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Professor İlknur ÖZCAN

Correspondence Address
Biruni University Faculty of Dentistry
Merkezefendi Mahallesi G75. Sokak No:13 Cevizlibağ
Zeytinburnu/İSTANBUL
edr@biruni.edu.tr

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A. Faruk ERTÜRK

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FROM THE EDITOR

We are very pleased to announce to you that our journal, Eurasian Dental Research, which is a new scientific journal in the field of dentistry, has started its publication life.

Eurasian Dental Research aims to contribute to the literature by publishing manuscripts at the highest scientific level on all fields of dentistry. The journal publishes original articles, and rare case reports that are prepared in accordance with ethical guidelines.

The journal is the official publication of Biruni University and published triannually in April, August, and December. The publication language of the journal is English.

No fees or charges are required for manuscript processing and publishing with Eurasian Dental Research.

We aim to be accepted in the internationally respected indices and discovery services in the coming years.

We will be happy to see your scientific studies and articles in Eurasian Dental Research, the journal of our Faculty.

Prof. Dr. İlknur ÖZCAN
Editor in Chief

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The Effects of Hyaluronic Acid Gel on Oral Mucositis in Children Receiving Chemotherapy

Serap KESKİN TUNÇ[1], Yusuf Rodi MIZRAK[2], Gamze AKSU[3], Kamuran KARAMAN[3], Mahide Büşra BAŞKAN[4]

Abstract

Aim Oral mucositis (OM) is a common side effect of systemic chemotherapy (CT) in cancer patients. The aim of this study was to investigate the effect of hyaluronic acid (HA) gel on OM in children receiving CT.

Material and method A total of 40 pediatric patients aged between 3 and 18 years who were diagnosed with leukemia and treated with CT in the inpatient setting were included. The patients were randomly divided into groups. The HA group (n=20) received HA gel and the control group (n=20) received sodium bicarbonate. The grade of OM was evaluated based on the World Health Organization Common Toxicity Criteria Scale. The pain severity was assessed using the Visual Analog Scale (VAS).

Results Of the patients, 21 (52.5%) were girls and 19 (47.5%) were boys. The mean age was 9.37±5.11 (range, 3 to 18) years. The majority of the patients (77.5%) had a diagnosis of pro-B-cell acute lymphoblastic leukemia (ALL). There was no statistically significant difference in the number of OM lesions and VAS scores between the groups (p>0.05).

Conclusion The study results show that both standard oral care with sodium bicarbonate and HA gel have similar effects on pain relief and regression of OM in pediatric cancer patients undergoing CT. The HA gel is a feasible alternative for the pediatric population.

Keywords Chemotherapy, Childhood leukemia, Hyaluronic acid gel, Oral mucositis, Pediatrics

Introduction

Oral mucositis (OM) is a common side effect of chemotherapy (CT) and radiation therapy (RT), characterized by erythematous and ulcerated oral mucosal lesions (1). It is seen in about 80% of patients receiving high-dose CT and in nearly 100% of patients receiving RT to the head and neck region (2).

Oral mucositis is associated with pain, dysphagia, loss of taste, weight loss, and secondary infections, leading to impaired quality of life (3). It is more common in young individuals than elderly (4). Due to the cytotoxic effects of CT on epithelial basal cell layer, as well as atrophy and tissue ulceration, the reparative and regenerative process of the tissues is reduced. In addition, nearly all CT agents suppress the bone marrow, leading to granulocytopenia and thrombocytopenia and predisposing the patient to infection and bleeding (5). The ulcerated oral epithelium prepares the ground for the entry of microbes into the body, thereby resulting in systemic and local infections. Then, patients become dehydrated and malnourished due to pain. As OM progresses following CT, cellular and molecular alterations occur, leading to breakage of the deoxyribonucleic acid (DNA) helix and release of reactive oxygen species (ROS) into the circulation. The ROS activates transcription factors such as P53 and nuclear factor-kappa B (NF-κB), leading to cellular apoptosis (6). Several factors are involved in these biological processes including the drug dose, drug toxicities, time interval between CT cycles, additional RT, the general condition of the patient, sensitivity of the patient to CT agents, and oral hygiene and dental status of the patient (7).

The management of CT-related side effects includes antimicrobial mouthwash, adhesive mucosal barrier, cryotherapy, and topical analgesics (2). In recent years, keratinocyte growth factor (KGF), low-level laser therapy (LLLT), and hyaluronic acid (HA) have been investigated in the treatment of OM (8).

Sodium Bicarbonate (SB) is a widely used agent for the prevention and treatment of OM, a condition that causes inflammation and ulceration of the mucous membranes in the mouth. It is also used as a cleansing agent due to its ability to dissolve mucus and loosen debris. The benefits of SB use are due to its alkalizing effect, which raises oral pH and prevents the growth of aciduric bacteria. This makes saliva more fluid and prevents the accumulation of detritus. Furthermore, its use is strongly encouraged due to its low cost, patient-friendly application, lack of side effects, and long shelf life (9).

The HA is a natural polysaccharide composed of D-glucuronic acid and N-acetyl-D-glucosamine and is synthesized as a linear polymer. The majority of the cells have a capacity to synthesize HA at a varying extent in the cell cycle. The main function of

Correspondence: Mahide Büşra BAŞKAN, busrademirok@gmail.com

[1] Health Science University, Faculty of Hamidiye Dentistry, Department of Oral and Maxillofacial Surgery, Istanbul, Türkiye

[2] Van Yüzüncü Yıl University, Faculty of Dentistry, Department of Oral and Maxillofacial Surgery, Van, Türkiye

[3] Van Yüzüncü Yıl University, Faculty of Medicine, Department of Pediatric Hematology, Van, Türkiye

[4] Istanbul University, Faculty of Dentistry, Department of Oral and Maxillofacial Surgery, Istanbul, Türkiye

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HA appears to be in tissue healing, by activating and modulating inflammatory responses, stimulating cellular proliferation, migration, and angiogenesis, inducing basal keratinocyte proliferation and re-epithelization by reducing collagen deposition and scarring (10). Animal (11, 12) and clinical studies (10, 13, 14) have shown that HA yields favorable results in reducing pain and inducing healing in wound healing and ulcerative aphthous lesions. It is also known that topical hyaluronic acid application may be effective in the symptomatic treatment of oral mucositis observed after CT (15). Although there are not enough studies on human subjects, animal experiments have shown that hyaluronic acid is certainly effective in the treatment of oral mucositis (16). In the present study, we aimed to investigate the effect of HA gel on OM in CT-treated pediatric patients.

Material and Methods

Study design and study population

This clinical cross-sectional study was conducted at the Department of Pediatric Hematology and Oncology of a tertiary care center in Van, Turkey, between June 1st, 2019, and June 2nd, 2020. The study included pediatric patients aged 3 to 18 years who were hospitalized with a diagnosis of malignancies, receiving chemotherapy (CT), and capable of cooperating with study procedures. Inclusion criteria required patients to meet these conditions, while exclusion criteria included the presence of other systemic diseases, prior exposure to radiotherapy, or cooperation difficulties.

A total of 59 patients were assessed for eligibility. 11 patients of these patients did not meet the inclusion criteria and were excluded. Among the 48 eligible patients, 43 agreed to participate, while 5 declined. The enrolled participants were randomly divided into two equal groups of 20 patients each, using the envelope randomization method. The remaining three patients discontinued participation during the study period (two from the control group and one from the HA group), leaving 20 patients in each group for final analysis. The study flowchart is shown in Figure 1.

ALLIC BFM (Acute Lymphoblastic Leukemia Berlin-Frankfurt-Münster study group trials) 2009 chemotherapy protocol, an internationally accepted treatment protocol, was applied at the clinic. The protocol is for childhood leukemia and lasts approximately 2.5 years. Both groups received equal or similar doses of CT as per the treatment protocol.

Prior to enrollment, written informed consent was obtained from the parents and/or legal guardians of all participants. The study protocol was approved by the Van Yuzuncu Yil University Faculty of Medicine Clinical Research Ethics Committee (No: 06/03.07.2019) and was conducted in accordance with the principles outlined in the Declaration of Helsinki.

The first group served as the control group. Patients and their caregivers received routine oral hygiene education prior to CT. This included instructions on brushing teeth and the tongue twice daily using a soft-bristled nylon toothbrush and fluoride toothpaste. Patients were advised to avoid foods that remain in the mouth for extended periods. Oral care was performed four times daily after meals using a bicarbonate serum solution (0.9% sodium chloride and 5% sodium bicarbonate). If oral mucositis (OM) developed, the lesions were treated with bicarbonate solution four times a day, regardless of OM severity. In cases of severe pain, topical local anesthetics were permitted.

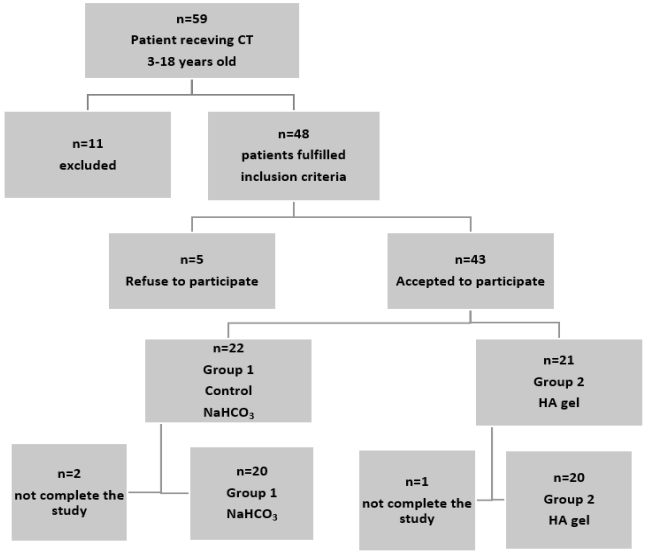

Figure 1: Study flowchart (CT: Chemotherapy, HA: Hyaluronic Acid)

The second group (HA group) also received routine oral hygiene education before CT. Once OM developed, the lesions were treated with high-molecular-weight hyaluronic acid (HA; sodium salt, 600 mg/100 g; Aftamed® protective barrier gel, Aktident, Istanbul, Turkey) four times daily (morning, afternoon, evening after meals, and night) for five to seven days, in accordance with the manufacturer's instructions. The gel was applied directly to the lesions, and patients were instructed to refrain from consuming food or beverages for 30 minutes post-application. Similar to the control group, topical local anesthetics were permitted in cases of severe pain.

