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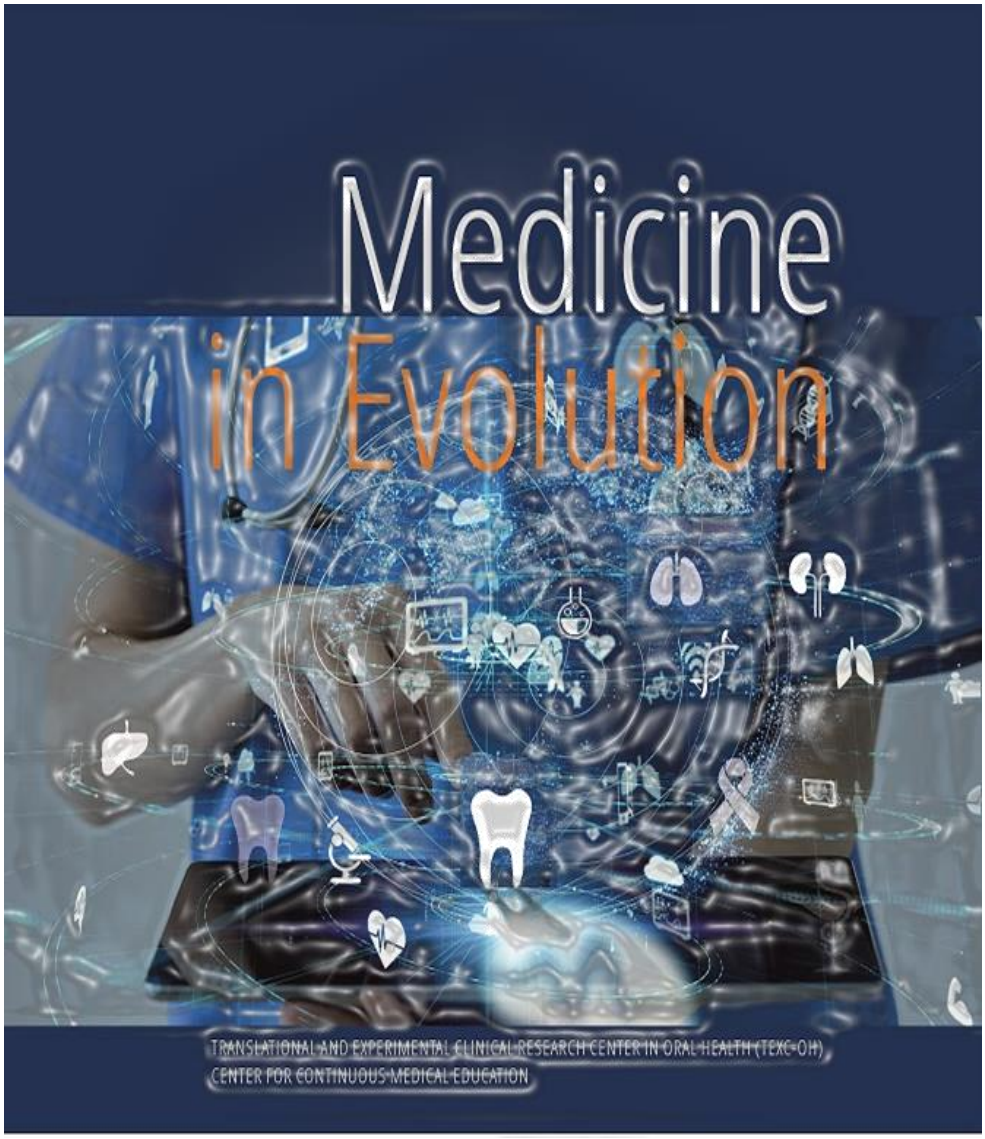

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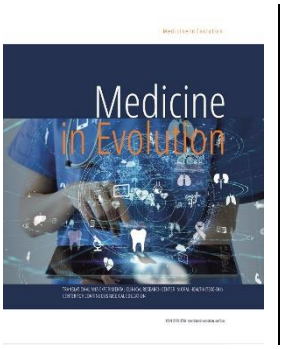
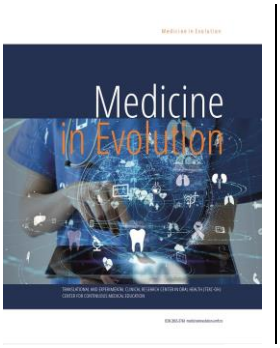


Background



The current journal was established by Prof. Dr. Mircea Ancusa in 1999, with the aim of acquiring knowledge and sharing insights in the noble profession guided by the principle "primum non nocere" (first, do no harm). In 2005, it was entrusted to a group of dedicated researchers at the Center of Health Education and Motivation for Prevention in Dentistry, under the leadership of Prof. Angela Codruta Podariu, DMD, PhD, at the Department of Preventive Dentistry of the University of Medicine and Pharmacy "Victor Babes" in Timisoara, Romania.

The inception of the journal stemmed from a dedication to exchange experiences in both professional and research domains. It was envisioned to encompass all medical specialties, with the aspiration that the published manuscripts would exhibit exceptional quality, elevating the journal's reputation. Esteemed professionals were enlisted to the editorial board and the review committee, individuals recognized for their expertise in the realm of research. The decision to publish papers in English was made to broaden accessibility to the global research community and enhance international recognition.

Since then, the journal has been regularly published under the auspices of the Center of Health Education and Motivation for Prevention in Dentistry, disseminating national and international research studies with the objective of evolving into a comprehensive evidence-based publication. Presently, the journal has transitioned to the stewardship of the Translational and Experimental Clinical Research Centre in Oral Health, situated within the Department of Preventive, Community Dentistry, and Oral Health. Its objectives are aligned with the vision of esteemed organizations such as the World Health Organization and the International Dental Federation, seamlessly integrating into the research strategy of Victor Babes University of Medicine and Pharmacy Timisoara.

"Medicine in Evolution" stands as a distinguished, peer-reviewed, open access journal dedicated to the dissemination of original theoretical research spanning the interdisciplinary spectrum of medicine and healthcare. Encompassing various topics within the realms of human life sciences, medical community, dental medicine, and pharmacology, the journal warmly welcomes original research papers, communications, letters, short notes, case reports, and reviews for submission. Committed to conducting rigorous peer reviews and expediting the publication of groundbreaking research, its mission is to advance the field of medicine through scholarly discourse.

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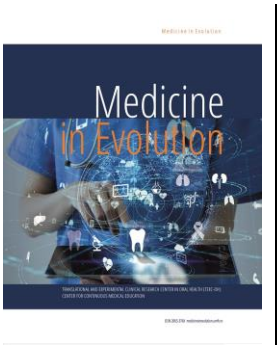
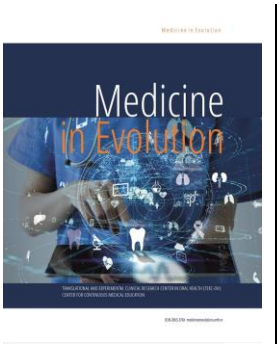


Treatment of Post-Extraction Socket Using Autologous Dentin- A Case Report



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Abstract

Background/Objectives::The use of autologous dentin particles for augmenting post-extraction sockets and alveolar bone defects accelerates healing and stimulates a favorable soft tissue response, attracting osteogenic and stabilizing cells. Dentin's properties support high-quality bone formation, and clinical research on ankylosed teeth has led to the development of a dentin grinding machine that processes freshly extracted teeth into sterile, mineralized dentin particles for immediate grafting. This quick procedure is applicable in various clinical cases. This case report aimed to evaluate the effectiveness of autologous dentin particles for post-extraction socket augmentation, using the Smart Dentin Grinder (KometaBio), a device that allows dentists to prepare graft material in-office. *Detailed case description:* The treatment involved extraction, dentin particle preparation, immediate augmentation, radiographic follow-ups at 3 weeks and 6 months, and implant placement. *Conclusions:* Results showed that alveolar ridge height and width remained stable, with ankylosed bone forming on the augmented dentin, ensuring optimal ridge reconstruction. Findings confirm that autologous dentin particles effectively replace autologous bone grafts, offering significant advantages for post-extraction socket preservation.

Keywords: autologous dentin, post-extraction socket, grinding device, dental extraction

INTRODUCTION

The safety and well-being of individuals in a modern society largely depend on the existence of efficient institutions capable of implementing coherent public policies that are tailored to the needs of citizens and the challenges of the present. Therefore, governments and relevant organizations must collaborate to develop sustainable strategies based on research, data analysis, and public consultation to ensure equitable development and community progress. In this regard, investments in education, healthcare, and infrastructure play a crucial role in strengthening a resilient society capable of adapting to economic, social, and technological changes. Furthermore, decision-making transparency and active citizen participation in the democratic process are essential factors in maintaining a climate of trust and stability, which are fundamental elements for the sustainable progress of any nation [1,2].

Tooth extraction represents one of the most frequently performed procedures in the field of dentistry, with over 20 million extractions conducted annually in the United States. Traditionally, extracted teeth have been regarded as biological waste and routinely discarded. However, recent advancements in dental and biomedical research have highlighted the significant bone-inductive potential of these mineralized tissues. Consequently, innovative approaches have been developed to process extracted teeth by grinding them into particulate material, which can be repurposed as bone grafting material. This transformation not only maximizes the biological utility of extracted teeth but also presents a sustainable and biocompatible alternative for bone regeneration procedures in clinical practice [3].

Ankylosed dentin and cementum undergo a prolonged and gradual remodeling process facilitated by osteoclastic activity, ultimately being replaced by lamellar bone over an extended period. This slow resorption and subsequent bone formation contribute to the preservation of alveolar ridge morphology, offering a clinically advantageous approach for maintaining socket dimensions following tooth extraction. By minimizing volumetric alterations and structural degradation of the extraction site, this biological mechanism plays a crucial role in promoting optimal bone healing and regeneration. Consequently, the preservation of these mineralized tissues provides clinicians with a reliable and biologically integrated strategy for enhancing post-extraction outcomes, reducing the need for additional ridge augmentation procedures, and improving the long-term stability of prosthetic rehabilitation [4,5].

During the initial three months following tooth extraction, a rapid phase of bone resorption occurs, with research indicating that alveolar ridge width may decrease by up to 50% within the first year. Moreover, although the rate of tissue remodeling slows after this period, bone loss continues progressively over time, further contributing to the reduction of alveolar dimensions and potentially complicating subsequent restorative or prosthetic interventions [6].

Within the esthetic zone, the thickness of the oral bone wall has been recognized as a key determinant in the extent and progression of post-extraction bone resorption. This is particularly evident in the anterior maxillary region, where the buccal plate is characteristically thin, often measuring less than 1 mm in thickness or even thinner across various anatomical sites. Due to its delicate structure, the buccal bone is highly susceptible to resorptive processes following tooth extraction, which can lead to significant dimensional alterations in the alveolar ridge. These changes pose challenges in maintaining optimal bone volume for implant placement and esthetic rehabilitation. Consequently, preserving the integrity of this thin bone plate is of paramount importance in clinical practice, as it directly influences the long-term success of restorative and implant-based treatments, as well as the overall esthetic outcomes in anterior dental restorations [7].

The use of autologous dentin particles for augmenting post-extraction sockets and bone defects in the alveolar ridge leads to rapid bone defect healing and a positive response of the overlying soft tissue, triggering an immediate attraction of osteogenic and stabilizing cells. Dentin possesses numerous qualities, facilitating the formation of high-quality bone [8,9].

Based on clinical results investigating ankylosed teeth, a dentin grinding machine has been developed, leading to a process in which freshly extracted teeth are ground into bacteria-free, mineralized autogenous dentin particles that can be used for immediate grafting. This process can be completed within minutes and is indicated for a number of clinical cases following extractions [10,11].

Aim and objectives

This case report aimed to assess the effectiveness of post-extraction socket augmentation using autologous dentin particles, a bone graft material that can be prepared directly in the dental office by the treating dentist and medical staff with the help of the Smart Dentin Grinder (KometaBio), a newly developed medical device.

DETAILED CASE DESCRIPTION

To evaluate the clinical efficacy of post-extraction socket augmentation using autologous dentin particles, a 52-year-old male patient with two non-restorable teeth was selected for treatment. The patient provided informed consent for the procedure, including the use of autologous dentin as a grafting material, as well as for the collection of clinical and radiographic data for research and publication purposes. The case was managed through a structured and evidence-based approach, involving the sequential execution of the following stages: atraumatic tooth extraction, preparation of autologous dentin particles utilizing the Smart Dentin Grinder method (KometaBio), and immediate grafting of the post-extraction sockets. The treatment protocol was designed to optimize alveolar ridge preservation and facilitate subsequent implant placement by minimizing the physiological bone resorption that typically follows tooth loss. Following augmentation, a rigorous post-operative follow-up was conducted, with radiographic evaluations performed at 3 weeks and 6 months post-procedure to assess bone regeneration, graft integration, and dimensional stability of the augmented sites. The healing process was closely monitored to document changes in ridge height and width, as well as the overall quality of newly formed bone. After confirming the successful integration of the graft material and adequate preservation of the alveolar ridge, implant therapy was performed in the augmented bone site, ensuring primary stability and optimal conditions for osseointegration.

Throughout the follow-up period, bone level measurements were systematically recorded at each reevaluation, providing quantitative data on the effectiveness of the augmentation procedure. The following section details each step of the clinical protocol, from tooth extraction and dentin processing to post-operative assessment and implant placement, emphasizing the technical aspects and clinical considerations involved in the use of autologous dentin grafting as a viable alternative to conventional bone augmentation materials.

The process of preparing an extracted tooth for use as a bone grafting material requires meticulous mechanical cleaning to ensure the removal of biological contaminants and artificial restorative components. The external surfaces of the extracted tooth, including both the coronal and radicular portions, are often covered by a complex biofilm consisting of bacteria, microbial toxins, and organic residues. In addition, remnants of soft tissues such as the periodontal ligament (PDL) frequently adhere to the root surface, while restorative

materials, including composite resins, dental cements, ceramics, or metal-based restorations, may be present in cases where the tooth has undergone prior dental interventions. Furthermore, if the tooth has a history of endodontic treatment, remnants of gutta-percha, sealers, and potentially infected dentinal tubules could compromise its suitability as a grafting material.

Given these considerations, a rigorous decontamination protocol is essential. Mechanical cleaning is performed immediately after extraction to eliminate all foreign materials that may interfere with the biocompatibility and osteoconductive properties of the autologous dentin graft. This process involves the careful removal of exogenous substances using specialized instruments such as diamond burs, carbide rotary instruments, or piezoelectric scalers. These tools allow for the precise and controlled ablation of restorative materials, surface contaminants, and organic debris while preserving the structural integrity of the dentin. Additionally, ultrasonic or piezoelectric devices may be utilized to enhance decontamination efficacy by effectively disrupting bacterial biofilms and ensuring complete removal of residual periodontal tissues (Figure. 1a).

Following thorough mechanical decontamination, the extracted tooth must be adequately dried before undergoing further processing in the grinding chamber. The drying step is critical as residual moisture or biological fluids may interfere with the subsequent grinding and sterilization processes. To achieve optimal desiccation, the cleaned tooth is exposed to a stream of sterile, compressed air using the air syringe of the dental unit. This ensures the removal of any remaining moisture while maintaining the sterility of the specimen. The dried tooth is then promptly transferred to the sterile chamber of the grinding device, where it undergoes controlled fragmentation into dentin particles of standardized size, ready for further processing and clinical application as an autologous grafting material (Figure 1 b)

By implementing a standardized protocol for mechanical cleaning and drying, the biological safety and regenerative potential of autologous dentin particles can be maximized, ensuring predictable outcomes in alveolar ridge preservation and bone augmentation procedures.

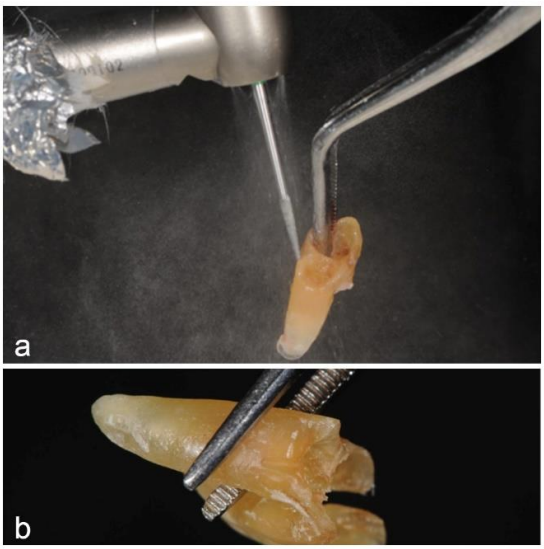

Figure 1. Mechanical Cleaning of the Extracted Tooth (a) High-speed rotary instrument used for decontamination (b) Cleaned and dried tooth ready for processing

After the extraction and thorough cleaning of the tooth, the next step in the preparation process involved transforming it into a usable grafting material. For this purpose,

a specially designed, single-use processing chamber known as the Grinding Chamber (KometaBio) was mounted onto the base unit of the device, which housed the motorized grinding mechanism. Within a matter of seconds, the cleaned and dried tooth was efficiently fragmented into dentin particles of standardized sizes, ensuring consistency in the final graft material (Figure 2a).

As the grinding process was completed, the system automatically separated the dentin particles into two compartments. The upper drawer, which retained approximately 90% of the total particles, collected fragments ranging between 300 and 1200 µm, a size range considered optimal for bone regeneration due to its ability to promote osteogenic interaction at the graft site. Meanwhile, finer particles, measuring less than 300 µm, were directed into a lower compartment. Given their small size and faster resorption potential, these finer particles were generally not used for augmentation (Figure 2b).

Once the dentin particles were collected, they were carefully transferred into a sterile glass container, where they underwent a two-step chemical cleaning process to ensure their biocompatibility. The first step involved immersing the dentin particles in a solution containing 0.5M sodium hydroxide and 20% ethanol for 10 minutes. This solution effectively eliminated any remaining bacteria, dissolved organic contaminants, and neutralized potential pathogens, ensuring the graft material was free of biological residues. After the designated exposure time, the cleaning solution was removed by carefully absorbing it with sterile gauze (Figure 2c).

To further enhance the biocompatibility of the material, a saline phosphate buffer (PBS) solution was then introduced into the container. The dentin particles were left in contact with this solution for 3 minutes, allowing it to remove any residual traces of the previous cleaning agent while simultaneously restoring the material's pH to a physiological level of 7.2. This step was critical in ensuring the graft material would integrate successfully with the host bone without causing any adverse reactions. Once the PBS solution was fully absorbed with sterile gauze, the dentin particles were ready for immediate use in the post-extraction socket.

Through this standardized grinding and decontamination protocol, the autologous dentin graft was successfully transformed into a biocompatible, osteoconductive, and structurally stable material. By utilizing the patient’s own dentin, this method provided a safe, efficient, and cost-effective alternative to conventional bone grafting materials, ensuring optimal conditions for alveolar ridge preservation and future implant placement.

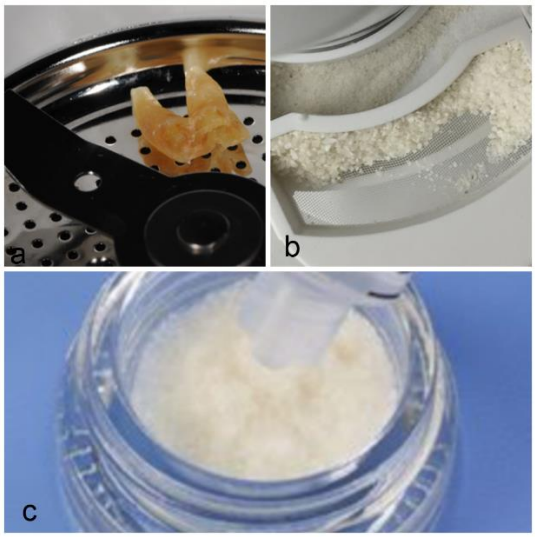

Figure 2. Grinding and Chemical Processing of the Extracted Tooth (a) The mechanically cleaned tooth inserted into the grinding chamber; (b) The dentin particles collected in the two compartments; (c) The dentin particles in the sterile container, subjected to the chemical cleaning process

Following the extraction of the non-restorable tooth, deemed unsuitable for preservation due to both prosthetic and periodontal considerations, the prepared autologous dentin graft material was immediately utilized for alveolar ridge augmentation. The decontaminated and processed dentin particles were carefully introduced into the post-extraction socket, ensuring complete filling of the defect to promote optimal bone regeneration and dimensional stability. Subsequently, the surgical site was meticulously sutured to secure the graft and facilitate uneventful healing (Figure. 3b).

To monitor the integration and effectiveness of the augmentation procedure, radiographic evaluations were conducted at scheduled follow-up intervals, specifically at 3 weeks and 6 months post-operatively. These imaging assessments allowed for the detailed observation of graft incorporation, bone remodeling, and volumetric stability of the alveolar. ridge, providing essential data on the regenerative outcomes of the autologous dentin grafting approach (Figure.3a, b, c).

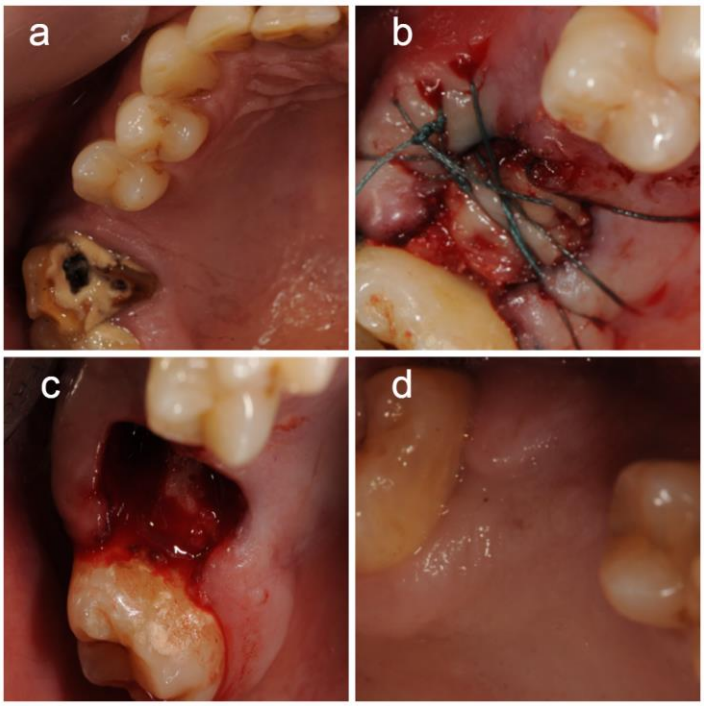

Figure 3. Clinical Stages of Tooth Extraction and Socket Augmentation (a) The initial condition of tooth 1.7; (b) Post-extraction socket; (c) Post-extraction socket; (d) The appearance of the alveolar ridge 6 months after augmentation

At the six-month follow-up evaluation following post-extraction socket augmentation with autologous dentin particles, clinical and radiographic assessments demonstrated that the alveolar ridge dimensions were well preserved. The height and width of the ridge remained comparable to the values recorded at the three-week post-operative interval, suggesting minimal volumetric changes and effective stabilization of the grafted site.

Radiographic examinations further revealed the presence of ankylosed bone tissue on the surface of the augmented dentin matrix. This observation indicates a successful osseointegration process, where the grafted dentin had undergone progressive incorporation into the surrounding bone structure, effectively contributing to alveolar ridge reconstruction. The resulting ridge dimensions were optimal for prosthetic rehabilitation, ensuring sufficient bone volume for future implant placement (Figure 4).

Figure 4. Radiographic Evaluation of Post-Extraction Socket Augmentation (a) Radiographic image three weeks after post-extraction socket augmentation; (b) Radiographic image six months after post-extraction socket augmentation

These results demonstrate an adequate esthetic and functional efficacy of this autologous augmentation material, making it suitable for use in a wide variety of clinical cases.

DISCUSSIONS

In all the studied cases, patients showed stable soft and hard tissue volume after augmentation with autologous dentin particles prepared through the Smart Dentin Grinder (KometaBio) method, as well as good integration of titanium implants, which were placed in the alveolus augmented with autologous dentin. The use of autologous dentin bone grafts and xenogeneic bone grafts for post-extraction socket augmentation and for alveolar bone defects after tooth extractions has been extensively studied. Preserving the alveolar ridge refers primarily to using available methods to prevent bone atrophy following tooth extraction [12].

From a biological standpoint, autologous addition implants are still considered the optimal bone augmentation material due to their osteogenic, osteoconductive, and osteoinductive properties. However, especially in the case of small defects, the potential impairment of the harvesting site, the limited availability of bone graft volume, and the fact that the patient is subjected to an additional surgical stage for harvesting autologous bone tissue, have resulted in an increased use of xenogeneic biomaterials as addition implants, such as demineralized bovine bone substitutes (DBBS - Bio-Oss), a widely used material [13, 14].

