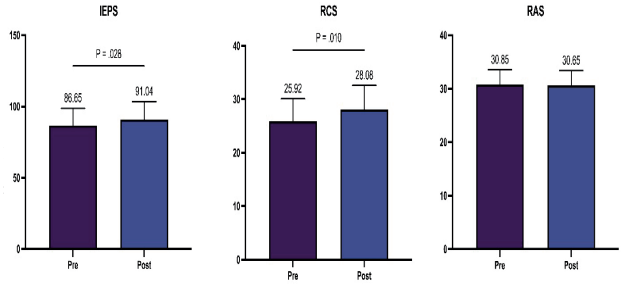

Figure 1: Bar Graph Comparing Mean Scores of Interdisciplinary Education Perception Scale (IEPS), Research Competency Scale (RCS), and Research Anxiety Scale (RAS) in Pre – and Post-Intervention Measurements.

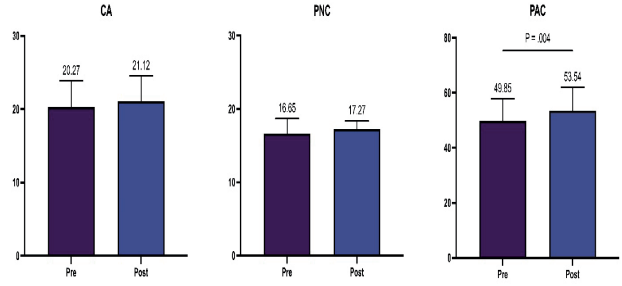

Figure 2: Competence and Autonomy (CA), Perceived Need for Collaboration (PNC), Perception of Actual Collaboration (PAC) subscale measurements of Interdisciplinary Education Perception Scale (IEPS).

DISCUSSION

Interdisciplinary Education Perception Scale(IEPS) and Research Competency Scale(RCS) showed significant different according to our results while Research Anxiety Scale(RAS) did not . And one of the subsclae of IEPS, The Perception of Actual Cooperation(PAC) showed a statistically significant increase. This meant that when postgraduate students work and were put into action together, their attitude to working interprofessionally is improving. Our results indicate that the course organized for the educational intervention positively impacted the perception of interdisciplinary education, research competency among postgraduate health students from three disciplines.

Interprofessional experiences can be designed through various approaches, including didactic sessions (Aleshire et al., 2019; Baker & Durham, 2013) clinical experiences (Hartnett et al., 2019; Janotha et al., 2019) a combination of didactic and clinical settings (Haber et al., 2017; Niranjan et al., 2019), simulations, or workshop activities (Christian et al., 2020; Haber et al., 2021). In our study, we combined didactic and workshop activities with two additional disciplines that might be challenging to include in a comprehensive curriculum. We believe interventions like ours can be beneficial, offering relatively cost-effective and efficient methods to enhance IPE.

Within the scope of interprofessional research activities, peer teaching provides a form of student interaction facilitated in formal professional contexts. In this context, learning becomes a socialization process where students have the opportunity to share their experiences from their own disciplines with students from other disciplines. This exchange not only enriches the learning environment but also fosters a broader understanding of different professional perspectives and approaches (Burgess et al., 2017; Burgess et al., 2019; van Diggele et al., 2020).

In the literature, there are IEPS studies in which attitudes towards interdisciplinary collaboration were questioned and the scores were found to be promisingly high (Büyüköztürk, 1997; Tosunöz et al., 2021; Williams & Webb, 2013). The IEPS is a multidimensional analysis. The sum of the scores obtained from the subscales and the scale are used together to interpret the perception of interdisciplinary education. In the literature, high values in these scores indicate an increased perception of interdisciplinary education and readiness for collaboration. According to the WHO definition, IPE is defined as two or more professionals receiving and learning information from each other and learning together (WHO, 2010). Similarly, in our study, total pre-post-IEPS scores were found high: 86.65 ± 12.20 and 91.04 ± 12.40, respectively. In the light of these data, we can interpret that the students in our study may be open to the WHO recommendations (2010) on interdisciplinary communication and cooperation for health professionals.

The post-test scores of IEPS subscales, CA and PNC were found to be high. These results showed that interdisciplinary collaboration was a desirable attitude among the participants in our study. In the PAC, the statistically significant increase in post-test scores indicates that the training improved students' perception of actual collaboration. In a similar study conducted with occupational therapy students, the greatest discrepancies in the responses of first-year students who were not in clinical rotation studies were found in the 9th item of the "perception of actual cooperation" subscale. Similar to this study, the increase we saw in our study supports the idea that interdisciplinary trainings

and simulations are the main lever of interdisciplinary collaborative approach (San Martín-Rodríguez et al., 2005). This approach is also an important requirement of modern healthcare (Bullard et al., 2019).

Similar to IEPS scores, RCS scores which shows researchers increased after the activity. Accurately assessing the level of RCS scores provides greater awareness of their research strengths and areas for improvement, and enables them to plan and implement strategies to further develop areas of research competence (Swank & Lambie, 2016). This also supports Picciotto's (1997) assertion about researcher competence: "In order for students to acquire research skills, they should be drawn into the research process and given the opportunity to participate in research activities themselves." (Picciotto, M., 1997).

Graduate students are required to complete one or more research studies during their continuing education. At the stage of designing these studies, methodological skills may be lacking because the training provided is often inadequate so students may experience anxiety when developing a research proposal. This anxiety can be multidimensional. After our activity, there was no significant change in anxiety scores of RAS. We think that the anxiety scale we used (Büyüköztürk, 1997) evaluates the researcher's attitude towards the act of "research" more and do not have factors that distinguish sub-anxiety topics. In conclusion, our study group consisted of volunteer research assistants with a high desire for multidisciplinary research. In order to evaluate multidisciplinary research anxiety, multifaceted scales such as Research Anxiety Rating Scale (RARS), which includes psychometric properties and consists of sub-headings such as library, writing, statistics, field research, research course, research utility and competence anxiety, are required (Mudra & Sastria, 2023).

The study observed that students from various health disciplines collaborated and exchanged knowledge, thereby strengthening their professional identities and enhancing teamwork. In the context of value-based healthcare systems, this development is expected to lead to better care outcomes in the long term (Sibbald et al., 2021). The participants' engagement in ice-breaking social activities before the main intervention further strengthened this collaboration (Shroque Zaher et al., 2022).

For future studies, we recommend adapting the current model to include other health professionals involved in designing joint research projects and patient care. This approach could continually and consciously encourage students to reflect on their professional and interprofessional identity development, but it would require investment in both student time and faculty development (Miller et al., 2023). Additionally, we advise allocating an extended time frame for planning research studies and propose longer follow-up studies to better understand the impacts of the conducted research. To ensure validity in different populations and settings, the designed measures should be tested with various research partners and stakeholders. This study can also be replicated with undergraduate students.

This study's limitations are as follows: First, the event only lasted two days, which limits our understanding of the long-term outcomes as no follow-up study was conducted. Second, the study focused on postgraduate students, highlighting the importance of structured learning opportunities for better preparation in interprofessional practices for this group. Third, the lack of a comparison group in the study limits the evaluation of the results; however, the consistency of findings across different disciplines and the significant changes observed between pre – and post-tests suggest the potential value of the experience. Fourth, the study is based on subjective evaluations, which could increase the risk of bias. Lastly, there is no definitive evidence on the replicability of the study and whether similar results can be achieved in different geographical locations and educational systems.

CONCLUSIONS

In conclusion, this easily replicable teaching method provides a straightforward tool to reinforce the importance of collaborative work in conducting multidisciplinary studies related to oral health. Particularly, this intervention offers a novel experience for postgraduate students across various disciplines, enhancing their readiness for interdisciplinary learning and collaboration. We encourage the adaptation of such interventions to increase students' engagement in interprofessional education and collaborative practices. As we move towards a more collaborative care environment, dental schools should seize opportunities to improve patient health while reducing costs and maximizing resources.

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ORIGINAL ARTICLE / ARAŞTIRMA MAKALESİ

Assessment of the Remineralization Effect of Hemp-Containing Toothpaste

Kenevir İçeren Diş Macununun Remineralizasyon Etkisinin Değerlendirilmesi

Elif ALKAN[1], Dilek TAĞTEKİN[2], Nesrin KORKMAZ[3], Funda YANIKOĞLU[4]

ABSTRACT

Objective: The study aimed to evaluate the remineralizing effect of hemp on initial enamel caries lesions.

Materials and methods: Initial caries lesions were created on twenty-eight intact enamel samples with demineralization solution (pH=4.5) in a shaking incubator for 72 hours at 37°C. Samples were divided into four groups (n=7) ((1) experimental toothpaste containing hemp (H) (SPC Kozmetik), (2) hemp oil (HO), (3) Sensodyne Repair and Protection toothpaste (S) (GSK), (4) Control (no treatment)). The agents were applied using a pH-cycle model for seven days. All agents were kept on the surface of samples for 2 minutes and then applied for 1 minute using an electric toothbrush (Oral-B Test Drive (Genius)). Samples were evaluated with microhardness device, a fluorescence-assisted imaging device (FluoreCam), laser fluorescence device (DIAGNOdent Pen). Data were statistically analyzed with ANOVA and Kruskal Wallis H tests ($p<0.05$).

Results: According to fluorescence and microhardness evaluations, the remineralization effect was similar in all treatment groups, except for hemp oil ($p<0.01$). Groups S (288.86±9.63), and H (284.86±10.41) showed significantly higher microhardness values compared to HO (238.57±10.89) ($p<0.001$). According to FluoreCam data, lesion size decreased in S (-1.83) and H (-1.07), while an increase was observed in HO (0.75). According to DIAGNOdent Pen data, the mineral increase in S (-8.42±1.18) and H (-8.29±1.03) was significantly higher than in HO (-3.57±2.06) ($p<0.001$).

Conclusions: Herbal toothpaste containing hemp (H) demonstrated a similar remineralization effect to Fluor and NovaMin-containing toothpaste (S).

Keywords: Initial Caries Lesion, Herbal Toothpaste, Demineralization, Hemp, Remineralization.

ÖZ

Amaç: Bu çalışma, kenevirin başlangıç mine çürük lezyonlarına remineralize edici etkisini değerlendirmeyi amaçlamıştır.

Gereç ve Yöntemler: Yirmi sekiz sağlam mine numunesi üzerinde demineralizasyon solüsyonu (pH=4.5) kullanılarak çalkalamalı inkübatörde 37°C'de 72 saat süreyle başlangıç çürük lezyonları oluşturulmuştur. Mine örnekleri dört gruba ayrılmıştır (n=7) ((1) kenevir içeren deneysel diş macunu (H) (SPC Kozmetik), (2) kenevir yağı (HO), (3) Sensodyne Onarım ve Koruma diş macunu (S) (GSK)), (4) Kontrol (tedavi yok)). Ajanlar yedi gün boyunca pH döngüsü modeli kullanılarak uygulanmıştır. Remineralizasyon ajanları diş yüzeyinde 2 dakika bekletildikten sonra elektrikli diş fırçası (Oral-B Test Drive (Genius)) ile 1 dakika süreyle uygulanmıştır. Örnekler mikrosertlik cihazı, floresans destekli görüntüleme cihazı (FluoreCam), lazer floresans cihazı (DIAGNOdent Pen) ile değerlendirilmiştir Veriler ANOVA ve Kruskal Wallis H testleri ile istatistiksel olarak analiz edilmiştir ($p<0,05$).

Bulgular: Floresans ve mikrosertlik sonuçlarına göre kenevir yağı hariç tüm tedavi gruplarında benzer remineralizasyon etkisi görülmüştür ($p<0.01$). Grup S (288,86±9,63) ve H (284,86±10,41), HO'ya (238,57±10,89) kıyasla anlamlı derecede yüksek mikrosertlik değerleri göstermiştir ($p<0,001$). FluoreCam verilerine göre S (-1,83) ve H'de (-1,07) lezyon boyutunda azalma görülürken, HO'da (0,75) artış gözlenmiştir. DIAGNOdent Pen verilerine göre S (-8,42±1,18) ve H'deki (-8,29±1,03) mineral artışı HO'ya (-3,57±2,06) göre anlamlı derecede yüksekti ($p<0,001$).

Sonuç: Kenevir içeren bitkisel diş macunu (H), flor ve NovaMin içeren diş macununa (S) benzer remineralizasyon etkisi göstermiştir.

Anahtar Kelimeler: Başlangıç çürük lezyonu, bitkisel diş macunu, demineralizasyon, kenevir, remineralizasyon.

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INTRODUCTION

Dental caries lesions are one of the most common diseases that may lead to tooth loss if it is not treated. The current dentistry aims to improve the aesthetic and function of the tooth by remineralization process and preventing caries lesions (Nagarathana et al., 2015). Demineralization occurs when organic acids produced by acidogenic bacteria in dental plaque dissolve mineral ions from dental hard tissues. This process of returning mineral ions to tooth tissue is called remineralization. There is a continuous

demineralization-remineralization cycle in the oral cavity. Demineralization is a reversible process; therefore, initial enamel caries can be remineralized with plaque control, regulation of diet, and application of antibacterial agents (Guerrieri et al., 2012). Remineralization is a conservative method with short-term, economical, and easy application. Nowadays, herbal extracts have gained special attention as antimicrobial agents by preventing and treating caries due to being not chemical and synthetic (Poureslami, 2012). Some natural plant extracts may likely prevent demineralization and maintain remineralization of the tooth tissue (Philip, 2019).