Assessment and follow-up

Both groups were followed for five and seven days and on Days 0, 1, 2, 3, 4, 5, 6, 7, and 11 according to the World Health Organization (WHO) Common Toxicity Criteria Scale (12). The pain severity was assessed using the Visual Analog Scale (VAS). Recurrence, grade of OM, and VAS scores were recorded, and the same treatment protocol was applied according to the group allocation. All patients were followed for OM, until CT was discontinued.

OM scoring

The OM grading was performed by the same team including a pediatric hematologist and a pediatrician based on the WHO Common Toxicity Criteria Scale. The lesions were classified as Grade 0 = absent; Grade 1 = pain and erythema; Grade 2 = erythema and ulcers with no difficulty in swallowing solid food; Grade 3 = ulcers requiring only liquid diet; and Grade 4 = requiring parenteral and enteral nutrition support. Oral examination and OM scoring were performed on Days 1, 2, 3, 4, 5, 6, 7, and 11, starting from the day of laser treatment. The dentist performing the laser and the pediatrician were excluded from OM grading.

Pain scoring

The VAS is a useful tool which has been widely utilized all over the world (17). In this study, it was also used to evaluate pain status of the patients at the same timepoints with OM grading. The score ranges from 0 (no pain) to 10 (worst pain). Using the VAS, the patients were asked to mark their pain intensity between 0 and 10 (Figure 2).

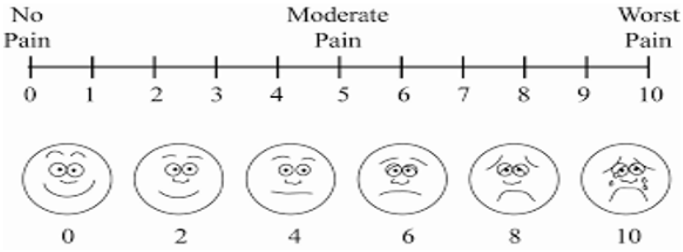

Figure 2: Visual Analog Scale for children

Statistical analysis

The effect size according to the difference in the OM measurements of the control and HA groups on the 11th day compared to the 0th day; 1.038 and post hoc power is 89.24%.

Statistical analysis was performed using the NCSS (Number Cruncher Statistical System) version 2020 software (NCSS LLC, Kaysville, UT, USA). Continuous data were presented in mean ± standard deviation (SD) or median (min-max), while categorical data were presented in number and frequency. The normality of distribution was checked using the Kolmogorov-Smirnov test. The Mann-Whitney U test was performed to compare non-normally distributed quantitative variables between the groups. The Pearson chi-square, Fisher exact, and Fisher-Freeman-Halton exact tests were used to compare qualitative variables between the groups. The Friedman test was used for the intra-group analysis of the non-normally distributed quantitative variables. A p value of <0.05 was considered statistically significant.

Results

A total of 40 patients were included in the study. Of these patients, 21 (52.5%) were girls and 19 (47.5%) were boys. The mean age was 9.37±5.11 (range, 3 to 18) years. There was no statistically significant difference in the age and sex between the groups (p>0.05).

Thirty-one patients (77.5%) were diagnosed with pro-B-cell acute lymphoblastic leukemia (ALL), one (2.5%) with T-cell ALL, one (2.5%) with Hodgkin lymphoma, three (7.5%) with acute megakaryoblastic leukemia (AML)-M7, and four (10%) with Burkitt lymphoma. The mean number of CT sessions was 5±1 (range, 2 to 8). There was no statistically significant difference in the distribution of diagnosis and number of CT sessions between the groups (p>0.05) (Figure 3).

The mean number of OM lesions was 3.77±2.04 (range, 1 to 9), indicating a statistically significant difference between the groups (p=0.014 and p<0.05, respectively). The number of OM lesions was statistically significantly higher in the HA group (p<0.05). Oral mucositis mostly affected the buccal mucosa in 20 (50%), sublingual mucosa in 17 (42.5%), palatal mucosa in 24 (60%), lips in nine (22.5%), and oral mucosa in 13 patients (32.5%). There was no statistically significant difference in the distribution of affected areas between the groups (p>0.05) (Table 1).

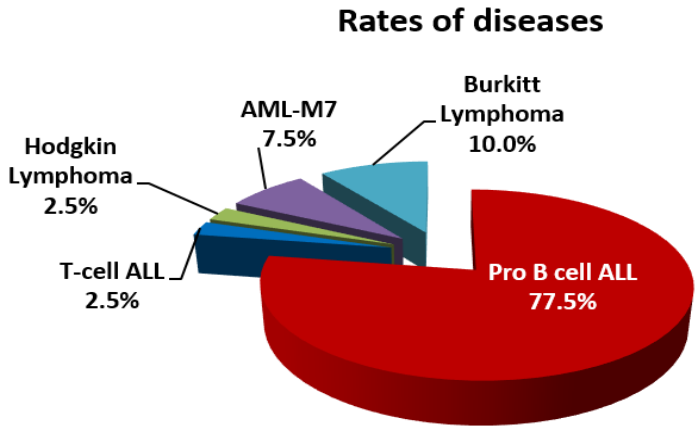

Figure 3: Distribution of diseases of children included in the study (AML: Acute Megakaryoblastic Leukemia; ALL: Acute Lymphoblastic Leukemia)

The number of OM lesions was the highest on Day 0 in both groups with a gradual decrease toward Day 11. The number of OM lesions was higher in the HA group than the control group on Days 0, 1, 2, 3, 4, and 7, while this number was reduced on Day 11. However, there was no statistically significant difference in the number of OM lesions on Days 0, 1, 2, 3, 4, 7, and 11 between the groups (p>0.05) (Figure 4).

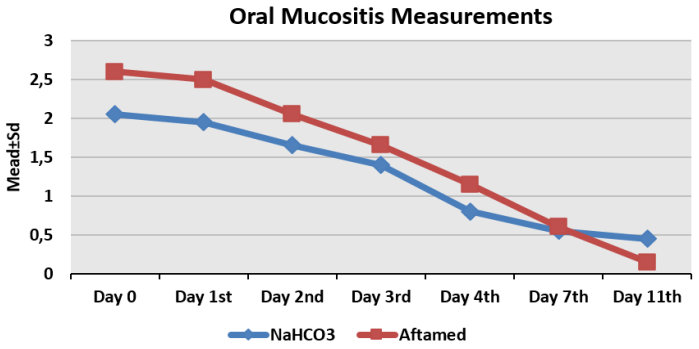

Figure 4: Distribution of oral mucositis measurements (Sd: Standard deviation)

According to the VAS pain scores, the highest score was observed on Day 0 with a gradual decrease toward Day 11. There was no statistically significant difference in the mean VAS scores on Days 0, 1, 2, 3, 4, 7, and 11 between the groups (p>0.05) (Table 2).

Table 1: Distribution of intraoral regions with oral mucositis

Regions with oral mucositis	n (%)
Buccal region	20 (50.0)
Sublingual region	17 (42.5)
Palatal region	24 (60.0)
Labial region	9 (22.5)
Other	13 (32.5)

Oral mucositis has been observed affecting multiple regions in a single patient.

Table 2: Comparison of VAS scores in the groups on days 1, 2, 3, 4, 7, and 11

VAS		$NaHCO_3$	Aftamed	p*
VAS day 0	Mean ± Sd	7.30 ± 1.62	7.20 ± 1.64	0.816
	Median (min - max)	8 (4 - 10)	7 (4 - 10)	
VAS day 1st	Mean ± Sd	7.10 ± 1.65	7.20 ± 1.64	0.907
	Median (min - max)	8 (4 - 10)	7 (4 - 10)	
VAS day 2nd	Mean ± Sd	6.20 ± 1.82	6.00 ± 1.94	0.831
	Median (min - max)	6 (2 - 10)	6 (2 - 8)	
VAS day 3rd	Mean ± Sd	5.00 ± 1.65	5.00 ± 1.90	1.000
	Median (min - max)	5 (2 - 8)	5 (2 - 8)	
VAS day 4th	Mean ± Sd	3.30 ± 2.53	3.60 ± 2 .11	0.685
	Median (min - max)	4 (0 - 8)	4 (0 - 6)	
VAS day 7th	Mean ± Sd	2.50 ± 2 .58	2.35 ± 2.03	0.978
	Median (min - max)	2 (0 - 8)	2 (0 - 6)	

VAS: Visual Analog Scale, Sd: Standard Deviation, Min: Minimum, Max: Maximum
p: Probability value*

Discussion

Oral mucositis is one of the most frequent complications of CT and RT. Despite a vast body of research on this topic in the literature, there is no completely effective treatment or prevention method for OM. The majority of studies have aimed to decrease the frequency and severity of OM rather than to prevent it. In the present study, we compared two methods which are commonly used in the clinical practice in pediatric patients receiving CT. The study's results showed that HA gel was as effective as sodium bicarbonate in reducing pain and the number of OM.