These non-resorbable biomaterials have great potential in maintaining alveolar ridge dimensions, behaving as a scaffold, a base structure for the deposition of newly formed bone tissue. Although DBBS presents a high osteoconductive potential and there is evidence that it is as effective as autologous grafts, either alone or combined with autologous addition material, it has the major disadvantage of having an incomplete and slow resorption rate.

Additionally, the use of these types of bone augmentation implants (such as xenografts - DBBS, Bio-Oss) increases treatment costs, making the procedure less accessible to a larger number of patients [15, 16].

Taking all these factors into consideration, it is interesting and necessary to test alternative bone augmentation materials that can reduce the cost of post-extraction socket preservation procedures, making them more accessible to more patients, while also improving the outcome in terms of quality and quantity of newly formed bone tissue [17, 18].

An impressive number of clinical studies have demonstrated that replanted teeth, after their endodontic treatment, are subject to the phenomenon of bone ankylosis, and dentin is gradually replaced by bone tissue. It is well known that dentin and bone tissue have a similar organic and inorganic structure. Recent studies have focused on the potential of dentin to substitute bone tissue both at the post-extraction socket level and for correcting defects at the alveolar ridge [19, 20].

It has been demonstrated that dentin, used as a material for autologous particulate augmentation or in the form of a dentin block, is capable of inducing bone remodeling as a result of its osteoinductive, osteoconductive, and osteo-neoformation properties. In addition to these advantages, in vitro studies have shown that proteins extracted from dentin influence the proliferation and differentiation of osteoprogenitor cells. The results suggested that TGF-β, likely in combination with other factors and constituents from dentin, are capable of regulating cellular behavior and, therefore, can influence the development, remodeling, and regeneration of mineralized bone tissue [21-23].

In humans, the use of a bone augmentation material made from autologous particulate dentin in the post-extraction socket and in alveolar ridge bone defects has demonstrated osteoconductive and osteogenic properties, resulting in high-quality bone tissue that allows for implant therapy after a short osteointegration waiting period [24, 25].

CONCLUSIONS

The use of extracted teeth as a bone augmentation material offers many advantages for the clinician. The material is completely autologous and contains mineralized tissue similar to bone, with a series of bioactive growth factors in the dentin matrix, additionally having the advantage of presenting no risk of disease transmission.

Based on the results obtained from preclinical data, dentin can be successfully ground into particles ranging from 300 to 1200 μm and added to the post-extraction socket or to bone defects in the alveolar ridge, where the material is gradually resorbed over time. Due to its mineral content, dentin particles are used as a material with a low substitution rate, which limits the dimensional changes that occur after extraction, especially in comparison to materials with a rapid absorption rate that are commonly used for augmentation.

Within the limits of the cases and arguments presented in this series, it has been demonstrated that autologous dentin particles used for post-extraction socket preservation can be an excellent alternative that successfully replaces autologous bone grafts, as demonstrated above with numerous advantages over other bone augmentation materials.

However, further randomized studies are necessary to confirm the advantages of this treatment option, as the method is still in its early stages. Future clinical studies are underway to investigate the regenerative potential of dentin in comparison with other standard biomaterials indicated for different clinical cases that require optimal bone levels and/or periodontal regeneration.

Conflicts of Interest

The authors declare no conflict of interest.

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Assessing the Diagnostic Potential of Brush Biopsy for Oral Cancer Detection

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Abstract

1.Background/Objectives: This study aims to assess the effectiveness of brush biopsy in detecting malignancies in the oral cavity through clinical examinations of patients attending regular dental check-ups. Additionally, it evaluates the diagnostic value of brush biopsies by analysing the cytological results, risk factors, and lesion localization while discussing the role of oral cancer prevention and the method's advantages and limitations in routine dental practice. 2.Material and methods: After a detailed inspection and palpation of the soft tissue in the oral cavity, cells from a suspicious, potentially precancerous lesion were collected using a cytobrush, which was stroked multiple times over the lesion in a rotating motion under light pressure in order to obtain as many cells as possible. The present study included 60 patients who met the eligibility criteria, selected based on age distribution (18 to 90 years old) and assessed for key risk factors such as alcohol consumption and smoking habits. 3.Results: The obtained results confirmed that leukoplakia was the most frequently diagnosed condition, summing 25% of all cases, that represent 17 out of the lesions identified, while lichen planus represented 19% of diagnoses, with 13 cases detected, both being recognized as premalignant lesions requiring careful monitoring. 4.Conclusions: Brush biopsy is a non-invasive, cost-effective, and easily integrated diagnostic tool for early oral cancer detection, complementing traditional biopsy methods by enabling timely intervention, reducing unnecessary surgical procedures, and supporting preventive dental care, with further research needed to validate its clinical role.

Keywords: Oral cancer, brush biopsy, early detection, cytology, oral pathology

INTRODUCTION

Oral cancer is a significant public health concern, with a rising global incidence and substantial morbidity and mortality rates [1]. Early detection plays a central role in improving patient outcomes and survival rates [1]. Traditional diagnostic techniques, such as visual examination and tissue biopsy, have diagnostic limitations in terms of invasiveness, subjectivity, and potential sampling errors. Therefore, there is a growing need for reliable and non-invasive methods that can aid in the early detection of oral cancer [2, 3]. The brush biopsy technique has emerged as a potential tool for detecting oral cancer. This technique involves the use of a specially designed brush to collect cells from suspicious oral lesions. Brush biopsy offers several advantages over conventional biopsy methods, including its simplicity, cost-effectiveness, and ability to be performed in an outpatient setting [4].

A brush biopsy is a diagnostic procedure used to detect oral cancer. It is a minimally invasive technique, in which a small sample of cells from the oral cavity gets collected for an examination under a microscope [4,5]. The brush biopsy procedure involves using a small brush with fine bristles to gently collect cells from the surface of suspicious areas in the mouth, such as lesions, ulcers, or abnormal tissue [6]. Each lesion must be sampled separately to ensure accurate localization of results. During routine dental visits, the oral mucosa should be examined for abnormalities, and any unclear changes suspected of neoplasia should be documented along with a brush biopsy. The collected cells are preserved in a liquid medium and sent to a pathologist for evaluation of abnormalities or cancer signs [7, 8].

Clinically conspicuous lesions, particularly those with high-grade dysplasia or invasive squamous cell carcinoma, should undergo morphological assessment for early detection, as prognosis is significantly better in early stages [9]. Since oral mucosal carcinoma primarily affects the epithelium, brush biopsy is a useful diagnostic tool, reducing the need for overdiagnosis associated with frequent surgical biopsies. Compared to conventional surgical biopsies, brush biopsy offers several advantages, including lower costs, minimal material requirements, and a simple, rapid procedure [10]. Its non-invasive nature makes it suitable even for anxious patients. While surgical biopsies are typically reserved for highly suspicious lesions, brush biopsies have a broader range of indications. They are effective for exclusion diagnosis, early detection, and monitoring of oral mucosal carcinoma and potentially malignant oral disorders. Oral cancer, predominantly oral squamous cell carcinoma (OSCC), represents a significant public health issue worldwide [11].

The incidence of OSCC has been rising, and despite advancements in treatment, survival rates remain low due to late-stage diagnoses [12]. Common risk factors for oral cancer include tobacco use, alcohol consumption, human papillomavirus (HPV) infection, and poor oral hygiene [13]. Early detection plays a crucial role in improving prognosis, as it allows for timely intervention and reduces the likelihood of disease progression. Current diagnostic methods for oral cancer rely heavily on conventional biopsy techniques, which, while accurate, are invasive and can cause patient discomfort [14]. The brush biopsy has emerged as a non-invasive alternative that enables clinicians to collect epithelial cells from suspect lesions with minimal discomfort to the patient. This technique holds potential as a screening tool for the early detection of oral malignancies, particularly in dental settings where routine examinations are conducted [15]. Despite its advantages, the diagnostic accuracy of brush biopsy remains under continuous evaluation [15]. This study aims to investigate its effectiveness compared to standard histopathological methods, assess its feasibility in routine dental practice, and explore its role in identifying potentially malignant, premalignant and malignant lesions. By analyzing patient demographics, lesion

characteristics, and cytological findings, this research seeks to provide valuable insights into the potential implementation of brush biopsy in primary dental care settings.

Aim and objectives

The aim of this observational, prospective study is to evaluate the outcome of the clinical extra-oral and endo-oral examination of the patients that are referring on a regularly basis to the dental office for check-ups or planned treatments, and quantify the presence potentially malignant, premalignant or malignant lesions, as well as the use and efficiency of the brush biopsy technique for the detection of malignancy in the oral cavity.

In addition, a further evaluation of the cytological diagnosis, the disease spectrum, risk factors and localization on the oral mucosal will be performed in order to evaluate the diagnostic value of brush biopsies. Furthermore, the importance of oral cancer prevention, the advantages and disadvantages of the oral brush biopsy in general dental routine and the limits of this method are discussed.

MATERIAL AND METHODS

The Clinic of Oral Pathology of the "Victor Babes" University of Medicine and Pharmacy conducted a study in collaboration with the dental office "Zahnarztpraxis Dr. Sautré" in Düsseldorf, Germany, during the period between July 2023 – December 2023.

Patients that presented in the dental office for all kind of treatments and regularly check-ups were screened for oral lesions. Those patients with any kind of oral lesions (benignant lesions, fungal lesions, denture related lesions), were included in the data colleection, as well as patients with potentially malignant lesions, including leukoplakia lesions, lichen planus and ulcerative lesions were quantified.

The inclusion criteria were represented by: >18 years of age, both genders, visible lesion in the oral cavity or need for oral cancer prevention, compliant patient

The exclusion criteria were represented by: <18 years of age, non-compliant patients

This examination protocol was divided into 3 parts: the medical history of the patient (questionnaire), the extraoral examination and the intraoral examination.

After a detailed inspection and palpation of the oral cavity, the cells from a suspicious, potentially precancerous lesion were collected, using a cytobrush (Figure 1, Figure 2). This type of brush wasstroked over the lesion several times, performing a rotating motion in the same direction and under light pressure to obtain as many cells as possible (Figure 3, Figure 4).

After the oral inspection that focused as well on the oral mucosa, a cytobrush (Rovers Orcellex Brush RT, Oral Cell Sampler) was brushed over the clinically suspicious lesion by rotating it around 10 times to remove squamous epithelia from the epithelial lining (so-called forced exfoliation). The head of the brush was then loosened and stored a solution (BD SurePath™) to preserve the collected cells (Figure5, Figure 6). An accompanying cytopathology form was filled out for each brush biopsy, containing at least the patient's name, date of birth and insurance details, but usually also information on localization, clinical picture and any previous illnesses and therapies.

The lesions were described in terms of their location, color, surface structure and size and in many cases a suspected diagnosis was made. Important risk factors, such as a previous squamous cell carcinoma diagnosis or a previously diagnosed lichen planus, were also noted on the accompanying form. The main concern of the question about malignancy was also made clear in all forms.

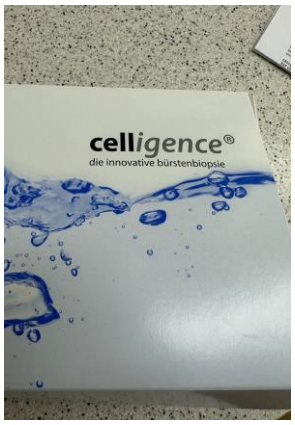


Figure 1. The Brush Biopsy Kit used (Celligence – die innovative Bürstenbiopsy - Mundwerk Deutschland GmbH & Co. KG)

Figure 2. The Brush Biopsy Kit used (Celligence – die innovative Bürstenbiopsy - Mundwerk Deutschland GmbH & Co. KG)

Figure 3. The Brush used for the Biopsy (Rovers Orcellex Brush RT, Oral Cell Sampler)

Figure 4. The Brush used for the Biopsy (Rovers Orcellex Brush RT, Oral Cell Sampler)

Figure 5. The Solution used: BD SurePath™

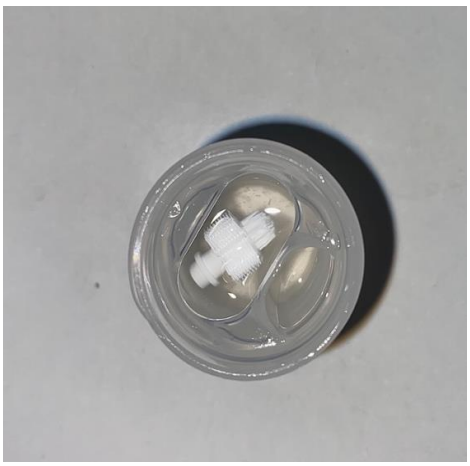


Figure 6. The Solution used: BD SurePath™

RESULTS

In a quarter, the dental clinic "Zahnarztpraxis Dr. Sautré" sees an average of 900 different patients. The study was conducted from July 2023 until December 2023, covering two quarters. This accounts for approximately 1800 different patients over the duration of the study. Among these 1800 patients, 60 met the criteria for inclusion in the study.

In the age groups of 18-30, 30-40, and 40-50, there were 6 patients each, accounting for 10% of the total patients each. Twelve patients fell within the 50-60 and 60-70 age brackets, representing 20% of the total patients each. The highest number of patients, 13, belonged to the 70-80 age group, accounting for approximately 22% of the total patients. Five patients were between 80-90 years of age, making up around 8% of the total patients. In total, the study included 60 patients.

The two most striking risk factors for oral cancer development are alcohol consumption and smoking. First, the risk factors from the whole patient collective were evaluated. From all patients, 28% claimed regular alcohol consumption and 10% tobacco consumption only. The combination of both risk factors significantly increases the risk of development of oral cancer and was stated by 17% of patients. Of the patient collective 45% did not mention any risk factors (Table 1). It has to be noted that some patients may feel prejudged by their doctor and fear to claim any risk factors.

Table 1. The risk factors of the patient collective

Risk Factors Mentioned	Percentage
No risk factors mentioned	45%
Alcohol consumption	28%
Smoking + Alcohol consumption	17%
Smoking	10%

Twenty-seven out of the total 60 patients denied any risk factors, including alcohol consumption or use of tobacco. Alcohol was consumed by 17 patients a regular basis. The combination of smoking and alcohol use was seen in 10 patients. Purely smoker were 6 patients. It can be seen that, if you are smoker, it is more likely that you also consume alcohol, than vice versa. In a subsequent analysis, the study examined the risk factors associated with patients who underwent brush biopsy. Among the patients included in the study, it was found that 11 individuals (42%) did not report any specific risk factors. However, a significant proportion, constituting 27% of the patients, reported a history of both smoking and alcohol consumption (Table 2). Additionally, four patients reported smoking only, while another four patients reported alcohol consumption only.

Table 2. The risk factors of the patient a Brush Biopsy was performed

Risk Factors Mentioned	Percentage
No risk factors mentioned	42%
Alcohol consumption	27%
Smoking + Alcohol consumption	16%
Smoking	15%

Most of the 69 lesions were located on the vestibular mucosa, the jugal mucosa, or tongue. A number of 16 lesions (24%) were localised in the vestibule (left and right combined) and a total of 14 lesions (20%) were found on the cheek (jugal mucosa, right and left combined). The tongue mucosa was involved in 12 cases (16%). Lesions were also found on the labial mucosa (7), the floor of the mouth (6), the edentulous ridge (5), the hard palate (4), the gingiva (3) and the retromolar area (2) (Table 3).

Table 3. Location of the Lesion

Area	Percentage
Vestibule	23%
Jugal Mucosa	20%
Tongue	18%
Labial Mucosa	10%
Floor of the mouth	9%
Edentulous Ridge	7%
Hard Palate	6%
Gingiva	4%
Retromolar Area	3%

In the clinical evaluation, the most frequently diagnosed condition was leukoplakia, accounting for 25% of all cases, with a total of 17 lesions identified. Following closely behind was lichen planus, comprising 19% of diagnoses with 13 lesions detected. Both leukoplakia and lichen planus are recognized as premalignant lesions, necessitating careful monitoring and management. In addition to leukoplakia and lichen planus, various other lesions were observed within the group of patients included. These cases represented by 8 cases of ulcerations (12%), 6 instances of hyperkeratinisation (9%), and 6 aphthous lesions (9%). Furthermore, 4 cases of hyperkeratinisation referring to bite marks, 3 instances of pressure point ulceration due to poorly fitting dentures, and 3 cases of candida were identified (Table 4). Less frequently observed were 2 cases of erythroplakia, along with individual instances of a burning lesion, prevention, petechiae, fibroma, and persisting irritation ulcer. Each of these conditions calls for specific attention and, where necessary, appropriate treatment to ensure the patient's oral health and well-being.

Table 4. Clinical diagnosed lesions

Condition/Lesion	Percentage
Leukoplakia	25%
Lichen Planus	19%
Ulcer	12%
Hyperkeratinization	9%
Aphthous lesion/Inflammation	9%
Bite marks	6%
Pressure Point Ulcer	4%
Candida	4%
Prevention of rezidive of OSCC	3%
Erythroplakia	2%
Burning lesion	2%
Prevention	1%
Petechiae	1%

From the 69 lesions which were included in the study, in case of 32 lesions a brush biopsy was performed. Out of these 32 brush biopsy samples, the most frequent diagnosis was leukoplakia, with 19 results in total (60%). The 2nd frequent cytological diagnosis was "no malignant cells" which refers to clinical diagnosis like ulcerations. Three cases of lichen planus were detected and each one case of mycosis, erythroplakia and candida (Table 5).

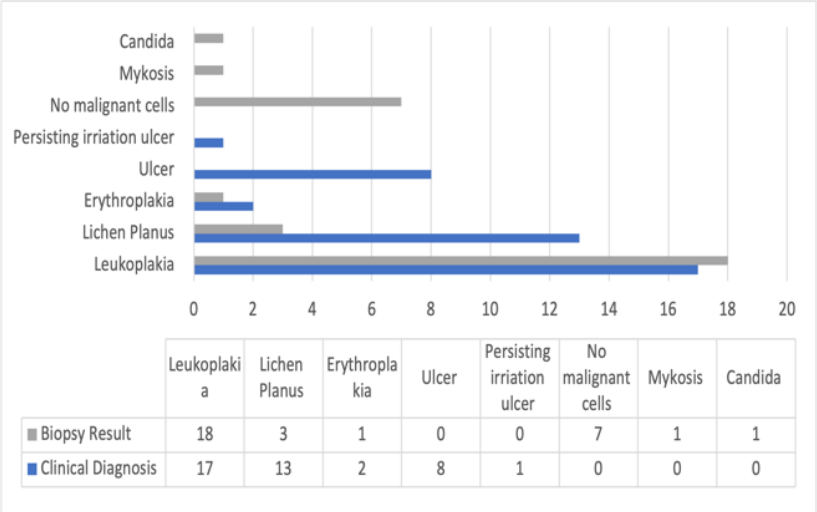
Table 5. Biopsy Results

Condition/Lesion	Percentage
Leukoplakia	60%
No malignant cells	22%
Lichen planus	9%
Mykosis	3%
Erythroplakia	3%
Candida	3%

Out of the 32 biopsies performed, 10 were taken from the vestibule, accounting for 31% of the total. Eight lesions were biopsied from the tongue, while seven were taken from the jugal mucosa. In three cases, biopsies were taken from the floor of the mouth, two from the hard palate, and one each from the retromolar area and the edentulous ridge. Interestingly, although seven lesions were found on the labial mucosa, no biopsies were taken from them. Similarly, no biopsies were taken from the three lesions located on the gingiva (Table 6).

Table 6. Location of the Brush Biopsy performed

Area	Percentage
Vestibule	31%
Tongue	25%
Jugal Mucosa	22%
Floor of the mouth	10%
Hard Palate	6%
Retromolar area	3%
Edentulous ridge	3%



	Leukoplakia	Lichen Planus	Erythroplakia	Ulcer	Persisting irriation ulcer	No malignant cells	Mykosis	Candida
Biopsy Result	18	3	1	0	0	7	1	1
Clinical Diagnosis	17	13	2	8	1	0	0	0

Figure 1. The Clinical Diagnosis of the Lesions vs. The Cytological Diagnosis

A comparison of clinical and cytological diagnoses revealed notable findings. Leukoplakia was clinically diagnosed in 18 lesions, with 17 confirmed by biopsy, indicating high diagnostic accuracy. However, lichen planus showed a significant discrepancy—while it was clinically diagnosed in 13 cases, only 3 were confirmed cytologically, suggesting challenges in its clinical identification (Figure 7). Erythroplakia was clinically identified in two cases, but only one was cytologically confirmed. The diagnosis of "no malignant cells" was mainly associated with biopsies of ulcerative lesions or those performed as a preventive measure, such as monitoring potential recurrence of oral squamous cell carcinoma (OSSC). Additionally, one case of Candida albicans infection and another of mycosis were identified, emphasizing the importance of cytological evaluation in accurately distinguishing various oral lesions.

DISCUSSIONS

The findings from this study align with the existing literature on the effectiveness of oral brush biopsy (OBB) in the early detection of oral cancer. The results of this study, which included 60 patients from July 2023 to December 2023, demonstrate that OBB is a reliable method for identifying precancerous and cancerous lesions in the oral cavity.

The patient cohort consisted of 29 females and 31 males, with a median age of 60 years. A total of 69 lesions were found, of which 32 were subjected to brush biopsy. The most common lesion identified was leukoplakia, with 18 clinically diagnosed cases and 17 confirmed by biopsy. This high prevalence underscores the importance of routine screening in detecting such lesions early.

Compared to conventional scalpel biopsy, brush biopsy provides a non-invasive alternative with high patient acceptance. Prior studies, including Neumann et al. (2022) and Deuerling et al. (2019), report high sensitivity and specificity for brush biopsy. The study highlights its potential as a routine screening tool in general dental practice, particularly in detecting leukoplakia and early-stage OSCC. However, discrepancies in diagnosing lichen planus underscore the need for combined diagnostic approaches. The findings of this study align with existing literature on the effectiveness of oral brush biopsy (OBB) for early oral cancer detection. Conducted between July and December 2023 with 60 patients, the study confirmed OBB as a reliable method for identifying precancerous and cancerous oral lesions. The patient cohort included 29 females and 31 males, with a median age of 60 years. Among

69 detected lesions, 32 underwent brush biopsy, with leukoplakia being the most common diagnosis.

Comparison with previous studies, such as Neumann et al., highlights similar findings, with leukoplakia being the most frequently detected lesion. The study by Neumann et al., conducted in Germany between 2014 and 2016, involved 670 patients and 814 brush biopsies analyzed using liquid-based cytology (LBC). The sensitivity for cancer detection was 100%, with a specificity of 86.5%, reinforcing the reliability of OBB in general dental practice.

A study by Deuerling et al. (2019) at the University of Leipzig further supported LBC's efficacy, analyzing 1,352 samples between 2012 and 2018. The findings showed a sensitivity of 95.6% and specificity of 84.9%, demonstrating that LBC is highly sensitive, minimally invasive, and an efficient alternative to traditional scalpel biopsy.

Gupta et al. [] in India compared exfoliative cytology, modified brush biopsy, and scalpel biopsy in 225 cases of oral precancerous lesions. The modified brush biopsy showed higher sensitivity (81.69%) than routine exfoliative cytology (48.57%), confirming its usefulness as a screening tool, particularly in resource-limited settings.

A 2023 study by Kokubun et al. in Japan analyzed 653 patients undergoing cytological and histological examinations. The findings indicated that while OBB had a sensitivity of 69% and specificity of 75%, some cases required histological confirmation, especially for deep-margin lesions.

Despite its advantages, oral brush biopsy presents certain limitations that must be considered. One of the main concerns is the possibility of false-negative results, particularly in cases of squamous cell carcinoma (SCC), where tumoral cells may be located in deeper layers, making them difficult to detect [36]. Additionally, the specificity of OBB is lower than that of scalpel biopsy, which means it may not always accurately distinguish between dysplastic and non-dysplastic lesions [28]. Some conditions, such as lichen planus and erythroplakia, also pose diagnostic challenges, often requiring additional histological confirmation to ensure an accurate diagnosis [24]. Another important factor influencing the reliability of the method is its dependence on sample quality. The accuracy of liquid-based cytology and brush cytology largely depends on proper sample collection and analysis, and any deficiencies in this process may lead to inadequate or inconclusive results [36]. Furthermore, while OBB is highly effective for early detection, its diagnostic value in advanced lesions remains limited, as it may not be sufficient for identifying deeply invasive or complex lesions, which necessitate histological follow-up [23].

Overall, these studies affirm that oral brush biopsy, particularly when combined with liquid-based cytology, is a highly sensitive, non-invasive, and practical tool for early oral cancer detection. It enhances diagnostic accuracy in general dental practice, supports early intervention, and reduces oral cancer mortality rates.

CONCLUSIONS

Brush biopsy proves to be a valuable diagnostic tool for early oral cancer detection. Its non-invasiveness, affordability, and integration into routine dental check-ups support its widespread adoption. While it does not replace traditional biopsy methods, it serves as an effective preliminary screening technique, prompting timely intervention. Further research and larger cohort studies are recommended to validate its role in clinical practice.