NovaMin, a commercial form of bioactive glass, rapidly releases calcium, sodium, and phosphorus ions which are essential for remineralization into the saliva, when it is present in the saliva and the pH in the oral cavity increases. The released ions attach to the tooth surface and remineralize the tooth surface forming hydroxycarbonate apatite. (Du et al., 2004).

Hemp (*Cannabis sativa L.*) has been used as many sources, including fiber, food, and medicinal products (Bonini et al., 2018). Especially the seeds of hemp have high oil content (Truta et al., 2009). Hemp containing products may be more effective in reducing the number of bacterial colonies in dental plaque compared to some existing oral hygiene products and may be a safer alternative to conventional oral hygiene products due to antimicrobial resistance (Stahl & Vasudevan, 2020). Previous research in dentistry on hemp oil is limited and the effect of hemp oil on dental hard tissues is not fully discovered.

This study aimed to investigate the effect of hemp-containing herbal experimental toothpaste on remineralization of initial caries lesions. The hypothesis of the study was that herbal toothpaste containing hemp has a similar remineralization effect compared to commercial toothpaste containing Fluor and NovaMin.

MATERIALS AND METHODS

Ethical approval of the study was obtained from the Clinical Research Ethics Committee of Marmara University Faculty of Dentistry (Date: 03.09.2020 Decision no: 2020/59).

Sample preparation

The number of samples was evaluated using G*power version 3.1.9.7 (α=0.05, 1-β=0.80) and the sample size was determined as four samples for each group based on previous study (Şivet et al., 2023). Twenty-eight enamel samples (n=7) were obtained by cutting the middle buccal surfaces of the extracted teeth using a handpiece (NSK EX-6, Japan) and diamond disc (Sigmadent, Turkey) under water cooling. Enamel samples were placed in acrylic molds with the dentin surface in acrylic and the enamel surface exposed. The surfaces of the samples were sanded under water for 5 minutes with 1200 silicon carbide sanding discs and then polished for 2 minutes with polishing pastes (CleanPolish (RDA:43.8) and SuperPolish (RDA:9.8), Kerr, Switzerland). After that, the samples were washed with distilled water and kept in a refrigerator at +4 □ in a container with distilled water until the measurements were made.

Experimental Groups

Study groups were divided into four groups (n=7) for enamel samples. The agents applied on the enamel samples and their contents are presented in Table 1. Hemp oil was obtained from hemp seeds by cold pressing at Yozgat Bozok University Hemp Institute. Hemp-containing experimental toothpaste was manufactured by SPC Kozmetik using hemp seed oil and aqueous hemp extract obtained from hemp leaves along with other ingredients showed in Table 1. In each group, remineralization agents were applied for a total of 3 minutes (Jo et al., 2014). They were kept on the tooth surface for 2 minutes and then applied for 1 minute with a rechargeable toothbrush (Oral-B Test Drive (Genius) rechargeable toothbrush, Germany). Hemp oil was applied on the enamel surface using a microbrush. In control group no treatment was applied on enamel surfaces. The samples were subjected remineralization-demineralization cycle for seven days with 6 hours of demineralization and 18 hours of remineralization each day (Carvalho et al., 2014). After each demineralization challenge samples were rinsed with distiled water and then placed in remineralization solution. All samples were evaluated with DIAGNOdent Pen, FluoreCam, and microhardness devices at baseline, after demineralization, and after remineralization stages as described below.

Table 1. Agents applied on the enamel samples and their contents.

Remineralization Agent	Content	Manufacturer
Hemp-containing experimental toothpaste (H) (%5 Hemp Oil and %5 Hemp Extract)	5% Hemp oil, 5% Hemp Extract, Mint oil, Mentol, Polisorbat 20, Xanthan Gum, Aqua, Glyserin, Sorbitol, Phenylpropanol, Capryly Glycol Stevia (Rebaudioside A), Hydrated Silica	SPC Kozmetik, Turkey
Hemp Oil (HO)	Hemp Seed Oil	Yozgat Bozok University, Turkey
Sensodyne Repair and Protect (NovaMin) (S)	Gliserin, Peg-8, Hydrated Silica, Calsium Sodium Phosphosilicat (NovaMin), Cocamidopropil Betain, Sodium Metyl Cocoyl Taurate, Aroma, Titanium Dioksit, Carbomer, Silica, Sodium Sakkarin, Sodium Flourid (1450 Ppm), Limonene.	Glaxosmithkline (Gsk), Ireland

DIAGNOdent Pen Analysis

The DIAGNOdent Pen (Kavo, Germany) was used to evaluate the surface changes of the enamel samples at baseline, after demineralization, and after remineralization stages. As recommended by the manufacturer, the instrument was calibrated prior to each measurement using standard ceramic. A recommended B-type probe was used for flat surface detection. The device was held vertically on the samples and measurements were made from 3 different points in each sample. The mean value was then calculated and recorded.

FluoreCam Analysis

Enamel samples were analyzed with a FluoreCam device (Daraza Corporate Headquarters, Indiana, USA) at baseline, after demineralization, and after remineralization stages. Before analysis, each sample was removed from the moist container and dried with a thin paper towel. Images were taken from the surfaces using the intraoral appliance of the FluoreCam system. The FluoreCam system can compare the intact enamel surface and demineralized-remineralized areas in terms of size and fluorescence values with images taken at different times. Analyzes were recorded in the FluoreCam Software program.

Surface Microhardness Analysis

The samples were measured using a Microhardness tester (Shimadzu Corporation, Japan) at baseline, after demineralization, and after remineralization stages. Measurements were made from 3 different areas of the lesion area by applying 200 g of force for 15 seconds on the flat surface of the samples. Then, the average of these three measurements was taken and the average sample value was recorded.

Formation of Artificial Initial Caries on Enamel Samples

Demineralization solution (2.0 mmol/lt $Ca(NO3)_2.H_2O$, 2.0 mmol/lt $NaH_2PO^4H_2O$, 0.04 μg F/ml (NaF) in 75 mmol/lt acetate buffer) (pH 4.7) was prepared in the Biochemistry Laboratory of the Marmara University Faculty of Dentistry (de Mello Vieira et al., 2005). Initial enamel lesions were formed on the samples by shaking 60 rpm at 37°C in a shaking incubator (ZWYR-240, LABWIT, Australia) for 72 hours. The solution renewed daily. The samples were removed from the demineralization solution after 72 hours, washed with distilled water, and kept in containers with distilled water in the refrigerator at +4 °C for measurements after demineralization.

Statistical analysis

Obtained data were analyzed with IBM SPSS V23. The conformity to the normal distribution was examined using the Shapiro-Wilk test. One-way Analysis of Variance (ANOVA) was used to compare normally distributed data according to groups, and multiple comparisons were examined with Duncan, Tamhane and Tukey HSD tests. The Kruskal Wallis H test was used to compare the data that were not normally distributed according to the groups, and multiple comparisons were examined with the Dunn test. In order to analyze within-group comparisons, Repetitive Analysis of Variance was used for data suitable for normal distribution, and Friedman Test for data not suitable for normal distribution. Analysis results are presented as mean ± standard deviation for quantitative data. Significance level was taken as $p<0.05$.

RESULTS

DIAGNOdent Pen Evaluation

There was no significant difference between the groups at baseline (T0) and after demineralization (T1) stages according to the data obtained from the DIAGNOdent Pen device. After remineralization process (T2), laser fluorescence values decreased significantly in toothpaste groups (H and S), while no significant decrease was observed in the hemp oil applied group and the control group. Toothpaste applied test groups (H and S) were found to have similar remineralizing effect according to DIAGNOdent Pen data (Table 2).

Table 2. The data obtained from DIAGNOdent Pen at baseline, after demineralization and after remineralization stages (mean ± standart deviation).

	Baseline (T0)	Demineralization (T1)	Remineralization (T2)	T1-T2	P**
Hemp-containing experimental toothpaste (H)	6.86 ± 1.46A	14.29 ± 1.03B	6 ± 0.53Aa	8.29 ± 1.03a	<0.01
Hemp oil (HO)	6.57 ± 1.29A	16 ± 1.2B	12.43 ± 2.77Cb	3.57 ± 2.06b	<0.01
Sensodyne Repair and Protect (NovaMin) (S)	5.86 ± 2.1A	14.43 ± 0.9B	6 ± 0.93Aa	8.43 ± 1.18a	<0.01
Control	5.57 ± 1.4A	15.14 ± 1.46B	14.57 ± 1.59Bc	0.57 ± 0.49b	<0.01
P*	0.686	0.114	<0.01	<0.01	

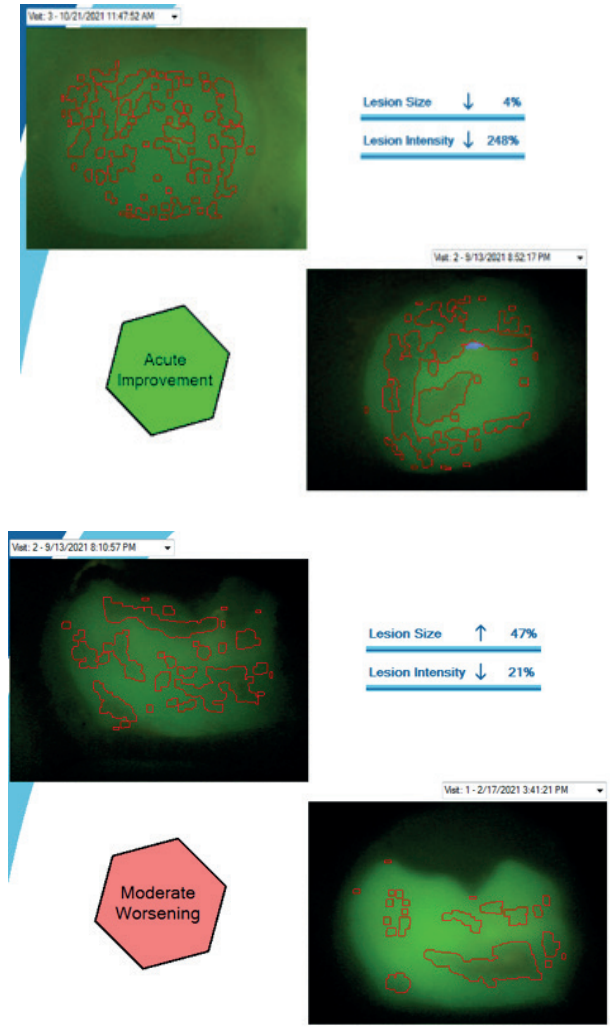
FluoreCam Evaluation

According to FluoreCam data, after remineralization stage (T2-T1), lesion size decreased significantly in both toothpaste applied groups (H and S) which had statistically similar results. There was a slight increase in lesion size values in the hemp oil and control groups. The increase in lesion size was bigger in the control group (Table 3). According to the FluoreCam System, toothpaste applied groups (H and S) had improvement (Fig. 1a and 1c), while Hemp oil applied group and the control group demonstrated worsening (Fig.1b and 1d).

Table 3. The lesion size data obtained from FluoreCam System at baseline, after demineralization and after remineralization stages (mean ± standart deviation).

	Baseline (T0)	Demineralization (T1)	Remineralization (T2)	T2-T1	P**
Hemp-containing experimental toothpaste (H)	5.18 ± 0.78	6.8 ± 1.31	5.13 ± 0.32	– 1.67 ± 1.07a	<0.01
Hemp oil (HO)	2.25 ± 1.55	3.51 ± 1.74	4.07 ± 2.2	0.55 ± 0.75b	<0.01
Sensodyne Repair and Protect (NovaMin) (S)	5.26 ± 0.45	6.77 ± 1.03	4.94 ± 0.54	– 1.83 ± 1.07a	<0.01
Control	3.13 ± 1.06	5.18 ± 2.01	6.2 ± 1.24	1.02 ± 1.34b	<0.01
P*	<0.01	<0.01	0.051	<0.01	

**Kruskal Wallis Test; **Friedman test; same letter codes have no significant difference*



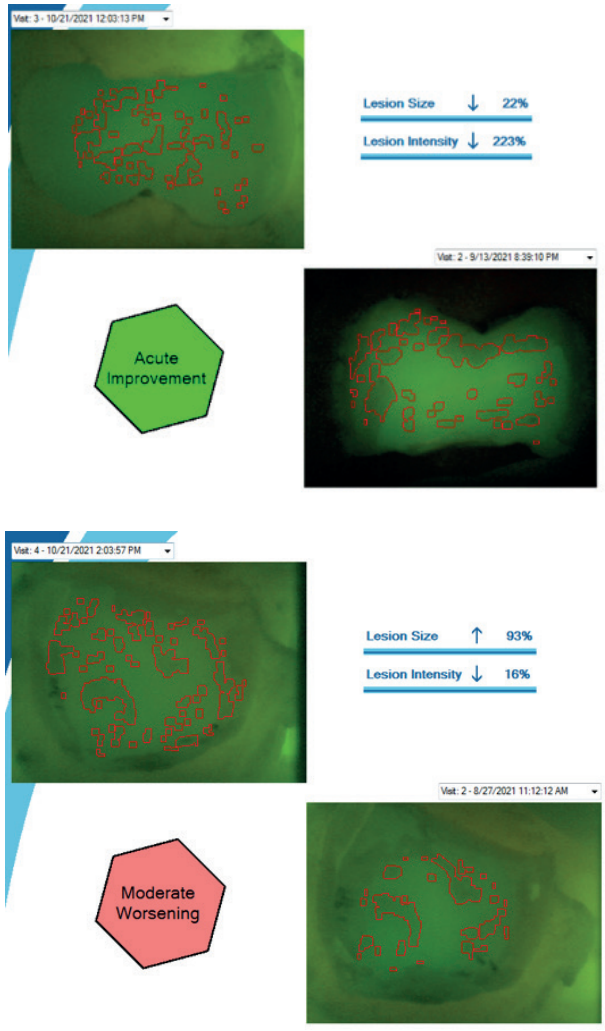


Figure 1: a) FluoreCam image of the sample applied experimental herbal toothpaste containing hemp. b) FluoreCam image of the sample applied hemp oil. c) FluoreCam image of the sample applied toothpaste containing Fluor and NovaMin. d) FluoreCam image of the sample from the control group.