Although there are several studies showing a direct correlation between the frequency of OM and the number of CT sessions, some authors have reported the opposite (18, 19). In the current study, both groups received an equal or similar number of CT sessions to prevent controversial outcomes.

Until now, several methods have been described for the prevention and treatment of OM. Topical HA application has been shown to be an effective method with rapid symptomatic relief for oral ulcers including recurrent aphthous stomatitis (20), which was the basis of the hypothesis that HA could be an effective method for the treatment of OM. In their study, Shahrabi et al. (15) reported that HA was significantly more effective than placebo for the management of pain. Similarly, in this study, the highest score was observed on Day 0, followed by a gradual decrease toward Day 11 in patients receiving HA gel, which is consistent with findings reported in the literature.

According to the Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology (MASCC/ISOO) clinical practice guidelines, basic oral hygiene methods are effective in the management of OM (1). Sodium bicarbonate ($NaHCO_3$) is one of the most common mouthwash agents used in the basic oral hygiene. The MASCC/ISOO guidelines state that there is no recommendation for the use of sodium bicarbonate in the management of OM due to the lack of strong evidence; however, it is advised to be used as one of the oral hygiene protocols for the prevention of OM. In a systematic review, McGuire et al. (21) reported that sodium bicarbonate was a beneficial and harmless method for both oral hygiene maintenance and patient comfort. Several studies have demonstrated that sodium bicarbonate rinse is beneficial and free from serious side effects; however, children may complain about its unpleasant taste (17). Of note, previous studies have reported no significant difference in the effectiveness of sodium bicarbonate and other mouthwashes in reducing OM symptoms (22). In a randomized clinical study, Saxen et al. (23) found no significant difference in the VAS scores between diclofenac sodium and HA gel applications.

Currently, high-molecular-weight HA is commercially available in various formulations (e.g., sprays, gels, and mouthwashes) and concentrations (0.2%, 0.8%, 2.5%, and 3%) (14, 23, 24). Several studies showing the effectiveness of HA in the management of OM have suggested that HA enhances the healing process and reduces the number of OM lesions (15, 25). In a randomized clinical study, Yıldırım et al. (26) evaluated the effect of two different HA concentrations (0.2% versus 0.8%) on postoperative pain and wound healing of palatal donor sites after free gingival graft surgery. They reported that the mean VAS score was improved with the 0.2% HA concentration. In the present study, we used Aftamed® protective barrier gel at 0.6% concentration; however, there is still a need for further studies comparing 0.2% and 0.6% HA concentrations to draw more reliable conclusions on this subject.

Nonetheless, there are some limitations to this study. First, this study's population consisted of pediatric patients and the application of HA gel was difficult to apply for the parents and/or caregivers. As NAHCO3 is liquid and is used as a mouthwash, it can exert positive effects on OM sites located in the throat and adjacently to the tongue root which are invisible, yielding similar results to HA. Further studies comparing HA gel and mouthwash formulations of HA would provide valuable information on this issue.

We believe that one of the reasons for the absence of a significant difference among the methods we compared is the varied application techniques. It is important to note that, due to the gargling form of sodium bicarbonate, it may be effective in the oropharynx; however, it should not be overlooked that HA can only be applied in the oral cavity. The fact that sodium was used as a mouthwash and HA was used as a gel during the study is the limitation of this study.

Conclusion

Oral mucositis is one of the most frequent complications of CT and RT. Despite a vast body of research on this topic in the literature, there is no completely effective treatment or prevention method for OM. The majority of studies have aimed to decrease the frequency and severity of OM rather than to prevent it. In the present study, we compared two methods which are commonly used in the clinical practice in pediatric patients receiving CT. The study's results showed that HA gel was as effective as sodium bicarbonate in reducing pain and the number of OM.

Declarations

Ethics Committee Approval: *The study protocol was approved by the Van Yuzuncu Yil University Faculty of Medicine Clinical Research Ethics Committee (No: 06/03.07.2019)*

Informed Consent: Written informed consent was obtained from patient who participated in this study.

Peer Review: Externally peer-reviewed.

Author Contributions: *Conception/Design of Study- S.K.T., Y.R.M., G.A., K.K., M.B.B.; Data Acquisition- G.A., K.K.; Data Analysis/Interpretation- S.K.T., Y.R.M., M.B.B.; Drafting Manuscript- S.K.T., Y.R.M., G.A., K.K., M.B.B.; Critical Revision of Manuscript- S.K.T., Y.R.M., G.A., K.K., M.B.B.; Final Approval and Accountability- S.K.T., Y.R.M., K.K.; Material and Technical Support- S.K.T., Y.R.M., G.A., K.K., M.B.B.; Supervision- S.K.T., M.B.B.*

Conflict of Interest: *Authors declared no conflict of interest.*

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Comparative Evaluation of Surface Hardness and Color Stability of Dental Composites with Different Photoinitiators

Zafer Ege KESER[1], Musa Kazım ÜÇÜNCÜ[2,3]

Abstract

Aim This study aims to comparatively investigate the color stability and microhardness values of dental composites with different photoinitiators.

Material and method In the study, Ivoclar Tetric N-Ceram, Dentac Parion, and FGM Llis composites were used. A total of 30 composite discs were evenly divided for surface microhardness and ΔE measurements. Each subgroup contained 5 composite discs (Diameter: 5 mm, Thickness: 2 mm). Before the experimental procedures, all composite discs were aged in a coffee solution for one week. Surface microhardness was measured using the Vickers Hardness Test device, while color stability was assessed with a spectrophotometer. One-way ANOVA and Two-Way Repeated Measures ANOVA with Bonferroni-adjusted pairwise comparisons were applied.

Results No statistically significant difference was observed among the three dental composite groups in terms of color stability ($p > 0.05$). However, their color stability performance ranked from highest to lowest as follows: Llis (3.13 ± 0.42) > Parion (2.76 ± 0.57) > Tetric N-Ceram (2.70 ± 0.76). In contrast, a statistically significant difference was detected among the groups regarding surface microhardness ($p < 0.05$). Llis exhibited significantly higher values compared to Tetric N-Ceram and Parion ($p < 0.05$).

Conclusion The compositional structure of the composite material and the photoinitiator mechanism used are directly related to the formation of its mechanical properties.

Keywords Camphorquinone, Color stability, Dental composite, Microhardness, Photoinitiator

Introduction

Advancements in dental composites have reached an unprecedented level, with modifications in both the inorganic and organic components yielding more aesthetic and functional restorative materials (1).

Technological innovations have facilitated the transition from chemically polymerized composites to light-cured materials, significantly enhancing color stability and other mechanical properties of composite restorations (2). This pivotal shift in composite polymerization has been largely driven by the incorporation of photoinitiators such as camphorquinone, which play a fundamental role in initiating the polymerization cascade through the generation of free radicals upon light activation (3,4). Among these, camphorquinone remains the most widely employed photoinitiator (5). Camphorquinone exhibits an absorption spectrum within the blue region of visible light, with a wavelength range spanning 360–510 nm (4,5). However, its most significant drawback lies in its intrinsic yellow coloration. The increased weight percentage of camphorquinone within the composite matrix results in a pronounced yellowish hue and reduced luminosity, which can, in turn, influence color stability, mechanical performance, and the degree of conversion (6). Resin-based composites may also incorporate various alternative photoinitiators with distinct chemical structures and formulations, such as benzophenone (7), 1-phenyl-1,2-propanedione (PPD) (8), dibenzoyl germanium (Ivocerin) (9), diphenyl(2,4,6-trimethylbenzoyl)-phosphine oxide (TPO) (10), and Lucirin TPO (11) each offering potential advantages in mitigating the limitations associated with camphorquinone.

In this context, our study aims to comparatively evaluate the microhardness values and color stability of three distinct dental composite materials, each containing a different photoinitiator, following a one-week aging process in a coffee solution. The null hypothesis of this study is stated as follows: There is no statistically significant difference among the three composite materials in terms of color stability and microhardness values.

Material and Methods

Design of study

This study was conducted at the Hard Tissue Laboratory of the Altınbaş University Faculty of Dentistry Dental Hospital.

Correspondence: Musa Kazım ÜÇÜNCÜ, ucuncumusakazim@gmail.com

[1] Student Dentist, Altınbaş University, Faculty of Dentistry, Istanbul, Türkiye

[2] Altınbaş University, Faculty of Dentistry, Department of Restorative Dentistry, Istanbul, Türkiye

[3] Health Sciences University, Faculty of Hamidiye Dentistry, Department of Restorative Dentistry, Istanbul, Türkiye

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Furthermore, ethical approval is not required for this study, as no live animal or human-derived products were used in its execution. It incorporated composite resins with distinct photoinitiator systems, specifically Tetric N-Ceram (Ivoclar; Schaan, Liechtenstein), FGM Llis (FGM Group; Brazil), and Parion (Dentac; Turkey) (Table 1). Prior to initiating the study, a power analysis was performed using the G*Power statistical software package (G*Power Ver. 3.0.10, Germany). Based on the parameters established by Yildirim Ucuncu et al. (12), the power analysis was conducted with a Type I error probability of 0.05 (95% confidence interval), a test power of 0.8 (Type II error = 0.20), and an effect size of 1.73. Under these conditions, the required sample size was determined to be five specimens per subgroup (n = 5). The study was conducted in two separate phases.