The daily use of brush biopsy in dental offices for cancer detection holds great potential. It is a time-efficient procedure that can be easily integrated into routine dental check-ups. Additionally, it is cost-effective for both patients and dentists, providing an affordable alternative for early cancer detection compared to invasive biopsy techniques.

While brush biopsy does not replace surgical biopsy, which remains essential for an accurate diagnosis, it helps reduce the need for unnecessary surgical interventions. In conclusion, liquid-based brush cytology is a highly sensitive and reliable method for diagnosing oral neoplasia. Its advantages over traditional invasive biopsy methods could facilitate early detection and treatment, ultimately improving patient outcomes.

Conflicts of Interest

The author declares no conflict of interest.

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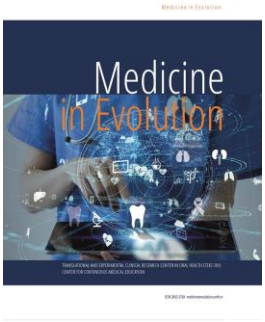
Evaluation of the Surface, Structural, And Optical Stability of a Single-Shade Universal Resin Composite After Exposure to Acidic Staining Solutions



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Abstract

1.Background/Objectives: Advances in adhesive dentistry have led to the development of single-shade universal resin composites (SsURCs), designed to simplify shade selection and enhance aesthetic outcomes, yet their long-term stability under acidic conditions remains a concern. This study aimed to evaluate the surface properties, zeta potential, Raman spectral characteristics, and color stability of Omnichroma, a single-shade universal resin composite, before and after immersion in staining solutions (coffee, Coca-Cola, and red wine). 2.Methods: A total of 20 disc-shaped specimens were prepared and divided into four subgroups: control (artificial saliva), coffee, Coca-Cola, and red wine. Surface roughness, contact angle, and color stability were assessed before and after immersion, while Raman spectroscopy analyzed structural modifications, and zeta potential measurements determined the point of zero charge (PZC). 3.Results: Coffee caused the most significant color change ($\Delta E = 10.84 \pm 1.03$) and roughness increase ($SR = 1.53 \pm 0.38$), followed by red wine ($\Delta E = 5.33 \pm 0.27$; $SR = 1.15 \pm 0.08$) and Coca-Cola ($\Delta E = 1.28 \pm 0.44$; $SR = 1.21 \pm 0.31$). The PZC was identified at pH 3.8, indicating a predominance of anionic ionizable groups. Raman analysis revealed molecular alterations, particularly in C=O stretching and C=C aromatic ring vibrations. 4. Conclusions: These findings suggest that acidic beverages affect the structural and optical stability of Omnichroma, with coffee having the greatest impact. Further in vivo studies are needed to assess its long-term performance in clinical settings.

Keywords: Single-shade universal resin composite, contact angle, zeta potential, hardness, roughness, Raman spectroscopy, colour stability

INTRODUCTION

Direct resin composite restorations are widely used in dental clinics, benefiting from advancements in adhesive dentistry. The "Natural Layering Concept" was developed to meet patients' aesthetic expectations by replicating the appearance of natural teeth [1]. While this technique is commonly applied in clinical practice, it demands a high level of restorative skill and extended chairside time. In contrast, recently introduced single-shade universal resin composites (SsURCs) streamline the restorative process, offering a more efficient alternative [2]. Composite resins have become increasingly popular as direct restorative materials in recent decades, largely due to the growing patient preference for aesthetically pleasing restorations. These materials are highly valued by clinicians for their ability to facilitate minimally invasive procedures, their excellent aesthetic results, their strong adhesion to dental tissues, and their enhanced durability. The ability of a resin composite to seamlessly match the colour of the dental structure is a key factor in patients' perception of aesthetic treatment quality. This aspect significantly influences both their satisfaction with the final result and their assessment of the clinician's professional competence [3].

Over time, significant advancements in dental composite technology have improved their physical, chemical, and aesthetic properties, enabling their use in a wide range of clinical scenarios. However, the modern diet poses new challenges to these materials. Increased consumption of acidic beverages such as carbonated drinks, coffee, black tea, and alcohol introduces potential risks to resin-based restorations. The acidic nature of these substances, with their low pH, can compromise the structural integrity of the composite, alter the properties of its fillers, and weaken the bond between the fillers and the resin matrix, ultimately reducing the longevity of restorations. Clinicians must carefully evaluate the structural composition of composite resins and their resistance to chemical and mechanical stresses when selecting materials for restorative treatments. Within the oral cavity, restorations are continuously exposed to environmental changes, whether through acidic foods and beverages or the mechanical forces of mastication and, in certain cases, excessive occlusal forces. These challenges can significantly influence the performance and durability of resin-based materials.

Single-shade universal resin composites (SsURCs) are designed to adapt to a wide range of tooth shades, eliminating the need for shade selection. Their ability to seamlessly integrate with surrounding tooth structures relies on the blending effect, which occurs through light reflection and scattering. When light interacts with the composite material, it disperses across the surface of the filler particles and scatters in various directions. This optical phenomenon is influenced by factors such as restoration size and the material's translucency. The terms "chameleon effect" and "colour adjustment potential" are also commonly used to describe this blending capability [4].

Omnichroma is a single-shade, structurally coloured universal composite designed for a wide range of direct restorative applications. Its extensive colour-matching capability eliminates the need for shade selection, streamlines the restorative process, and reduces composite inventory. This allows clinicians to minimize chair time, decrease material waste, and lessen dependence on traditional shade-matching techniques [5].

The available literature on Omnichroma provides limited data, primarily focusing on its color adjustment potential [6, 7], shade-matching ability [8], optical behavior [9], and color stability [1]. Some studies also explore its cytotoxicity [10], as well as its flexural strength (FS) and elastic modulus (EM) [11, 12]. However, comprehensive research on its mechanical, spectral, and structural properties remains scarce, highlighting the need for further investigations to fully understand its clinical performance.

Aim and objectives

The aim of this study is to evaluate the surface properties (contact angle, zeta potential and roughness) and Raman spectral characteristics of a single-shade composite, as well as its colour stability before and after immersion in staining solutions (coffee and acidic carbonated beverage).

MATERIALS AND METHODS

A disc-shaped specimen was prepared using a custom-made plexiglass mold with an internal diameter of 10 mm and a height of 2 mm. Omnichroma, a light-cured, radiopaque, single-shade universal composite (Tokuyama Dental, Tokyo, Japan; Batch No. 123E83), was used as the restorative material. Omnichroma is a single-shade universal resin composite that utilizes structural color technology to match a wide range of tooth shades without the need for additional tints or pigments. Its color-matching ability is based on the uniform size and arrangement of filler particles, which enable it to blend seamlessly with surrounding tooth structures. Its filler system consists of 79% by weight (68% by volume) of spherical silica-zirconia filler, with a mean particle size of 0.3 µm (ranging from 0.2 to 0.6 µm), along with a composite filler. The resin system comprises urethane dimethacrylate (UDMA) and triethylene glycol dimethacrylate (TEGDMA), with additional components including Mequinol, dibutyl hydroxyl toluene, and a UV absorber. The composite was carefully compacted into the mold using a Teflon-coated plastic filling instrument, and excess material was removed with an explorer. A celluloid strip was placed over the compacted resin, followed by a 1 mm thick glass slide to flatten the surface and extrude any remaining excess material. The resin was then light-cured for 40 seconds through the Mylar strip and glass slide using an LED curing unit (3M Elipar DeepCure-S LED, USA) with a light intensity of 400 mW/cm² in a uniform continuous curing mode. The light intensity was verified after every five samples.

A total of 20 Omnichroma composite disc-shaped specimens were prepared. The specimens were divided into four subgroups (n = 5 each), with one group serving as a control and the other three immersed in different staining solutions: artificial saliva (control), coffee, Coca-Cola, and red wine. The solutions were prepared as follows:

- Control Group
- Coffee Group: Specimens were immersed in a Nespresso coffee solution, prepared by dissolving one capsule of black coffee (Nespresso, Switzerland) in 100 ml of boiling distilled water and allowing it to cool to room temperature.
- Coca-Cola Group: Specimens were stored in Coca-Cola (Coca-Cola Co., USA), a carbonated soft drink composed of carbonated water, high fructose corn syrup, caramel color, phosphoric acid, and caffeine. To maintain carbonation, tightly sealed containers were used, and a fresh bottle was opened daily.
- Red Wine Group: Specimens were immersed in 150 ml of red wine (Feteasca Neagra, Purcari, Romania). The wine was poured into sealed glass containers to prevent oxidation, and a fresh bottle was used daily.

All specimens were stored at 37°C in an incubator to simulate oral conditions, and the solutions were replaced daily to ensure consistency. The pH of the solutions was measured and stabilized using a calibrated digital pH meter (Hanna Instruments HI 5221, Romania), with an accuracy of ±0.01 pH. Measurements were taken before specimen immersion to ensure consistency in the storage environment.

The primary color of Omnichroma was recorded using a digital spectrophotometer (Vita Easyshade®V, Compact, Vita Zahnfabrik, Bad Säckingen, Germany). To ensure accurate measurements and minimize absorption effects, each specimen was placed on a white

background. The probe tip of the spectrophotometer was positioned perpendicularly at the center of the specimen and brought into direct contact with its surface.

To assess its hydrophobicity and surface interaction properties, the water contact angle was measured on two distinct surfaces of the material: a smooth, polished area (Surface 1) and a rough, uneven area (Surface 2). These measurements provide insight into the wettability and potential influence of surface texture on the composite's clinical performance. Water contact angle measurements were performed using the Drop Shape Analyzer-DSA25 (KRÜSS GmbH, Germany). The Double Sessile Drop method was employed with distilled water at a drop volume of 1 µL. The temperature was maintained at 20°C throughout the experiment. Each composite material was subjected to six to seven measurements per surface to ensure statistical reliability. Water served as the drop phase, with air as the surrounding phase. The system recorded parameters such as contact angle (CA) at right (r), left (l), and mean (m) positions, surface free tension (SFT), and volume of the applied liquid droplets. The mean contact angle and standard deviation were calculated for each surface of the samples. The instrument's software (KRÜSS ADVANCE 1.14.1.16701) automatically analyzed the drop profiles. The experimental process was designed to ensure replicability and eliminate variability by maintaining identical environmental and procedural settings for both sets of measurements. Additional SFE (surface free energy) results were calculated using the OWRK model, focusing on polar and dispersive contributions.

The zeta potential was measured using a Particle Charge Detector Mutek PCD-03 (Mütek GmbH, Neckartailfingen, Germany). This device is designed to assess the concentration of water-soluble ionic polymer solutions and determine the zero-charge point of composite micro- and nanoparticles. For the analysis, 10-20 mg of solid powder was dispersed in 10 mL of PBS solution, ensuring a uniform suspension. After an equilibration period of 10 minutes, the streaming potential was recorded directly from the instrument's display (Figure 1).

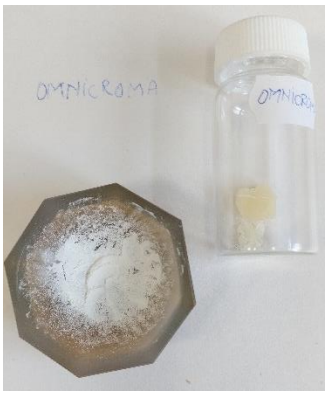

Figure 1. Streaming Potential Analysis of a Dental Composite: Powderization and Measurement Using the PCD Device

The vibrational properties of Omnichroma composite resin were analyzed before and after immersion in coffee, red wine, and Coca-Cola using the LabRAM Soleil™ Raman Microscope (HORIBA Scientific). Raman spectra were acquired with a 532 nm laser, utilizing QScan™ lightsheet confocal imaging for enhanced spatial resolution and SmartSampling™ technology for rapid spectral acquisition. Measurements were performed with four accumulations to improve signal clarity and minimize noise. A 5× magnification objective lens was used to precisely focus on the sample surface, covering a spectral range of 200 to 3200 cm^{-1}. To prevent thermal damage and ensure optimal spectral quality, a neutral density (ND) filter at 10% (8.9 mW) was applied. Data collection and spectral analysis were conducted using LabSpec 6 software for precise evaluation of structural changes.

The surface characterization of the dental resin composite samples was conducted using a Mitutoyo SJ-201 Roughness Tester (Mitutoyo Europe GmbH, Germany). To determine the arithmetic average roughness (Ra), each specimen was analyzed through three-line measurements. The profilometer, featuring a 5 µm radius diamond tip, recorded two-dimensional surface profiles at a scanning speed of 0.5 mm/s, with a cut-off value of 0.8 mm and a total measuring length of 4 mm. Measurements were performed in three distinct areas on each sample, and the arithmetic mean of these readings was calculated to represent the Ra (peak-valley roughness) value.

Color measurements were performed using the VITA Easyshade V digital spectrophotometer (Vita Zahnfabrik, Bad Säckingen, Germany), designed for accurate and reliable shade determination of teeth and restorations. The color parameters L*, a*, and b* were analyzed according to the Commission Internationale de l'Eclairage (CIE) standards, while hue angle (°) and relative color saturation (C*) were derived from these values. Specimens were immersed daily for 20 minutes over 10 days in red wine (Fetească Neagră), black coffee (Nespresso), or Coca-Cola, followed by air drying. Color changes were recorded before and after immersion, and the total color difference (ΔE) was calculated using the formula:

$$\Delta E = ([\Delta a^*]2 + [\Delta b^*]2 + [\Delta L^*]2)1/2$$

A $\Delta E > 2.7$ indicated very distinct changes, $1.2 \leq \Delta E \leq 2.7$ denoted distinct changes, and $\Delta E < 1.2$ was considered non-distinct.

Statistical analysis of surface roughness, color change, and hardness of the Omnichroma composite before and after immersion in coffee (Nespresso), Coca-Cola, and red wine (Fetească Neagră) was performed using SPSS 23.0 software (SPSS, Chicago, IL, USA). One-way ANOVA and one-sample t-tests were used to compare the variations in these properties across the different staining solutions, with statistical significance set at $p < 0.05$.

RESULTS

The pH measurements of the immersion solutions revealed variations in acidity levels, which could influence the discoloration of the composite specimens. The coffee solution (Nespresso) exhibited a mildly acidic pH of 5.0, while the red wine (Fetească Neagră, Purcari, Romania) showed a more pronounced acidity with a pH of 3.5. Coca-Cola had the lowest pH value of 2.5, indicating a highly acidic environment.

For Omnichroma, the average diameter of droplets was recorded as 1.58 mm ± 0.05 mm for the first measurement set and 1.67 mm ± 0.03 mm for the second. The mean contact angle was 64.94° ± 4.82° in the first test and 76.97° ± 3.08° in the second, indicating variations in wettability under consistent conditions. The average droplet volume was 0.564 µL ± 0.079 µL in the first test and 0.877 µL ± 0.049 µL in the second. Corresponding three-phase points (r) and (l) were recorded as 3.6 mm ± 0.1 mm and 2.0 mm ± 0.1 mm for the first set and 3.7 mm ± 0.0 mm and 2.1 mm ± 0.0 mm for the second (Figure 2). The SFE analysis revealed the total surface free energy and its polar and dispersive contributions, aligning with the expected hydrophilic characteristics of the material.

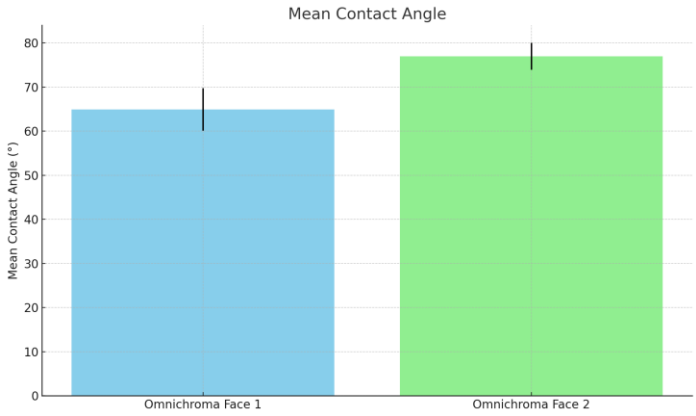

Figure 2. Mean Water Contact Angle of Omnichroma on Different Surface Textures

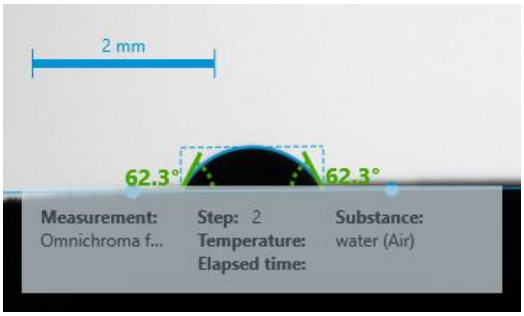

Figure 3. Example of Contact Angle Measurement for Omnichroma Composite

To determine the point of zero charge (PZC)—the pH at which the streaming potential reaches zero—a pH titration was conducted on the Omnichroma sample (Figure 3). The titration process began in an acidic medium using a 0.5% HNO_3 solution and gradually transitioned toward the basic region by incrementally adding NaOH solution. The results indicated that the PZC was observed at pH 3.8, suggesting that the composite material contains a significantly higher number of anionic ionized/ionizable groups compared to positively charged ones (Figure 4).

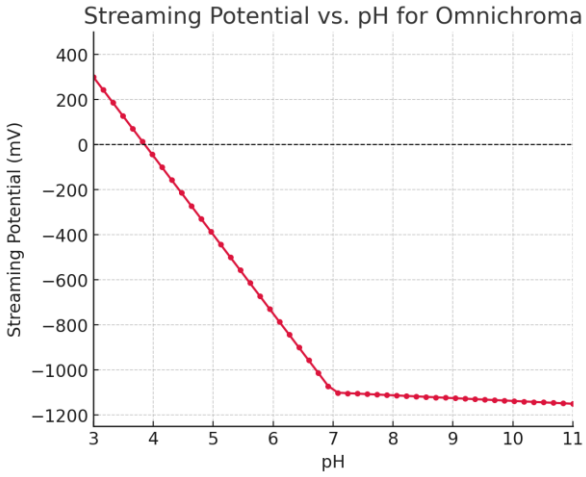

Figure 4. Streaming Potential vs pH for Omnichroma

Initially, Omnichroma exhibited a surface roughness (SR) of 1.06 ± 0.09. After 10 days of immersion, the roughness increased to varying degrees depending on the solution. Coffee immersion had the most pronounced effect, increasing the roughness to 1.53 ± 0.38, indicating a moderate abrasive impact. Red wine led to a slight increase, with a final SR of 1.15 ± 0.08, while Coca-Cola caused a minor increase to 1.21 ± 0.31, showing a less significant effect than coffee but comparable to red wine (Figure 5).

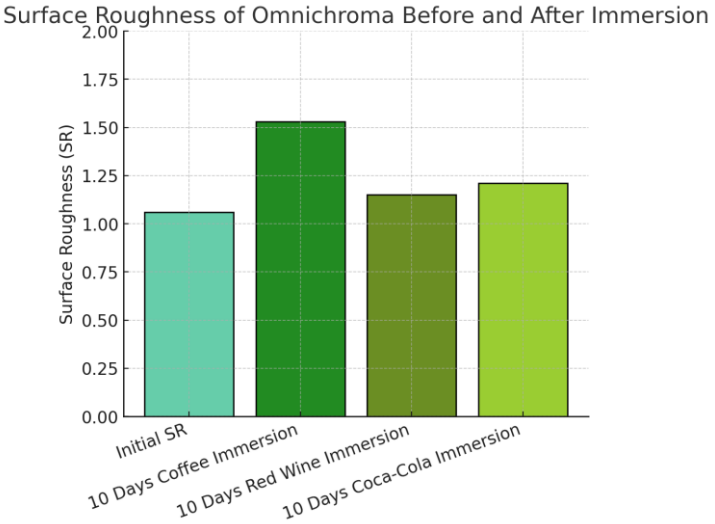

Figure 5. Surface Roughness of Omnichroma before and after immersion

Omnichroma exhibited the most significant color change in coffee ($\Delta E = 10.84 \pm 1.03$), a moderate color alteration in red wine ($\Delta E = 5.33 \pm 0.27$), and the least noticeable change in Coca-Cola ($\Delta E = 1.28 \pm 0.44$).

The Raman analysis revealed structural modifications in the Omnichroma composite resin after immersion in staining solutions. Compared to the control sample, notable variations in vibrational intensities were observed, particularly in the C=O stretching (1700 cm^{-1}) and C=C aromatic ring vibrations (1600 cm^{-1}). The coffee-immersed sample (A) exhibited the most pronounced spectral changes, indicating polymer network alterations. The Coca-Cola (B) and red wine (C) samples showed moderate shifts, suggesting minor interactions with the resin matrix. The control sample (D) maintained a stable vibrational profile, confirming the integrity of the unexposed composite (Figure 6).

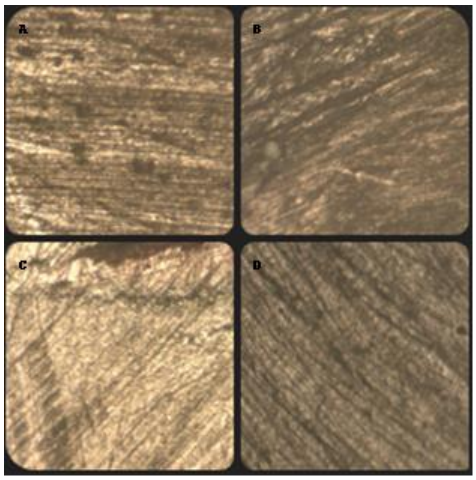

Figure 6. Surface Morphology of Omnichroma After Immersion in Staining Solutions: (A) Coffee, (B) Coca-Cola, (C) Red Wine, (D) Control

DISCUSSIONS

The pursuit of natural-looking restorations has recently led to the development of restorative systems that incorporate multiple shades and varying translucency levels, including enamel shade resin composites available in high, medium, and low value [13].

Single-shade universal resin composites are increasingly used in clinical practice due to their ability to simplify shade selection, provide good aesthetics, and minimize material waste from expired products [14]. For long-term success, resin-based composite restorations must exhibit optimal physical, mechanical, and biological properties to withstand the erosive and abrasive conditions of the oral environment [15]. While most existing studies primarily focus on the aesthetic properties of SsURCs, limited research has been conducted on their surface characteristics and stability. Therefore, this study aims to evaluate key properties of SsURCs, including contact angle, surface roughness, microhardness, zeta potential, Raman spectral characteristics, and colour stability before and after immersion in staining solutions (coffee and acidic carbonated beverage), providing a comprehensive analysis of their performance in clinical applications.

According to the manufacturer, Omnichroma does not contain pigments; instead, its colour properties rely on structural colour, a smart chromatic technology designed to control the optical characteristics of the resin composite. This innovation enables the composite to interact with light waves at specific frequencies, reflecting precise wavelengths within the tooth colour spectrum. To achieve this structural colour effect, the composite's filler must consist exclusively of uniformly sized spherical particles. Tokuyama's research has demonstrated that 260 nm spherical fillers generate the necessary a and b colour parameters to match natural teeth. Any variations in the size or shape of the filler material can disrupt or hinder the structural colour phenomenon, ultimately affecting the composite's shade-matching capability. Therefore, Omnichroma exclusively incorporates 260 nm spherical filler (Omnichroma Filler) to ensure optimal colour adaptation [16].

Our study results indicate that the varying pH levels of the immersion solutions may play a significant role in the staining susceptibility of the composite material, with more acidic environments potentially enhancing discoloration over time.

Several studies [17, 18] have reported an average critical surface roughness threshold of 0.2 μm, though no universally accepted value for surface roughness assessment currently exists. A clinical study by Jones et al. [19] found that patients could perceive surface irregularities when the mean roughness (Ra) reached 0.3 μm. In the present study, all tested composite resins exhibited a significant increase in mean surface roughness following immersion in staining solutions, suggesting potential implications for both aesthetic durability and patient-perceived texture changes. This increase in surface roughness may be attributed to the acidity of the beverages used, as well as the surface irregularities that develop during the finishing process.

The long-term color stability of commercial resin-based composite materials used in aesthetic restorative procedures remains a concern, as discoloration and poor color matching are among the primary reasons for restoration replacement [20]. The methodology employed in this study aligns with previous research utilizing spectrophotometry and the CIE Lab coordinate system*, which is widely recommended for dental applications. This system is particularly suited for detecting subtle color variations, offering advantages such as high sensitivity, repeatability, and objective measurement, making it an effective tool for assessing color stability in dental materials. The findings of this study align with previous research indicating that coffee induces greater discoloration in composite materials compared to other beverages [21, 22]. Bagheri et al. [23] reported that while cola compromises the surface integrity of composites due to its low pH, it does not cause as much discoloration as coffee and tea, as it lacks yellow dye pigments. Similarly, Sirin Karaarslan et al. [24] observed a decrease in L-values across all samples after an aging process, signifying darker shades in the tested composites. In the present study, values decreased in all Omnichroma samples following immersion in coffee, Coca-Cola, and red wine, confirming the darkening effect of these beverages. The results are consistent with previous studies [25, 26] analyzing color

changes in composite resins exposed to staining solutions, further supporting the observation that discoloration leads to negative ΔL values, indicating a shift toward darker shades over time.