Microhardess Evaluation

There was no statistically significant difference between all test groups at the baseline (T0) and after demineralization (T1) stages. After remineralization (T2), herbal hemp containing toothpaste and Sensodyne Repair and Protect toothpaste showed similar remineralization effects with increase in microhardness values, while hemp oil applied group had lower values. The hemp oil and control group showed similar results, with significantly lower values than the toothpaste applied groups (Table 4).

Table 4. The microhardness values obtained at baseline, after demineralization and after remineralization stages (mean ± standart deviation).

	Baseline (T0)	Demineralization (T1)	Remineralization (T2)	P**
Hemp-containing experimental toothpaste (H)	301 ± 14.95A	188.43 ± 9.32B	284.86 ± 10.41Ca	<0.01
Hemp oil (HO)	302.29 ± 13.77A	187.86 ± 8.66B	238.57 ± 10.89Cb	<0.01
Sensodyne Repair and Protect (NovaMin) (S)	303.57 ± 1.49A	194 ± 8.52B	288.86 ±7.95Ca	<0.01
Control	303.57 ± 10.62A	194.14 ± 7.18B	230.57 ± 9.81Cb	<0.01
P*	0.985	0.465	<0.01	

*One Way Analysis of Variance; **Repeated measures analysis of variance; same letter codes have no significant difference.

DISCUSSION

The process of tooth decay depends on biological factors present in saliva and dental plaque. The amount of cariogenic bacteria present in saliva and plaque is an important determinant in caries formation. The concentration of bacteria in saliva and plaque is highly related to the oral hygiene of the individual, as well as the type of carbohydrate consumption and the frequency of carbohydrate intake (Hicks et al., 2004). Initial enamel lesions can remineralize by applying appropriate antibacterial agents and controlling plaque formation (Guerrieri et al., 2012).

In remineralization of dental tissues, fluoride is regarded as the gold standard. Fluoride prevents demineralization by creating fluorapatite crystals which are larger in size and more resistant to acid attacks compared to hydroxyapatite (Arifa et al., 2019). Additionally, fluoride prevents caries-causing bacteria from producing acid (Soi et al., 2013). High concentrations of fluoride is toxic, and even levels slightly above therapeutic levels may cause fluorosis and therefore its use is limited (Ullah et al., 2017).

Because of the possible toxic effects of fluoride, researchers have sought alternative materials that can provide remineralization effects. NovaMin (calcium sodium phosphosilicate) is a synthetic and highly biocompatible product developed for the regeneration of bone (Layer, 2011). NovaMin has been used as a remineralization agent by adding it to toothpaste and prophylaxis pastes. When NovaMin is

present in the oral cavity, calcium and phosphate ions are released with a rapid increase in pH. The release of the ions lead to the formation of a hydroxycarbonate apatite layer which is similar to natural hydroxyapatite in chemical and structural composition, for a potential replacement for hydroxyapatite (Haghgoo et al., 2016). In this study, Sensodyne Repair and Protection toothpaste containing NovaMin and Fluor was used to compare its positive effects with the herbal products containing hemp.

Herbal extracts have been considered therapeutic agents in traditional medicine. Nowadays, herbal extracts attract special attention because they are not chemical and synthetic. If the effects of herbal products are supported by evidence from scientifically based studies, they may be safer alternatives for the treatment of initial enamel lesions (Shaheen et al., 2015). Kanth et al. showed plant extracts and essential oils can be used in oral and dental care products, mouthwashes, topical gels, etc. However, they stated that herbal products should be converted into a suitable form for regular use in oral hygiene products and future research studies are needed to evaluate the quality and effectiveness of these products (Kanth et al., 2016).

Various studies have investigated various aspects of hemp, such as its components, biological activities and industrial applications. Hemp may have a therapeutic effect on the treatment of dental caries because of its antibacterial properties (Bellocchio et al., 2023). Hemp-containing mouthwashes, when applied to dental plaque, showed bacterial inhibition with the same efficacy as chlorhexidine, which is a common agent for disinfection. In addition, hemp-fortified tooth polishing powder has been expressed to limit bacteria present in dental plaque (Vasudevan & Stahl 2020). Despite the large number of hemp-based oral products available, the scientific evidence on the safety, toxicity, and efficacy of these products is restricted.

In the present study, herbal hemp-containing experimental toothpaste showed a similar effect in the remineralization of initial enamel lesions as a conventional toothpaste containing fluoride and NovaMin. According to the microhardness data obtained in this study, the group in which hemp toothpaste was applied was the group whose microhardness values increased the most after the remineralization process (T2-T1) (Table 4).

Fluorescence techniques may be used in the diagnosis of initial enamel caries lesion in modern dentistry (Sudjalim et al., 2007). Structurally, enamel tissue is highly mineralized and semi-transparent. Enamel tissue with different degrees of mineralization shows different fluorescence effects. Based on laser fluorescence technique (DIAGNOdent Pen) and FluoreCam device, the mineral loss of the tooth can be expressed visually and quantitatively. For this reason, in the present study, the FluoreCam device was used to measure the remineralization amount of demineralized enamel tissue. It has been suggested that the FluoreCam device is a clinically applicable, non-invasive, repeatable and reliable method (Korkut et al., 2017). According to the results of this study, the FluoreCam and DIAGNOdent Pen data were consistent with the microhardness data.

For thousands of years, natural products have been considered a promising therapeutic, especially for oral diseases such as dental caries (Ancuceanu et al., 2019; Cruz Martinez et al., 2017; Jawale et al., 2017). Fluoride-containing toothpastes were used as positive controls to evaluate the remineralizing activity of herbal agents. Recently, oral care products containing bioactive substances obtained from extracts of plants have been launched. Similar to the this study, Janakiram et al. reported that herbal toothpaste was as effective as non-herbal toothpaste but was not superior to fluoride toothpaste (Janakiram et al., 2020). The results of the present *in vitro* study showed that herbal toothpastes have similar positive effects on remineralization as fluoride containing conventional toothpaste.

Using natural and fluoride-free systems for remineralization may decrease the risk of fluoride toxicity. Herbal-based products may maintain remineralization of the initial enamel lesions. Because of that, they may be preferable for individuals than fluoride-based systems used in caries prevention.

The present study has its limitations as being a short-term and an *in vitro* study. This study was conducted in *in vitro* conditions although a demineralization-remineralization cycle was used to imitate the oral environment. Agents were used for seven days to evaluate their remineralizing effect. The number of days agents were applied may be increased in further studies.

CONCLUSIONS

The use of experimental herbal toothpaste containing hemp oil and hemp extract had similar positive effects on enamel remineralization as traditional toothpaste containing Fluor and NovaMin. The application of hemp oil alone was not effective on enamel remineralization. All treatment groups except hemp oil demonstrated a remineralization effect on initial enamel lesions. The effect of hemp oil was found similar to the control group.

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Conflict of Interest

The authors declare no conflict of interest related to this study.

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CASE REPORT / OLGU SUNUMU

Bilateral Basis Mandibulariste Görülen Langerhans Hücreli Histiyositozis: Nadir Bir Olgu

Langerhans Cell Histiocytosis in Bilateral Basis Mandibularis: A Rare Case

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ÖZ

Otoimmün bir hastalık olan Langerhans hücreli histiyositoz (LHH), kemik iliği kaynaklı atipik histiositlerin anormal proliferasyonu ile karakterize nadir görülen bir hastalık grubudur. Sistemik hastalığı olmayan 57 yaşında erkek hasta kliniğimize konsültasyon amacı ile başvurdu. Hastada bilateral mandibula korpusta hafif düzeyde ağrı ve deride kaşıntı şikayeti mevcuttu. KIBT incelemesinde mandibula alt sınırında baziste, bilateral yıkım alanları izlendi. Kemikte ekspansiyon ve periost reaksiyonu izlenmedi. LHH tanısı alan hastada ekstraskeletal yayılım görülmediğinden eozinofilik granülom varyantı olarak kabul edildi. Bu olgu sunumunun amacı, bilateral basis mandibulada yıkıma sebep olmuş nadir yerleşimli LHH olgusunu sunmaktır. Ayrıca ilk tutulum bölgesi genellikle baş ve boyun bölgesi olması nedeniyle diş hekimlerinin erken tanıda önemli rol aldığı bu hastalığın radyografik verilerini sunmaktır.

Anahtar Kelimeler: Langerhans hücreli histiyositoz, Eozinofilik granülom, Konik ışınlı bilgisayarlı tomografi

ABSTRACT

Langerhans cell histiocytosis (LCH), an autoimmune disease, is a rare group of diseases characterized by abnormal proliferation of atypical histiocytes originating from the bone marrow. A 57-year-old male patient with no systemic disease applied to our clinic for consultation. The patient had mild pain in the bilateral mandible corpus and itching on the skin. CBCT examination revealed bilateral destruction areas on the mandible basis. No bone expansion and periosteal reaction were observed. The patient diagnosed with LCH was accepted as an eosinophilic granuloma variant since no extraskeletal extension was observed. This case report aims to present a rare case of LCH that destroyed the bilateral basis mandible. In addition, it is to present the radiographic data of this disease, in which dentists play an important role in early diagnosis since the first involvement area is usually the head and neck region.

Keywords: Langerhans cell histiocytosis, Eosinophilic granuloma, Cone beam computed tomography

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GİRİŞ

Langerhans hücreli histiyositoz (LHH), soliter eozinofilik granülom, Letterer-Siwe hastalığı ve Hand-Schuller-Christian hastalığının dahil olduğu hastalık grubunu kapsar. Genellikle iskelette ve ender olgularda yumuşak dokuda görülür. Kemik lezyonlarının %1'inden azını oluşturur. LHH tek odak halinde olabileceği gibi multifokal, agresif bir hastalık olarak da görülebilir. Hand-Schüller-Christian hastalığı çoklu kemik tutulumu, diabetes insipidus ve ekzoftalmus ile birlikte görülebilir. Letterer-Siwe hastalığı çoğunlukla 3 yaşından önce görülen LHH'nin en ağır formudur. Granülomatöz reaksiyonun vücudun her tarafına yayıldığı bu formda aralıklı ateş, hepatosplenomegali, anemi, lenfadenopati, hemoraji göze çarpan belirtilerdir (Kumar et al., 2015; Luz et al. 2018).

Maksillofasial bölgede en çok mandibula etkilenir. Tüm LHH hastalarının %10'unda oral bulgular mevcuttur. LHH lezyonları genellikle hızla gelişir ve künt, sürekli bir ağrıya neden olur. Çenelerde görülen LHH olgularında gingivitis, diş eti kanaması, kemikte büyüme, yumuşak doku kitlesi, dişlerde mobilite, diş kaybı, ağrı ve ülserasyon gibi belirtiler gözlemlenir (Madrigal-Martínez-Pereda et al. 2009; Coleman et al. 2013; Lajolo et. al. 2012).

LHH lezyonları kemikte yıkıma, dişlerde yüzen diş görünümüne, mobilite ve minör kök rezorpsiyonuna neden olabilir. İntraosseöz lezyonlar periosteal kemik reaksiyonunu uyarabilir. Dış kortikal tabakanın yıkıma uğradığı lezyonlarda yumuşak doku uzanımı izlenebilir.

Mandibula maksillaya göre daha sık etkilenir. Her iki çenede posterior bölgede anterior bölgeye göre daha sık rastlanır. Kemik içi lezyonlar soliter bir yerleşim gösterirken alveolar bölgede yerleşen lezyonlar multipldir. Çenelerdeki soliter lezyonlara başka kemiklerdeki lezyonlar eşlik edebilir. Kemik içi lezyonlar radyografide düzensiz, oval veya dairesel bir görünüme sahip olabilir. Alveolar lezyonlar genellikle diş kökünün orta bölümünden başlar ve kepçe ile oyulmuş görüntü oluşturur. Çenelerde görülen LHH lezyonları genellikle radyolusenttir (Madrigal-Martínez-Pereda et al. 2009; Coleman et al. 2013; Lajolo et. al. 2012).