Table 1: The compositional information and lot numbers of the dental composites

Brand of dental composites	Origin	Contain	Photoinitiator	Recommend Polymerization Technique	Lot Number
Tetric N-Ceram	Ivoclar Group, Schaan, Liechtenstein	UDMA, Bis-EMA, Bis-GMA, copolymer, Si-Zr mixed oxide, ytterbium trifluoride, inorganic fillers: 54-56 vol% particle size: 0.11 µm – 15,5 µm	Dibenzoil germanium	500-900 mW/cm2 : 20 s 1000-1300 mW/cm2 : 10 s 1800-2200 mW/cm2 : 5 s	Z04ZB2
Parion	Dentac, T-Resto, Türkiye	Bis-GMA, Bis-EMA, UDMA, TEGDMA inorganic filler, silica, quartz Inorganic fillers: 77-78 w% & 66 v%	Camphorquinone	≥800 mW/cm2 20 s	PN220122
Llis	FGM Dental Group, Brasil	Bis-GMA, TEGDMA, Bis-EMA, UDMA camphorquinone, co-initiators, Silane, Barium-Aluminum Silicate Glass, Silicon Dioxide Inorganic fillers: 56-59 v% & 77.5 -78.5 w% Particle size: 40 nm -0.7 µm (average size: 0.7 µm)	Camphorquinone + co-initiator (tertiary amine)	1200 mW/cm2: 20 s (translucent & enamel) – 40 s (dentin & body) (2.7 -3.0 mm) 700 mW/cm2 : 20 s (translucent & enamel) – 40 s (dentin & body) (2.2 -2.9 mm) 500 mW/cm2: 20 s (translucent & enamel) – 40 s (dentin & body) (1.9 – 2.5 mm)	310823

Measurement of color stability

Baseline and post-staining color measurements were conducted under standardized conditions, at the same time of day, using a spectrophotometer (Vita Easy Shade Compact, VITA Zahnfabrik, Bad Säckingen, Germany). Prior to each measurement, the device was calibrated according to the manufacturer's instructions using the built-in ceramic reference block. Specimen preparation was carried out using Teflon molds, each with a diameter of 5 mm and a thickness of 2 mm, to ensure uniformity. Five composite resin discs were fabricated for each subgroup (n=5; per group), and this phase of the study was conducted with a total of 15 composite discs. A transparent celluloid strip was first placed on a microscope slide, followed by stabilization of the Teflon mold. Composite resin was then carefully introduced into the mold using a plastic spatula, ensuring the absence of air bubbles. Subsequently, another transparent celluloid strip and a microscope slide were placed atop the mold. Gentle finger pressure was applied to eliminate excess material and ensure a smooth, uniform surface. Following this, only the microscope slide was removed, and polymerization was carried out directly through the transparent celluloid strip, adhering to the designated polymerization protocols (ValoTM Cordless, Ultradent, Cologne, Germany). This approach effectively prevented the formation of an oxygen inhibition layer, ensuring optimal polymerization quality. The light-exposed upper surfaces of the specimens were carefully marked and removed from the molds without deformation. Each specimen was then placed in a tube containing distilled water and stored in a dark incubator at 37°C for 24 hours to ensure proper hydration and stabilization. For baseline color measurements, the specimens were removed from the distilled water, gently dried, and analyzed using the CIELAB color system. Measurements were performed three times for each specimen, precisely at the center of the resin surface. The arithmetic mean of these three measurements was calculated to obtain the average L, a, and b values. To simulate staining and aging, a coffee solution was prepared by dissolving 2 g of coffee in 200 mL of boiling water, followed by filtration through a filter paper to remove residues. The specimens were then immersed in 5 mL of the prepared coffee solution within separate tubes and stored in a 37°C incubator for 24 hours (13). At the end of the immersion period, the specimens were removed from the coffee solution, gently dried, and subjected to post-staining color measurements, following the same protocol as the baseline assessments.

The changes in color coordinates were determined using the following equations:

$\Delta L^*=L2-L1, \Delta a^*=a2-a1, \Delta b^*=b2-b1$

The total color change $(\Delta E)^*$ was calculated using the formula:

$$\Delta E^*_{ab} = \sqrt{(L^*_2 - L^*_1)^2 + (a^*_2 - a^*_1)^2 + (b^*_2 - b^*_1)^2}$$

Measurement of microhardness

The Vickers hardness test was employed to assess the surface hardness of both the upper and lower surfaces of the specimens and to determine their hardness ratio. Specimen preparation followed the same protocol described in Section 2.2. Measurement of Color Stability, utilizing Teflon molds with a diameter of 5 mm and a thickness of 2 mm to ensure uniformity. Five composite resin discs were fabricated for each subgroup (n=5; per group), and this phase of the study was conducted with a total of 15 composite discs. The light-exposed upper surfaces of the specimens were carefully marked and removed from the molds without deformation. Subsequently, the specimens were stored in tubes containing distilled water and incubated in a dark environment at 37°C for 24 hours. Following the incubation period, hardness measurements were performed using a Vickers hardness testing device (Shimadzu HMV-2, Japan). This device features a touchscreen panel, allowing precise adjustment of test load, test duration, and other parameters. The test load is adjustable between 98.07 mN and 19.914 N, while the test duration ranges from 5 to 999 seconds. Additionally, the device is equipped with two ocular lenses providing 10x and 40x magnification. A 50 g load was applied for 30 seconds to the upper surfaces of the specimens, creating a diamond-shaped indentation. The projection corners of this indentation were marked under 40x magnification for precise measurement. Three hardness measurements were obtained from distinct locations on the upper surface of each specimen, ensuring a minimum spacing of 100 µm from the specimen's edges and between measurement points. The arithmetic mean of these three measurements was recorded as the Vickers Hardness Number (VHN) for the upper surface.

Statistical analysis

All statistical analyses were conducted using GraphPad Prism software (GraphPad Software, Inc., California, USA). Descriptive statistical methods, including mean, standard deviation, and median, were employed to summarize the study data. The normality of quantitative variables was assessed using the Shapiro-Wilk test alongside graphical inspections. For comparisons involving three or more normally distributed groups, a One-Way ANOVA was performed. In cases where measurements were taken at different time points on the same material with two independent variables, a Two-Way Repeated Measures ANOVA was utilized. To control for multiple comparisons, Bonferroni-adjusted pairwise comparisons were applied, ensuring the identification of statistically significant differences between groups. A significance threshold of $p < 0.05$ was considered indicative of statistical relevance.

Results

The mean microhardness values are presented in Table 2. Microhardness test results were analyzed using a Two-Way Repeated Measures ANOVA, revealing a statistically significant difference among composites aged in the coffee solution ($p < 0.05$). To determine the source of this variation, a Bonferroni-adjusted multiple comparison test was conducted. No statistically significant difference was observed between the microhardness values of N-Ceram and Parion dental composites ($p > 0.05$). However, Llis dental composite exhibited significantly higher microhardness values than both counterparts ($p < 0.05$) (Table 3). Post-immersion color stability, assessed through ΔE values, was analyzed via One-Way ANOVA. No statistically significant difference was detected among the dental composites in terms of color stability ($F = 0.7476$; $p > 0.05$) (Table 4). Notably, ΔE values for all three composites remained below the clinically perceptible threshold of 3.3, ranking from worst to best as Llis > Parion > Tetric N-Ceram.

Table 2: The microhardness values of the dental composites

	Microhardness (VHN)	
	Before aging	**After aging**
Tetric N-Ceram	35.18 ± 3.59	35.82 ± 3.95
Dentac Parion	36.84 ± 5.07	34.26 ± 4.26
Llis	45.01 ± 11.21	41.86 ± 10.57

Table 3: Post-hoc analysis multiple comparisons

Microhardness	Mean Differences	95,00% CI of differences	Adjusted P Value
N- Ceram vs. Parion	1.450	-0.3570 to 3.257	>0.9999
N- Ceram vs. Llis	-6.457	-11.97 to -0.9395	0.0016*
Parion vs. Llis	-7.907	-14.06 to -1.755	<0.0001*

*Two-Way Repeated Measures ANOVA -Pairwise comparisons with Bonferroni correction *p<0.05*

Table 4: The comparison of ΔE values

	ΔE	p
Tetric N-Ceram	2.70 ± 0.76	>0.05
Dentac Parion	2.76 ± 0.57	
Llis	3.13 ± 0.42	

One-Way ANOVA

Discussion

Based on the findings, the null hypothesis of this study was partially rejected. While no statistically significant difference was observed among the composites in terms of color stability, a significant difference was detected in microhardness values.

It is well established that various systems, such as CIELAB, CIEDE2000, and CMC, are utilized in devices designed to quantify color data and calculate ΔE values (14,15). Among these, CIELAB is recommended for dental applications, as it characterizes color based on human perception and provides a suitable framework for detecting subtle color differences (16). Spectrophotometers, developed to facilitate rapid color analysis while ensuring adequate color information, direct light onto the sample surface and provide readings in CIE L* a* b* units. In this study, the VITA Easy Shade spectrophotometer—a widely employed device in the literature—was used for this purpose (13,17,18). Extensive research has been conducted to determine the acceptability and perceptibility thresholds of different color systems (14,19). Paravina et al. (19) defined the 50:50% perceptibility threshold for CIELAB as 1.2 and the acceptability threshold as 2.7, while Ruyter et al. identified the

threshold for an unacceptable ΔE value at approximately 3.3 (20). Additionally, studies have proposed higher thresholds, such as 4.2 (21) and 5.5 (22). In light of this information, composite materials with ΔE values below 3.3 were considered clinically acceptable in this study, and no statistically significant differences were found among the tested composites.