The color stability of resin-based composite materials is influenced by multiple factors, including the degree of monomer conversion and the chemical composition of the material. A higher degree of conversion results in fewer unreacted monomers, reduced solubility, and enhanced resistance to discoloration. In contrast, unconverted double carbon bonds trap residual monomers within the composite, making it more prone to staining. Additionally, hydrophilic organic matrices, which promote water absorption, can accelerate the degradation of the polymeric network, leading to the release of by-products such as formaldehyde and methacrylic acid, both of which contribute to discoloration. Increased water sorption further compromises color stability by expanding the free volume within the polymer, allowing greater diffusion of water molecules, which first degrades the material and subsequently leads to staining [6].

The Raman spectroscopy findings highlight the varying degrees of chemical interactions between Omnichroma and acidic staining solutions, influencing its surface composition and structural stability. Due to Omnichroma's structural color technology, which relies on diffraction and light scattering from its microscopic structure, the small color changes observed in this study may be even less perceptible in a clinical setting. Additionally, Omnichroma’s resin matrix is primarily composed of urethane dimethacrylate (UDMA), a hydrophobic monomer known for its ability to enhance the water resistance of the material. This increased hydric stability reduces the likelihood of polymer degradation and minimizes further color alterations, contributing to the long-term aesthetic durability of the restoration [6, 27].

A key limitation of this study is the in vitro design, as laboratory conditions cannot fully replicate the complexities of the intraoral environment. Additionally, the research focused solely on single-shade universal resin composites, without including other universal composite types, such as multi-shade or bulk-fill composites. Another constraint was the absence of an aging process for the tested SsURC samples, which limits insights into their long-term performance. To gain a more comprehensive understanding, further in vivo studies are needed to evaluate the clinical effectiveness of SsURCs, particularly in terms of discoloration, wear resistance (including erosive, abrasive, and mechanical factors), bacterial adhesion, plaque accumulation, and potential toxicity.

CONCLUSIONS

This study demonstrated that acidic staining solutions significantly influence the surface properties and color stability of Omnichroma composite resin. Among the tested solutions, coffee had the most pronounced effect, causing the greatest increase in surface roughness and color change, followed by red wine and Coca-Cola, which exhibited lesser but still notable alterations. Raman spectral analysis indicated structural modifications in the composite’s chemical matrix, while zeta potential measurements reflect the composite’s surface charge behavior in acidic environments. Although Omnichroma’s structural color technology enhances shade matching, its long-term stability in acidic conditions remains a concern. The findings highlight the need for further in vivo research to evaluate the composite’s performance under real intraoral conditions, considering factors such as aging, wear resistance, bacterial adhesion, and mechanical degradation.

Conflicts of Interest

The authors declare no conflict of interest.

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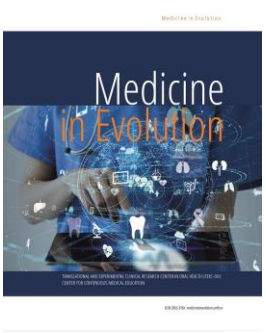
Whitening Efficacy and Enamel Mineralization Effects of Hydrogen Peroxide-Based and Peroxide-Free Whitening Products



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Abstract

1.Background/Objectives: Tooth discoloration can negatively impact self-esteem and social interactions, driving the demand for effective and safe whitening treatments. Whitening agents vary in composition, with hydrogen peroxide-based products being widely used for their strong bleaching effect, while peroxide-free alternatives incorporating remineralizing agents aim to balance whitening efficacy with enamel preservation. 2.Methods: This study evaluated the whitening performance and impact on enamel mineralization of Crest 3D White Professional Effects, a hydrogen peroxide-based product, and My White Secret, a peroxide-free alternative containing hydroxyapatite. Sixty extracted human teeth were divided into two equal groups and subjected to whitening treatments according to the manufacturers' protocols. Color and enamel mineralization were assessed using the VITA Classical Shade Guide and the DIAGNOdent Pen before and after each whitening session. 3. Results: My White Secret demonstrated a rapid initial whitening effect while maintaining enamel mineralization, whereas Crest 3D White exhibited a delayed but more pronounced whitening outcome, raising concerns regarding potential demineralization. Whitening response variability suggests that factors such as enamel structure and baseline mineralization influence treatment outcomes. 4.Conclusion: These findings emphasize the significance of formulation differences in whitening treatments, as hydrogen peroxide may impact enamel integrity, while hydroxyapatite-based alternatives provide a more balanced approach by by combining whitening efficacy with remineralization benefits. Selecting a whitening treatment should consider both aesthetic outcomes and enamel health.

Keywords: tooth whitening, enamel mineralization, hydrogen peroxide, remineralization, aesthetic dentistry

INTRODUCTION

The World Health Organization defines health as a state of complete physical, mental, and social well-being [1]. A bright, healthy smile is often seen as a reflection of overall psychosomatic well-being. In everyday culture, smiling is associated with happiness and serves as a key tool for communication and social connection, impacting not only aesthetic perceptions but also deeper aspects like self-esteem. Physical appearance can influence or enhance personal qualities and behaviours [2,3]. Beyond their primary function in chewing, teeth play a vital role in speech and social interactions. Poor oral health, which prevents a person from smiling confidently, can significantly hinder social relationships and overall quality of life [4, 5].

The importance of aesthetic dentistry and the way individuals perceive their smiles has grown significantly among the population. The visual appeal of a smile has become a key psychological and social factor, with dental appearance and conditions often influencing self-confidence and self-image [6–8]. Many people seek to improve aspects of their smile, especially tooth colour, as discoloration can lead to discomfort, embarrassment, and anxiety in social situations [5, 9].

Due to the increasing demand for aesthetic treatments in the 21st century, dentistry has advanced to meet public expectations. The growing interest in smile enhancement has led clinicians and researchers to develop minimally invasive procedures, such as teeth whitening, as a safer alternative to veneers or crowns, which can be more invasive and potentially damaging when used solely for cosmetic purposes [10].

In the late 1980s, both professional and over-the-counter whitening products were introduced to the U.S. market in response to the growing demand for achieving bright, white teeth. The effects of carbamide peroxide (CP) on dental structures were initially identified during World War I when it was used as an antiseptic for treating acute necrotizing ulcerative gingivitis (ANUG). In 1962, Klusmier proposed the application of a CP-containing gel to manage periodontal inflammation following orthodontic treatments. This led to the unexpected discovery of peroxide's ability to lighten enamel, paving the way for its use in teeth whitening. However, Kusmier's communication to the Arkansas Dental Society regarding this finding remained unnoticed until 1989 when Haywood and Heymann formally described the technique [11].

An imbalance in the shape and colour of the teeth can directly impact the aesthetics of a smile, potentially affecting an individual's personal relationships, psychological well-being, and professional demeanor. These factors may lead to considerable negative consequences for overall health and quality of life [12, 13].

Teeth whitening has become the primary method for addressing discoloration, offering beneficial results depending on the cause and severity of tooth staining. Various techniques are available, including in-office whitening, which utilizes hydrogen peroxide at concentrations of 35-37%, and at-home treatments under professional supervision, where patients apply carbamide peroxide in concentrations between 10% and 22% [14, 15].

Whitening agents primarily function by oxidizing organic compounds. Due to their high instability, these agents release free radicals, particularly nascent oxygen, upon contact with dental tissue. This oxygen penetrates the dentinal tubules and interacts with highly pigmented carbon ring compounds, breaking them down into lighter, less pigmented substances. For an effective whitening process, several factors must be considered, including the concentration of the bleaching agent, its ability to penetrate the dental structure to reach chromophoric molecules, and the duration and frequency of its exposure to these molecules. A well-balanced combination of these elements ensures optimal whitening results. [13, 16].

The most commonly suggested treatment is at-home whitening; however, some patients may feel uneasy about wearing a whitening tray for extended periods [17]. Besides professionally supervised whitening techniques, there are also over-the-counter whitening products available in pharmacies and supermarkets, which do not require professional oversight. This method has gained popularity, driven by patients' growing desire to achieve brighter, whiter teeth [13].

Aim and objectives

This study aims to evaluate and compare the whitening efficacy and impact on enamel mineralization of Crest 3D White Professional Effects and My White Secret by analyzing shade changes and mineralization levels over multiple days using the VITA Classic Shade Guide and DIAGNOdent Pen, providing insights into their effectiveness and safety in aesthetic dentistry.

MATERIAL AND METHODS

For the analysis, a total of 60 extracted human teeth from the maxillary and mandibular anterior regions were used. These teeth were intact, non-carious, and extracted for orthodontic reasons or due to periodontal disease affecting their supporting bone structure. Prior to inclusion in the study, informed consent was obtained from all patients. The teeth were initially cleaned under a water jet to remove organic residues and then stored in a physiological saline solution.

After selection, the teeth were randomly divided into two equal groups of 30 specimens each to ensure an accurate and detailed comparison. The first group was assigned to whitening with Crest 3D Whitestrips Professional Effects, a hydrogen peroxide-based product, while the second group underwent whitening with My White Secret, a product formulated by UK-based dentists that does not contain hydrogen peroxide.

Before starting the whitening process, the initial mineralization and color of all teeth were recorded using the Vita Classical shade guide. Whitening was then performed following the manufacturers' instructions. In both groups, the whitening strips were applied for 30 minutes per session. After this period, the strips were removed, and each tooth was thoroughly rinsed with water to eliminate any residual whitening agents. Subsequently, the mineralization and color of each tooth were re-evaluated before being stored in saline solution until the next whitening session.

To mimic an in vivo scenario, as recommended by both manufacturers, the whitening procedure was conducted once daily for several consecutive days. Each session followed the same protocol, including mineralization and color assessment after the application of the whitening strips. The second and third whitening sessions were carried out under identical conditions, ensuring consistent monitoring of changes in both enamel integrity and color throughout the whitening process.

Two at-home tooth whitening solutions were utilized, each with distinct active ingredients. Crest 3D White Professional Effects Level 18, manufactured by Procter & Gamble, contains hydrogen peroxide as the primary whitening agent, which acts through an oxidative mechanism to break down stains on the enamel surface [18]. In contrast, My White Secret, produced by Smile Beauty Care, is a peroxide-free alternative that employs phthalimidoperoxycaproic acid (PAP) and hydroxyapatite, components known for their enamel-safe whitening properties and remineralizing effects [19]. The application of both whitening products was carried out strictly in accordance with the manufacturers' guidelines to ensure standardized conditions, optimal efficacy, and safe use throughout the study. (Table 1)

Table 1. Composition and Manufacturer Details of Whitening Products Used in the Study

Materials	Manufacturer	Ingredients
Crest 3D White Professional Effects Level 18	Procter & Gamble Global Privasi Tim	PVP, Water, PEG-8, Acrylates Copolymer, Hydrogen Peroxide, Sodium Hydroxide, Sodium Saccharin
My white secret	Smile beauty care	Glycerin, Water/Aqua, PVP, Ethylcellulose, Alcohol, SodiumPolyacrylate, Phthalimidoperoxycaproic Acid (PAP) Xylitol,Potassium Citrate, Hydroxyapatite, Rebaudioside A, Menthol.Sodium Citrate, Xanthan Gum, PVM/MA Copolymer, C12-15 Pareth-3

Colour Assessment

A spectrophotometer (Vita Easyshade® V Compact, Vita Zahnfabrik, Bad Säckingen, Germany) was utilized to measure colour [20]. Calibration was carried out using standard tiles from the National Institute of Standards and Technology (NIST). The testing conditions included a spectral range of 360 to 750 nm, a wavelength interval of 10 nm, and a reflectance angle of 45°. Measurements were conducted against a black background, with each specimen undergoing an average of three scans [21]. The recorded tooth colour was noted according to the Vita Classical shade guide. Tooth shades were numerically coded based on an ordered scale, assigning higher values to darker shades and lower values to lighter ones, following the VITA Classic guide.

Assessment of Dental Mineralization

To assess the level of tooth mineralization, the DIAGNOdent Pen 2190 (Kavo) device, based on LASER fluorescence technology, was used. This device measures the fluorescence of dental tissues through a laser beam with a wavelength of 655 nm [22]. Demineralization of dental structures leads to a loss of autofluorescence, which appears as darkened areas. For accurate use, the equipment was individually calibrated for each tooth, considering variations in dental mineralization [23]. According to the DIAGNOdent classification, values were interpreted as follows: 1-13 indicates healthy enamel, 14-20 suggests early enamel caries, 21-29 signals deep enamel caries, and values above 30 indicate dentin caries [24]. To ensure measurement accuracy, each assessment was performed twice, and all measurements were conducted by the same researcher.

Statistical analysis

Statistical analysis was performed using SPSS version 24.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics, including mean values and standard deviations, were calculated for each whitening product at different time points.

Ethical approval

All participants willingly signed a written informed consent form prior to their inclusion in the study. The research adhered to the ethical principles outlined in the Declaration of Helsinki and was officially approved by the Ethics Committee of the University of Medicine and Pharmacy "Victor Babeş," Timişoara, Romania (Approval No. 09/11.03.2024).

RESULTS

The comparative analysis of Crest 3D White Professional Effects Level 18 and My White Secret over three days demonstrated distinct patterns of whitening efficacy. At baseline, My White Secret exhibited a higher mean value (3.26) compared to Crest 3D White (1.6), indicating a stronger initial whitening effect. However, while My White Secret showed a gradual and consistent increase in whitening over time, reaching a final mean of 4.73 on Day 3, Crest 3D White displayed a more rapid and pronounced improvement after Day 2, increasing from 1.6 to 4.2. This suggests that Crest 3D White may have a delayed but more

intense whitening effect, whereas My White Secret provides a more stable but progressively improving outcome.

The standard deviation (SD) values provide additional insights into the variability of the products' effects among participants. My White Secret exhibited greater inter-individual differences, with an SD of 1.66 on Day 3 compared to 1.22 for Crest 3D White. This indicates that while My White Secret maintained a relatively steady progression in whitening, the extent of its effectiveness varied more significantly between individuals. On the other hand, Crest 3D White showed a lower initial mean but a more uniform response among participants, as indicated by its lower SD values in the early days of application (Table 2, Figure 1).

These findings suggest that the choice between these two whitening products may depend on individual preferences and expectations. Users seeking a faster and more dramatic improvement in whitening might benefit more from Crest 3D White, which demonstrated a substantial increase in effectiveness after Day 2. Conversely, individuals preferring a gradual, more consistent whitening effect, despite potential variability in outcomes, may find My White Secret to be a better option. Further studies with larger sample sizes and extended assessment periods could provide deeper insights into the long-term efficacy and stability of these whitening treatments.

Table 2. Mean Values and Standard Deviations of Whitening Products

Moment assessment	Crest(Mean)	Crest (SD)	My White secret(Mean)	My White Secret(SD)
Initial	1.6	0.67	3.26	1.43
Day 1	1.6	0.63	3.26	1.43
Day 2	2.86	0.83	3.93	1.49
Day 3	4.2	1.22	4.73	1.66

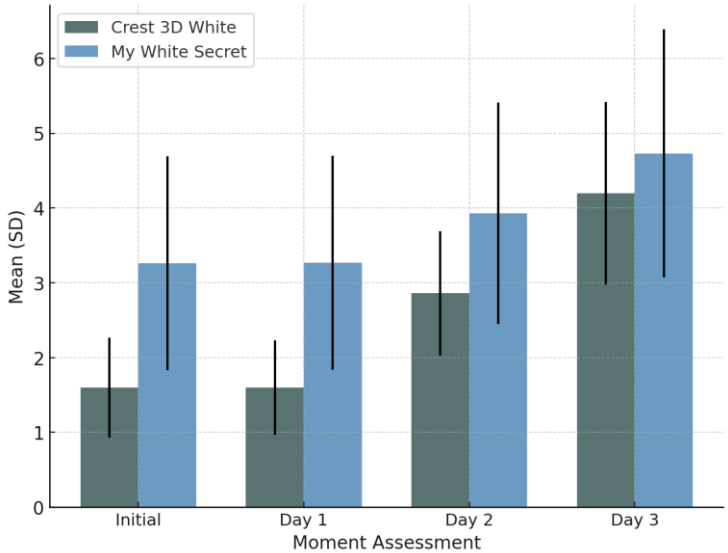

Figure 1. Comparison of Crest 3D White Professional Effects Level 18 and My White Secret

At the initial assessment, both groups exhibited relatively high average colour values, indicating darker shades. By day 1, a significant reduction in shade value was observed for both treatments, with My White Secret demonstrating a steeper decline, suggesting a more rapid whitening effect compared to Crest. As the study progressed to day 2 and day 3, the downward trend continued, although the rate of change slowed. By the final assessment on day 3, My White Secret reached the lowest shade values, indicating a stronger overall

whitening effect, while Crest also showed improvement, but with a more gradual reduction in colour values. These findings suggest that My White Secret may offer a faster whitening outcome, whereas Crest provides a steadier but less pronounced effect over the same period (Figure 2).

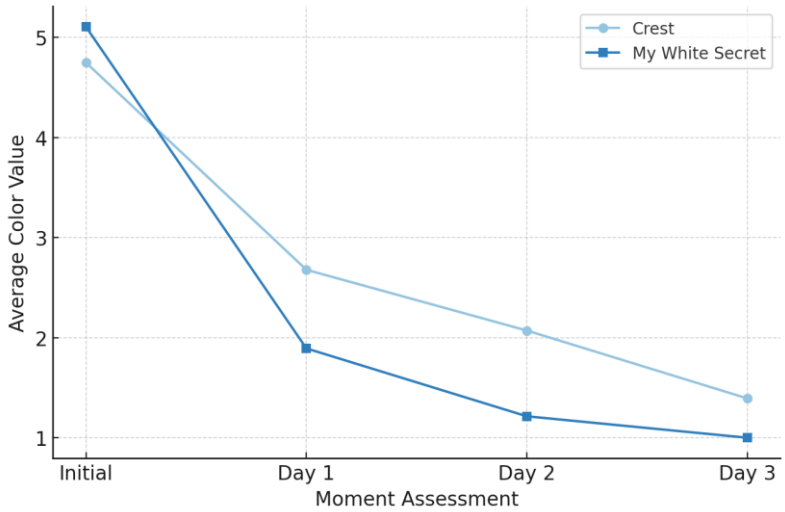

Figure 2. Comparing colour evolution Crest versus My White Secret (Vita Shade Guide)

DISCUSSIONS

The findings of this study demonstrate notable differences in the whitening efficacy and impact on enamel mineralization between hydrogen peroxide-based (Crest 3D White Professional Effects) and peroxide-free (My White Secret) whitening products. My White Secret exhibited a rapid initial whitening effect, while Crest 3D White showed a delayed but more pronounced improvement after the second day. The variability in whitening responses among samples suggests that factors such as enamel composition and baseline mineralization levels may influence treatment outcomes. Additionally, the oxidative mechanism of hydrogen peroxide raises concerns regarding potential enamel demineralization, whereas the inclusion of hydroxyapatite in My White Secret may contribute to a gradual whitening effect while supporting remineralization.

These findings align with previous research indicating that hydrogen peroxide is an effective bleaching agent due to its ability to oxidize chromogenic molecules. However, studies such as that of Li et al. (2024) emphasize its potential adverse effects, including enamel demineralization and increased tooth sensitivity. Our study supports this observation, as Crest 3D White produced a strong whitening effect but also raised concerns about its impact on enamel integrity. On the other hand, My White Secret, which utilizes phthalimidoperoxycaproic acid (PAP) and hydroxyapatite, exhibited a more gradual but controlled whitening effect, potentially reducing the risks associated with peroxide-based formulations. The variability in whitening response observed in our study may also be linked to individual differences in enamel structure and mineral content, a factor highlighted in previous research exploring the penetration depth of bleaching agents and their interaction with dental tissues.

In comparison to Agarwal et al. (2024), who evaluated over-the-counter whitening products available in online marketplaces, our findings highlight similar concerns regarding the role of active ingredients in determining whitening efficacy and enamel safety. Their study found that the most effective over-the-counter product achieved results comparable to a dentist-prescribed whitening agent, while lower-quality formulations led to enamel surface

alterations and reduced microhardness. Similarly, our study suggests that the formulation of a whitening product plays a critical role in both effectiveness and enamel protection. The presence of acidic agents in some over-the-counter whitening products has been associated with increased enamel erosion and susceptibility to staining, reinforcing the importance of selecting formulations that incorporate remineralizing agents to counteract potential damage.

Furthermore, our results are consistent with the study by Loguercio et al. (2024), which explored the role of hydroxyapatite-capsaicin (HAp-CAP) composites in reducing hydrogen peroxide diffusion and preventing enamel demineralization. Their findings suggest that bioactive components in whitening formulations can help mitigate the adverse effects of bleaching while maintaining whitening efficacy. This aligns with our observation that hydroxyapatite-containing My White Secret provided a more controlled whitening process while potentially preserving enamel integrity. The inclusion of bioactive compounds in whitening products represents a promising direction for future research, offering a balance between effective bleaching and enamel preservation.

An important aspect to consider is the potential impact of whitening agents on dental sensitivity, a commonly reported side effect in the literature. Previous studies have shown that hydrogen peroxide can induce structural changes in enamel, increasing porosity and microcracks, which may lead to short- and medium-term tooth sensitivity [25]. Although this study did not directly assess dental sensitivity, it is essential to highlight that patients using hydrogen peroxide-based whitening agents may experience temporary discomfort after treatment, especially if the product is applied incorrectly or for longer durations than recommended by the manufacturer. In contrast, peroxide-free formulations, such as My White Secret, may reduce this risk due to the presence of remineralizing components like hydroxyapatite. The findings of this study support the idea that peroxide-free alternatives may represent a safer option for individuals prone to dental sensitivity or those seeking a gentler whitening treatment. Further research is necessary to determine to what extent prolonged use of these products affects enamel strength and the longevity of the whitening effect over time.

Despite the insights provided by this study, several limitations should be acknowledged. The in vitro design does not fully replicate the complex oral environment, where factors such as saliva, diet, and bacterial activity may influence whitening efficacy and enamel mineralization. Additionally, the sample size was limited to 60 extracted teeth, which, although providing controlled conditions, may not fully represent natural variations in enamel composition. The relatively short evaluation period also prevents conclusions about the long-term effects of these whitening treatments on enamel integrity. Finally, this study focused on only two commercially available whitening products, limiting the generalizability of the findings to other formulations. Future research should incorporate in vivo assessments, larger sample sizes, and extended follow-up periods to better understand the long-term safety and effectiveness of different whitening approaches.

This study reinforces the importance of balancing whitening efficacy with enamel health when selecting a bleaching treatment. While hydrogen peroxide-based formulations offer strong and rapid whitening effects, their potential impact on enamel integrity should be carefully considered. Peroxide-free alternatives, particularly those incorporating remineralizing agents, may provide a safer option for long-term use while still achieving effective whitening results.

CONCLUSIONS

This study highlights the distinct whitening efficacy and impact on enamel mineralization of hydrogen peroxide-based and peroxide-free whitening products. My White

Secret provided a rapid initial whitening effect while maintaining enamel mineralization, whereas Crest 3D White exhibited a delayed but more pronounced whitening outcome, raising concerns about potential demineralization. These findings emphasize the critical role of ingredient composition in whitening formulations, as peroxide-based treatments may compromise enamel integrity, while peroxide-free alternatives incorporating remineralizing agents such as hydroxyapatite offer a more balanced approach. The results underscore the need to consider both whitening efficacy and enamel preservation when selecting a whitening treatment, as the long-term impact on dental health is an essential factor in aesthetic dentistry.

Conflicts of Interest

The authors declare no conflict of interest.

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A Snapshot of Oral Health, Quality of Life, And Lifestyle Factors in Diabetic Patients

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Abstract

1.Background/Objectives: Diabetes Mellitus (DM) is a major public health concern, significantly impacting quality of life (QoL) and increasing the risk of oral health complications. This study aims to explore the relationship between oral health, QoL, and lifestyle factors in diabetic patients, with a focus on Western Romania. 2. Methods: A total of 60 patients diagnosed with Type 1 or Type 2 diabetes participated in a descriptive observational survey. Data on oral health status, self-care behaviors, dental visit frequency, and lifestyle habits were collected through a structured questionnaire.3. Results: A total of 60 patients diagnosed with Type 1 or Type 2 diabetes participated in a descriptive observational survey. Data on oral health status, self-care behaviors, dental visit frequency, and lifestyle habits were collected through a structured questionnaire. Findings revealed poor adherence to oral hygiene practices, with 50% of participants brushing twice daily and only 25% flossing regularly. Additionally, 53.3% visited a dentist in the past year, while a significant proportion sought care only in emergencies. The OHIP-14 scores indicated a moderate impact of oral health on QoL, with psychological and physical discomfort affecting daily activities. Correlation analysis showed a link between oral health knowledge, diabetes duration, and self-care behaviors. 4.Conclusion: The study highlights the urgent need for improved oral health education within diabetes management programs. Integrating preventive dental care, lifestyle modifications, and patient awareness strategies may contribute to better metabolic control and enhanced QoL in diabetic populations.