Lokalize çene lezyonları genellikle cerrahi küretaj ile tedavi edilir. Tutulan kemik ve lezyon sayısı, lezyonun büyüklüğü, lokalizasyonu ve hastanın yaşına bağlı olarak küretaj, kemoterapi, radyoterapi ayrı ayrı veya birlikte uygulanabilir (Coleman et al. 2013; Fang & Jiang 2017).

Bu olgu sunumunun amacı, bilateral basis mandibulada yıkıma sebep olmuş nadir yerleşimi ile langerhans hücreli histiyositozis olgusunu sunmaktır.

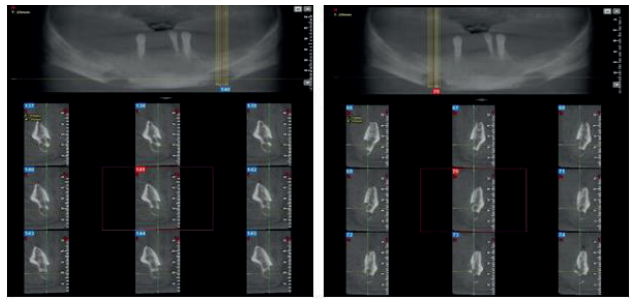
OLGU SUNUMU

İstanbul Üniversitesi Diş Hekimliği Fakültesi Ağız, Diş ve Çene Radyolojisi kliniğine 57 yaşında erkek hasta konsültasyon amacı ile başvurdu. Anemnezinde herhangi bir sistemik hastalığı olmadığı öğrenildi. Hasta 5 ay önce korpus mandibulada bilateral deri kaşıntısı başladığını bildirdi. Ayrıca 4 ay önce bilateral mandibular birinci premolar dişlerin çekildiğini, çekimlerinin zor ve ağrılı geçtiğini ardından ilgili bölgede ağrı şikayeti başladığını belirtti. Bu şikayet ile farklı diş hekimlerine başvuran hastanın defalarca antibiyotik ve ağrı kesici kullandığı ancak şikayetlerinin geçmediği öğrenildi. Hastanın ilgili bölgelerde hafif düzeyde sürekli ağrı ve deride kaşıntı dışında semptomu yoktu. Yapılan intraoral muayenede hastanın diş eksiklikleri dışında bir bulgu gözlenmedi. Ekstraoral muayenede ise palpasyonda artan ağrı mevcuttu, ancak krepitasyon veya fluktuasyon alınmadı. Lenf muayenesinde anormal bulgu görülmedi (Resim 1).

Resim 1: Hastaya ait ekstraoral ve intraoral görüntüler

Hastada yakın tarihte implant planlaması için alınan panoramik ve konik ışınlı bilgisayarlı tomografi (KIBT) görüntüleri mevcuttu. KIBT incelemesinde korpus mandibulada, mental foramen hizasında, mandibular kanal inferiorunda, sağ tarafta daha geniş olmak üzere bilateral kemik yıkım alanları tespit edildi. Lezyonlar mandibula bazisten mandibular kanalın alt sınırına kadar uzanım gösteriyordu. Mandibula alt sınırında baziste, bukkal ve lingual kortikal kemikte yıkım izlendi. Her iki tarafta bukkal kemik yıkımı lingual kemik yıkımından daha fazlaydı. Mandibular kanalın deplase olmadığı, kanalın inferior ve bukkal kemik sınırının incelmiş olduğu görüldü. Lezyonların ekspansiyon yapmadan kortekste yıkıma neden olduğu ancak periost reaksiyonu oluşturmadığı görüldü. (Resim 2,3).

Histopatolojik değerlendirme sonrası LHH tanısı alan hastada yapılan medikal konsültasyonda mandibula tutulumu dışında LHH tutulumu olmadığı öğrenildi. Ekstraskeletal yayılım görülmediğinden eozinofilik granülom varyantı olarak kabul edildi. Ayrıca düşük doz radyoterapi tedavisi alan hastanın 2 senelik takibinde nüks gelişmediği bildirildi.



Resim 2: Hastaya ait KIBT görüntüleri

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Resim 3: Hastaya ait 3 boyutlu rekonstrüksiyon görüntüsü

TARTIŞMA

Langerhans hücreleri (histiyositler) kemik iliğinden köken alan, antijenleri yakalayan, işleyen ve lenfositlere sunan dentritik hücrelerdir. İmmun sistemin önemli bir parçası olan bu hücrelerin aşırı çoğalması ve değişik organlarda birikmesi LHH hastalığına neden olur (Kapukaya et al. 2013).

LHH nadir görülen bir hastalıktır. Erkek hastalarda kadın hastalara göre daha fazla görülür. Klinik olarak tek sistem veya mulltisistem tutulum olabilir. Tek sistem formunda genellikle deri, lokalize akciğer, kemik ve lenf nodu tutulumu görülür. Multisistem formunda ise karaciğer, akciğer, dalak, gastrointestinal sistem ve hematopoetik sistem tutulumu ile karşılaşılabilir. Genellikle asemptomatiktir. İskelet lezyonları genellikle rastlantı sonucu fark edilir. Semptomatik lezyonlarda en sık görülen belirtiler ağrı ve şişliktir. Etkilediği organa bağlı olarak farklı belirtilere neden olabilir. Birçok olguda spontan regresyon bildirilen LHH, hızlı progresyon gösterip ölüme de sebep olabilir (Kumar et al. 2015; Kapukaya et al. 2013).

Erken dönemde LHH lezyonları agresif bir görünümde olabilir. İntraosseöz lezyonlar ekspansiyona ve perforasyona sebebiyet verebilir. Kortikal kemik etkilendiğinde periosteal kemik reaksiyonuna neden olabilir. Sklerotik sınırlar, iyi sınırlı bir lezyonun iyileştiğinin göstergesi olabilir (Lieberman et al 1996).

LHH'nin en sık etkilediği kemikler kafatası kemikleri, femur, mandibula, pelvis ve omurlardır. Olguların %30'unda oral ve perioral lezyonlar bulunur. Oral semptomları genellikle ağrı, şişlik, kemik kaybı, mobil dişler, diş kayıpları ve gingivitistir. Oral bölgede izole tonsil tutulumu sadece birkaç olguda bildirilmiştir (Atalay et al. 2014).

LHH için intraoral bölge genellikle ilk tutulum alanıdır. Bu nedenle diş hekimleri erken teşhiste önemli rol oynamaktadırlar. Semptomlarının spefisik olmaması nedeniyle yanlış teşhisler konabilmektedir. Hastalığın yıkıcı doğası nedeniyle agresif periodontitis, osteomyelit ve malignite ile karışabilmektedir (Xie et al. 2021). Periodontal hastalıktan, LHH'ın karakteristik kepçe ile oyulmuş görünümü ile ayrılabilir. Kemik yıkımının merkezi kökün orta üçlüsüdür (White & Pharoah 2009). Skuamöz hücreli karsinom genellikle soliter, kötü tanımlanmış bir radyolusensi gösterir ve bir yumuşak doku kitlesi ile ilişkili olabilir. Osteomiyelitte ise en belirgin belirti sekestr oluşumudur. Ancak LHH için kesin tanı histopatolojik inceleme ile konmaktadır (Hwang et al. 2019; Koong 2017).

Çene tutulumu alveolar proçesde ve çenenin başka bölgelerinde kemik içi olabilir. Kemik içi lezyonlar genellikle soliterken, alveolar lezyonlar multipldır. Mandibula maksillaya oranla daha fazla tutulur ve posterior bölgelerde tutulum daha sıktır. Ramus mandibula kemik içi lezyonların en sık tutulduğu bölgedir. Alveolar lezyonlar genellikle diş köklerinin ortasından başlar ve kepçe ile oyulmuş görünüm mevcuttur. Diş köklerinin çevresindeki kemiğin yıkımı sonucu yüzen diş görünümü oluşabilir. Kemik içi lezyonlar ise düzensiz, oval ya da dairesel şekilli olabilir. Çenelerin herhangi bir bölgesinde korteksi harap edip yumuşak doku lezyonu oluşumu görülebilir. Periost reaksiyonu tabloya eşlik edebilir (White & Pharoah 2009; Koong 2017).

LHH yaşa ve klinik tabloya göre üçe ayrılır. Letterer-siwe hastalığı çocuk ve bebeklerde görülür. Çoklu sistem tutulumu ile karakterizedir. Hand-Schuller-Christian hastalığı iskelet dışı lezyonların çoklu olduğu kronik dissemine formudur. Eozinofilik granülom hastalığında ise soliter veya multipl iskelet lezyonları ve nadiren iskelet dışı yayılım gösteren kronik lokalize formudur (Yashoda-Devi et al. 2012; Aruna et al. 2011).

Diabetes insipidus hipofiz bezi tutulumu nedeniyle yaygın bir LHH komplikasyonudur. Bu ömür boyu hormon replasmanı gerektirebilir (Grois et al. 2016).

Bizim olgumuz literatür geneliyle uyumlu olacak şekilde erkek hastada ve mandibulada görülmekteydi. Ekstraskeletal yayılım görülmediğinden eozinofilik granülom varyantı olarak kabul edildi ve yapılan medikal konsültasyonda diabetes insipidus olmadığı öğrenildi. Lezyonlarda kemik içi tutulum görüldü ancak alveolar tutulum mevcut değildi. Kemik içi lezyonlar genellikle ramusta ve soliter olarak izlenirken bizim olgumuzda korpus mandibulada baziste bilateral tutulum izlendi. Kortekste yıkım görülürken periost reaksiyonu izlenmedi.

SONUÇ

LHH genellikle iskelet sistemini tutan ve nadir görülen bir hastalıktır. İlk tutulum bölgesinin genellikle baş ve boyun bölgesi olması nedeniyle diş hekimleri erken tanıda önemli rol almaktadır. Ayırıcı tanı periodontal hastalıklar, osteomyelit ve malignite ile yapılmalıdır. Olguların yaşı ve radyografik değerlendirme ile ayrım yapılabilir. Kesin tanı için histopatolojik değerlendirme gereklidir.

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ORIGINAL ARTICLE / ARAŞTIRMA MAKALESİ

Plaut-Vincent Stomatitis: A Case Report

Plaut-Vincent Stomatitis: Bir Olgu Sunumu

Suay Yağmur ÜNAL, Gaye KESER, Filiz NAMDAR PEKİNER

ABSTRACT

Necrotizing ulcerative stomatitis or Plaut-Vincent's Stomatitis is a complication of necrotizing ulcerative gingivitis that extends beyond the gingiva and is involved in other parts of the oral mucosa, with Fusiform bacillus, Borrelia vincenti and other anaerobic microorganisms being the most common associated bacteria. It starts with sore throat, bad smell in the mouth, bleeding gums in young adults with poor oral hygiene and decreased immune resistance. In this case, clinical findings of Plaut-Vincent Stomatitis belonging to a male patient are presented. In a 22-year-old male patient, erythematous, ulcers with irregular margins and grayish-white fibrin were observed in the soft tissue of the right third molar region of the mandible and in the buccal mucosa. The patient has halitosis, difficulty in swallowing, pain in the oropharynx, and lymphadenopathy. In the treatment of infected tissues, improvement was observed after systemic antibiotics and hydrogen peroxide mouthwash were applied for 6-7 days. Plaut-Vincent Stomatitis is frequently seen in young adults and poor oral hygiene, smoking, emotional stress, alcohol consumption and malnutrition are stated as etiological factors that predispose to this disease. Detection of ulcerated lesions in soft tissue examination is important in diagnosis and treatment.

Keywords: Necrotizing ulcerative stomatitis, Plaut-Vincent Stomatitis, Third molar, Oral Diagnosis, Treatment

ÖZ

Nekrotizan ülseratif stomatitis ya da Plaut – Vincent Stomatitisi nekrotizan ülseratif gingivitisin bir komplikasyonu olup gingivanın ötesine uzanarak oral mukozanın diğer bölgelerinde tutulum gösteren, Fusiform basillus, Borrelia vincenti ve diğer anaerobik mikroorganizmaların en yaygın ilişkili bakteriler olduğu tablodur. Ağız hijyeni iyi olmayan, immün direnci düşmüş genç erişkinlerde, boğaz ağrısı, ağızda kötü koku, dişeti kanamasıyla başlar. Bu olguda erkek hastaya ait Plaut – Vincent Stomatitisi klinik bulguları sunulmaktadır. 22 yaşında erkek hastada mandibula sağ üçüncü molar bölge yumuşak dokuda ve bukkal mukozada eritemli, ülserlerle birlikte düzensiz marjinler ve kirli beyaz, grimsi fibrin izlenmiştir. Hastada halitozis, yutkunmada zorluk, orofarenkste ağrı ve lenfadenopati mecvuttur. Enfekte dokuların tedavisinde 6-7 gün süreyle sistemik antibiyotik ve hidrojen peroksitli gargara uygulandıktan sonra iyileşme gözlenmiştir. Sıklıkla genç erişkinlerde görülmekle birlikte kötü ağız hijyeni, sigara, duygusal stres, alkol tüketimi ve yetersiz beslenme bu hastalığa zemin hazırlayan etiyolojik faktörler olarak belirtilmektedir. Hastalarda yumuşak doku muayenesinde ülsere lezyonların tespit edilmesi, tanı ve tedavide önem taşımaktadır.