Hardness testing methods, including Brinell, Knoop, and Vickers, employ distinct techniques and application protocols (23). Among these, the Vickers test is widely used in dentistry due to its applicability across a broad range of materials. As a non-destructive method, it determines microhardness by automatically measuring the diagonal length of the quadrilateral indentation created by a diamond indenter (12,23,24). The literature indicates that various loading weights have been used in conjunction with different holding times (12,24–26), and an ISO standard has been established for this purpose (27). Based on the microhardness test results, the highest values—both before and after a one-week aging period in a coffee solution—were observed in the Llis group. Statistically significant differences were found between Llis and both Tetric N-Ceram and Parion. However, no significant difference was detected between Tetric N-Ceram and Parion, with their values exhibiting close similarity. The Llis composite, when immersed for varying durations in acidic solutions such as ferrous sulfate (pH: 4.5) and paracetamol (pH: 3.6), exhibited lower microhardness values in ferrous sulfate compared to paracetamol (26). Acidic solutions may lead to surface degradation by inducing matrix breakdown and dissolution within the composite structure, thereby compromising key properties such as surface roughness and microhardness (26,28). According to the literature, the pH of coffee is reported to range between 4.85 and 5.13. However, the absence of direct pH measurement using an indicator in our study represents a limitation. Consequently, restorative materials subjected to prolonged exposure in coffee solutions may be expected to exhibit reduced microhardness values and diminished color stability over time (29).

The inorganic filler composition of Llis comprises smaller particles compared to Tetric N-Ceram and Parion, while its volumetric filler content is notably higher. The type and content of inorganic fillers incorporated into the chemical composition of resin-matrix composites exert a direct influence on their polymerization mechanism (30). Increasing the filler content has been shown to enhance VHN (12,31), whereas the degree of conversion may remain unaffected, potentially leading to reduced polymerization shrinkage (32). This fundamental principle accounts for the superior hardness values observed in the Llis composite compared to the others. To address the inherent limitations of camphorquinone-based or camphorquinone-amine-based dental composites—such as their yellowish hue, which compromises esthetics, and their rapid photopolymerization under ambient light—alternative photoinitiators, including phenylbis(2,4,6-trimethylbenzoyl)phosphine oxide (BAPO), dibenzoyl germanium (Ivocerin), and diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide (TPO), have been introduced and integrated into composite formulations (3,9,33). Notably, TPO-containing composites have been demonstrated to offer superior color stability compared to conventional camphorquinone-based resin composites (11,33). Ivocerin, a germanium-based photoinitiator with broad-spectrum short-wavelength absorption, has been developed to enhance polymerization efficiency. Materials incorporating this photoinitiator have been reported to achieve significantly higher reactivity and polymerization efficiency than those formulated with camphorquinone or TPO (3,9). Consequently, composites containing such advanced photoinitiators are expected to exhibit superior color stability, a finding that aligns well with our study's results and existing literature.

The limitations of this study include the absence of an investigation into the mechanical properties—particularly the degree of conversion—of the composites in aqueous environments other than coffee, such as artificial saliva or effervescent tablets. Future studies may consider these factors and employ extended aging protocols. Additionally, the precise quantity of photoinitiators within the composite formulations is not explicitly disclosed on product labels. To address this limitation, high-sensitivity chromatographic or spectroscopic analyses could be conducted to accurately determine photoinitiator concentrations.

Conclusion

The compositional structure of resin-based composites, particularly the quantity and size of inorganic filler particles, directly influences their mechanical properties, such as microhardness. A dental composite incorporating an Ivocerin-based photoinitiator may yield superior outcomes in terms of color stability compared to other formulations.

Declarations

Ethics Committee Approval: *Since this study did not involve the use of any live animals or human-derived materials, ethical approval was not required.*

Informed Consent: *Since no human-derived materials were used in this study, informed consent was not required.*

Peer Review: *Externally peer-reviewed.*

Author Contributions: *Conception/Design of Study- Z.E.K., M.K.Ü.; Data Acquisition- Z.E.K., M.K.Ü.; Data Analysis/Interpretation- Z.E.K., M.K.Ü.; Drafting Manuscript- Z.E.K., M.K.Ü.; Critical Revision of Manuscript- Z.E.K., M.K.Ü.; Final Approval and Accountability- Z.E.K., M.K.Ü.; Material and Technical Support- Z.E.K., M.K.Ü.; Supervision- M.K.Ü.*

Conflict of Interest: *Authors declared no conflict of interest.*

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Comparative Evaluation of Trueness and Precision of PMMA Three-Unit Bridges Fabricated Using Three Milling Devices

Gökçen DİNÇER[1], Münir DEMİREL[2]

Abstract

Aim This in vitro study aimed to evaluate the trueness and precision of three-unit bridge restorations fabricated using different milling devices.

Material and method A dental model prepared for bridge restorations in the right first premolar and first molar was scanned using a laboratory scanner (inEos X5, Dentsply Sirona). The data were imported into dental design software (DentalCAD 3.1 Rijeka; exocad GmbH) to create a bridge restoration design, saved as a reference (R-STL). Ten bridges were milled from polymethylmethacrylate blocks (Telio CAD LT A2 B55, Ivoclar Vivadent, Liechtenstein) using three milling devices: Cerec MC XL (C-STL), Cerec Primemill (P-STL), and inLab MC X5 (X-STL). The restorations were rescanned with an intraoral scanner (Cerec Primescan, Dentsply Sirona), and the datasets were analyzed using a 3D analysis program (Geomagic Control X v.2020.1, 3D Systems, NC, USA). Statistical analyses included one-way ANOVA, post hoc Tukey tests, and the Shapiro-Wilk test ($\alpha = 0.05$).

Results Significant differences in trueness were observed among the groups ($p < 0.001$), with the inLab MC X5 device (X-STL, RMS = 32 μm) showing the highest trueness and the Cerec MC XL group (C-STL, RMS = 44 μm) the lowest. No significant differences in precision were found ($p = 0.117$).

Conclusion The choice of milling device significantly affects the trueness of three-unit bridge restorations, with the inLab MC X5 device producing the most accurate results. However, precision did not differ significantly among the devices.

Keywords Milling devices, Polymethylmethacrylate, Precision, Three-unit bridge, Trueness

Introduction

The advent of computer-aided design/computer-aided manufacturing (CAD/CAM) technology has revolutionized restorative dentistry by improving the accuracy, efficiency, and reproducibility of dental prostheses (1,2). In contrast to conventional techniques, CAD/CAM systems allow for digital design and production of restorations, eliminating many manual steps and reducing potential errors (3). This digital workflow presents opportunities and challenges, particularly when evaluating the milling device performance (4).

In CAD/CAM workflows, milling accuracy is a critical determinant of the clinical success of the restorations. Two parameters, trueness and precision, are commonly used to evaluate milling quality. Trueness reflects how closely a milled object matches its original digital design, whereas precision indicates the consistency of repeated measurements or processes (5). Both factors directly affect the fit of restorations, which influences longevity, marginal integrity, and patient satisfaction (6). For instance, a poorly fitted restoration may lead to plaque accumulation, secondary caries, or marginal discoloration, compromising the long-term success of the prosthesis (4,7).

Polymethyl methacrylate (PMMA) is widely used in dental applications because of its biocompatibility, machinability, and aesthetic properties. It is frequently employed in temporary restorations and serves as a test material for evaluating milling systems. The relatively low hardness of the material makes it ideal for testing the capabilities of different milling strategies and devices under controlled conditions (8,9).

The performance of milling devices depends on several factors including the number of axes, spindle control, tool geometry, and milling strategies (10). Variations in the design of milling machines and implementation of distinct machining methodologies may significantly affect the outcomes of the milling process (11). In dental practice, three- or four-axis milling machines are predominantly employed, whereas in dedicated milling centres, five-axis machines are more frequently utilized. The prevalent machining methodology is the Z-level strategy, in which the restoration is machined based on two-dimensional curves analogous to contour lines (4,11).

This study aims to compare the trueness and precision of three milling devices, focusing on the fabrication of three-unit PMMA bridges. The hypothesis was that there would be no significant differences in the trueness and precision of the three milling devices.

Correspondence: Gökçen DİNÇER, gokcenates@istanbul.edu.tr

[1] Istanbul University, Faculty of Dentistry, Department of Prosthodontics, Istanbul, Türkiye

[2] Biruni University, Faculty of Dentistry, Department of Prosthodontics, Istanbul, Türkiye

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Material and Methods

Design of study

This in vitro study aimed to assess the trueness and precision of three-unit polymethylmethacrylate (PMMA) bridges fabricated using three distinct CAD/CAM milling systems: Cerec MC XL, Cerec Primemill, and inLab MC X5. The study adhered to the guidelines set forth in ISO 12836:2015 (12), which establish the accuracy criteria for digitizing devices utilized in dentistry. Thirty specimens were fabricated, with each milling system producing 10 bridges (n = 10 per group). Ethics committee approval was not required for this study as it was conducted in vitro using only CAD/CAM-fabricated PMMA specimens.

Digital Design and Specimen Preparation

A master dental model prepared for a three-unit bridge restoration involving the right first premolar and first molar served as the basis of this study. The reference model was digitized using a high-precision laboratory scanner (inEos X5; Dentsply Sirona). The bridge restoration was then virtually designed with dedicated dental CAD software (DentalCAD 3.1 Rijeka; Exocad GmbH), and the finalized design was saved as the reference standard STL file (R-STL).

Using the R-STL data, three-unit PMMA bridges were fabricated from prefabricated PMMA blocks (Telio CAD LT A2 B55; Ivoclar Vivadent) using three different milling systems. The resulting STL files were classified according to their respective milling devices: Cerec MC XL (C-STL), Cerec Primemill (P-STL), and inLab MC X5 (X-STL). All milling procedures were performed in accordance with the manufacturer's recommendations to ensure standardization. The milling systems employed in this study differed in their technological configurations and operational parameters (Table 1).