Keywords: Oral Health, OHIP-14, Lifestyle habits, Diabetes Mellitus

INTRODUCTION

Diabetes Mellitus (DM) is a chronic condition that impacts approximately 422 million people worldwide, accounting for 8.5% of the global population. Individuals with DM are at a higher risk of developing both microvascular and macrovascular complications, including retinopathy, nephropathy, neuropathy, and cardiovascular diseases [1].

DM encompasses a group of metabolic disorders characterized by hyperglycemia and is generally classified into four main categories: type 1 diabetes, type 2 diabetes, gestational diabetes, and other specific forms of diabetes [2]. DM is a major global public health concern, with its prevalence rising sharply across most countries. Recent estimates project that the number of individuals with DM will surge from 171 million in the year 2000 to 366 million by 2030, highlighting the growing burden of the disease worldwide [3].

Diabetes complications significantly contribute to morbidity among individuals with DM, leading to a substantial decline in quality of life (QoL). The quality of life (QoL) of individuals with type 2 diabetes mellitus (T2DM) is significantly influenced by disease progression and response to medication therapy. Health behaviors are often considered key determinants of health-related quality of life (HRQoL), as they directly impact overall well-being. Diabetes self-care is an ongoing process that involves acquiring knowledge and adapting to the complex nature of T2DM within a social context. Given that the majority of daily diabetes management falls on patients and their families, it is crucial to establish reliable and valid measures for assessing self-management effectiveness. Individuals with diabetes must engage in multifaceted self-care activities, including maintaining a balanced diet, engaging in regular physical activity, monitoring blood glucose levels, practicing foot care, and adhering to medication regimens. Studies indicate that poor adherence to self-care behaviors, such as lack of exercise or inconsistent medication use, is associated with lower HRQoL. Conversely, patients who actively adhere to diabetes self-care routines tend to experience improved HRQoL, emphasizing the critical role of self-management in diabetes care [4].

The Oral Health Impact Profile-14 (OHIP-14) elaborated by Slade and Spencer in 1994 is one of the most widely used indicators for assessing subjective oral health status in oral epidemiology. Initially designed to evaluate individuals' perceptions of their oral health, OHIP-14 is frequently employed as a measure of oral health-related quality of life (OHRQoL)[5]. It captures the physical, psychological, and social impacts of oral health conditions, aligning with the World Health Organization's (WHO, 1993)[6] broader definition of quality of life, which considers individuals' well-being within their cultural and personal contexts. When examining the effects of oral health on quality of life, it is crucial to distinguish between disease-specific measures like OHIP-14 and more generic health-related quality of life (HRQoL) assessments.

Studies have demonstrated a strong link between DM and various oral health complications, with periodontitis being the most well-established association. Periodontitis is now recognized as a complication of diabetes, and recent research suggests that its treatment can positively influence glycemic control in type 2 diabetes (T2DM) by improving HbA1c levels, highlighting a bidirectional relationship between the two conditions[7]. Beyond periodontitis, individuals with DM are also at a higher risk for other oral health issues, including dry mouth, Candida infections, and even oral cancer. These conditions are likely to negatively impact oral health-related quality of life (OHRQoL), as has been observed in cases of periodontitis and xerostomia (dry mouth)[8]. Additionally, poor self-perceived oral health has been linked to a decline in general health-related quality of life (HRQoL) in T2DM patients. Given these significant implications, international organizations, such as the

International Diabetes Federation (IDF) and the American Diabetes Association (ADA), emphasize the importance of integrating oral health awareness into diabetes care to improve overall well-being in individuals living with diabetes [1].

Lifestyle factors, including physical activity, diet, and stress, play a crucial role in the development and progression of type 2 diabetes (T2DM). Adopting healthier dietary habits and increasing physical activity (such as walking) and exercise (such as running or cycling) are essential components of T2DM management. Clinical guidelines strongly recommend lifestyle modifications for both the prevention and effective management of the disease[9].

In Romania, the PREDATORR study was the first national-level investigation to systematically assess the prevalence of diabetes among adults. The study reported a DM prevalence of 11.6% and a prediabetes prevalence of 16.5%, with higher rates observed in men and the elderly. Regional variations in diabetes prevalence highlight the need for targeted interventions, especially in Western Romania, where lifestyle factors, healthcare accessibility, and awareness about the diabetes-oral health link may vary. Compared to other European countries, Romania's diabetes prevalence falls within a moderate to high range (10-20%), exceeding the global (8.3%) and European (7.9%) prevalence reported by the International Diabetes Federation (IDF) in 2014. These findings emphasize the importance of integrating oral health awareness, quality of life assessments, and lifestyle modifications into diabetes care strategies [10].

Aim and objectives

This study aims to explore the link between oral health, quality of life (OHQoL), and lifestyle factors in diabetic patients, with a focus on the Western Romania region. Given the high prevalence of DM and prediabetes in Romania, understanding how oral health status and self-care behaviors influence the quality of life of diabetic individuals is crucial. Additionally, this study seeks to assess patients' awareness of the bidirectional relationship between diabetes and oral health, as well as their dental care utilization patterns. By identifying gaps in knowledge and self-care practices, the findings can contribute to the development of integrated health strategies aimed at improving both metabolic and oral health outcomes for people living with diabetes.

MATERIAL AND METHODS

This study was a descriptive observational survey conducted on 60 patients diagnosed with diabetes in the Western region of Romania. The research was carried out at the Outpatient Diabetes Care Facility of the Pius Brinzeu County Emergency Hospital in Timisoara, a specialized healthcare facility providing comprehensive diabetes management and multidisciplinary care. The study took place over a defined period, specifically in March 2024, during which eligible patients attending the Diabetes Center's outpatient services were invited to participate. All individuals with Type 1 or Type 2 diabetes, who met the inclusion criteria and sought medical care at the center during the assessment period, were considered for the study. This setting allowed for the collection of relevant clinical and self-reported data regarding oral health status, quality of life, and lifestyle factors in diabetic patients, providing valuable insights into the diabetes-oral health connection in the regional population.

For this study, participants were selected based on specific inclusion and exclusion criteria to ensure the reliability and relevance of the findings. The inclusion criteria required participants to be diagnosed with Type 1 or Type 2 diabetes, regardless of gender, aged 18 or older, and living with the condition for at least six months. Additionally, all participants needed to have at least one natural tooth, as the study aimed to evaluate the impact of oral health on quality of life and diabetes management. Exclusion criteria were set to eliminate

factors that might interfere with the accuracy of the results. Individuals with severe mental or physical disabilities were excluded, as their ability to participate in self-reported assessments and maintain regular oral health care routines might be compromised. Furthermore, medical personnel suffering from diabetes were also excluded to prevent potential bias, as their professional knowledge and access to healthcare resources could influence their oral health behaviors and overall diabetes management in ways that differ from the general diabetic population. By defining these clear inclusion and exclusion parameters, the study ensures that the collected data accurately reflects the oral health status, lifestyle factors, and quality of life of individuals with diabetes, particularly within the general population of diabetic patients. All participants provided informed consent, and none were involved in the study's development. This research was conducted in accordance with the principles of the Declaration of Helsinki (2013 version) and received ethical approval from the Ethics Committee of the University of Medicine and Pharmacy "Victor Babeş" in Timisoara, Romania (Approval No. 05/30.01.2024).

A questionnaire was developed in Romanian to assess diabetic patients' knowledge, attitudes, and habits, along with relevant demographic, medical, and oral health factors. The 18 multiple-choice, closed-ended questions covered various aspects, including social background (age, gender, education, and place of residence), medical history (diabetes type, duration, treatment, and other health conditions), and oral health knowledge, particularly awareness of the diabetes-oral health connection. Additionally, the questionnaire explored dental care utilization, evaluating the frequency of dental visits, reasons for avoiding dental care, and access to professional treatment. To assess oral hygiene behaviors, participants reported their toothbrushing frequency, use of fluoride toothpaste, and interdental cleaning practices. Oral health complaints such as oral pain, dry mouth (xerostomia), and bad breath were also recorded. The data collected provided valuable insight into oral hygiene practices, access to dental care, and perceived oral health issues among diabetic individuals, contributing to a better understanding of the relationship between diabetes and oral health-related quality of life. At the end of the survey, participants received general oral health education, emphasizing the impact of diabetes on oral health and promoting better self-care practices.

Oral health-related quality of life (OHRQoL) was assessed using the validated Romanian version of the short-form Oral Health Impact Profile (OHIP-14-RO), a self-administered questionnaire. Participants responded to 14 items, rated on a scale from 0 (never) to 4 (very often), covering seven subdomains: functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap. The total OHIP-14-RO score ranged from 0 to 56, with higher scores indicating a greater negative impact on oral health-related quality of life. Additionally, responses were dichotomized, with a threshold of "occasionally" or more indicating an impact on OHRQoL. Only fully completed questionnaires were included in the final analysis. This validated tool has been implemented in Romania to evaluate the effect of oral health conditions on quality of life in diabetic patients.

The study was designed as a questionnaire-based survey, collecting information on oral health, lifestyle, and quality of life in diabetic patients without any dental intervention or oral examination. Participation was entirely voluntary, and all respondents provided written informed consent before completing the questionnaire, ensuring ethical compliance and respect for participants' autonomy.

Participants were classified based on their diabetes type (Type 1 or Type 2), while glycated hemoglobin (HbA1c) levels were categorized as <5.7% (good glycemic control), 5.7–6.4% (moderate control), and >6.5% (poor control). The study also assessed behavioral factors, including smoking status, by categorizing participants as smokers or non-smokers. Self-care

behaviors related to oral hygiene were evaluated, including brushing techniques, brushing frequency, and interdental cleaning habits using aids such as dental floss. Additionally, participants reported on their utilization of available dental services, specifying the frequency and type of dental care accessed, as well as any existing oral health conditions. To assess knowledge and attitudes toward oral health and diabetes, the questionnaire included cognitive components examining participants' understanding of the link between diabetes and periodontal disease. Their perception of oral health importance was measured using a Likert scale, with response options ranging from "completely agree" to "totally disagree". This comprehensive approach provided valuable insights into oral health behaviors, service utilization, and awareness levels among diabetic patients, helping to better understand their quality of life and self-care practices.

Data analysis was conducted using SPSS statistical software (version 23, Chicago, IL). Descriptive statistics, including means, standard deviations, and percentages, were used to summarize demographic variables since the data followed a normal distribution. Frequency tables were generated for all variables, providing a clear overview of the dataset. To examine the associations between categorical variables, the chi-square test was applied, while Student's t-test and ANOVA were used to compare means across different groups. A $p<0.05$ level of significance was set for all statistical analyses.

RESULTS

A total of 60 patients were invited to participate in this survey, all of whom successfully completed it, resulting in a 100% response rate. Participants ranged in age from 28 to 85 years, with an average age of 62.1 years (SD = ±11.4), and the most frequently reported age was 64 years. In terms of gender distribution, 31 participants (51.7%) were female, while 29 (48.3%) were male. The majority of participants (60.5%) resided in urban areas, while 39.5% lived in rural areas. Regarding educational background, the largest proportion of participants (49.7%) had completed 10 grades of school, followed by 21.8% who had finished high school, and 12.2% who held a university degree.

Most participants (82.3%) were diagnosed with Type 2 diabetes, with 22.4% having been diagnosed within the past 1 to 5 years, followed by 17.8% who had been living with diabetes for 6-10 years. A smaller proportion (16.4%) had been diagnosed for less than one year. The number of participants gradually decreased with longer disease duration, with 14.4% diagnosed for 10-14 years, 11.6% for 15-19 years, and 12.3% for 20-24 years. Very few participants had been diagnosed for 25-29 years (2.1%) or more than 30 years (2.7%) (Figure 1).

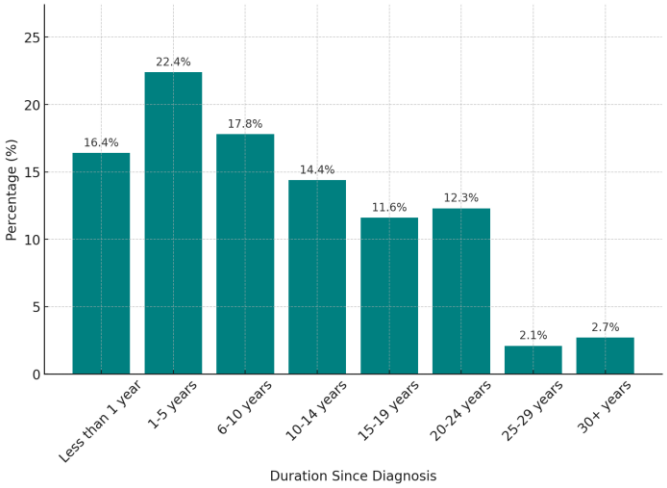

Figure 1. Distribution of Type 2 Diabetes Diagnosis Period

In the study sample of 60 patients, the majority, 45 participants (75%), were diagnosed with Type 2 diabetes, while 11 (18.3%) had Type 1 diabetes. A small proportion, 2 patients (3.3%), were uncertain about their diabetes type (Figure 2).

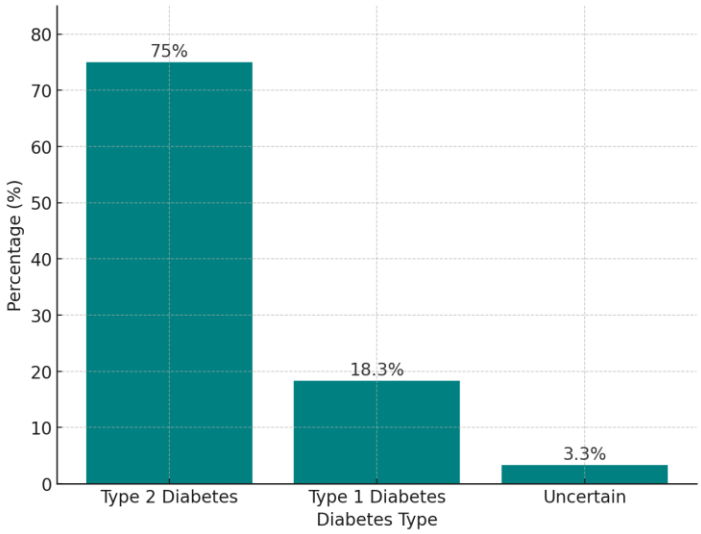

Figure 2. Diabetes Type Distribution Among Study Participants

Regarding dental visit frequency, a significant number of participants, 24 (40%), reported that they never visit the dentist, while 18 (30%) attended once a year. Only 6 patients (10%) visited the dentist twice a year, whereas 1 patient (1.7%) reported going three times a year. Meanwhile, 11 participants (18.3%) stated that they visited the dentist four or more times a year, indicating a small group with higher dental care engagement (Figure 3).

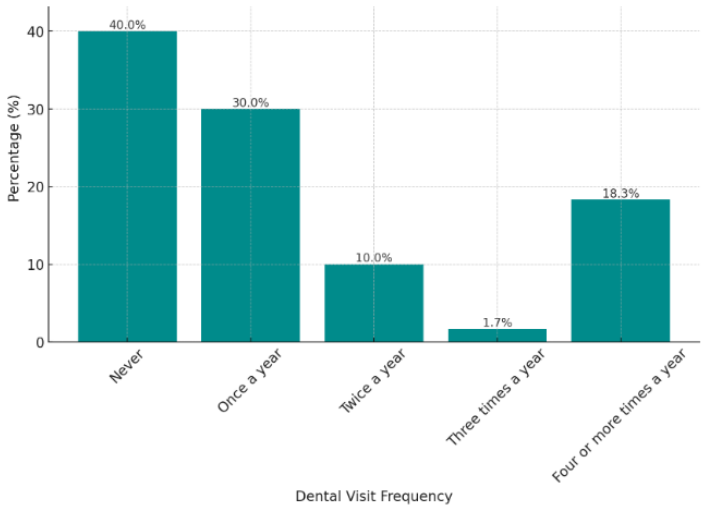

Figure 3. Distribution of Dental Visit Frequency by Percentage of Respondents

Hemoglobin A1c (HbA1c) levels, which indicate glycemic control, were recorded for all participants. As shown in the analysis, 45.2% of patients had an HbA1c level of ≥6.5%, suggesting poor glycemic control. The reported HbA1c values were based on participants' medical evaluation records.

Among the 60 participants in this study, many reported comorbidities frequently associated with diabetes. Arterial hypertension was the most common, affecting 24 individuals (40%), posing an additional cardiovascular risk when combined with diabetes.

Thyroid disorders were present in 4 participants (6.7%), potentially complicating metabolic control and diabetes management. Additionally, 2 participants (3.3%) had ischemic cardiopathy, further highlighting the increased prevalence of cardiovascular diseases in diabetic individuals. Other reported conditions included respiratory diseases, glaucoma, and gastrointestinal disorders, underscoring the multiple health challenges faced by people living with diabetes.

Regarding exercise frequency, defined as any form of sustained physical activity, the majority of participants, 30 individuals (50%), reported being inactive. Among those who engaged in physical activity, 14 participants (23.3%) exercised 1–2 times per week, 10 participants (16.7%) reported exercising 3–4 times per week, while 6 participants (10%) engaged in physical activity 5 or more times per week (Figure 4).

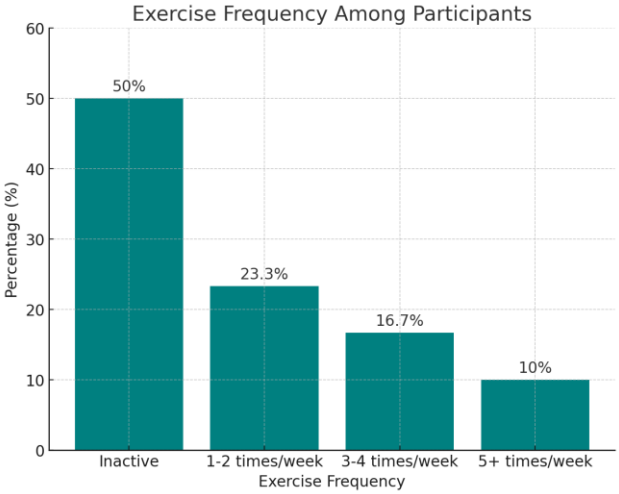

Figure 4. Exercise Frequency Among Participants

For the 60 participants in this study, the mean OHIP-14 score was recalculated at approximately 0.55, reflecting the general oral health-related quality of life (OHRQoL) in this diabetic population. Regarding speech and taste disturbances, 70.8% of participants reported never having pronunciation difficulties, while 18.6% experienced them occasionally. Taste disturbances were slightly more common, with 58.4% reporting no issues and 15% experiencing them occasionally. About 63.7% of participants never reported mouth pain, while 18.6% occasionally experienced it. Similarly, 57.5% had no discomfort while eating, but 23% felt it occasionally. Nearly 48.7% of participants never felt self-conscious due to oral health, though 23% experienced occasional discomfort. Additionally, 57.5% never reported distress related to oral appearance, but 21.2% occasionally did. For daily activities, 61.9% had no limitations, while 18.6% reported occasional difficulties. Eating or speaking discomfort affected 18.6% of participants occasionally, while 62.8% reported no issues. Feelings of frustration or helplessness were uncommon, with 66.4% reporting no psychological impact, though 19.5% experienced occasional distress. Most participants (62.8%) reported no social restrictions due to oral health, but 20.4% occasionally faced challenges in social interactions. Feelings of disadvantage due to oral health were never reported by 63.7% of participants, though 20.4% occasionally experienced this issue.

The nonparametric correlation analysis identified several significant relationships regarding age, education, environment, oral health status, and specific oral health impacts among diabetic patients. A negative correlation was found between education level and diabetes duration (Rho = -0.07, $p < .05$), suggesting that individuals with higher education levels tend to have been diagnosed with diabetes more recently. Additionally, a positive

correlation was observed between age and poor diet due to dental problems (Rho = 0.09, $p < .05$), indicating that older participants are more likely to experience dietary difficulties related to oral health issues. Lastly, a negative correlation was found between irritability caused by dental problems and frequency of dental visits (Rho = -0.08, $p < .05$), implying that individuals who experience oral health-related discomfort tend to visit the dentist infrequently, typically once or twice a year.

To further explore the impact of oral health knowledge on quality of life, participants were grouped based on their self-reported understanding of the diabetes-oral health link. Two groups were formed: a high-knowledge group (participants rating their knowledge as "Good" or "Very Good") and a low-knowledge group (participants rating their knowledge as "Satisfactory" or "Poor"). The mean OHIP-14 score for the high-knowledge group was 2.73, while the low-knowledge group had a mean score of 3.82. Although the results indicate a trend where greater knowledge was associated with better oral health-related quality of life (reflected by lower OHIP-14 scores), a t-test comparison produced a p-value of 0.20, suggesting that the observed difference was not statistically significant. However, these findings highlight a potential relationship between increased awareness of oral health risks and improved quality of life, which should be further explored in future studies with larger sample sizes.

DISCUSSIONS

This study highlights that the majority of diabetic patients experienced one or more dental issues, yet did not receive a dental referral or visit a dentist for routine check-ups, seeking care only in cases of severe pain or emergencies. This pattern suggests that oral health concerns are often overlooked in diabetes management, despite the fact that diabetic individuals require greater dental care attention compared to non-diabetic patients. Similar findings have been reported in previous research, emphasizing the need for greater integration of oral health into diabetes care. These observations reinforce the importance of preventive measures and the promotion of oral hygiene practices among diabetic individuals. Some studies have advocated for the implementation of healthcare programs aimed at improving oral health monitoring, routine check-ups, and treatment accessibility for diabetic patients. Moreover, research has shown that oral health problems share common risk factors with other non-communicable diseases such as obesity, cardiovascular diseases, stroke, and diabetes, suggesting a link between lifestyle habits and systemic health complications.

A key finding of this study was that most diabetic patients lack awareness of the relationship between diabetes and oral health complications. Additionally, more than half of the participants had insufficient knowledge regarding the impact of diabetes on oral health. These findings are in line with research conducted both in Romania and internationally, where diabetic individuals often remain unaware of the potential oral health risks associated with their condition. However, a subset of patients recognized that diabetes contributed to dry mouth and had negative effects on periodontal health, reinforcing the need for better patient education and awareness campaigns.

The findings of this study indicate that most individuals with diabetes have limited awareness of the bidirectional relationship between diabetes and periodontal disease and lack sufficient knowledge about their increased risk for oral health complications. As expected, a higher level of awareness regarding oral health risks was significantly associated with better oral hygiene practices and oral care habits. However, the majority of people with diabetes do not receive adequate information about the impact of diabetes on oral health or guidance on oral care from their diabetes care providers. This aligns with evidence from a recent scoping review [11], which highlighted that diabetes care providers rarely discuss oral health in

clinical settings. The main barriers identified include insufficient knowledge of the diabetes-oral health link, lack of structured oral health assessment tools and guidelines, and the absence of clear referral pathways for oral health care. These findings underscore the need for integrating oral health education and preventive strategies into diabetes management to improve overall health outcomes.

The findings indicate that individuals with diabetes in this study had low adherence to oral hygiene practices and dental visits. Less than half, 30 participants (50%), reported brushing their teeth twice daily, while flossing was even less common, with only 15 participants (25%) using dental floss daily for interdental cleaning. Additionally, only 32 participants (53.3%) had visited a dentist in the past 12 months, reflecting a pattern of inadequate dental care engagement among diabetic individuals. Comparatively, large national studies have shown that people with diabetes seek dental care less frequently than those without diabetes. These figures are notably lower than those observed in high-income countries, such as England, where 75% of adults brush twice daily and 73% visit the dentist annually, and the United States (64%) and Australia (60.3%), where a significantly higher proportion of the general population reports regular dental visits. This delay in seeking dental care among people with diabetes is particularly alarming, given that periodontal disease can worsen glycemic control and contribute to diabetes-related complications [11]. These findings emphasize the need for targeted oral health education and preventive measures within diabetes care to improve both oral and overall health outcomes for individuals living with diabetes.

The ambiguity regarding patients' uncertainty about their diabetes classification. often arises due to the complexities in distinguishing between diabetes types, particularly in adults. For instance, individuals initially diagnosed with type 2 diabetes based on phenotypic characteristics may later exhibit clinical features or undergo further analyses that prompt a re-evaluation and subsequent reclassification to type 1 diabetes. This scenario is not uncommon; studies have shown that more than 40% of type 1 diabetes diagnoses occur after the age of 30, leading to frequent misclassification as type 2 diabetes due to overlapping symptoms and the higher prevalence of type 2 diabetes in adults. Additionally, some patients initially diagnosed with type 2 diabetes may develop clinical signs suggestive of secondary diabetes, necessitating further investigations to accurately determine the diabetes type. This underscores the importance of continuous monitoring and comprehensive evaluation in diabetes care to ensure accurate diagnosis and appropriate management [12,13].