Anahtar Kelimeler: Nekrotizan Ülseratif Gingivitis, Plaut-Vincent Stomatiti, 3.Molar Diş, Oral Diagnoz, Tedavi

INTRODUCTION

Plaut-Vincent's Stomatitis is a complication of necrotizing ulcerative gingivitis that extends beyond the gingiva and is involved in other parts of the oral mucosa, affecting <1% of the population. Trench mouth, acute necrotizing ulcerative gingivitis, necrotizing ulcerative stomatitis, fusospirochetal gingivitis, Vincent's stomatitis, and Vincent infection are additional names for this medical condition (Horning & Cohen, 1995).

Periodontal disease known as necrotizing ulcerative gingivitis (NUG) causes severe gingival ulcerations that may lead to the gradual destruction of the gingivae. Young people are more likely to have NUG, especially severely undernourished children and young adults who have HIV infection (Hu et al., 2015).

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An impaired capacity to handle psychological stress, immunosuppression, and tobacco use have all been reported to be substantially related epidemiologically with the emergence of NUG, according to prospective clinical research. It has been demonstrated that these variables reduce the host immunological response, which promotes bacterial pathogenicity. Psychological stress decreases salivary flow and gingival microcirculation while increasing adrenocortical secretions, which can change how polymorphonuclear leukocytes and lymphocytes operate. This affects the patient's behavior and mood as well as the immunological response, leading to poor dental hygiene, malnutrition, and increased tobacco use. (Pitzura & Loos, 2020, Aaron & Deblois, 2023).

Despite a low prevalence, this disease has a strong clinical significance because it is the most serious ailment linked to the dental biofilm. Fusiform and spirochete bacteria are mostly linked to NUG, which is frequently caused by an opportunistic bacterial infection (Alshagroud et al., 2023).

NUG is primarily defined by the presence of necrosis/ulcer of the interdental papillae, gingival bleeding, and pain. Secondary symptoms include halitosis, pseudomembrane formation, regional lymphadenopathy, fever, and sialorrhea. According to studies, the interdental papilla necrosis or ulcer, gingival bleeding, discomfort, pseudomembrane development, and halitosis were the most important clinical findings. There were extraoral symptoms including adenopathy or fever. Children were more likely to experience fever, adenopathy, and sialorrhea than they were to experience pain or bad breath. (Sivapathasundharam et al., 2018; Khademi & Aryan, 2015).

Many viral diseases as well as other bacterial conditions might cause diagnosis to be misinterpreted. Bacterial infections like gonococcal or streptococcal gingivitis, infectious mononucleosis, acute herpetic gingivostomatitis, as well as some mucocutaneous conditions like multiforme erythema, desquamative gingivitis, and pemphigus vulgaris, should be taken into consideration for a differential diagnosis (Malek et al., 2017).

Treatment should be administered in stages: first, the acute phase should be treated; next, the underlying condition should be treated; and last, the disease's aftereffects should receive corrective treatment. Finally, the phase of support or maintenance (Dufty et al., 2017).

Two key goals of therapy for the acute phase are to stop the disease process and tissue damage and to regulate the patient's overall pain and discomfort, which interferes with nutrition and maintaining good oral hygiene. These goals can be reached through thorough superficial ultrasonic debridement and chemical detersion of the necrotic lesions using oxygen-releasing chemicals ''local oxygen therapy''. If a debridement response is inadequate or systemic effects are present, systemic antimicrobials may be used. Since metronidazole is effective against stringent anaerobes, it can be a good first choice medication. Other systemic medications, such as penicillin, tetracyclines, clindamycin, amoxicillin, or amoxicillin plus clavulanate, have also been proposed with positive outcomes. Because of the numerous bacteria present in the tissues, where the local medicine will not be able to acquire acceptable concentrations, locally given antimicrobials are not advised. Patients with immunodepression who are receiving antibiotic therapy should use antifungal medications (Herrera et al., 2014; Folayan, 2014).

The prior chronic condition, such as preexisting chronic gingivitis, should be treated once the acute phase has been brought under control. It is important to enforce oral hygiene guidelines and incentive. Predisposing local variables that already exist, like partially impacted teeth and overhanging restorations, should be carefully assessed and addressed. Smoking, getting enough sleep, and reducing stress are all systemic predisposing variables that should be regulated and taken into account. In some cases, the illness's changed gingival topography should be corrected since gingival craters may encourage plaque buildup and disease recurrence. Gingivectomy and/or gingivoplasty techniques, periodontal flap surgery, or even regenerative surgery, may be beneficial for treating superficial craters. Additionally, this phase's primary objectives are managing the risk factors and adhering to the recommended dental hygiene routines (Brad et al., 2019; Santos et al., 2020).

A considerable amount of epidemiologic data indicates that Plaut-Vincent's disease occurs primarily to individuals who have been subjected to stress, immunosuppression, malnutrition, poor oral hygiene, and smoke. Yet, we present a case of a young male patient with only poor oral hygiene and smoking that leads a severe necrotising stomatitis companied by lymphadenopathy.

CASE REPORT

A 22-year-old male patient presented at the Department of Oral and maxillofacial Radiology at Marmara University Faculty of Dentistry with complaints of difficulty in swallowing and pain around the right retromolar region. He also had halitosis, pain in the oropharynx and lymphadenopathy in submandibular lymph nodes. Patient had a poor plaque control without any parafunction and had no other significant medical history or known allergies. He was smoking a pack of cigarettes a day. Intraoral examination showed erythematous, ulcers with irregular margins and grayish-white fibrin in the soft tissue of the right retromolar region of the mandible and in the buccal mucosa (Fig. 1). Panoramic radiography image revealed the partially impacted third molar existence in both sides and multiple caries caused by poor oral hygiene (Fig. 2). In the treatment of infected tissues, systemic antibiotics and hydrogen peroxide mouthwash were applied for 6-7 days and extraction of the third mandibular molar tooth was recommended. In this case, the patient was referred to us due to his acute condition and he went to another clinic out of the city for dental treatment. After 1 week of antibiotic and mouthwash use, improvement was observed in the related lesion (Fig. 3).

Figure 1: Patient's intraoral examination; along with the halitosis and limited jaw movements, an erythematous area covered with fibrin was observed on retromolar area.

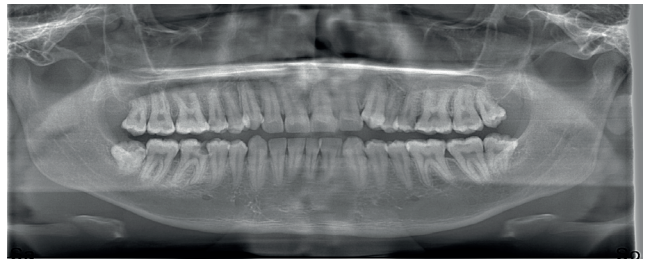

Figure 2: Patient's panoramic image; partially impacted third molar which triggered the stomatitis can be seen

Figure 3: Patient's intraoral image within a week; after the systemic antibiotics and regular mouthwash treatment combined with oral hygene and diatery regulation, lesion healed.

DISCUSSION

An endogenous polymicrobial infection called Vincent's stomatitis primarily affects those who have weakened immune systems. Pioneers Plaut and Vincent independently identified the disease's link with the fusiform-spirochete in the 1890s. The most common word for the acute ulcerative condition affecting the gingiva is acute necrotizing ulcerative gingivitis, and the term used for fuso-spirochetal infection of the oropharynx and throat, with a severe membranous ulceration of the throat, is Vincent's angina (Mizrahi 2014; Stoker & Gauer, 2021).

Despite the fact that there are precise diagnostic requirements for the diagnosis of necrotizing stomatitis, patients may display vague signs and symptoms or only meet some of the requirements. numerous studies stress the

importance of preventing periodontitis and the necessity of individualized interventions (Tonetti et al., 2015).

With this method of treatment, ulcer healing can be anticipated in a couple of days and the condition is typically stopped in its tracks with adequate treatment. However, if untreated, disorders like necrotizing ulcerative periodontitis (NUP) and even cancrum oris (noma), which can be fatal, can worsen and become more severe (Khammissa et al., 2022).

The most common anaerobic bacteria now being associated with necrotizing periodontal illnesses include Treponema and Selenomonas spp., Prevotella intermedia, Fusobacterium nucleatum, Porphyromonas gingivalis, and Fusobacterium necrophorum. Numerous predisposing variables, including poor oral hygiene, smoking, mental stress, nutritional inadequacy, systemic disorders, or a compromised immune system, have been hypothesized for the etiology of necrotizing periodontal diseases (Yousefi et al., 2020; Ferrisse et al., 2019).

Pain, ulceration, and bleeding are the diagnostic triad for necrotizing periodontal diseases. Halitosis, pseudomembranes, a "wooden" sensation in the teeth, a metallic taste, tooth mobility, ropy saliva, lymphadenopathy, fever, and malaise are some of the secondary clinical indications of necrotizing periodontal diseases (Marty et al., 2016; Kashyap & Kashyap ,2022). Even while clinical characteristics differ from patient to patient, our patient had some of the most typical characteristics such as pain, ulceration covered with pseudomembrane, halitosis and lymphadenopathy.

Kashyap and Kashyap (2022) presented a case of Vincent's stomatitis with the acute ulcerative involvement of gingiva and pseudomembranous ulceration of tonsils in a general medical practitioner. Antibiotics such as penicillin and metronidazole are the medications of choice due to the microbial nature. Yet, Khademi and Aryan (2015) reported a 17-year-old girl who experienced emotional stress and developed signs of Vincent's angina. Clinical improvement was not much found with antibiotic medication, amoxicillin and cephalexin, although improvement was attained with mouthwash and salt water. The management should concentrate on removing local causes and microbial buildup. As a result, we seek non-surgical treatment for the issue. Antibiotics like metronidazole and penicillin are the preferred treatments due to the microbial nature of the condition (Özbayrak 2010). However, systemic antibiotics do not completely remove local etiological variables. Using antibacterial mouthwashes with 0.12% chlorhexidine can assist to locally control the infection. After the acute phase has passed, surgical debridement and recontouring are typically advised (Martos et al., 2019; Özberk et al., 2018).

CONCLUSIONS

Plaut-Vincent Stomatitis is frequently seen in young adults and poor oral hygiene, smoking, emotional stress, alcohol consumption and malnutrition are stated as etiological factors that predispose to this disease. Detection of ulcerated lesions in soft tissue examination is important in diagnosis and treatment. Clinicians face a diagnostic challenge when treating necrotizing ulcerative gingivitis and the variety of gum disease presentations, which is best handled by an interprofessional team approach.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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REVIEW / DERLEME

Endodontide Post-operatif Ağrı Yönetimine Güncel bir Yaklaşım: Kriyoterapi

A Current Approach to Post-operative Pain Management in Endodontics: Cryotherapy

Sevda DÜRÜST BARIŞ[1], Ali TÜRKYILMAZ[2]

ÖZ

Endodontik tedavinin önemli zorluklarından biri, tedaviden sonra hastalar tarafından sıklıkla bildirilen post-operatif ağrı ve rahatsızlığın yönetimidir. Post-operatif ağrı tüm vakaların %3 ile %58'inde ortaya çıkar. İşlem öncesi hasta sakinleştirici yaklaşımlar ve açıklamalar, oklüzal redüksiyonlar ve glide-path uygulamaları gibi mekanik teknikler ve uzun etkili anestezi enjeksiyonları, antihistaminikler, non-steroid antienflamatuar ilaçlar, salisilik asit, asetaminofen, ibuprofen ve asetaminofen kombinasyonları ve narkotik analjezikler gibi farmakolojik ilaçlar dahil olmak üzere ağrı insidansını azaltmak için çeşitli protokoller kullanılmıştır. Soğuk terapi olarak da bilinen kriyoterapinin kas-iskelet ağrısı, kas spazmları, bağ dokusu gerginliği, kanama, iltihaplanma ve sinir iletkenliğini azalttığı fizyolojik ve klinik olarak kanıtlanmıştır. Kriyoterapi dokularda kan akışını ve sıcaklığını düşürmede, kimyasal mediyatörler tarafından uyarılan nosiseptörleri inhibe etmede ve metabolik aktiviteyi azaltmada etkilidir. Tıp alanında cerrahi işlemler sonrası ağrı kontrolünde uzun yıllardır kullanılmaktadır. Diş hekimliğinde kriyoterapi, özellikle cerrahi işlemlerden sonra postoperatif ağrı kontrolü için uzun süredir uygulanmaktadır. Endodontik tedavide de kriyoterapi güncel konulardan biridir. Bu derlemenin amacı endodontik tedavi sonrası post-operatif ağrı kontrolünde kriyoterapinin rolü hakkında genel bilgi vermektir.