Table 1: Milling Devices

Milling System	Type	Spindle Speed (RPM)	Bur Type	Cooling System
Cerec MC XL	4-axis chairside milling system	20000	Dual cutting burs designed for milling ceramics, and hybrid materials PMMA	Air-based cooling system to prevent overheating
Cerec Primemill	Upgraded 4-axis milling system	22000	Enhanced diamond burs with optimized cutting edges for precision	Integrated liquid cooling to maintain material integrity
inLab MC X5	5-axis laboratory milling system	25000	Multi-directional cutting burs capable of milling complex geometries	Advanced liquid cooling system with continuous temperature monitoring

Following milling, each bridge was subjected to digital scanning using an intraoral scanner (Cerec Primescan, Dentsply Sirona). To ensure optimal data acquisition and minimize the influence of extrinsic variables, scanning was performed in an environment that was specifically controlled to eliminate dust and mechanical vibrations. The scanning protocol involved capturing multiple perspectives to generate high-resolution three-dimensional (3D) models, which were subsequently exported as STL files.

The obtained STL files were imported into a dedicated metrology software (Geomagic Control X; version 2020.1, 3D Systems, NC, USA) for accuracy assessment. The trueness and precision of the fabricated restorations were evaluated through a comparative analysis of the scanned STL data and the original reference STL model (R-STL).

Trueness was evaluated by calculating the root-mean-square (RMS) deviation between the scanned STL file of each fabricated bridge and the original reference STL (R-STL). This approach provides a quantitative assessment of the overall accuracy of milled restorations relative to their digital design. Each sample was analyzed at more than 50,000 data points to ensure a comprehensive evaluation, and the mean RMS deviation (μm) across the entire surface was recorded. The precision was assessed by determining the standard deviation of the RMS deviations within each milling group, reflecting the consistency of the milling process. Lower standard deviation values indicate greater reproducibility of the milling outcome.

Statistical Analysis

All measurements were statistically analyzed to determine significant differences among the three milling systems. Data distribution was assessed using the Shapiro–Wilk test to verify normality. One-way analysis of variance (One-Way ANOVA) was performed to identify overall differences between groups, followed by Tukey's post hoc test for pairwise comparisons, with the level of statistical significance set at $\alpha = 0.05$. Statistical analyses were conducted using SPSS Version 28.0 (IBM Corp., Armonk, NY, USA).

Results

The trueness of the fabricated PMMA bridges was assessed by evaluating the RMS deviation between the scanned STL models and reference STL file (R-STL). One-way ANOVA revealed significant differences between the three milling devices ($F = 29.345$, $p < 0.001$).

Among the three milling systems, inLab MC X5 demonstrated the highest trueness with an average RMS deviation of 32 ± 2.5 μm. Cerec Primemill exhibited moderate trueness, with an RMS deviation of 38 ± 2.8 μm. In contrast, Cerec MC XL showed the lowest trueness, with an RMS deviation of 44 ± 3.0 μm (Table 2). Post-hoc Tukey analysis confirmed that the inLab MC X5 group differed significantly from the other two groups ($p < 0.001$). Furthermore, a statistically significant difference was observed between Cerec Primemill and Cerec MC XL ($p = 0.017$) (Figure 1). Precision was evaluated by analysing the consistency of the RMS deviations within each group. One-way ANOVA indicated no statistically significant differences in precision between the three devices ($F = 2.146$, $p = 0.117$) (Figure 2). The inLab MC X5 exhibited the highest consistency, with a standard deviation of 2.5 μm. Cerec Primemill achieved similar precision, with a standard deviation of ±2.8 μm, whereas Cerec MC XL displayed the lowest consistency, with a standard deviation of 3.0 μm (Table 2).

Table 2: Comparison of Trueness and Precision Among Different Milling Systems

Milling System	n	Trueness (Mean ± SD, µm)	95% CI (Trueness	Range (Median)	p-value (Trueness)	Precision (Mean ± SD, µm)	95% CI (Precision)	Range (Median)	p-value (Precision)
inLab MC X5	10	32 ± 2.5	[29.5, 34.5]	27 – 39 (32)	<0.001**	2.5 ± 0.8	[1.8, 3.2]	1.8 – 3.5 (2.5)	0.017*
Cerec Primemill	10	38 ± 2.8	[35.0, 41.0]	35 – 42 (38)	–	2.8 ± 0.9	[2.0, 3.6]	2.0 – 4.0 (2.8)	–
Cerec MC XL	10	44 ± 3.0	[40.5, 47.5]	37 – 49 (44)	–	3.0 ± 1.0	[2.2, 3.8]	2.2 – 4.2 (3.0)	–
p-value	–	–	–	–	<0.001**	–	–	–	0.017*

*ANOVA Test *p<0,05 **p<0,01*

Figure 1: Box Plot Representation of Trueness Values for Different Milling Devices

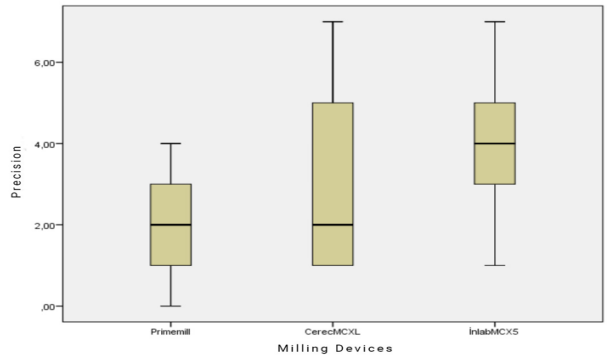

Figure 2: Box Plot Representation of Precision Values for Different Milling Devices

Discussion

This study evaluated the trueness and precision of three different CAD/CAM milling systems for the fabrication of three-unit PMMA bridges. The trueness exhibited significant differences among the milling systems ($p < 0.001$), indicating that the accuracy of the fabricated restorations varied depending on the milling device used. In contrast, the precision analysis revealed minimal differences among the milling systems ($p = 0.117$), suggesting that all devices produced consistent results across multiple fabrications. Therefore, the null hypothesis was rejected for the trueness analysis but partially accepted for the precision analysis.

The use of digital workflow in the fabrication of provisional restorations has significantly enhanced manufacturing efficiency and improved clinical outcomes, particularly in terms of marginal adaptation and mechanical strength (13,14). One of the primary functions of a provisional bridge is to maintain proper occlusal function and tooth stability until definitive restoration is achieved (15). An optimally fabricated provisional bridge also plays a key role in preventing postoperative complications such as hypersensitivity, pain, and abutment mobility or migration (16,17). In this regard, CAD/CAM technology has become a widely adopted approach, owing to its precision and reproducibility. Subtractive manufacturing, which is the most commonly used CAD/CAM technique, relies on milling machines equipped with power-driven tools that mechanically shape material blocks into the desired geometry under computer-controlled conditions (18,19). Various materials are used for interim prostheses, with polymethylmethacrylate (PMMA) being one of the most established options owing to its high strength, colour stability, and ease of repair (20). In the present study, a PMMA-based provisional material was used to fabricate three-unit bridges, allowing for a standardized evaluation of milling accuracy among different CAM systems.

Among the three milling systems evaluated, Cerec MC XL and Cerec Primemill are both 4-axis chairside milling systems, with Primemill offering enhanced accuracy, whereas InLab MC X5 is a 5-axis laboratory milling system designed for high-accuracy restorations, allowing for greater flexibility in milling complex geometries. 5-axis milling units seem to result in better-adapted restorations compared with 3-axis (21,22) and 4-axis units (4,6,23). The design of 5-axis milling machines, which can move in the X, Y, and Z directions and rotate around two axes, typically the A-axis and C-axis, enables milling complex contoured surfaces and intricate geometries without repositioning the workpiece (3). Only one study reported better marginal integrity and smaller gaps for a 3-axis than for a 5-axis machine (24). Therefore, a milling unit with an additional axis achieves better angles, more effective and accurate processing, and better surface topography and finishing, particularly for multiunit restorations (4,6,21,25).

Trueness is a critical parameter for ensuring the proper fit of restorations, particularly in areas such as margins and occlusal surfaces. Poor trueness can result in overmilling or undermilling, leading to marginal gaps that compromise the long-term success of restoration. Marginal gaps facilitate plaque accumulation and increase the risk of secondary caries, gingival inflammation, and prosthetic failure (26). In this study, inLab MC X5 consistently produced bridges with minimal deviations, making it particularly suitable for complex restorative cases requiring high accuracy.

Studies comparing 3-, 4-, and 5-axis milling machines in the same context are lacking, making it impossible to rank the efficiency of the machines however, the inLab MC X5 showed superior trueness. All three systems demonstrated consistent precision, as indicated by the lack of significant differences in standard deviations across groups. This suggests that under standardized conditions, even 4-axis systems such as Cerec MC XL and Primemill can achieve reliable repeatability in milling results. Nonetheless, the limitations of 4-axis systems in accurately reproducing intricate features, particularly undercuts and marginal details, were evident in the trueness analysis (10, 22).

Moreover, the precision reflects the consistency of the

milling process. While precision has a less direct impact on clinical fit compared to trueness, high precision ensures predictable outcomes and reduces variability in restorations produced by the same system (22). The comparable precision observed across all devices in this study underscores the reliability of modern CAD/CAM technologies in maintaining a consistent milling quality, even across different hardware configurations. For clinicians, the choice of milling system should be guided by the specific requirements of the restorative task. The inLab MC X5 is recommended for laboratory-based workflows and complex cases that require high trueness, such as full-arch restorations or prostheses with intricate features. Chairside systems such as Cerec MC XL and Primemill, while providing slightly less accuracy, offer sufficient precision for simpler restorations and convenience in same-day dentistry. Balancing accuracy, efficiency, and cost-effectiveness is key to optimizing patient care.