Furthermore, the level of education may influence patients' understanding of their diabetes status. Individuals with lower educational attainment might have limited health literacy, affected their comprehension of medical information and contributed to uncertainty regarding their diagnosis. Research indicates that patients with lower education levels often have less knowledge about diabetes management, which can impact their ability to effectively engage in self-care and understand their condition [14, 15].

Recent research highlights the crucial role of oral health awareness and lifestyle factors in improving oral health-related quality of life (OHRQoL) among diabetic patients. A study by Oluwatoyin et al. (2024) [16] found that individuals with greater awareness of oral health risks reported better OHRQoL scores on the OHIP-14 scale. This connection was further validated through clinical assessments of oral hygiene and mucosal health, demonstrating that oral health education and proactive self-care behaviors can significantly enhance quality of life. Similarly, Poudel et al. (2020) [17] examined diabetic patients in Australia and found that those who better understood the link between diabetes and oral health reported lower OHIP-14 scores, indicating fewer oral health-related challenges and improved overall well-being. Beyond oral health knowledge, lifestyle factors such as diet, physical activity, and smoking habits also play a key role in maintaining both oral and systemic health in diabetic

individuals. Unhealthy habits can exacerbate oral health complications, while an active lifestyle and a well-balanced diet may contribute to better glycemic control and reduced oral disease burden.

This study has several limitations that should be acknowledged. Its cross-sectional design limits the ability to determine causal relationships between diabetes and oral health outcomes. Additionally, reliance on self-reported data may introduce reporting bias, as participants could either overestimate or underestimate their oral health status and behaviors.

To enhance the validity and reliability of future findings, research should incorporate objective oral health assessments conducted by dental professionals. Evaluations of periodontal status (PPD, CAL, BOP), dental caries (DMFT index), and salivary flow rates would provide a more accurate and comprehensive analysis of oral health in diabetic patients. Integrating both self-reported and clinically assessed data could strengthen the evidence base and contribute to more targeted interventions aimed at improving oral health outcomes in this population. Another limitation is the absence of a control group, which restricted direct comparisons between diabetic and non-diabetic individuals. This lack of comparative data prevents a clearer understanding of how diabetes uniquely affects oral health and quality of life. Future studies should include a non-diabetic control group to assess differences more precisely and strengthen the findings on the interaction between diabetes, oral health, and lifestyle factors.

CONCLUSIONS

This study underscores the significant impact of oral health on the quality of life of diabetic patients, revealing low adherence to dental hygiene and preventive care. Many participants lacked awareness of the diabetes-oral health connection, which was associated with poorer self-care behaviors and reduced dental service utilization. The findings reinforce the importance of integrating oral health education and preventive strategies into diabetes care protocols. Future research should include larger samples and objective oral health assessments to further investigate this relationship and promote comprehensive diabetes management strategies that address both systemic and oral health needs.

Conflicts of Interest

The authors declare no conflict of interest.

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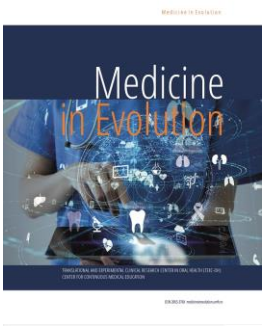
Impact of Myasthenia Gravis on Oral Health-Related Quality of Life: A Multidisciplinary Perspective



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Abstract

1.Background/Objectives: Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disorder that impairs nerve impulse transmission, leading to muscle weakness affecting mastication, speech, and swallowing, significantly impacting oral health-related quality of life (OHRQoL). This study aims to evaluate the impact of MG on OHRQoL using the OHIP-14 questionnaire, assessing functional limitations, psychological distress, and social impairments. 2.Methods: A cross-sectional study was conducted on 100 MG patients who completed a self-administered OHIP-14 questionnaire while awaiting medical consultations. The OHIP-14 evaluates seven domains, including functional limitation, physical pain, psychological discomfort, and handicap, using a 4-point Likert scale. 3.Results: Results showed that MG significantly affects OHRQoL, with participants frequently reporting speech difficulties (mean score: 2.28 ± 1.11), oral discomfort (1.16 ± 1.07), self-consciousness (1.94 ± 1.42), and eating disruptions (2.18 ± 1.31). Many also experienced social disability, reduced well-being, and functional impairments. 4.Conclusion: These findings highlight the need to integrate oral health assessments into MG management. A multidisciplinary approach involving neurologists, dental specialists, and mental health professionals is essential to improving patient outcomes.

Keywords: Myasthenia gravis, oral health-related quality of life, OHIP-14, neuromuscular impairment

INTRODUCTION

Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disorder characterized by an abnormal immune response, wherein the body's immune system mistakenly generates antibodies against specific membrane proteins at the neuromuscular junction. This immune-mediated disruption impairs the normal transmission of nerve impulses to muscles, resulting in fluctuating muscle weakness and fatigue. The clinical manifestations of MG vary widely, often affecting the ocular muscles, leading to drooping eyelids (ptosis), and causing difficulties in swallowing (dysphagia) and breathing. Additionally, limb muscles, particularly those in the arms and legs, are commonly involved, resulting in generalized muscle weakness that can significantly impact daily activities [1].

Beyond limb and respiratory involvement, MG frequently affects muscles responsible for facial expressions and mastication, leading to functional impairments that influence essential activities such as chewing, swallowing, and speaking (dysarthria). As a consequence of facial muscle weakness, many patients exhibit an expressionless appearance, which can further impact their oral health. Moreover, weakness in the soft palate muscles can lead to a nasal speech tone and restricted lip movement. In severe cases, MG can also extend to the diaphragm and neck extensors, potentially leading to breathing difficulties (dyspnea) [2].

Epidemiological studies indicate that MG affects approximately 140 to 150 individuals per million people worldwide, with an incidence rate ranging between 1.7 and 30 new cases per million annually [3]. The persistent nature of muscle weakness, coupled with the need for long-term treatment, imposes a significant physical and psychological burden on affected individuals. Many patients with MG also suffer from associated mental health conditions, such as anxiety and depression, further emphasizing the necessity of a multidisciplinary approach that addresses both the physical and psychological aspects of the disease [4]. The introduction of immune-based therapies, particularly corticosteroids in the 1970s, has significantly improved MG prognosis, rendering the disease less life-threatening in many cases. However, complete and sustained remission remains rare, with many patients continuing to experience persistent fatigue, functional impairments, and adverse effects associated with long-term immunosuppressive therapies [5]. These ongoing challenges highlight the need for further research and the development of more effective therapeutic strategies.

Beyond its systemic effects, MG has a notable impact on oral health, influencing it both directly—through neuromuscular impairments affecting mastication, swallowing, and speech—and indirectly, through behavioral adaptations due to disease progression and long-term treatment effects. Conversely, changes in oral health can also have broader implications for systemic well-being [6]. Given that oral health is an integral component of general health, maintaining optimal oral function is essential for preserving overall quality of life [7, 8].

Oral Health-Related Quality of Life (OHRQoL) is a well-established concept that reflects the impact of oral health on physical, psychological, and social well-being, influencing essential activities such as eating, speaking, and social engagement (14–16). To assess OHRQoL, various measurement tools have been developed, with the Oral Health Impact Profile (OHIP) being one of the most widely used and validated instruments. The strength of OHIP lies in its ability to measure changes in patients' perceptions of their oral health, bridging the gap left by conventional clinical assessments that often fail to capture the broader psychosocial impact of oral disorders [9].

The OHIP-49 questionnaire, consisting of 49 questions grouped into seven dimensions of OHRQoL, has been extensively validated and is recognized for its reliability, sensitivity to change, and cross-cultural applicability. However, despite its effectiveness, its extensive

length and the time required for completion have posed limitations in both clinical and research settings, reducing its practicality. To address these challenges, a shortened version—OHIP-14—was introduced. This version retains the core dimensions of the OHIP-49 but condenses the questionnaire to just 14 items, providing a more time-efficient alternative without compromising validity or reliability. The development of OHIP-14 has made it a preferred tool in both research and clinical practice, offering a more practical approach to evaluating the impact of oral health on quality of life [10].

The OHIP-14 questionnaire was selected as the primary tool for assessing the impact of MG on oral health-related quality of life due to its well-established validity, reliability, and sensitivity in capturing patient-reported oral health challenges. Given that MG predominantly affects neuromuscular function, leading to impairments in mastication, swallowing, and speech [11], a patient-centered measure such as OHIP-14 is essential for understanding the broader implications of these dysfunctions. Unlike conventional clinical assessments that primarily evaluate physiological symptoms, the OHIP-14 provides a comprehensive evaluation of how oral health issues influence physical, psychological, and social well-being [12]. Its ability to measure subjective experiences related to oral function aligns with the study's objective of assessing the real-world impact of MG-related neuromuscular impairments on quality of life. Additionally, the OHIP-14's brevity and ease of administration make it a practical tool for individuals with MG, who may experience fatigue and difficulty completing lengthy surveys, ensuring reliable and meaningful data collection.

Given the interplay between systemic diseases such as MG and oral health, it is crucial to assess how oral impairments influence the overall well-being of affected individuals. Understanding these relationships can lead to better multidisciplinary management strategies, ensuring that oral health considerations are integrated into the broader treatment framework for MG patients.

Aim and objectives

This study aims to evaluate the impact of myasthenia gravis (MG) on oral health-related quality of life using the OHIP-14 questionnaire. It examines how neuromuscular impairments affect mastication, speech, and swallowing, along with their psychological and social consequences. The objective is to highlight the need for integrating oral health assessments into MG care and to support multidisciplinary strategies for improving patient well-being.

MATERIAL AND METHODS

A structured and detailed information sheet outlining the objectives, methodology, and potential implications of the study was provided to all prospective participants. This document also addressed any concerns or questions they had to ensure transparency and allow for an informed decision regarding their participation. The study was conducted on a voluntary basis, and only individuals who met the inclusion criteria were invited to participate. Those who agreed to take part in the research were required to provide written informed consent before proceeding. Following the consent process, participants were given a self-administered questionnaire designed to assess oral health-related quality of life, which they were asked to complete while waiting for their scheduled medical appointment. To minimize any inconvenience, the estimated time for completion of the questionnaire was approximately 5 to 8 minutes, ensuring that it did not interfere with their clinical consultation.

This study is a cross-sectional observational study designed to evaluate the impact of myasthenia gravis (MG) on oral health-related quality of life (OHRQoL) using the OHIP-14 questionnaire.

To maintain the validity and reliability of the collected data, all completed questionnaires were carefully reviewed to verify that they met the inclusion criteria. A total of 110 questionnaires were initially distributed; however, only 100 were deemed eligible for inclusion in the final analysis. The remaining 10 questionnaires were excluded due to missing or incomplete responses or failure to satisfy the predefined inclusion criteria. The exclusion of these incomplete responses helped ensure the integrity of the dataset, allowing for more accurate and meaningful conclusions regarding the impact of myasthenia gravis (MG) on oral health and quality of life.

Individuals aged 18 years or older with a confirmed diagnosis of MG were considered eligible to participate in the study. Additionally, participants were required to have the cognitive ability to provide informed consent and actively engage in the research process. The selection criteria were designed to ensure that all included participants had a clear understanding of the study's objectives and were capable of accurately completing the questionnaire.

Exclusion criteria were established to maintain methodological rigor and ensure that the study population was homogenous. Individuals diagnosed with other severe neuromuscular disorders that could potentially interfere with the assessment of MG-specific symptoms were excluded from participation. Moreover, individuals with cognitive impairments or psychiatric conditions that hindered their ability to provide informed consent were not included in the study. Individuals diagnosed with other severe neuromuscular disorders were excluded to ensure that the symptoms assessed were specifically attributable to myasthenia gravis (MG) and not confounded by overlapping neuromuscular dysfunctions. This methodological approach aimed to enhance the accuracy of the findings by reducing variability in the study population and ensuring that the observed impact on oral health-related quality of life (OHRQoL) was directly associated with MG. Additional exclusion criteria included significant barriers to completing the questionnaire, such as illiteracy, language difficulties, or severe motor dysfunction that impaired the ability to respond to survey items. The implementation of these inclusion and exclusion criteria was essential to reducing variability in the study population and ensuring a reliable analysis of the effects of MG on oral health and quality of life.

All participants voluntarily provided written informed consent before enrolling in the study, and none of the respondents were involved in the study's design or methodological development. The research was conducted following the ethical principles established by the Declaration of Helsinki and received official approval from the Ethics Committee of the University of Medicine and Pharmacy "Victor Babeș," Timișoara (Approval No. 07/11.04.2024).

The assessment of Oral Health-Related Quality of Life (OHRQoL) was carried out using the Romanian-adapted version of the 14-item Oral Health Impact Profile (OHIP-14)[13]. This instrument is widely recognized as a validated and reliable tool for evaluating the impact of oral health on overall well-being. The OHIP-14 measures oral health-related quality of life across seven distinct domains: Functional Limitation (difficulties in pronunciation and alterations in taste perception), Physical Pain (oral discomfort and pain while eating), Psychological Discomfort (tension and self-consciousness caused by oral health concerns), Physical Disability (dissatisfaction with diet and disruptions in eating habits), Psychological Disability (embarrassment and difficulty in relaxation), Social Disability (irritability and challenges in daily activities), and Handicap (reduced overall well-being and functional limitations due to oral health issues).

Participants completed the OHIP-14 questionnaire by responding to items on a 4-point Likert scale, where "very often" was assigned a score of 4, "often" a score of 3, "sometimes" a score of 2, "rarely" a score of 1, and "never" a score of 0. The total OHIP-14 score ranged from 0 to 56, with lower scores indicating a higher OHRQoL [14,15]. This scoring system allowed for a standardized evaluation of how oral health-related factors affected various aspects of the participants' lives, providing valuable insights into the challenges faced by individuals with MG in maintaining oral health and overall well-being.

By employing a validated assessment tool and adhering to strict inclusion and exclusion criteria, this study aimed to provide a rigorous evaluation of the relationship between MG and oral health-related quality of life. The methodological approach ensured that the findings were both reliable and generalizable, contributing to a better understanding of the specific challenges faced by individuals with MG and supporting the development of targeted interventions to improve their oral and overall health.

Statistical analysis was performed using SPSS version 24.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics, including mean values and standard deviations, were calculated for each whitening product at different time points.

RESULTS

The results of the OHIP-14 questionnaire provide a comprehensive perspective on the impact of oral health on various aspects of participants' daily lives, particularly in the domains of functional limitation, physical pain, psychological discomfort, physical disability, social disability, and handicap. The findings reveal substantial variability in how individuals perceive and experience oral health-related challenges, with some reporting minimal interference, while others encounter persistent difficulties that significantly affect their well-being and daily activities.

Within the functional limitation domain, the extent to which oral health affected speech and taste perception was evaluated. The mean score for pronunciation difficulties was 2.28 (SD = 1.11), suggesting a moderate level of impairment among participants. The distribution of responses showed that 7% of individuals never experienced speech difficulties, while 17% reported them very rarely and 30% occasionally. A substantial proportion of respondents (33%) reported experiencing pronunciation problems fairly often, while 13% indicated that these issues occurred very often. These results indicate that while speech impairments were not universally reported, a considerable percentage of participants encountered them frequently, potentially affecting communication and social confidence.

In contrast, taste disturbances were less prevalent, with a mean score of 0.89 (SD = 1.09). More than half of the participants (51%) never experienced taste alterations, while 20% reported them very rarely and 21% occasionally. Only a small fraction of respondents encountered more frequent occurrences, with 5% experiencing taste disturbances fairly often and 3% very often. These findings suggest that although taste disturbances were less frequently reported than speech difficulties, they remained relevant to a subset of participants and could influence dietary choices and overall eating experiences.

The physical pain domain assessed oral discomfort and pain experienced while eating. The mean score for general oral discomfort was 1.16 (SD = 1.07), indicating that most participants experienced minimal pain. Among respondents, 34% never reported discomfort, 30% experienced it very rarely, and 24% occasionally. A smaller proportion reported more frequent discomfort, with 10% indicating it occurred fairly often and 2% reporting very frequent episodes.

For pain while eating, the mean score was slightly higher at 1.33 (SD = 1.18), suggesting a somewhat greater impact compared to general oral discomfort. The response

distribution revealed that 31% never experienced pain while eating, 27% reported it very rarely, and 26% occasionally. A minority of participants (10%) indicated experiencing pain while eating fairly often, while 6% reported it very often. These results suggest that while oral pain and discomfort were not dominant concerns, they were still present for some individuals, with potential consequences for dietary habits and overall oral function.

The psychological discomfort domain explored the emotional impact of oral health, focusing on self-consciousness, guilt, and tension related to oral conditions. The mean score for self-consciousness was 1.44 (SD = 1.39), indicating that while it was not a widespread issue, some participants experienced moderate emotional distress. The response distribution showed that 36% of individuals never felt self-conscious, 19% experienced it very rarely, and 23% occasionally. A smaller subset of participants (9%) felt self-conscious fairly often, while 13% experienced this issue very often. (Table 1, Figure 1)

Table 1. Distribution of Responses for the OHIP-14 Domains in Patients with Myasthenia Gravis

		Never N(%)	Rarely N(%)	Sometimes N(%)	Often N(%)	Very often N(%)	Mean	Std. Deviation
Functional Limitation	**Item 1**	7%	17%	30%	33%	13%	2.28	1.11
	Item 2	51%	20%	21%	5%	3%	0.89	1.09
Physical Pain	**Item 3**	34%	30%	24%	10%	2%	1.16	1.07
	Item 4	31%	27%	26%	10%	6%	1.33	1.18
Psychological Discomfort	**Item 5**	36%	19%	23%	9%	13%	1.44	1.39
	Item 6	59%	13%	19%	3%	6%	0.84	1.19
Physical Disability	**Item 7**	40%	20%	14%	16%	10%	1.36	1.40
	Item 8	21%	20%	24%	14%	21%	1.94	1.42
Psychological Disability	**Item 9**	40%	19%	19%	9%	13%	1.36	1.41
	Item 10	13%	17%	31%	17%	22%	2.18	1.31
Social Disability	**Item 11**	28%	20%	18%	20%	14%	1.72	1.41
	Item 12	15%	15%	31%	17%	22%	2.16	1.33
Handicap domain	**Item 13**	44%	18%	18%	7%	13%	1.27	1.41
	Item 14	52%	24%	9%	10%	5%	0.92	1.21

In terms of guilt related to oral health problems, the mean score was 0.84 (SD = 1.19), suggesting that this concern was less frequently reported than self-consciousness. The majority of participants (59%) never experienced guilt, while 13% reported it very rarely and 19% occasionally. Only a small fraction of respondents reported frequent feelings of guilt, with 3% experiencing it fairly often and 6% very often.

Additionally, tension related to oral health was evaluated separately, with a mean score of 1.36 (SD = 1.40). The results indicated that while some individuals experienced mild to moderate distress, it was not a dominant issue. A total of 40% of respondents never reported tension, 20% experienced it very rarely, and 14% occasionally, while 16% stated they felt tension fairly often, and 10% very often.

The mean score for self-consciousness due to oral health concerns was higher at 1.94 (SD = 1.42), indicating that this concern was more prevalent than tension. The response distribution showed that 21% of participants never felt self-conscious, 20% reported experiencing it very rarely, and 24% occasionally. A considerable proportion of respondents (14% and 21%) reported experiencing self-consciousness fairly often and very often, respectively.

The physical disability domain assessed the extent to which oral health contributed to diet dissatisfaction and disruptions in eating habits. The mean score for diet dissatisfaction was 1.36 (SD = 1.41), suggesting that while not widespread, a subset of participants experienced moderate concerns. Among respondents, 40% never felt dissatisfied with their diet, 19% reported this very rarely, and another 19% occasionally. A smaller group

experienced dissatisfaction more frequently, with 9% feeling it fairly often and 13% very often.

For disruptions in eating habits, the mean score was 2.18 (SD = 1.31), indicating that this issue was more prevalent than diet dissatisfaction. The response distribution showed that 13% never experienced disruptions, 17% reported them very rarely, and 31% occasionally. Meanwhile, 17% of participants experienced these disruptions fairly often, and 22% very often.

The social disability domain examined how oral health influenced irritability and challenges in daily activities. The mean score for irritability was 1.72 (SD = 1.41), suggesting that while many participants did not frequently experience this issue, a notable proportion still did. Among respondents, 28% never felt irritable, 20% reported experiencing it very rarely, and 18% occasionally. Meanwhile, 20% of participants reported feeling irritable fairly often, and 14% very often.

The assessment of difficulty in daily activities revealed a mean score of 2.16 (SD = 1.33), suggesting that this issue was more frequently reported compared to irritability. The distribution of responses indicated that 15% of participants never experienced difficulties, while 15% reported them very rarely and 31% occasionally. A notable proportion of respondents experienced more frequent disruptions in daily activities, with 17% reporting difficulties fairly often and 22% very often. These findings highlight that challenges in performing routine tasks were a significant concern for a substantial subset of participants, potentially impacting their overall quality of life and social functioning.

The handicap domain assessed the impact of oral health on overall well-being and functional limitations. The mean score for reduced well-being was 1.27 (SD = 1.41), indicating moderate distress among some participants. The response distribution showed that 44% of participants never reported a reduction in well-being, while 18% experienced it very rarely and another 18% occasionally. A smaller proportion reported more frequent well-being concerns, with 7% experiencing them fairly often and 13% very often. These findings suggest that while the majority of participants did not perceive a significant reduction in well-being due to oral health issues, a notable minority experienced moderate to frequent distress

For functional impairments related to oral health, the mean score was 0.92 (SD = 1.21), suggesting that this issue was reported less frequently than well-being concerns. Among respondents, 52% never experienced functional limitations, 24% reported them very rarely, and 9% occasionally. Meanwhile, 10% faced functional difficulties fairly often, and 5% very often. These findings indicate that while most participants did not perceive significant functional impairments due to oral health issues, a small proportion reported experiencing frequent limitations.

Overall, these findings suggest that while oral health-related issues did not significantly limit daily activities for most participants, they had a substantial impact on psychological well-being, eating habits, and social interactions for certain individuals. These results underscore the importance of addressing oral health not only from a clinical perspective but also in terms of its broader implications for quality of life. (Table 1, Figure 1)

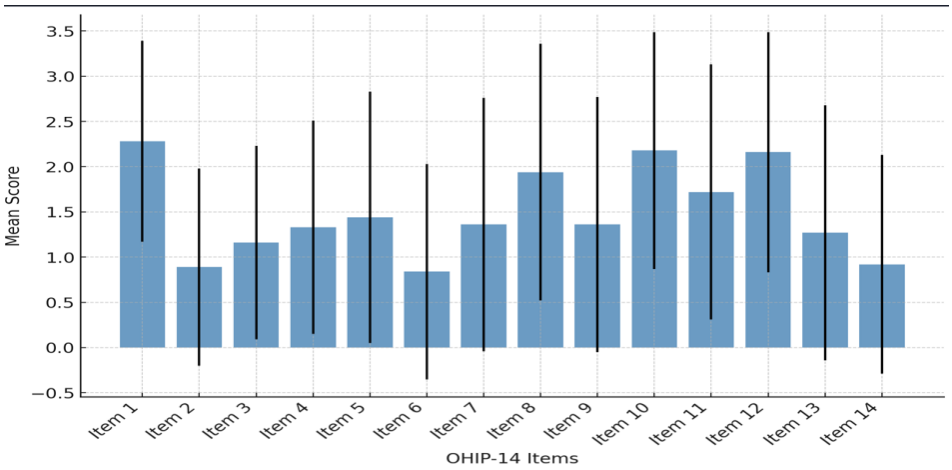

Figure 1. Mean OHIP-14 Scores with Standard Deviations in Patients with Myasthenia Gravis

DISCUSSIONS

The results of this study provide valuable insights into the significant impact of myasthenia gravis (MG) on oral health-related quality of life, emphasizing the interplay between neuromuscular dysfunction and oral impairments. The findings demonstrate that MG-related muscle weakness affects essential oral functions, including mastication, speech, and swallowing, leading to functional limitations, psychological distress, and social impairments. These results are consistent with previous studies evaluating the broader quality of life in MG patients, reinforcing the need for a multidisciplinary approach to disease management. By comparing our findings with existing literature, we further highlight the necessity of integrating oral health assessments into routine MG care, as addressing oral impairments may contribute to overall improvements in patient well-being.

The findings of this study reaffirm the substantial impact of myasthenia gravis (MG) on oral health-related quality of life, highlighting functional limitations, psychological discomfort, and social impairments as key factors influencing daily well-being. Our results align with those of previous studies, including Rodakowska et al. (2014), Szczudlik et al. (2020), and Wu et al. (2023), which have similarly demonstrated the multidimensional burden of MG on patient quality of life. Across different populations, oral impairments extend beyond mechanical difficulties, influencing social interactions, emotional well-being, and overall disease burden.