Anahtar Kelimeler: Ağrı, apikal periodontitis, diş hekimliği, endodonti, kriyoterapi

ABSTRACT

One of the major challenges of endodontic treatment is the management of post-operative pain and discomfort frequently reported by patients after treatment. It occurs in 3% to 58% of all post-operative cases. Mechanical techniques such as patient calming approaches and explanations prior to the procedure, occlusal reductions, glide-path applications, application of different mechanical techniques and movements during root canal treatment, and pharmacological drugs such as long-acting anesthetic injections, antihistamines, non-steroidal anti-inflammatory drugs, and narcotic analgesics various protocols have been used to reduce the incidence of pain. Cryotherapy also known as cold therapy, has been physiologically and clinically proven to reduce musculoskeletal pain, muscle spasms, connective tissue tension, bleeding, inflammation, and nerve conductivity. Cryotherapy is effective in reducing blood flow and temperature in tissues, inhibiting nociceptors stimulated by chemical mediators, and reducing metabolic activity. It has been used in the medical field for many years to control pain after surgical procedures. Cryotherapy in dentistry has long been applied for postoperative pain control, especially after surgical procedures. Cryotherapy is one of the current topics in endodontic treatment in recent years. The aim of this review is to give general information about the role of cryotherapy in post-operative pain control after endodontic treatment.

Keywords: Apical periodontitis, cryotherapy, dentistry, endodontics, pain.

GİRİŞ

Genel Bilgiler

Hastaların diş hekimlerini ziyaret etmelerinin temel sebepleri arasında diş ağrısı ilk sıralardadır. Endodontik tedavi sırasında ve sonrasında görülen ağrı hem hasta hem de klinisyen için istenmeyen bir durumdur ve genellikle hastalar tarafından klinisyenin becerilerinin bir ölçütü olarak kabul edilir (Siqueira ve ark., 2002). Kanal tedavisi uygulamalarının en önemli hedeflerinden biri işlem esnasında ve sonrasında diş ağrısının kontrol altına alınmasıdır (Attar ve ark., 2008).

Hastalar kök kanal tedavisi öncesinde, esnasında ve sonrasında farklı seviyelerde ağrı hissedebilirler. Bir

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sistematik inceleme, hastaların %3 ile %58'inin post-operatif endodontik ağrı yaşadığını göstermiştir (Liesinger ve ark., 1993). Kök kanal tedavisinden sonra görülen ağrının en önemli sebeplerinden biri periapikal doku inflamasyonudur. Mekanik ve kimyasal yaralanmalar ile mikroorganizmalar gibi etkenler de postoperatif ağrı gelişimini etkileyebilir (Sathorn ve ark., 2008). Periradiküler doku yaralanmasını takiben vazodilatasyon ve vasküler geçirgenlik artışı meydana gelir ve enflamasyon olaylarına aracılık eden çok sayıda kimyasal salınır. Hargreaves ve Hutter özellikle tedavi öncesi ağrısı ve/veya pulpa nekrozu olan dişlerde postoperatif ağrının beklenebileceğini bildirmişlerdir (Hargreaves ve Hutter, 2002). Albashaireh ve ark ise; vital olmayan pulpaya sahip dişlerde post-operatif ağrı görülme sıklığının vital pulpaya sahip dişlere göre daha fazla olduğunu, ayrıca tek ve çok seansta yapılan kök kanal tedavileri arasında postoperatif ağrı görülme sıklığında anlamlı bir fark olmadığını bildirmişlerdir (Albashaireh ve Alnegrish, 1998).

Kök kanal sisteminin yetersiz şekillendirilmesi ve temizlenmesi, irrigasyon solüsyonunun, kanal içi ilaçların veya debrisin apikalden taşması, hiperoklüzyon, gözden kaçırılmış kök kanalları ve kalıcı periapikal patolojinin varlığı kök kanal tedavisi sonrası ağrıyı etkileyen yaygın faktörler arasındadır. Post-operatif ağrı, çalışma uzunluğunun belirlenmesi ve tedavi boyunca korunması, kanalın uygun şekilde temizlenmesi ve şekillendirilmesi, irrigasyon maddelerinin etkili kullanımı konusunda dikkatli olunması halinde büyük ölçüde önlenebilir.

Endodontik tedavi sonrası ağrı en sık kanal tedavisinden sonraki ilk 24 ile 48 saat içinde ortaya çıkar ve bazen birkaç gün sürebilmesine rağmen genellikle sonraki birkaç saat içinde geriler (Bashetty ve Hegde, 2010). İşlem öncesi hastayı sakinleştirici yaklaşımlar ve açıklamalar, oklüzal redüksiyon uygulamaları (Parirokh ve ark., 2013) ve kök kanalı boyunca düzgün ve pürüzsüz bir giriş yolu oluşturulması gibi mekanik teknikler (Pasqualini ve ark., 2004) ve uzun etkili anestezi uygulamaları (Crout ve ark., 1990), antihistaminikler, non-steroid antienflamatuar ilaçlar (NSAID'ler), salisilik asit, asetaminofen, ibuprofen ve asetaminofen kombinasyonları ve narkotik analjezikler gibi farmakolojik ilaçlar (Torabinejad ve ark., 1994; Ryan ve ark., 2008) ağrı görülme sıklığını azaltmak için etkilidir (Arslan ve ark., 2016).

Ağrı kontrolünde farmakolojik bir yöntem olan analjezik ajanların kullanımı, hızlı etkileri ve kolay uygulanabilmeleri nedeniyle yaygındır (Crout ve ark., 1990; Ergün ve Güneri, 2009). NSAID'ler günümüzde diş hekimliğinde en çok önerilen; analjezik, antipiretik ve antiinflamatuar etkileri olan ilaçlardır (Arslan ve Çelebioğlu, 2006; Ergün ve Güneri, 2009). Nispeten güvenli ilaçlar olmalarına rağmen, gastrointestinal intolerans ve böbrek, karaciğer ve solunum bozuklukları gibi yan etkileri olabileceği bildirilmiştir (Arslan ve Çelebioğlu, 2006; Ergün ve Güneri, 2009).

Histamin akut inflamasyon belirtilerinin birçoğunu ortaya çıkarabilir. Bu nedenle postoperatif ağrı, ödem ve enflamasyonun kontrolünde antihistaminikler tercih edilir. Antihistaminikler, histaminin kan damarlarının düz kasları üzerindeki etkisini antagonize ederek damar geçirgenliğini azaltır. Böylece tedavi sonrası ağrı, ödem ve iltihaplanmayı elimine ederler. Ayrıca antihistaminikler analjezik sınıflandırmasında yer almamakla birlikte bazı durumlarda ağrı kontrolünde etkili olan adjuvan analjezik ilaçlar grubuna dahildir (Seymour ve Walton, 1984).

Ağrı kontrolüne bir başka alternatif ise farmakolojik olmayan yöntemlerdir. Farmakolojik olmayan bu yeni yöntemler analjezik kullanma gereksinimini azaltma, yaşam kalitesini iyileştirme, analjeziklerde gözlenen bazı yan etkilerin olmaması ve kolay uygulanma gibi çeşitli avantajlara sahiptir. (Seymour ve Walton, 1984). Düşük seviyeli lazer uygulamaları (Arslan ve ark., 2017; Doğanay ve ark., 2018), oklüzal redüksiyon (Parirokh ve ark., 2013) ve akupunktur uygulamaları da (Arslan ve ark., 2019) farmakolojik olmayan yöntemler arasındadır.

Ağrı üzerine yapılan çalışmalarda plasebo ilaçlar da kullanılmıştır (Nath ve ark., 2018; Shamszadeh ve ark., 2021). Plasebonun, çeşitli nörogörüntüleme yöntemleri kullanılarak ağrının duyumsama ve kontrolünde yer alan bazı beyin bölgelerini uyararak ilaçların etkisini taklit ettiği gösterilmiştir. Plasebo yanıtında dopamin, serotonin ve opioid sistemleri etkili olmaktadır (Seymour ve Walton, 1984). Etkilerini endojen opioid sistemlerini uyararak gösterdikleri düşünülmektedir. Bu etkiyi gösterirken beyindeki nörokimyasal yollar izole değildir ve fonksiyonel etkiler ortak mekanizmalar tarafından ortaya konur. Tanımı zor ve içeriği bilinmemekle birlikte plasebo etkisinin varlığı tıbbın tüm dallarında genel olarak kabul görmektedir. Ancak ne düzeyde etkili olduğu halen tartışmalıdır.

Kriyoterapi Tanımı

Kriyoterapi, tedavi amaçlı doku sıcaklığının düşürülmesini tanımlar. Terim, "soğuk" anlamına gelen Yunanca "cryos" ve "tedavi" anlamına gelen "therapeia"

sözcüklerinden türetilmiştir. Bu nedenle kriyoterapi, düşük sıcaklıklar kullanılarak yapılan tedavileri ifade etmektedir (Belitsky ve ark., 1987). Kriyoterapi kavramı aslında hedef dokuyu soğutmayı değil, daha yüksek sıcaklıktaki dokudan daha düşük sıcaklıktaki nesneye ısı çekmeyi ifade eder. Sıcaklık değişiminin ve dokulardaki biyofiziksel değişikliklerin büyüklüğü, nesnenin sıcaklığı ile soğuk veya sıcak uygulaması arasındaki farka, maruz kalma süresine, dokuların termal iletkenliğine ve ısıyı veya soğuğu uygulamak için kullanılan ajanın tipine bağlıdır. Bu tarz bir tedavinin insan dokularında kullanılması konağın lokal sıcaklığında değişikliklere neden olur (Belitsky ve ark., 1987).

M.Ö. 3000'de eski Mısırlılar, yaralanmaları tedavi etmek ve enflamasyonu azaltmak için soğuk tedavisini ilk olarak uygulamışlardır. Hipokrat Antik Yunan'da kriyoterapiyi, tedavi amacıyla lokal veya sistemik olarak kullanmayı önermiştir. Bununla birlikte, 1851'de James Arnott, malign hastalıkta bir tuz ve buz karışımı kullanarak soğutma tedavisini bildiren ve gösteren ilk kişidir (Nayeema ve Subha, 2013). Günümüzde kriyoterapi, 1960'lardan beri ağrı tedavisi için çeşitli klinik uygulamalarda kullanılmaktadır.

Tıpta Kriyoterapi Uygulamaları

Kriyoterapi dokularda kan akışını ve sıcaklığını düşürmede, kimyasal mediyatörler tarafından uyarılan nosiseptörleri inhibe etmede ve metabolik aktiviteyi azaltmada etkilidir. İlaç dışı yöntemlerden biri olan kriyoterapi tıp alanında cerrahi işlemler sonrası ağrı kontrolünde uzun yıllardır kullanılmaktadır. Öncelikle tıpta; spor yaralanmalarında, tendinitte, burkulmalarda, artrit ağrısında, kalça veya diz replasmanından sonra, alçı veya atel altında ağrı veya şişmeyi önlemek ve bel ağrısını tedavi etmek gibi çeşitli amaçlarla kullanılmaktadır. Ayrıca displastik dokuyu yok etmek için kullanılmıştır (McDowell ve ark., 1994; Watkins ve ark., 2014; Ahdoot ve ark., 2019).

Kriyoterapinin tıpta ortopedi, karın, jinekoloji ve fıtık ameliyatlarında kısa süreli uygulanarak ödem, ağrı ve iltihaplanmayı azaltarak iyileşme süresini hızlandırdığı bildirilmiştir (Kwekkeboom, 2001; Watkins ve ark., 2014). Tıp literatüründe kriyoterapinin ameliyat sonrası dönemde narkotik kullanımını azalttığı da bildirilmiştir (Kwekkeboom, 2001; Watkins ve ark., 2014). Bu nedenle özellikle geriatrik veya alerjik hastalarda, işlem sonrası ağrıyı az yan etkiyle veya hiç yan etki olmaksızın en aza indirmek için güvenli ve etkili bir yöntem olarak önerilmektedir.

Kriyoterapinin Etki Mekanizması

Kriyoterapinin vasküler, nörolojik ve doku metabolizması olmak üzere üç temel fizyolojik doku etkisi bulunmaktadır. Doku 15 dakikadan daha uzun süre düşük sıcaklığa maruz kaldığında, ilk refleks olarak vazokonstrüksiyon meydana gelir ve daha sonra bunu soğuk kaynaklı vazodilatasyon izler. Vazodilatasyona, histamin benzeri madde "H"nin (substance H) salınımı aracılık eder. Bunun sonucunda bölgede sıcak kan akışı tekrar vazokonstrüksiyon ve ardından tekrar vazodilatasyona neden olur. vazokonstrüksiyon kan damarlarının adrenerjik elemanları tarafından tetiklenen bir nöral refleks olarak vazodilatasyonu takip eder ve hücre duvarını bir arada tutan vasküler geçirgenliği azaltır. Azalmış geçirgenlik, eksüda veya transüda olarak periradiküler dokuya sızan sıvı miktarını azaltmak için anahtar bir faktördür. Böylece kemomekanik hazırlıktan sonra periapikal dokuda yaygın olarak meydana gelen doku ödemi ve şişmesini azaltır (Sahuquillo ve Vilalta, 2007). Periradiküler cerrahi sonrası hematomun önlenmesi, yalnızca ağrıyı kontrol altına almak için değil, aynı zamanda iyileşme sürecini hızlandırmak, cerrahi sonrası komplikasyon insidansını azaltmak için de çok önemlidir. Bu nedenle soğuk uygulama ile cerrahi bölgenin sıcaklığının düşürülmesi, cerrahi sonrası destekleyici tedavide önerilen bir uygulama haline gelmiştir (Sahuquillo ve Vilalta, 2007; Herrera ve ark., 2010).