This study has several limitations. First, research was carried out in a controlled in vitro setting, which does not fully duplicate the complex intraoral environment, where occlusal forces, salivary exposure, and patient-specific anatomical variances can all impact on the long-term accuracy and longevity of dental restorations. Additionally, the study focused solely on PMMA discs, a material commonly used for temporary restorations; however, its mechanical properties differ significantly from definitive materials like zirconia and lithium disilicate. Another limitation is that the study utilized a standardized scanning protocol and a limited number of milling devices with different axis configurations. Variability introduced by different intraoral or laboratory scanners, scanning strategies, operator skills, and software settings was not assessed, which may impact clinical outcomes. Finally, the study employed a single Z-level milling strategy, whereas alternative strategies such as spiral, adaptive, or zigzag milling may yield different accuracy and surface characteristics.

To address these limitations, future research should focus on assessing milling accuracy under clinical loading settings, taking into account occlusal forces and salivary exposure. Expanding the range of restorative materials, including zirconia, lithium disilicate, and hybrid ceramics, would provide a broader understanding of milling system performance across different substrates. Additionally, further research should investigate the impact of various scanning devices, scanner types (intraoral vs. laboratory), scanning strategies on the trueness and precision of milled restorations. Another significant field for future research is comparing different milling processes, such as spiral, adaptive, and zigzag milling, to enhance digital workflows for a variety of clinical applications. Moreover, including a broader range of milling devices with different axis configurations (three-, four-, and five-axis systems) would help determine the influence of machine configuration on milling accuracy and efficiency. Finally, long-term clinical studies are needed to evaluate restoration survival rates, marginal adaptation, and patient satisfaction, ensuring that the findings of in vitro analyses translate effectively into real-world clinical applications.

Conclusion

Within the limitations of this in vitro study, restorations fabricated using the 5-axis milling system (inLab MC X5) demonstrated the highest trueness, achieving greater dimensional accuracy in reproducing complex geometries. In contrast, the 4-axis milling units (Cerec MC XL and Cerec Primemill) exhibited lower trueness, with Cerec MC XL showing the least accuracy. However, no significant differences were observed in the precision among the three systems, indicating consistent reproducibility across multiple fabrications. The findings suggest that the increased range of motion in 5-axis systems enhances milling accuracy, making them more suitable for cases requiring high precision, while 4-axis systems remain a viable option for less complex restorations where efficiency and chairside convenience are prioritized.

Declarations

Ethics Committee Approval: *Since this study did not involve the use of any live animals or human-derived materials, ethical approval was not required.*

Informed Consent: *Since no human-derived materials were used in this study, informed consent was not required.*

Peer Review: *Externally peer-reviewed.*

Author Contributions: *Conception/Design of Study- M.D.; Data Acquisition- M.D.; Data Analysis/Interpretation- G.D.; Drafting Manuscript- G.D.; Critical Revision of Manuscript- M.D.; Final Approval and Accountability- G.D.; Material and Technical Support- M.D.; Supervision- M.D.*

Conflict of Interest: *Authors declared no conflict of interest.*

Financial Disclosure: *Authors declared no financial support.*

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Low Grade Mucoepidermoid Carcinoma Localized in the Posterior Hard Palate: Case Report

İlknur ENİNANÇ[1], Aslıhan ŞAHAN KESKİN[1]

Abstract

Aim Mucoepidermoid carcinoma (MEC) is the most commonly diagnosed malignant tumor of the salivary glands. While it predominantly occurs in the parotid gland, it may also affect the submandibular, submental, and minor salivary glands. This case report aims to contribute to the literature by presenting a low-grade MEC, clinically resembling benign lesions, detected asymptomatically in the hard palate.

Case Report A 30-year-old female patient with no systemic health issues visited the Department of Dentomaxillofacial Radiology at Sivas Cumhuriyet University Faculty of Dentistry for a routine examination. An asymptomatic, well-defined swelling with a slightly erythematous mucosal covering was detected at the junction of the hard and soft palate. The patient was not aware of the lesion. Histopathological analysis of the tissue sample, obtained through an incisional biopsy, confirmed features indicative of low-grade MEC.

Discussion Low-grade MEC can mimic benign salivary gland tumors, particularly pleomorphic adenoma, when presenting as an asymptomatic palatal lesion. This highlights the necessity of biopsy for accurate diagnosis. Early detection enables conservative treatment and improves prognosis. While surgical excision with clear margins is the preferred approach, long-term follow-up is essential due to the risk of recurrence.

Conclusion Asymptomatic low-grade mucoepidermoid carcinoma can be confused with pleomorphic adenoma when it occurs in the palatal region and must be considered in the differential diagnosis. Early-stage diagnosis of MEC is associated with a better prognosis and allows for more conservative treatment approaches.

Keywords Low-grade, Mucoepidermoid carcinoma, Oral mucosa, Pleomorphic adenoma, Salivary gland

Introduction

Mucoepidermoid carcinoma (MEC) constitutes approximately 10% of all salivary gland tumors and represents 35% of malignant cases within this group (1). It primarily occurs in the parotid salivary gland, with the minor salivary glands, submandibular, and sublingual glands being less frequently affected (1). The incidence is relatively higher in women, with the most frequently affected age group being the third to fifth decades of life (2). Histologically, it consists of a mixture of epidermoid, mucoid or squamous cells (3). Among salivary gland tumours, MEC is the most important tumour group in which prognosis varies according to the grading system (4). Numerous studies have highlighted the importance of grading systems in MEC (4-7). Three histological grades have been defined as low, intermediate and high (8, 9).

The treatment protocol for MEC varies based on its grade. While only surgical excision is performed in low grade MEC, radiotherapy and neck dissection can also be performed in high grade MEC (7). Low-grade MECs generally do not exhibit bone infiltration or mucosal ulceration (10). Because of its benign appearance, MEC may be confused with dental lesions, submucosal lesions, mucoceles, lymphomas, and lipomas (11, 12).

This case report aims to provide insights into the clinical and radiological characteristics of a low-grade MEC that resembles benign lesions, contributing to the existing literature.

Case Report

A 30-year-old woman was admitted to the Department of Dentomaxillofacial Radiology Radiology, Faculty of Dentistry, Sivas Cumhuriyet University, for routine dental examination and it was determined that she was systemically healthy. During intraoral examination, a swelling covered with mild erythematous mucosa was detected in the posterior region of the maxilla at the junction of the hard palate and soft palate (Figure 1). The patient was unaware of the swelling in the region, and palpation of the lesion did not elicit any pain. Periapical lesions were identified in the posterior maxillary teeth near the affected region on the patient's panoramic radiograph. However, periapical infection was ruled out due to the small size of these lesions, their distance from the region, the asymptomatic nature of the teeth on intraoral examination, and the firm consistency of the swelling mass rather than being fluctuant (Figure 2). It was established that the patient had not recently undergone anaesthesia in the palatinal region and there was no history of irritation causing trauma in the region. The patient was sent to the Department of Dentomax-

Correspondence: Aslıhan ŞAHAN KESKİN, asli1907sahan@gmail.com

[1]Sivas Cumhuriyet University, Faculty of Dentistry, Department of Dentomaxillofacial Radiology, Sivas, Türkiye

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illofacial Surgery for further evaluation and tissue sampling with a prediagnosis of pleomorphic adenoma and low grade adenocarcinoma. In the aspiration biopsy performed for the preliminary diagnosis, no material was aspirated. Due to concerns of bleeding and malignancy in the region, the patient was referred to the Department of Otorhinolaryngology. In this department, the requested computed tomography (CT) examination revealed no pathology in the palatal bone (Figure 3), and an incisional biopsy was performed in the relevant region. Histopathological examination resulted in a diagnosis of MEC arising from the minor salivary glands for the lesion. One week later, the remaining mass was removed by excisional biopsy, and the area was left for secondary healing (Figure 4-5). In postoperative controls, it was observed that the palatinal region was covered with healthy mucosa and healing was complete (Figure 6). Contrast-enhanced computed tomography (CECT) and magnetic resonance (MR) imaging performed nine months after the operation revealed no pathology in the adjacent structures and lymph nodes (Figure 7). In the third-year follow-up cone beam computed tomography (CBCT) examination, no pathological findings were detected in the relevant region, and the surrounding bone structures were evaluated as healthy (Figure 8). Radiotherapy and chemotherapy were not recommended by the oncologists in the postoperative period. The patient has been under follow-up for approximately three years without any signs of recurrence.

Figure 1: During intraoral examination, a smooth-surfaced swelling covered with slightly erythematous mucosa was observed in the posterior maxillary region.

Figure 2: Periapical lesions observed on the right and left maxillary molars in the panoramic radiograph of the patient

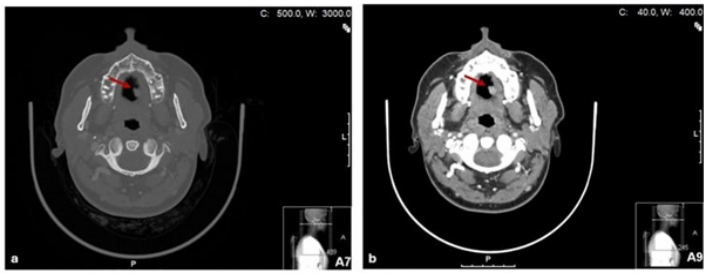

Figure 3: The patient's pre-biyopsy (a). non-contrast, (b). contrast-enhanced CT images. An increased density of contrast material was observed in the lesion.