The comparison with Rodakowska et al. (2014) underscores the reliability of OHIP-14 in assessing OHRQoL and highlights the necessity of rigorous inclusion criteria to ensure data validity [16]. While response fatigue in self-reported questionnaires has been noted in other studies, careful participant selection in our study minimized this risk, ensuring that the data accurately captured the impact of MG on oral health. The alignment between these findings suggests that despite differences in the underlying pathology, oral health remains a critical determinant of overall well-being, further supporting the need for integrated healthcare approaches.

The significant role of disease severity in shaping quality of life outcomes is also evident in our comparison with Szczudlik et al. (2020), who demonstrated that more severe MG symptoms correlate with greater impairment in physical and mental health. While their study employed the SF-36 questionnaire to assess general quality of life, our use of OHIP-14 allowed for a focused evaluation of oral health-related impairments [17]. Both studies underscore the importance of functional limitations, psychological distress, and social impairments as determinants of quality of life, reinforcing the necessity of integrating oral

health assessments into routine MG management. Neuromuscular dysfunctions affecting mastication, speech, and swallowing contribute significantly to the disease burden, necessitating a multidisciplinary approach that considers both systemic and oral health factors.

Additionally, our findings are consistent with those of Wu et al. (2023), who highlighted the profound impact of MG on psychological well-being [18]. Both studies identify self-consciousness and emotional distress as major concerns for MG patients, suggesting that oral health impairments contribute not only to physical difficulties but also to mental health burdens. These results reinforce the importance of psychological support alongside dental and neurological interventions to improve overall quality of life in MG patients.

Given the neuromuscular nature of MG and its direct effects on masticatory and facial muscles, dental professionals should play a more active role in the multidisciplinary care team. Collaboration between neurologists and dental specialists is essential for monitoring and addressing oral health challenges, particularly functional impairments affecting speech, mastication, and swallowing. Regular evaluations by dental professionals can aid in the early detection of oral dysfunction, allowing for timely interventions that prevent further complications. Moreover, since oral health issues in MG patients may extend beyond mechanical difficulties to include pain and discomfort, targeted management strategies should be developed to alleviate these symptoms and improve overall quality of life.

Beyond physical impairments, the psychological implications of oral health disturbances in MG should not be overlooked. Many participants in this study reported varying degrees of self-consciousness, emotional distress, and frustration related to their oral condition. The presence of such psychological burdens suggests that mental health support should be integrated into patient care to ensure that individuals receive appropriate counseling and coping strategies. Speech therapy and dietary counseling may also play an essential role in helping patients adapt to their limitations while maintaining their ability to communicate and eat effectively. Furthermore, tailored dental interventions, including occlusal adjustments, prosthodontic treatments, and specialized oral appliances, may significantly enhance comfort and functionality in affected individuals. The incorporation of these therapeutic strategies into routine care could mitigate the impact of oral health impairments on daily activities and social participation.

Despite the valuable insights provided by this study, several limitations must be acknowledged. The cross-sectional design, while useful for evaluating the prevalence and severity of OHRQoL issues in MG patients, does not allow for causal inferences regarding the progression of oral health deterioration. Longitudinal studies would be more informative in assessing how oral health challenges evolve in response to disease progression, treatment modifications, and rehabilitative interventions. Additionally, while self-reported data provide important patient-centered insights, they may be subject to response bias, with individuals potentially underestimating or overestimating their oral health challenges. Future research should incorporate objective clinical assessments alongside patient-reported outcomes to develop a more comprehensive understanding of the relationship between MG and oral health.

To refine our understanding of this interplay further, future studies should explore interventions specifically tailored to address the unique challenges faced by MG patients. Randomized controlled trials evaluating the efficacy of oral health interventions, such as customized prosthetic solutions, targeted physical therapy for oral musculature, and pharmacological management of oral discomfort, could provide valuable evidence for optimizing patient care. Additionally, investigating the impact of multidisciplinary approaches that integrate dental, neurological, and psychological care may yield novel

strategies for improving the overall well-being of individuals with MG. By addressing these research gaps, healthcare providers can develop more effective, evidence-based interventions that enhance the quality of life of MG patients, ensuring that both systemic and oral health needs are met comprehensively.

CONCLUSIONS

This study highlights the significant impact of myasthenia gravis on oral health-related quality of life (OHRQoL), demonstrating that neuromuscular dysfunctions affecting mastication, speech, and swallowing contribute to functional limitations, psychological distress, and social impairments. The findings underscore the necessity of integrating oral health assessments into routine MG management, as addressing these impairments may improve overall patient well-being. Given the multidimensional burden of MG on oral function, a multidisciplinary approach that incorporates dental, neurological, and psychological care is essential.

Conflicts of Interest

The authors declare no conflict of interest.

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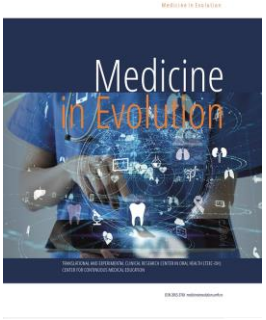
Modern Stragies for Diagnosing Occlusal Caries in Permanent Teeth



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Abstract

1.Background/Objectives: This study evaluates the diagnostic reliability of three methods for detecting occlusal caries: International Caries Detection and Assessment System (ICDAS-II) visual criteria, light-induced fluorescence (VistaCam iX, Dürr Dental), and laser-induced fluorescence (DIAGNOdent Pen, KaVo). Early caries detection is crucial for preventive strategies and minimizing invasive treatments. 2.Methods: A total of 97 permanent molars meeting the inclusion criteria were examined by two calibrated evaluators ($\kappa = 0.95$ for both fluorescence devices). Carious lesions were classified as non-cavitated, enamel lesions, or lesions extending to dentin. 3.Results: The analysis revealed significant differences among the three diagnostic methods. Laser-Induced Fluorescence was more effective in identifying sound teeth and advanced lesions but showed lower sensitivity to early-stage caries. In contrast, Visual Examination (ICDAS) and Light-Induced Fluorescence demonstrated greater effectiveness in detecting early lesions. These findings highlight the need for a combined diagnostic approach to enhance accuracy in caries detection. 4.Conclusion: Visual and Light-Induced Fluorescence methods were more responsive to early caries, while Laser-Induced Fluorescence better detected advanced lesions. These findings support a multimodal approach for improved diagnostic accuracy and early intervention.

Keywords: dental caries; oral health; ICDAS-II; VistaCam iX; DIAGNOdent Pen; digital dentistry

INTRODUCTION

Dental caries, a non-communicable disease (NCD) that is largely preventable, continues to pose a significant public health challenge, with reports indicating little to no improvement in oral health over the past 25 years. In response to this persistent issue, the World Health Organization (WHO) emphasized the urgent need to enhance global oral health through its most recent resolution in 2021. Achieving optimal oral health necessitates, among other measures, the early detection and treatment of dental caries. As oral health is a critical component of overall well-being, maintaining a healthy oral cavity and dentition free from pathological conditions such as caries or periodontal diseases remains a key objective, requiring continuous advancements in both primary and permanent dentition care [1].

According to the Global Burden of Disease Study (2019), untreated dental caries in permanent teeth remains the most prevalent condition worldwide, affecting an estimated 2.3 billion people. Furthermore, disparities in oral health persist between high-income and low-income countries, with limited access to dental care exacerbating the burden of the disease. The World Health Organization (WHO) has recognized the need for a global strategy to improve oral health, highlighting the importance of early diagnosis and prevention in reducing caries incidence. This underscores the necessity of improving diagnostic methodologies to facilitate timely intervention and prevent disease progression [1;2].

Efforts to improve the detection of carious lesions have intensified in recent years. Traditionally, dental healthcare providers have focused primarily on clinically visible lesions during diagnostic assessments. The most commonly employed diagnostic methods include visual and tactile examinations, involving direct observation of the tooth surface or the use of a dental probe. However, one of the significant challenges in caries diagnosis is the quantification of clinical observations into objective numerical data. To address this, the DMFT index—measuring the number of decayed (D), missing (M), and filled (F) teeth—was introduced as a tool to quantify an individual's oral health status [2]. Despite its widespread use, the DMFT index has proven to be insufficient, often failing to provide insights into the severity of the disease or the need for extensive dental treatment. Furthermore, without the inclusion of radiographic analysis, the DMFT index has been shown to underestimate carious lesions in approximately 44% of cases [3].

To enhance diagnostic accuracy, the International Caries Detection and Assessment System (ICDAS II) was developed as a universal scoring system. This system relies exclusively on the visual inspection of carious lesions and, according to Coelho (2020), provides up to 43% more diagnostic information than the DMFT/dmft index. ICDAS II classifies lesions as either active or inactive, thereby assisting dental professionals in determining prognosis and appropriate treatment plans [4].

The ability to evaluate lesion activity allows for more informed decisions regarding preventive versus therapeutic interventions. For instance, an in vivo study conducted by Ferreira et al. (2012) in Puerto Rico demonstrated that early interventions, such as sealing pits and fissures, are recommended for lesions with ICDAS scores of 3 and 4, while lesions with scores of 1 and 2 should be monitored for progression [5].

In addition to visual assessments, other diagnostic technologies have been introduced to improve caries detection. Laser fluorescence-based devices measure emitted infrared fluorescence and present results as numerical values. This technique leverages the principle that chromophores in dental enamel and dentin generate autofluorescence, which diminishes in the presence of demineralization. Furthermore, chromophores such as porphyrins, present in carious lesions and bacterial biofilms, produce fluorescence that can be quantified by comparing the fluorescence of healthy tooth surfaces to that of carious lesions [6]. Factors

such as the presence of blood or other fluids in the oral cavity can affect fluorescence readings, making it essential to ensure that tooth surfaces are thoroughly dried before measurement. To enhance patient compliance and facilitate long-term monitoring, intraoral cameras have been developed to capture and store clinical images of patients' teeth, allowing for continuous evaluation of incipient lesions over time [7].

Given the evolving approaches in cariology, where early-stage caries is considered reversible through infiltration techniques, the ability to detect lesions at their earliest stages is critical. This study aims to investigate the extent to which laser fluorescence and light-induced fluorescence devices can improve diagnostic outcomes derived from visual examinations. Additionally, the research seeks to evaluate the diagnostic reliability of laser-induced fluorescence and light-induced fluorescence in detecting occlusal caries in permanent teeth [6;7].

Aim and objectives

This study aims to evaluate the diagnostic performance of Visual Examination (ICDAS), Laser-Induced Fluorescence, and Light-Induced Fluorescence in detecting occlusal caries in permanent teeth. The objective is to assess their sensitivity and specificity in identifying early and advanced carious lesions and to explore the potential benefits of an integrated, multimodal diagnostic approach to enhance accuracy and early intervention.

MATERIAL AND METHODS

The research focused on patients aged between 7 and 17 years, who were referred to the Department of Dental Prevention, Community Dentistry, and Oral Health at the Victor Babeş University of Medicine and Pharmacy in Timişoara, Romania. The research adhered to the principles of the Declaration of Helsinki (1975) and its subsequent amendments, with written informed consent obtained from all participants before data collection.

Clinical examinations were conducted by two dentists who had undergone calibration to ensure consistency in diagnostic procedures. To assess the level of agreement between the two examiners, the kappa statistic was utilized, yielding a value of 0.95. This rigorous calibration protocol minimized subjective bias and ensured the reliability of visual assessments throughout the study. According to the criteria established by Landis and Koch (1977), this score reflects an almost perfect level of agreement [8].

Participants included in the study exhibited signs of pit and fissure caries in at least one permanent posterior tooth. Each tooth was subjected to a thorough clinical evaluation under appropriate lighting conditions, following careful cleaning of the tooth surfaces. It is important to note that any samples previously involved in the pilot phase were excluded from the main study to maintain data integrity. In total, 97 permanent posterior teeth were analyzed. The selected teeth were either intact or displayed early-stage, subtle carious lesions, with or without visible color alterations.

Teeth presenting occlusal restorations, enamel hypoplasia, hypomineralization, structural anomalies, or pulp necrosis were excluded from the study (Figure 1). For comparative analysis, the two calibrated dentists employed both a laser fluorescence device (DIAGNOdent, Kavo, Biberach, Germany) and an intraoral fluorescence camera equipped with a light-induced fluorescence head (Dürr Dental, Germany) to evaluate the teeth.

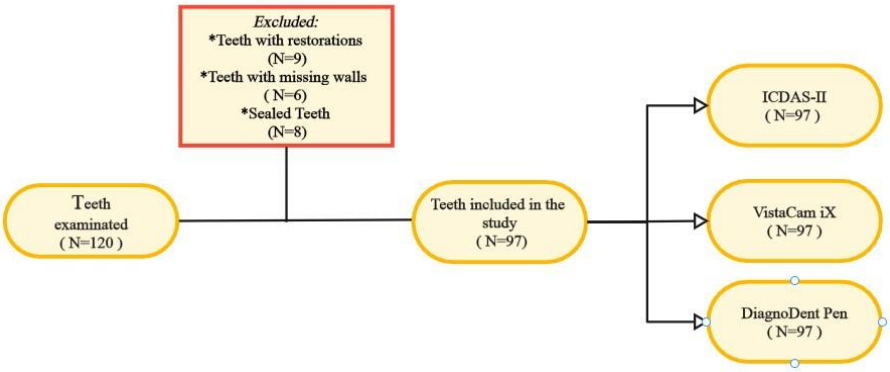

Figure 1. Flowchart of Inclusion and Exclusion Criteria for Teeth Examination

The visual examination of occlusal caries was conducted in accordance with the ICDAS II criteria. Prior to the assessment, the occlusal surfaces of the teeth were thoroughly cleaned to eliminate plaque and debris, using water spray and cotton pellets when necessary.

The ICDAS II system classifies carious lesions on a scale from 0 to 6. A score of 0 indicates a sound tooth surface, showing no evidence of caries even after five seconds of air drying. A score of 1 reflects the first visual changes in enamel, where slight opacity or discoloration (white or brown) becomes visible at the entrance to pits and fissures following prolonged air drying. When distinct visual changes in enamel are noticeable while the tooth is wet and become more pronounced upon drying, the lesion is assigned a score of 2.

A score of 3 corresponds to localized enamel breakdown without any visible clinical signs of dentinal involvement, observable both when the tooth is wet and after extended drying. If an underlying dark shadow from the dentine is detected beneath the enamel, the lesion receives a score of 4. A distinct cavity with visible dentine exposure is classified as a score of 5. Finally, a score of 6 is given to extensive cavities affecting more than half of the tooth surface, where dentine is clearly visible.

This systematic approach ensured consistent and reliable detection and classification of occlusal caries throughout the study.

The assessment utilizing light-induced fluorescence (VistaCam iX, Dürr Dental, Bietigheim-Bissingen, Germany) involved a camera hand piece equipped with two interchangeable lenses (Figure 2). This design enabled the device to function both with the fluorescence attachment for caries detection and as a standard intraoral camera. Patients were positioned in a supine position on the dental chair, with cotton rolls placed in the oral cavity, and the area was thoroughly dried using an air syringe. The fluorescence device was linked to a computer system, and ambient lighting was turned off to enhance imaging accuracy. Initially, images were captured using the fluorescence lens, followed by photographs taken with the white light lens.

The fluorescence scoring system categorized the findings as follows: 0–1.2 indicated healthy tissue, 1.3–1.5 corresponded to enamel caries, and values above 1.5 suggested dentinal caries. To assess the diagnostic accuracy of the applied methods, measurements were coded numerically as 0, 1, or 2 [9;10].

The Wilcoxon signed-rank test was selected for statistical analysis due to the non-parametric nature of the data. Given that the diagnostic scores were ordinal and not normally distributed, a non-parametric approach was required to compare the effectiveness of the three diagnostic methods. The Wilcoxon test allowed for pairwise comparisons of the methods while accounting for the ranked nature of the data. Additionally, Spearman's rank correlation coefficient was applied to assess the degree of association between the diagnostic scores

obtained from different methods, providing further insight into their comparative performance. All statistical evaluations were conducted using R software.

Figure 2. VistaCam iX

Figure 3. DiagnoDent Pen

Assement through laser-induced fluorescence were performed using a laser fluorescence device (DIAGNOdent Pen, KaVo, Biberach, Germany) (Figure 3). Calibration was carried out by selecting a healthy dental surface from a central or lateral incisor to establish a baseline reference. Following calibration, laser fluorescence readings were obtained for each occlusal surface, with three measurements taken per site. The highest recorded value from these readings was used for analysis [9; 10].

RESULTS

The outcomes of the three diagnostic methods applied in this study reveal notable differences in caries detection. Through visual examination using the ICDAS system, 42.26% (N = 41) of the assessed teeth received a score of 0, while 52.57% (N = 51) were categorized with a score of 1, and 5.15% (N = 5) were assigned a score of 2. The analysis conducted with the laser-induced fluorescence device demonstrated that 75.26% (N = 73) of the teeth were given a score of 0, whereas 7.22% (N = 7) obtained a score of 1, and 17.52% (N = 17) received a score of 2. In contrast, the light-induced fluorescence device indicated that 35.05% (N = 34) of the teeth were classified with a score of 0, 52.57% (N = 51) were assigned a score of 1, and 12.37% (N = 12) obtained a score of 2 (Table 1).

Table 1. Outcomes of Diagnostic Methods

Score	Visual Examination (ICDAS)	Laser-Induced Fluorescence (DiagnoDent Pen)	Light-Induced Fluorescence (VistaCam iX)
0	42.26% (N = 41)	75.26% (N = 73)	35.05% (N = 34)
1	52.57% (N = 51)	7.22% (N = 7)	52.57% (N = 51)
2	5.15% (N = 5)	17.52% (N = 17)	12.37% (N = 12)

The observed differences among these diagnostic methods underscore their respective strengths and limitations. Visual Examination (ICDAS) and Light-Induced Fluorescence demonstrate greater effectiveness in detecting early-stage caries, making them valuable tools for preventive care. In contrast, Laser-Induced Fluorescence appears to be more proficient in identifying advanced lesions, though it may underestimate early-stage cases.

These findings indicate that no single diagnostic method provides a fully comprehensive assessment of carious lesions. Integrating multiple diagnostic approaches could enhance accuracy and reliability, facilitating the early detection and appropriate management of both initial and advanced lesions.

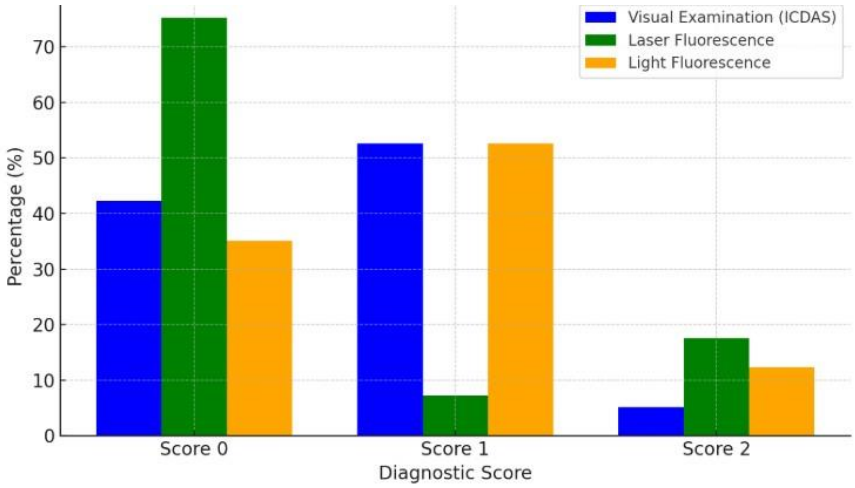

Figure 4. Comparison of Diagnostic Methods

The analysis of diagnostic trends across three methods—Visual Examination (ICDAS), Laser-Induced Fluorescence, and Light-Induced Fluorescence—reveals distinct patterns in their effectiveness at detecting carious lesions. Laser-Induced Fluorescence exhibits a sharp decline from score 0 (75.26%) to score 1 (7.22%), indicating a reduced ability to identify early-stage lesions compared to the other methods.

In contrast, Visual Examination (ICDAS) and Light-Induced Fluorescence follow a similar trend, capturing a high percentage of score 1 cases (52.57%), highlighting their greater sensitivity to early-stage caries. Moreover, Laser-Induced Fluorescence demonstrates a more pronounced increase in score 2 cases (17.52%), suggesting superior efficiency in detecting advanced lesions compared to Visual Examination (5.15%) and Light-Induced Fluorescence (12.37%) (Figure 5).

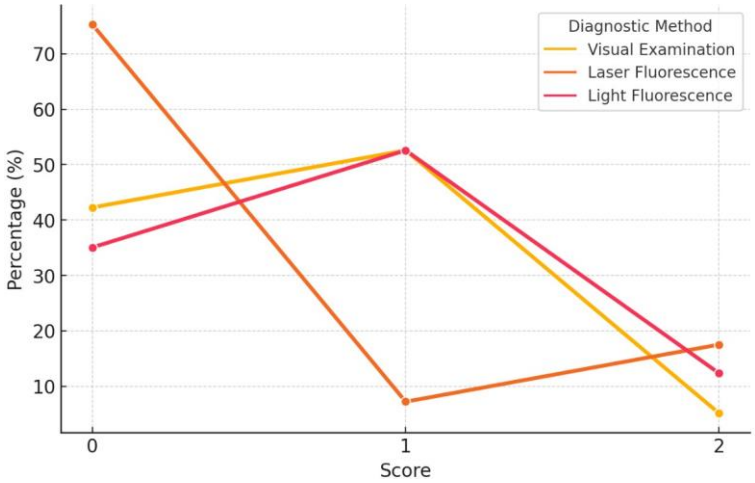

Figure 5. Trend of Diagnostic Scores Across Methods

DISCUSSIONS

The findings of this study provide valuable insights into the comparative diagnostic performance of Visual Examination (ICDAS), Laser-Induced Fluorescence, and Light-Induced Fluorescence in detecting occlusal caries in permanent teeth. The results highlight the strengths and limitations of each method, reinforcing the necessity of an integrated diagnostic approach to enhance caries detection accuracy [11].

Visual Examination (ICDAS) and Light-Induced Fluorescence demonstrated greater sensitivity to early-stage caries, as evidenced by their classification of a high percentage of cases with a score of 1 (52.57%). This aligns with previous studies suggesting that ICDAS is highly effective in identifying enamel demineralization and early carious lesions (Coelho, 2020). Similarly, Light-Induced Fluorescence, which captures autofluorescence variations in enamel, yielded comparable results, reinforcing its role as a reliable tool in detecting incipient lesions (Ferreira et al., 2012). These findings suggest that both methods are well-suited for preventive dental care, facilitating early intervention strategies such as fissure sealants and remineralization therapies [12;13].

Conversely, Laser-Induced Fluorescence demonstrated a significantly lower detection rate for early-stage caries (7.22% classified as score 1) but exhibited superior performance in identifying advanced lesions (score 2: 17.52%) compared to Visual Examination (5.15%) and Light-Induced Fluorescence (12.37%) [14]. This suggests that Laser-Induced Fluorescence may underestimate early enamel changes due to its reliance on fluorescence intensity, which is influenced by bacterial byproducts and the extent of demineralization. Prior research supports this observation, indicating that laser fluorescence devices tend to produce higher specificity but lower sensitivity for initial caries detection (Neuhaus et al., 2010). The ability of Laser-Induced Fluorescence to detect deeper enamel and dentinal involvement highlights its potential utility in confirming advanced caries diagnoses and guiding treatment planning [15].

A key implication of this study is the recognition that no single diagnostic method provides a fully comprehensive assessment of carious lesions. The observed discrepancies between the three methods underscore the need for a multimodal approach that leverages the advantages of each technique. Given the shift towards minimally invasive dentistry, where early detection and intervention are paramount, integrating fluorescence-based techniques with visual examination could improve diagnostic reliability and support individualized patient care.

Despite the strengths of this study, several limitations should be acknowledged. First, the sample size was relatively small (97 permanent posterior teeth), which may limit the generalizability of the findings. Additionally, the study focused exclusively on occlusal caries, and further research is needed to assess the efficacy of these diagnostic methods in detecting proximal and root caries. Another limitation is the potential influence of external factors such as saliva, plaque, and staining on fluorescence readings, which may have affected measurement accuracy. Future studies should explore standardized protocols to mitigate these variables and improve diagnostic consistency.

Future research directions should focus on the integration of fluorescence-based technologies with adjunctive diagnostic methods, such as optical coherence tomography and artificial intelligence-driven image analysis. AI-based image recognition systems have shown promise in enhancing caries detection by providing automated, quantitative assessments of lesion severity. Additionally, longitudinal studies assessing the clinical outcomes of different diagnostic approaches could provide further insights into their long-term effectiveness in caries management.

In conclusion, the results of this study reaffirm the necessity of refining caries detection methodologies to align with the evolving paradigm of preventive and minimally invasive dentistry. By combining Visual Examination (ICDAS), Laser-Induced Fluorescence, and Light-Induced Fluorescence, dental practitioners can improve diagnostic precision, optimize treatment planning, and contribute to more effective caries management strategies in clinical practice [16;17].