Kriyoterapinin nörolojik etkisi ile ilgili olarak analjezi nosiseptif duyusal sinir liflerinin sinir iletim hızı ile yakından ilişkilidir (Herrera ve ark., 2010). Soğutma, sinir iletiminin hızını yavaşlatarak analjezi sağlar. Bununla birlikte, miyelinli sinir liflerinde (A-delta lifleri) miyelinsiz liflere (C lifleri) kıyasla bu etki daha belirgindir (Ernst ve Fialka, 1994). Ayrıca soğuk uygulama, endorfin gibi nöro-etkili ajanların salınımını uyararak analjezik etkinin başlamasını sağlayabilir. Endorfinler, medüller dorsal boynuzdaki opioid reseptörlerine bağlanır. Böylece impulsların merkezi sinir sistemine nosiseptif iletimini engeller. Ek olarak, soğuk uygulama doku yaralanmasından sonra aktive olan özel sinir uçlarının (doku nosiseptörlerinin) aktivasyon eşiğini düşürebilir ve bu da soğukla uyarılmış nöropraksi olarak tanımlanan lokal anestezik etkiyi sağlayabilir. Böylece, soğutmanın analjezik etkisi, ağrının kimyasal aracılarının azalmış bir salınımı ve nöral ağrı sinyallerinin daha yavaş yayılmasının bir kombinasyonu ile üretilir (Ernst ve Fialka, 1994; Malanga ve ark., 2014). Kriyoterapinin doku metabolizması üzerindeki etkisi ile ilgili olarak; yaralanan doku, daha sonra doku hipoksisi ve nekrozu ile daha fazla

oksijen tüketme eğilimindedir. Kriyoterapi, doku kan akışını ve hücre metabolizmasını %50'den fazla azaltır (Malanga ve ark., 2014).

Sonuç olarak bu durum, dokularda serbest radikallerin üretimini sınırlayarak biyokimyasal reaksiyonların hızını yavaşlatır; oksijen tüketim oranını azaltır; ve doku hipoksisini ve doku yaralanmasını önler (Malanga ve ark., 2014).

Kriyoterapinin lokal fizyolojik etki mekanizmaları da araştırılmıştır. Soğuk uygulaması temel olarak dokulardan ısıyı uzaklaştırır ve sıcaklığın düşmesine neden olur. Sıcaklık düştüğünde vazokonstrüksiyon meydana gelir ve ödem oluşumu kısıtlanır. Vazokonstrüksiyon ayrıca hücre metabolizmasını yavaşlatarak, hücrelerin oksijen ihtiyacını azaltır ve dokularda serbest radikal üretimi sınırlanmış olur. Enflamatuar enzimlerin de artan sıcaklıkla miktarlarının arttığı bildirilmiştir (McLean, 1989). Cilde lokal olarak soğuk uygulamanın ağrı eşiğini değiştirdiği ve ağrıyı azalttığı gösterilmiştir (McLean, 1989). Ayrıca kriyoterapi sinir iletim kapasitesini de etkiler (Sambroski ve ark., 1992). Doku sıcaklığındaki değişikliklerle aktive olan, sıcaklığa duyarlı sinir uçlarına sahip termoreseptör olarak adlandırılan ağrı reseptörlerinin kriyoterapi ile aktivasyonu spinal kord içindeki nosisepsiyonu bloke edebilir (McLean, 1989; Sambroski ve ark., 1992; Ernst ve Fialka, 1994; Malanga ve ark., 2014).

Farklı bir açıdan yaklaşılacak olursa, kriyoterapinin tıpta yaygın olarak kullanılmasına rağmen, etkin uygulamada kullanılan yöntemlerin çok az bilimsel temeli vardır. Bir alanı soğutmak için gerekli süre, bu alanın soğutma maddesinin uzaklaştırılmasından sonra yeterince soğuk kaldığı süre ve soğutma maddesiyle temas halinde olan alanın ötesine geçen soğutma miktarı gibi faktörlerin sistematik olarak anlaşılması bilimsel literatürde şimdiye kadar yetersiz kalmıştır. Bir başka belirsizlik kaynağı da hücre ölümü için gerekli olan sıcaklıktır. Çoğu doku 2,2 °C' de donmasına rağmen, 20 °C' den yüksek sıcaklıklarda hücre ölümünün meydana gelmediği görülmektedir (Modabber ve ark., 2013). Kriyoterapi ile doku hasarı farklı mekanizmalar yoluyla meydana gelebilir. Buz ve benzeri yöntemlerle soğuk uygulama 0 °C civarındadır ve bu düşük sıcaklık lenfatik drenajı azaltabilir (Farah ve Savage, 2006).

Endodontide Kriyoterapi Uygulamaları

Kriyoterapi tıpta olduğu gibi diş hekimliğinde de periodontal cerrahi (Odrich ve Kelman, 1967), çekimler ve implant yerleştirme gibi ağız içi cerrahi işlemlerden sonra şişlik ve ağrı kontrolünde (Rana ve ark., 2011) ve temporomandibular eklem bozuklukları ile ilişkili artriti azaltma (Lande ve Templeton, 1988) gibi bazı durumlarda sıklıkla uygulanmaktadır. Ağız içi cerrahi uygulamalarda kriyoterapi, tipik olarak üçüncü molar diş çekildikten sonra ortaya çıkan ödem ve ağrıyı azaltmak için kullanıldığında olumlu sonuçlar göstermiştir (Rana ve ark., 2011; Fayyad ve ark., 2020).

Kök kanalında kanal içi kriyoterapi uygulaması, endodontik tedavi sonrası post-operatif ağrının yönetimi için basit ve uygun maliyetli bir teknik olarak önerilmektedir (Al-Nahlawi ve ark., 2016; Bazaid ve ark., 2018; Jain ve ark., 2018). İltihaplı periradiküler dokulara kriyoterapi uygulamanın bir yolu, kök kanal sistemini genişlettikten sonra soğuk bir madde ile kanal içi irrigasyondur. EndoVac (Kerr Endo, Orange Country, CA, ABD) sistemi gibi bir negatif basınçlı irrigasyon aktivasyon sistemi kullanıldığında bu işlemin daha başarılı olduğu kanıtlanmıştır (Schoeffel, 2008). Kanal içi kriyoterapinin periapikal dokuların enflamasyonunu azaltmak için diş kökünün dış yüzey sıcaklığını düşürme etkisine dair ilk çalışma 2015 yılında Vera ve ark. tarafından yapılmıştır (Vera ve ark., 2015). Bu *in vitro* çalışmada kanal içi soğuk salin solüsyonlarının irrigasyonda kullanılmasının, dış kök yüzey sıcaklığını 10 °C'den fazla azalttığı ve 4 dakika boyunca koruduğu gösterilmiştir. Bu azalmanın periradiküler dokularda lokal bir anti-inflamatuar etki oluşturmak için yeterli olabileceği teorize edilmiştir Vera ve ark., 2015.

Kriyoterapi için en uygun doz belirlenmemiştir. Dokunun yapısına göre uygun doz değişmektedir. Minimal yağ ve kas dokusu mevcut olduğunda (örneğin bir parmağa uygulandığında), 3 ile 5 dakikalık kriyoterapi önerilmiştir. Kas ve yağ dokusu gibi daha büyük bir hacme sahip olan bölgeler için önerilen süre yaklaşık 20 dakikadır (Bleakley ve Hopkins, 2010).

Kök kanallarında kriyoterapi uygulanmasının zorluklarından biri de apikal ve koronaldeki dentin özelliklerinin (genişlik ve mineralizasyon) farklı olması nedeniyle kökün apikal ve koronal kısımlarında periodontal ligamente soğuk geçişinin farklı olabilmesidir. Ayrıca servikal dentin, daha büyük dentin tübüllerine sahiptir ve iyileştirici uyaranların bitişik dokulara iletilmesini zorlaştırır. Apikal dentinin daha az tübül ile daha mineralize ve daha yoğun olması soğuk iletimini daha etkin hale getirecektir (Xu ve ark., 2016).

Aynı zamanda, ekstremitelerde küçük kan damarlarını etkileyen Raynaud hastalığı ve bölgenin tekrar ısıtılmasından sonra meydana gelen histamin salınımı nedeniyle ürtiker ile ortaya çıkabilen soğuk hipersensitivitesi gibi kriyoterapi için bazı riskler ve kontrendikasyonlar bulunmaktadır. Bu durum ciltte kırmızı noktalara ve soğuğa bağlı eriteme neden olarak tedavi sonrası kızarıklık, kaşıntı, şiddetli ağrı ve kas spazmı ile sonuçlanabilir (Houghton ve ark., 2010). Hemoglobinüri kriyoterapinin bir başka kontrendikasyondur. Bu durumda ise kırmızı kan hücrelerinin hızlı ayrışması sebebiyle hemoglobin kan proteinleri ile birleşemez. Sinir duyarlılığının değiştiği veya daha büyük sinirlerin yüzeye yakın olduğu bölgelerde soğuk tedavi önerilmez (Houghton ve ark., 2010). Ayrıca sistemik olarak aritmi, anjina pektoris, hipertansiyon gibi bazı hastalıkları veya kardiyak rahatsızlıkları olan hastalarda vazokonstriksiyon kan basıncını yükselteceği için kriyoterapi kullanımı da tartışmalıdır (MacAuley, 2001).

Dokunun doğasına bağlı olarak değiştiğinden, kriyoterapi için en uygun dozaj konusunda kesinlik yoktur. Çalışmaların çoğunda kanal içi kriyoterapi süresi 5 dakika olarak tutulmuştur. Vera ve ark. (2015) kök kanallarının 2,5 °C soğuk salin solüsyonu ile 5 dakika irrigasyonunun, dış kök yüzey sıcaklığını düşürdüğünü bildirdikleri için, benzer uygulama süresi çeşitli yazarlar tarafından da kullanılmıştır.

Vera ve ark., (2015) kök kanalında soğuk salin solüsyonunun irrigasyonda kullanılmasının, dış kök yüzey sıcaklığını 10 °C'den fazla azalttığını ve 4 dakika boyunca koruduğunu göstermesi bu konuda yeni çalışmalara öncülük etmiştir Vera ve ark., 2015. Bu bilgiler ışığında son yıllarda endodontik tedavi sonrası ağrıyı azaltmak için kriyoterapinin kanal içi kullanımına yönelik birçok çalışma yapılmıştır (Al-Nahlawi ve ark., 2016; Keskin ve ark., 2016; Bazaid ve ark., 2018; Vera ve ark., 2018; Vieyra ve ark., 2019).

2016 yılında kriyoterapi klinik olarak ilk kez Keskin ve ark., (2016) tarafından endodontide tek seansta kanal tedavisi sonrası postoperatif ağrıyı en aza indirmek için kullanılmıştır. Keskin ve ark., (2016) rastgele iki gruba ayrılan 175 vital dişte, tek seansta yapılan kök kanal tedavisinde son irrigasyon solüsyonu olarak soğuk salin solüsyonunun kullanılmasının post-operatif ağrı üzerindeki etkinliğini değerlendirmişlerdir. Kriyoretapi grubunda kök kanal hazırlığının tamamlanmasından sonra 5 dakika boyunca 2,5 °C %0,9 fizyolojik salin solüsyonu ile irrigasyon yapılırken, kontrol grubunda oda sıcaklığında saklanan fizyolojik salin solüsyonu kullanılmıştır. Ağrı, dolumdan 24 ve 48 saat sonra görsel analog skala (VAS) kullanılarak değerlendirilmiştir. Sonuçlar, kontrol grubuna kıyasla 2,5 °C soğuk salin kullanılan grupta post-endodontik ağrı düzeylerinde önemli bir azalma olduğunu ortaya koymuştur. Kanal içi kriyoterapi grubunda kontrol grubuna göre istatistiksel olarak anlamlı derecede daha düşük ağrı düzeyleri bulunmuştur.