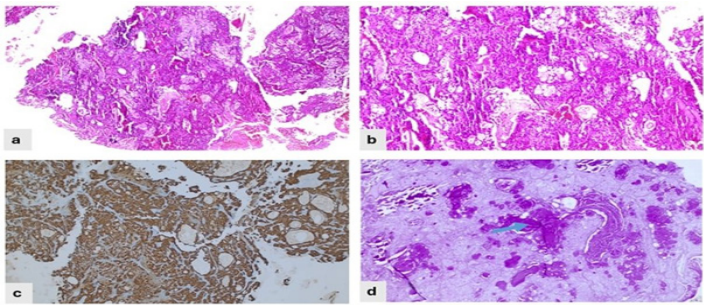

Figure 4: Histopathological images of material obtained from the palatal region. a-b. In the mucinous epithelial tumor cells forming low-grade mucoepidermoid carcinoma, eosinophilic or clear, broad cytoplasm, small nuclei with a uniform appearance, and intracellular and extracellular mucin production are observed. The structural morphological features of the salivary gland are lost. No squamous cell content is observed. (H&E X 50, H&E X 100). c. Immunohistochemical expression of cytokeratin 7 in the epithelial cells forming the tumor in low-grade mucoepidermoid carcinoma. (IHC X 50) d. Demonstration of extracellular mucin secretion with PAS stain marked by a blue arrow in mucoepidermoid carcinoma (PAS X50).

Figure 5: Three days after the surgery.

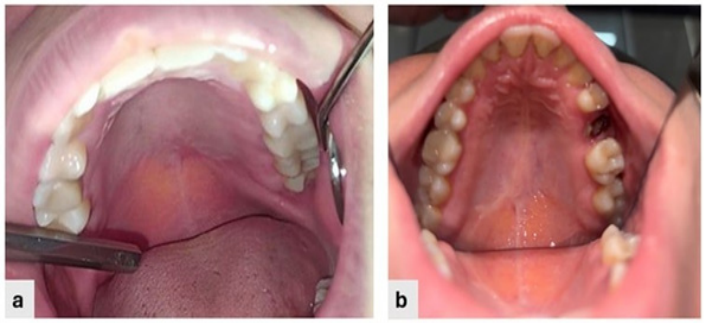

Figure 6: The appearance of the healed palatal region a. three months, b. three years after the excision of the mass.

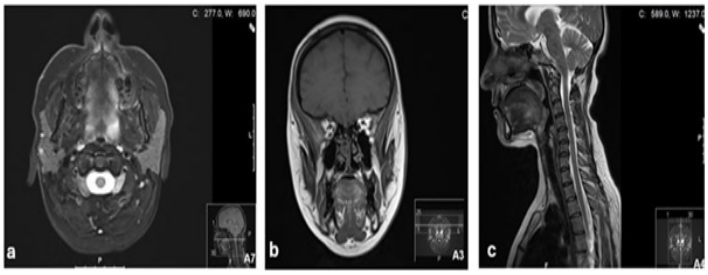

Figure 7: a. Axial, b. Coronal, and c. Sagittal contrast-enhanced MR images obtained in the 9th month after the surgery indicate no pathology.

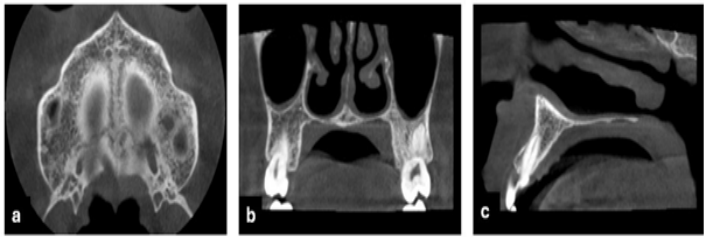

Figure 8: a. Axial, b. Coronal, and c. Sagittal CBCT images obtained during the patient's third-year follow-up.

Discussion

Minor salivary gland tumours are uncommon, with studies indicating that 44% of these tumours are malignant (13, 14). The most prevalent malignant tumour among salivary glands is MEC (13, 15). Although the parotid gland is frequently affected (16), in this case, MEC originated from the minor salivary glands in the palatine region.

Soft tissue swellings localised in the palatal region may have many different causes. In routine dental examinations, these swellings can often be considered as simple infections or lesions resulting from dental interventions. However, such lesions may also be an asymptomatic and unrecognised neoplasm. When evaluating suspicious lesions, ensuring that a potential neoplasm is not overlooked is crucial for accurate diagnosis and effective treatment planning. Clinical differentiation of palatinal swellings from neoplasms may not always be possible (17). Pleomorphic adenoma is the most frequently occurring salivary gland tumor among asymptomatic lesions found in the hard palate. Therefore, this tumor may be considered in the preliminary diagnosis of such swellings (16). In these cases, histopathological evaluation is of critical importance (16, 17). Generally, these tumours present as slow-growing, asymptomatic, bluish purple swellings (18). In high-grade tumours, it may appear as painful or painless, rapidly growing lesions that may cause metastasis to neighbouring tissues, lymph nodes, lung and bone (17, 19). Malignant lesions infiltrating the surrounding tissues may cause tooth displacement, mobility and resorption (17, 20). In this case, radiological and clinical examination revealed no mobility or resorption in the teeth near the region. Considering the painless and slow development of the lesion, pleomorphic adenoma, which is a benign tumour, was the first thought in the differential diagnosis for this case. In similar cases with asymptomatic course, the risk of malignancy should always be considered.

MEC is more frequently seen in female patients, especially between the third and fifth decades of life (2, 17). In this case, the patient's sex and age aligned with the findings in the literature.

Tumours arising in the minor salivary glands are localised in the buccal mucosa, lips, palate, floor of the mouth and tongue (16). The malignancy potential of tumours developing in the minor salivary glands varies depending on their location. For example, the incidence of malignant tumours in the palate varies between 40-60%, while this rate increases up to 90% as it progresses towards the floor of the mouth and tongue (21). The size and location of the tumour play a decisive role on signs and symptoms. Symptoms can differ based on the tumour's location. While it typically appears as a painless submucosal swelling, occasional small ulcerated areas may also be observed (21, 22). Tumours arising in the oropharyngeal region usually cause a painless mass, but when the tumour spreads to the nasopharynx or nasal cavity, it may cause symptoms such as facial pain, nasal obstruction or bleeding (21, 22). The location of the tumour, age of the patient, carcinoma type and stage at the time of diagnosis are critical parameters in determining the prognosis (21, 22).

Treatment options vary depending on the grade of MEC. In low-grade MECs, only surgical excision is sufficient, whereas in high-grade tumours, radiotherapy and chemotherapy are applied in addition to excision (7, 23). 5-year survival rate is 0-43% in high-grade MECs and 92-100% in low-grade tumours (7). The recurrence rate is less than 10% in low and intermediate grade tumours (24). The literature presents various treatment approaches for MEC. Considering that approximately 75% of MEC tumors are low-grade and rarely metastasize, local excision is often preferred for well-demarcated lesions (14, 25). For larger lesions infiltrated into bone, partial maxillectomy or palatal fenestration may be recommended (14). Eversole et al. managed low and moderate-grade minor salivary gland tumours through local and wide excision. In cases with bone erosion, resection was performed, achieving a 100% success rate (26). In addition, Melrose et al. suggested that more conservative treatments can be applied when there is no bone invasion and neighbouring bone and anatomical structures can be preserved (27). While some researchers endorse this conservative approach, others recommend more aggressive treatment strategies. Olsen et al. analyzed 54 patients with intraoral MEC over a 25-year period and proposed that all lesions, irrespective of grade, should be treated with partial maxillectomy (28).

In this case, postoperative contrast-enhanced computed tomography (CT) and positron emission tomography (PET) imaging of the lesion, which was completely excised without bone invasion, showed no metastasis in the neighbouring structures and lymph nodes. Therefore, radiotherapy and chemotherapy were not recommended by oncologists. In addition, no recurrence was observed in the patient who was followed up for about 2 years. In the present case, the patient had a low grade tumour and the surgical margins were clean, which led to a successful outcome. However, long-term follow-up remains important in such cases. In the literature, it is reported that recurrence in MEC is more common in the first 3-5 years after treatment (21). Therefore, maintaining regular radiological and clinical follow-up is critical for the long-term survival of patients.

Conclusion

In the palatal region, swellings can arise from various causes, including simple infections, dental interventions, and neoplasms. The rarity of minor salivary gland tumours poses significant challenges during the diagnostic and therapeutic process. As seen in this case, malignant mucoepidermoid carcinomas can clinically mimic benign lesions, potentially leading to delays in diagnosis. Histopathological examination stands out as the gold standard for definitive diagnosis, crucially informing treatment planning and prognosis. In this case, the low-grade tumour was successfully treated, with no recurrence observed during the follow-up period. However, long-term follow-up in such tumours remains important against the potential risk of recurrence.

Declarations

Informed Consent: *Written informed consent was obtained from patient who participated in this study.*

Peer Review: *Externally peer-reviewed.*

Author Contributions: *Conception/Design of Study- İ.E., A.Ş.K.; Data Acquisition- İ.E., A.Ş.K.; Data Analysis/Interpretation- İ.E., A.Ş.K.; Drafting Manuscript- İ.E., A.Ş.K.; Critical Revision of Manuscript- İ.E., A.Ş.K.; Final Approval and Accountability- İ.E., A.Ş.K.; Material and Technical Support- İ.E., A.Ş.K.; Supervision- İ.E., A.Ş.K.*

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