Vera ve ark., (2015) ayrıca buhar kilit etkisini ortadan kaldırmak ve soğuk irrigasyonun apikal üçtebir bölgesine sürekli iletilmesini sağlamak için bir negatif apikal basınç sistemi olan EndoVac'ı (Kerr Endo, Orange Country, CA, ABD) kullanmışlardır (Vera ve ark., 2015). EndoVac kullanımının apikalden irrigasyon solüsyonunun taşma riskini en aza indirerek olası periapikal inflamatuar reaksiyonları azalttığı bildirilmiştir (Siu ve Baumgartner, 2010). Keskin ve ark., (2017) ise tüm hastaların kanal tedavisinde çalışma boyundan 2 mm kısa yerleştirilen yandan perfore 31 gauge NaviTip iğne ile konvansiyonel iğne irrigasyonu uygulamışlardır. Konvansiyonel iğne irrigasyonunun, negatif apikal basınç sistemlerinden önemli ölçüde daha fazla irrigasyon solüsyonunun taşmasına ve post-operatif ağrıya neden olduğu gösterilmiştir (Siu ve Baumgartner, 2010; Keskin ve ark., 2017). Bu nedenle, güvenli bir irrigasyon uygulaması elde etmek için önceki çalışmalarda önerildiği gibi irrigasyon iğnesi, çalışma uzunluğundan 2 mm kısa olacak şekilde kullanılmıştır (Nielsen ve Baumgartner, 2007; Siu ve Baumgartner, 2010). Keskin ve ark.'nın çalışmasında, konvansiyonel yandan perfore iğne ile irrigasyon yapılmış olmasına rağmen; kriyoterapi grubunda, kontrol grubundaki hastalara göre post-operatif ağrı azalmıştır.

Al-Nahlawi ve ark., (2016) 75 adet vital tek köklü dişte tek seansta yapılan kök kanal tedavisi sırasında irrigasyon aşamasında EndoVac kullanarak kanal içi kriyoterapinin post-operatif ağrıya etkisini değerlendirmişlerdir. Kontrol grubunda salinle irrigasyon yapılmamış, deney gruplarında 20 ml oda sıcaklığındaki salin ile 5 dakika boyunca irrigasyon ya da 20 mL 2 ile 4°C'deki soğuk salin ile 5 dakika irrigasyon uygulanmıştır. Ağrı skoru değerlendirmesi, kanal dolumundan sonra 6, 12, 24, 48 saat ve 7 gün sonra VAS kullanılarak yapılmıştır. Çalışmadan elde edilen sonuçlar, soğuk salinle irrigasyon yapılan grupta 6, 12, 24 ve 48 saat sonra VAS ağrı değerlerinin hem oda sıcaklığında salinle irrigasyon yapılan gruptan hem de kontrol grubundan daha düşük olduğunu göstermiştir.

Vieyra ve ark., (2019) yaptıkları çalışmada, farklı sıcaklıklarda üç farklı irrigasyon rejimi kullanarak tek seansta yapılan kök kanal tedavisinden sonra post-operatif

ağrıdaki azalmayı değerlendirmişlerdir. Çalışma için konvansiyonel kök kanal tedavisi gereksinimi olan vital dişlere sahip toplam 240 hasta seçilmiş ve kök kanal hazırlığından sonra, son irrigasyon 4 °C, 2,5 °C ya da oda sıcaklığında %17 EDTA ve 10 mL soğuk salin solüsyonu kullanılarak yapılmıştır. Ağrı seviyesi VAS kullanılarak değerlendirilmiştir. Çalışmadan elde edilen verilere göre, 4°C ve 2,5 °C grupları arasında ağrı derecesi veya ağrı süresinde istatistiksel olarak anlamlı fark bulunamamıştır. Bununla birlikte, oda sıcaklığında EDTA ile irrige edilen hasta grubu, diğer gruplara göre anlamlı derecede daha yüksek post-operatif ağrı göstermiştir.

Vera ve ark., (2015) tarafından sunulan aynı protokolü izleyen diğer çalışmalar, kriyoterapinin vital pulpalı dişlerde tek seansta yapılan kök kanal tedavisinden sonra post-operatif ağrıyı azalttığını doğrulamıştır (Al-Nahlawi ve ark., 2016; Vieyra ve ark., 2019). Bununla birlikte, iltihabın pulpa içinde sınırlı olduğu ve periapikal dokuya yayılmadığı geri dönüşümsüz pulpitiste, iltihaplı pulpanın ekstirpasyonu genellikle hasta rahatlatılarak yapılır. Bu nedenle bu durumda kriyoterapinin post-operatif ağrıyı azaltmadaki doğrudan etkisi bu çalışmalarla belirlenememiştir.

Vera ve ark., 2018 yılında yaptıkları başka bir çalışmada pulpa nekrozu tanılı ve semptomatik apikal periodontitisli dişlerin kök kanal tedavisi sırasında kriyoterapi irrigasyonundan sonra post-operatif ağrı insidansını ve yoğunluğunu incelemişlerdir. Semptomatik apikal periodontitisli ve preoperatif VAS skoru (0-10) 7'den büyük olan toplam 210 tek köklü diş, kanal şekillendirme işlemi tamamlandıktan sonra kontrol grubu ve kriyoterapi deney grubu olmak üzere rastgele iki gruba ayrılmıştır. Kriyoterapi grubu için son irrigasyon, EndoVac kullanılarak 5 dakika boyunca 20 mL 2,5°C salin solüsyonu ile yapılmıştır. Kontrol grubu için ise son irrigasyonda oda sıcaklığında salin solüsyonu uygulanmıştır. Post-operatif ağrı, VAS kullanılarak kanal dolumundan 6, 24 ve 72 saat sonra değerlendirilmiştir. Kontrol ve kriyoterapi grupları arasında post-operatif ağrı insidansı ve yoğunluğu arasında anlamlı bir fark bulunmuştur. Kriyoterapi grubundaki hastalar daha az post-operatif ağrı bildirmişlerdir.

Gündoğdu ve ark., (2018) semptomatik apikal periodontitis tanısı konan azı dişlerinde kanal içi, ağız içi ve ağız dışı kriyoterapinin post-operatif ağrı üzerindeki etkinliğini değerlendirmişlerdir. Yüz dişi; kontrol grubu, kanal içi kriyoterapi, ağız içi kriyoterapi ve ağız dışı kriyoterapi olmak üzere rastgele dört gruba ayırıp ağrı değerlendirmesini VAS kullanarak yapmışlardır. Post-operatif ağrı, endodontik tedaviden 1, 3, 5 ve 7 gün sonra kaydedilmiştir. Sonuç olarak kriyoterapi uygulanan gruplarda, tüm ölçüm günlerinde önemli ölçüde daha az perküsyon ağrısı ve daha az post-operatif ağrı olduğunu bildirmişlerdir.

Alharthi ve ark., (2019) yaptıkları çalışmalarında, endodontik tedaviden sonra post-operatif ağrı kontrolünde, son irrigasyon solüsyonu olarak soğuk veya oda sıcaklığında salin kullanılmasının etkinliğini değerlendirmişlerdir. Kök kanal tedavisi için endikasyonu olan 105 hastanın vital ve vital olmayan dişleri; kriyoterapi grubu, oda sıcaklığında normal salin grubu ve kontrol grubu olmak üzere rastgele üç gruba ayrılmıştır. Post-endodontik ağrı, tedaviden 6, 24 ve 48 saat sonra değerlendirilmiştir. Sonuçlar, kriyoterapi grubunun tedaviden 6 saat, 24 saat ve 48 saat sonra en düşük post-operatif ağrıyı sergilediğini göstermiştir. Genel olarak, kontrol grubu en yüksek post-operatif ağrıyı göstermiştir, ancak ağrı tüm gruplarda zamanla azalmıştır.

Ayrıca bir çalışmada kriyoterapinin post-operatif ağrıyı azaltmadaki etkisi apikal periodontitisi olan ve apikal periodontitisi olmayan geri dönüşümsüz pulpitisli dişler arasında karşılaştırılmıştır (Bazaid ve ark., 2019). Geri dönüşümsüz pulpitisi olan 40 hasta arasında rastgele dağılım yapılmıştır. Hastalar, kullanılan son irrigasyon solüsyonunun sıcaklığına göre rastgele olarak; oda sıcaklığında salin kullanılan kontrol grubu ve soğuk salin kullanılan deney grubu olmak üzere iki gruba ayrılmıştır. Daha sonra gruplar pulpa teşhisine göre apikal periodontitisi olan geri dönüşümsüz pulpitis veya apikal periodontitisi olmayan geri dönüşümsüz pulpitis olmak üzere iki alt gruba daha ayrılmıştır. Bu çalışmanın sonucunda apikal periodontitisli geri dönüşümsüz pulpitisli hastalarda kanal içi kriyoterapi kullanımının post-operatif ağrının azaltılmasında etkili olduğu ancak apikal periodontitis olmayan irreversbl pulpitisli hastaları etkilemediği bildirilmiştir (Bazaid ve ark., 2019). Bu çalışmanın sonuçları daha önce asemptomatik olan ve periapikal patolojisi olmayan vakalarda kriyoterapinin etkisizliğini doğrulayan Alharthi ve ark.,'nın yaptığı çalışmayla uyumludur. Jain ve ark., (2018) da kanal içi kriyoterapiyi sadece apikal periodontitisli semptomatik geri dönüşümsüz pulpitiste post-operatif ağrıyı azaltmak için önermişlerdir.

Yakın zamanda yapılan bir başka çalışmada, Emad ve ark., (2021) semptomatik apikal periodontitisli vakalarda farklı irrigasyon protokollerinin post-operatif ağrı ve interlökin-6 ekspresyonu üzerindeki etkisini araştırmışlar ve 2-5 ml soğuk irrigasyon solüsyonu kullanan tüm irrigasyon

uygulamalarında, oda sıcaklığında solüsyon kullanılan uygulamalara kıyasla önemli ölçüde daha düşük ağrı skoru belirlenmiştir. Ayrıca temizleme ve şekillendirmenin başından sonuna kadar 2-5 ml soğuk sodyum hipoklorit ile irrigasyon yapılan grup, en düşük interlökin-6 seviyesini göstermiştir.

Yakın zamanda yapılan bir çalışmada kriyoterapi, biyoseramik materyallerle birlikte vital pulpa tedavisinde hemostaz sağlamak için denenmiş ve başarılı bulunmuştur (Bahcall ve ark., 2019). Bir vaka raporunda doğrudan pulpa kuafajında pulpa kanamasının kontrolü için kriyoterapinin başarıyla uygulandığı bildirilmiştir. Steril su buzu (0 °C) doğrudan ekspoze olan pulpa dokusuna ve tüm diş yüzeyine 1 dakika süreyle uygulanmış ve daha sonra yüksek emişli aspirasyonla pulpa çıkarılmış ve kök kanalı EDTA ile irrige edilmiştir. Son olarak, ekspoze bölgesi biyoseramik bir materyal ve kalıcı restorasyon ile kapatılmıştır. Tedavi edilen dişler 2 hafta sonra asemptomatik hale gelmiş ve 12-18 aylık bir takip süresi boyunca asemptomatik, canlı ve işlevsel kalmıştır. Vital pulpa kriyoterapisinin uzun vadeli prognozunu belirlemek için daha fazla klinik çalışma yapılması önerilmiştir (Bahcall ve ark., 2019).

Topçuoğlu ve ark., (2019) pre-operatif ağız içi kriyoterapi uygulamasının inferior alveolar sinir bloklarının başarı oranı üzerine etkisini araştırmışlardır. Ağız içi kriyoterapi kullanımının, özellikle semptomatik geri dönüşümsüz pulpitisli dişlerde, alt alveolar sinir bloğunun etkisini arttırdığını bulmuşlardır Topçuoğlu ve ark., 2019. Bununla birlikte, birçok durumda derin pulpal anestezi sağlamak için ek anestezi teknikleri hala gerekli olabilir.

SONUÇ

Diş hekimliğinde ağız içi cerrahi işlemlerden sonra uygulanan ağız dışı soğuk uygulamaların post – operatif ağrı üzerinde gösterdiği olumlu etkiye benzer şekilde kök kanallarında soğuk salin uygulamalarının da olumlu etkiler gösterdiği çalışmalarla desteklenmektedir. Kriyoterapinin etki mekanizması ve etkinliği iyi tanımlanmıştır; bununla birlikte; periyodu, süre, uygulama şekli ve kullanılan soğuk ajan gibi önemli faktörlerin standart hale getirilmesinin yanı sıra, sonuçlarını destekleyecek güçlü kanıtlar sınırlıdır. Bu derlemedeki bilgilere dayanarak kriyoterapinin semptomatik apikal periodontitis vakalarında post-operatif ağrı kontrolü sağlayarak, ağrıyı en aza indirgemek ve vital pulpa tedavisi sırasında pulpa kanamasını kontrol etmek için basit ve ucuz bir yöntem olduğu sonucuna varılabilir. Kriyoterapi uygulamalarının post-operatif ağrıya olan etkisini konu alan birçok çalışma yapılmış olmasına rağmen, kriyoterapinin kök kanal tedavisi sonrasında biyokimyasal belirteçler üzerine olan etkisi ile ilgili literatür bilgisi oldukça kısıtlıdır. Kriyoterapinin post-operatif ağrıya olan etkisi dışında biyokimyasal belirteçler üzerindeki etkisi hakkında literatürü destekleyecek daha fazla araştırmaya gereksinim vardır.

Çıkar çatışması

Yazarlar çalışmada herhangi bir çıkar çatışması olmadığını beyan eder.

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