CONCLUSIONS

This study highlights the comparative diagnostic performance of Visual Examination (ICDAS), Laser-Induced Fluorescence, and Light-Induced Fluorescence in detecting occlusal caries in permanent teeth. The findings emphasize the superior sensitivity of Visual Examination and Light-Induced Fluorescence in identifying early-stage caries, while Laser-Induced Fluorescence demonstrated greater specificity in detecting advanced lesions. These results underscore the limitations of relying on a single diagnostic method and reinforce the need for an integrated, multimodal approach to improve diagnostic accuracy and early intervention. Given the growing emphasis on minimally invasive dentistry, combining fluorescence-based technologies with visual assessment could enhance caries detection and optimize treatment planning. Future research should focus on refining fluorescence-based diagnostics, integrating artificial intelligence-driven image analysis, and evaluating long-term clinical outcomes to further advance caries management strategies.

From a clinical perspective, these findings highlight the necessity of integrating multiple diagnostic modalities to enhance caries detection. Given that early intervention is fundamental in minimally invasive dentistry, the combined use of visual examination and fluorescence-based methods can aid in identifying lesions at reversible stages, reducing the need for invasive restorative procedures. In clinical practice, practitioners should consider utilizing light-induced fluorescence for routine screening, supplemented by laser fluorescence for confirmation of advanced lesions. Moving forward, the development of standardized diagnostic protocols incorporating these modalities could lead to more accurate, evidence-based decision-making in caries management.

Conflicts of Interest

The authors declare no conflict of interest.

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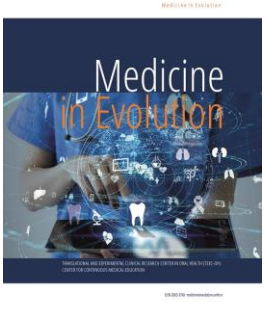
Stress Distribution in Dental Implants under Occlusal Forces – A Digital Simulation.



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Abstract

Aim and objectives: To analyze implant mechanics underloading using Finite Element Analysis (FEA) to assess micro-movements, identify failure points, and optimize design for improved clinical outcomes. Materials and methods: A numerical simulation of mechanical loading on a prosthetic abutment attached to a dental implant was conducted using ANSYS R18.2 Academic®. Measurements, material specifications, and photographs were analyzed to model the implant system with a 6-degree conical connection. Results: Stress analysis under vertical and oblique forces showed all values within permissible titanium alloy limits. Vertical forces led to uniform stress distribution, while oblique forces caused asymmetric stress with localized detachment tendencies. Conclusions: Masticatory forces impact implant stress and may contribute to microleakage, highlighting the need for patient-specific prosthetic alignment.

Keywords: implants, occlusal forces, peri-implantitis, mechanical loading, implant failure

INTRODUCTION

The dental implant therapy is experiencing significant growth, with a rising number of patients opting for dental implants globally, often instead of more invasive procedures. This trend inevitably leads to an increase in potential complications that dental professionals must adeptly manage [1].

Peri-implantitis can arise from various factors, primarily attributed to bacterial infections in the peri-implant area. The mechanisms by which bacteria adhere to the implant surface and socket share similarities with those observed in natural teeth and their surrounding gingival sulcus. However, the distinct materials and technical properties of dental implants result in markedly different clinical pathways and responses to targeted treatments [2, 3].

It is widely acknowledged that dental implants and their prosthetic components are subjected to vertical, oblique, and horizontal forces. Regardless of the chosen prosthetic design, the primary function of such prosthetics is masticatory efficiency, while also considering aesthetic and phonetic factors. Understanding how these forces are transmitted, their destabilizing effects, clinical implications, and potential corrective measures, is crucial. The present study seeks to elucidate these mechanical interactions through numerical computer analysis. The simulations and digital assessments conducted will precisely identify the types and magnitudes of forces responsible for micro-movements of the prosthetic abutment in relation to the implant, facilitating a three-dimensional visualization of the contact pressure distribution and potential gaps at the interface [4, 5].

The study employs Finite Element Analysis (FEA), a technique extensively utilized across engineering disciplines and beyond. One of the primary advantages of FEA is its ability to address complex problems that would otherwise pose significant analytical challenges. This method allows for the examination of both linear and non-linear phenomena and can be applied in dynamic, thermal, fluid flow, or electromagnetic analyses [6, 7].

The impetus for this type of investigation stems from the necessity to analyze complex structural strengths that traditional analytical methods cannot effectively manage. The core concept involves subdividing the structure into numerous smaller components, known as finite elements, to apply relevant design theories for each segment. This discretization process simplifies the modeling of the overall structure into manageable finite elements. The FEA model is an approximate representation, constructed by assembling the finite elements while considering the structure's geometry. These elements connect only at specific points called nodal points or nodes, which are intersections of the finite elements' lines. Finite elements can vary in dimensionality, being one-dimensional, two-dimensional, or three-dimensional, depending on the modeled structure's geometry [8, 9].

The inherent approximation of the finite element method arises from the necessity to replace the real geometry with a finite element mesh that simulates the actual shape, albeit with limitations due to the finite number of elements. Consequently, computational accuracy improves with an increase in the number of finite elements. Various approximation functions are utilized to compute unknown values throughout the finite element domain. It is crucial to highlight that the performance of the finite element method is closely tied to the quality of these approximation functions, especially regarding continuity at the interfaces of the elements. Originally applied in the design of strength structures, the finite element method has expanded to encompass nearly all research fields, including medicine [10, 11].

Dental implant therapy has evolved significantly over the past few decades, becoming a widely accepted and preferred solution for edentulism and tooth replacement. The success of implant therapy is largely dependent on various biomechanical factors, including implant

design, surface modifications, osseointegration, and the forces exerted on the implant during mastication. Understanding how these forces interact with the implant-abutment complex is crucial in predicting implant longevity and minimizing complications such as mechanical fatigue, screw loosening, and implant failure. Digital simulations, particularly Finite Element Analysis (FEA), have become an essential tool in modern dentistry, allowing researchers to model and analyze stress distributions in a controlled and reproducible manner. These computational models offer valuable insights into how different loading conditions affect implants, helping clinicians optimize their design and placement to enhance clinical outcomes.

Digital analysis thus presents numerous research opportunities within the medical domain, owing to its versatility and broad applications. In the context of this study, digital analysis may unveil new insights into the clinically undetectable phenomena at the implant-bone interface influenced by mechanical forces [12, 13, 14].

Aim and objectives

The aim of this study is to investigate the mechanical behavior of dental implants and their prosthetic components under various loading conditions using Finite Element Analysis (FEA). By simulating the forces acting on the implant-abutment interface, the study seeks to provide insights into the micro-movements and stress distribution that occur during masticatory functions. This understanding will help in optimizing implant designs and improving clinical outcomes by identifying potential failure points associated with mechanical forces.

MATERIAL AND METHODS

For the numerical simulation of mechanical loading on a prosthetic abutment attached to a dental implant, the ANSYS R18.2 Academic® software was employed. The study utilized an implant system featuring a precision conical connection with an angle of 6 degrees and a diameter of 4 mm, which is one of the most commonly used in private practice. Initially, measurements of the implant and the prosthetic abutment were taken both separately and in conjunction following their fixation (Figure 1). These measurements, along with photographs and the technical and chemical specifications of the materials used in their fabrication, were subsequently submitted to the numerical simulation department at the Polytechnic University of Timişoara.

To ensure the accuracy of the digital model, a high-resolution micro-computed tomography (micro-CT) scan was performed on the implant system before simulation. This imaging technique allowed for a precise 3D reconstruction of the implant-abutment complex, ensuring that its geometry and material properties closely matched real-life conditions. The reconstructed model was then imported into ANSYS software for further processing.

The digital model underwent meshing, where the structure was subdivided into finite elements to enhance simulation precision. A tetrahedral mesh was applied to optimize element distribution and ensure that stress concentrations were accurately captured. The mesh quality was assessed using convergence tests, ensuring that the element density was sufficient to achieve reliable results without excessive computational burden.

To simulate realistic oral conditions, two different force application scenarios were analyzed:

1. **Vertical loading:** A force of 150 N was applied along the implant's longitudinal axis, simulating masticatory forces in the posterior region.
2. **Oblique loading:** A force of 150 N was applied at a 30-degree angle to the implant axis, mimicking lateral chewing forces.

The boundary conditions were defined by fixing the implant base to simulate osseointegration within bone. The contact interactions between the implant and abutment were modeled using a frictional coefficient of 0.3, reflecting realistic mechanical interactions. The material properties used in the simulation included:

- **Titanium alloy (implant and abutment):** Young's modulus = 110 GPa, Poisson's ratio = 0.34.
- **Cortical bone (surrounding bone structure):** Young's modulus = 14 GPa, Poisson's ratio = 0.3.
  Trabecular bone: Young's modulus = 1.5 GPa, Poisson's ratio = 0.3.

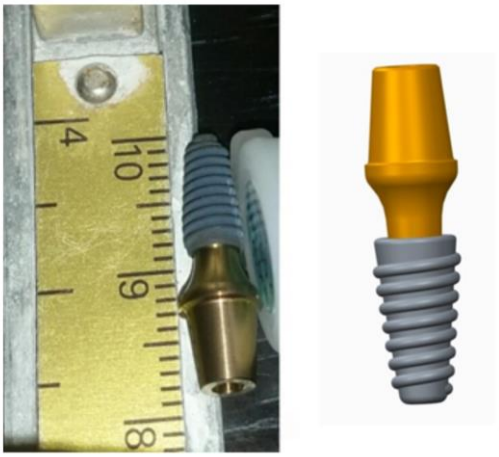

Figure 1. Measuring the implant with the screwed-on abutment at the torque recommended by the manufacturer. b) Digital design of the implant-prosthetic abutment complex

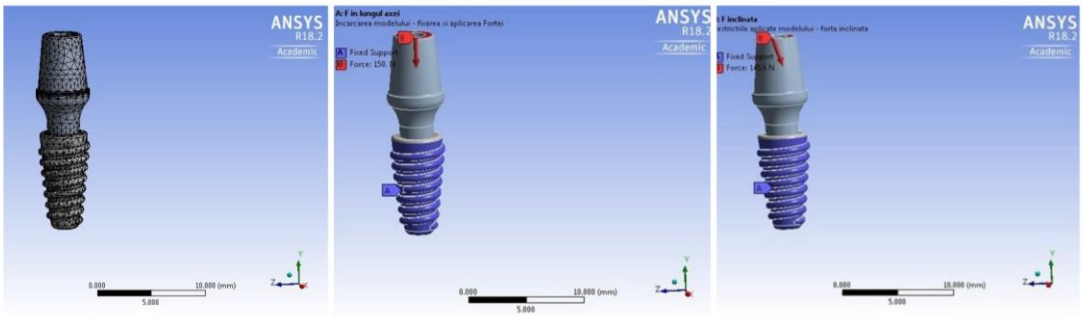

Figure 2. a) Discretization of the implant-bridge model; b) Application of vertical forces on the model; c) Applying oblique forces on the model

All relevant data was input into the system to digitally reconstruct the two components—the implant and the abutment—and to analyze their interactions under mechanical loading. Following the data input and creation of the implant-bridge model, the next step involved discretization, which entails dividing the entire structure into several three-dimensional segments (Figure 2a). This process enables a more detailed analysis of the model and enhances the accuracy of the results obtained.

As an initial parameter, a vertical force was applied along the axis of the implant, set at an intensity of 150 N, which approximates the forces generated during mastication in the posterior area. The force application in the numerical simulation was singular, transitioning from zero to maximum intensity—150 N—over the course of one second, as illustrated in

Figure 2b. After each simulation, both a color map depicting the intensity and location of mechanical stress, along with its numerical quantification, were generated.

Subsequent simulations were conducted to model the application of oblique forces on the implant-abutment assembly (Figure 2b). The use of oblique forces was chosen to closely replicate the conditions within the oral cavity, where various intensities and directions of forces occur during mastication.

For both types of simulations, the following parameters were calculated: stress generated in the implant and abutment, the contact area state between the implant and the abutment, frictional stress at the contact point, pressure distribution at the interface, the tendency of the abutment to slide relative to the implant, interlocking of the abutment with the implant at the contact area, and the likelihood of detachment of the abutment from the implant.

RESULTS

The initial recording focused on the stress observed in the model when subjected to vertical forces (Figure 3a). The results included a graphical representation, with areas exhibiting higher stress values shown in yellow and red (maximum), while regions without stress were depicted in blue. The numerical values varied from 3309 to 29.709 MPa.

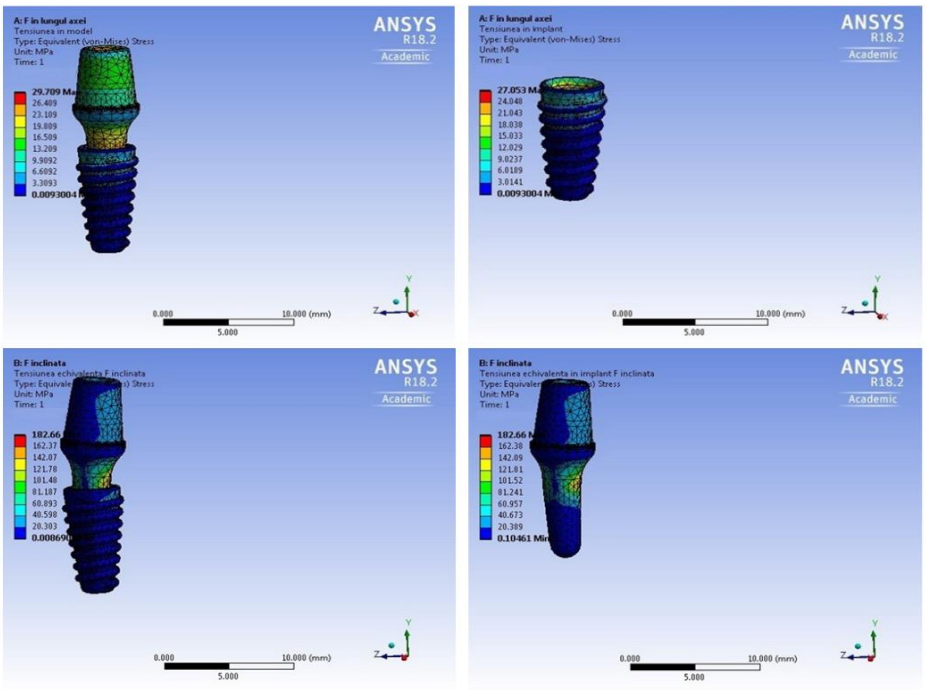

Figure 3. a) Stress in the model when vertical forces are applied; b) Stress in the implant when vertical forces are applied; c) Stress in the model when oblique forces are applied; d) Implant tension when oblique forces are applied

It can be seen from the graph that the highest stress occurs at the collar of the abutment, at the junction with the implant body, but it is not a destabilizing factor, being well below the permissible limit for titanium alloy. The second analysis focused on the stress occurring in the implant body during mechanical loading of the abutment with vertical forces (Figure 3b).

The forces recorded are similar to those at the bungs, but again, they are well below the permissible limit for the material from which they are made. The third analysis was to

determine the stresses appearing in the abutment under the influence of oblique forces (Figure 3c).

It should be noted that the tilt of the bump in the image is not real, the program only graphically represents its tendency to move under the action of the forces, for a better representation of their distribution and direction in the model. The fourth analysis was the determination of the stress occurring in the implant body under the influence of oblique forces (Figure 3d).

The levels attained in both the implant and the abutment are within the permissible limits for the alloy from which they are made, but the distribution of the stress zones is completely different from when the vertical force was applied.

The numerical results are very similar to the analysis under the two types of forces, but the positioning is completely different. While there is a uniform distribution of pressure and tension when vertical forces are applied, under oblique forces, there is a tendency for one-sided detachment (marked light green and yellow) in the area opposite to the direction of the force.

DISCUSSIONS

The results of the numerical analysis were different depending on the direction of the force being simulated. When the forces were vertical, the stresses and pressure areas generated were usually much more evenly distributed over the entire model. This means that at the connection level, as well as at the level of the whole assembly, vertical forces of the masticatory caliber are not able to generate destabilizations, micro-fractures or deformations. However, purely vertical forces are a rarity in the human masticatory pattern, most of which have both oblique and horizontal components. There are also significant differences between the developed forces, depending on the general condition of the patient, age, gender and the absence or presence of parafunctions [15, 16, 17, 18].

The oblique forces produced in the program are significantly more representative of the actual conditions found in the oral cavity. While chewing, patients engage in complex closing and opening, lateral, and forward movements that occur in countless subconscious sequences. The way these forces interact with both teeth and implants is much more intricate than any computer simulation could accurately portray. However, one conclusion can be drawn from this study: certain areas of the two components, particularly the interface between them, experience greater masticatory stress than others. For instance, even though the tensile and shear forces at the implant-butt connection, when subjected to oblique mechanical loading, remain within the safety limits of the titanium alloy, ongoing fatigue from repeated stress can eventually lead to wear and micro-cracking over time.

As illustrated in the previous images, specific regions of the connection between the implant and the abutment consistently experience masticatory stress. These forces can accumulate over time, and after a certain number of cycles, some areas of the alloy, or even the abutment screw, may begin to show signs of change.

The digital simulation was conducted using individual forces of 150 N, applied over a total duration of one second (from 0 to 150 N). Consequently, the implant, abutment, and their connection may behave differently in the actual dynamics of the oral cavity, where there are far more repetitions, varying humidity and temperature conditions, and potentially much higher masticatory forces in certain situations. Nevertheless, the areas highlighted in the current simulations represent the critical "key points" for maintaining implant stability over time.

The results of this study provide valuable insights into the mechanical behavior of dental implants subjected to various occlusal forces. By employing Finite Element Analysis

(FEA), the stress distribution and micro-movements at the implant-abutment interface were analyzed in detail, revealing the complex interplay of forces encountered in clinical settings. The findings highlight the crucial role of load directionality in determining implant stability and mechanical fatigue.

The present study corroborates findings from previous research demonstrating that vertical forces lead to a more uniform stress distribution across the implant structure, whereas oblique forces create asymmetrical stress patterns with a greater likelihood of micro-movements. Dhatrak et al. (2018) conducted a similar FEA-based study and reported that vertical loading conditions resulted in well-distributed stress, supporting the notion that axial loading is less detrimental to implant longevity compared to non-axial forces [22]. However, they also noted that oblique loads produced stress concentrations at the implant neck, a finding consistent with our results.

In another study, Datte et al. (2018) investigated the influence of restorative materials on stress distribution in dental implants. They found that material properties significantly affected stress propagation, with more rigid materials exhibiting less deformation but transmitting higher stress to the implant and surrounding bone [23]. Our study, while not directly assessing material influence, reinforces the importance of stress distribution patterns in maintaining long-term implant integrity. This suggests that selecting optimal prosthetic materials is as crucial as optimizing implant geometry to withstand mechanical fatigue.

Ghadiri et al. (2016) explored the effect of implant geometry on stress distribution and reported that tapered implants exhibited lower stress concentrations at the crestal bone compared to cylindrical implants [24]. Although our study focused on a conical implant-abutment connection, our findings align with their observations regarding the importance of implant design in mitigating excessive stress.

One of the key implications of this study is the role of repetitive occlusal forces in mechanical fatigue. While the forces applied in our simulations were limited to 150 N over one-second intervals, real-life masticatory cycles involve thousands of loading and unloading sequences daily. Kogawa et al. (2006) found that individuals with temporomandibular disorders exhibited significantly altered bite force patterns, which could lead to unpredictable mechanical fatigue in dental implants [25]. This underscores the need for patient-specific assessments when designing prosthetic restorations.

Furthermore, Varga et al. (2011) demonstrated that bite force varies significantly with age and gender, with younger males exerting higher forces than older individuals or females [26]. These variations must be factored into clinical decision-making, as higher bite forces may necessitate modifications in implant selection, prosthetic design, and occlusal adjustments to prevent excessive stress accumulation.

From a clinical standpoint, the findings of this study emphasize the importance of proper occlusal loading in implant-supported restorations. The observed stress concentration at the implant-abutment interface highlights the necessity for precise prosthetic alignment to minimize mechanical overload. Malocclusion or excessive lateral forces may accelerate abutment loosening, screw fractures, and even implant failure. Misch (2015) previously emphasized that occlusal adjustments should be an integral part of implant therapy, particularly in patients with parafunctional habits such as bruxism [27].

Additionally, the study reinforces the necessity of employing conical connections in implant systems to enhance mechanical stability. Previous research by Tetsch et al. (2015) suggested that internal conical connections distribute forces more evenly compared to external hexagonal connections, which are more susceptible to micro-movements [28]. Our findings align with this view, as the conical connection in our model exhibited stress localization but remained within permissible limits for titanium alloy.

While this study provides valuable insights, it has some limitations that must be addressed in future research. First, the simulations were conducted under idealized conditions without accounting for biological variables such as bone remodeling, soft tissue adaptation, and patient-specific occlusal dynamics. Hu et al. (2020) highlighted that real-world conditions introduce additional factors, including variations in bone density and implant osseointegration, which may alter stress distribution [29].

Future studies should incorporate dynamic simulations that mimic prolonged loading conditions to better represent clinical realities. Additionally, experimental validation using strain gauges or clinical follow-up studies would enhance the reliability of numerical findings. The integration of patient-specific data through advanced imaging techniques, such as CBCT and intraoral scanning, could further refine digital simulations, providing more personalized implant treatment planning.

The complexity of masticatory forces makes them challenging to measure and represent, regardless of technological advancements. The variety and subconscious coordination of movement patterns and intensities make it seem nearly impossible to break them down into mathematical components. Nevertheless, by aligning the current data with findings from other studies and existing literature [19, 20, 21], some significant conclusions can be drawn.

CONCLUSIONS

At the interface between the implant and the abutment, forces of tension, pressure, and notably, loosening are present. Although these forces are relatively small in individual trials at predetermined conditions (one second, 150 N), their existence and specific locations indicate a concentration map of masticatory stress.

Masticatory cycles are also highly variable, influenced by numerous factors. The extent of mouth opening, the force used for closing, and the frequency of closing-opening cycles are all subconsciously regulated and depend on aspects such as the individual's age, gender, overall health, and the type or hardness of the food consumed. These factors complicate the mechanism of force transmission to a patient's teeth and implants, while also highlighting the potential for long-term mechanical fatigue.

By correlating the numerical analysis data—particularly concerning pressure, tension, and detachment forces at the implant-abutment connection—with previous research findings, it can be concluded that masticatory forces play a contributing role in the development of microleakage when subjected to mechanical fatigue under specific conditions. However, it is crucial to note that occlusal balance and the integration of prosthetic restorations must be aligned with the implant systems utilized and the patient's local, regional, and systemic characteristics. All studies, whether clinical or paraclinical, should be considered within the context of the patient's overall situation to maintain relevance.

Masticatory forces are highly complex, dynamic, and influenced by numerous physiological and mechanical factors, making them challenging to quantify and analyze. The forces exerted at the implant-abutment interface, including tension, compression, and detachment, contribute to mechanical stress distribution and may play a role in microleakage under fatigue conditions. While these forces are relatively minor in controlled experimental settings, their cumulative effect over time highlights the potential for prosthetic instability.

Conflicts of Interest

The authors declare no conflict of interest.

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Assessment of Parental Knowledge and Behaviour Regarding the Oral Hygiene of Preschool Children

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Abstract

In young age, oral health is strongly influenced by the primary caregivers' attitude towards oral health. Parental factors such as socioeconomic status, education level, and dental anxiety of the parent may play a role in their knowledge about dental hygiene practices. 1.Background/objectives: The objective of this paper is to identify the gaps in parental knowledge regarding children's oral hygiene and to highlight the influence that variables such as the parent's level of education, fear of the dentist, or even gender may have on their knowledge about dental caries, tooth eruption and oral health habits. 2.Material and methods: The present work is an analytical cross-sectional study of parental attitude towards oral health of their children, aged between 0 and 6 years. Data collection was done by questionnaire and the sample population included 50 respondents and the results were statistically analysed. 3.Results: Regarding the parent's level of knowledge about dental eruption and oral health practices, no statistically significant differences were identified between the two sexes ($p=0.853$), between different levels of education ($p=0.628$), and also the absence or presence of parents' fear of the dentist and their level of knowledge are not correlated ($p=0.723$). However, the differences between dental fear of parents and their children proved to be statistically significant according to the chi-square test ($p<0.001$). 4.Conclusions: The study showed that the parent's gender, level of education and fear of the dentist do not influence their knowledge about dental caries, eruption of temporary teeth, eruption of permanent teeth and oral health. However, there seems to be a correlation between the dental fear of the parent and that of the children, and also between oral hygiene practices of parents and their children.

Keywords: oral hygiene; children; parental knowledge; education level; dental fear

INTRODUCTION

The concern for oral hygiene among the general population has made considerable progress from the previous century to the present, but nevertheless dental caries is one of the diseases with a high prevalence all over the world [1,2]. A comprehensive global epidemiological study published in 2017 estimated that 2.3 billion people suffer from cavities in permanent teeth, and more than 530 million children have cavities in primary teeth [2]. Although it is relatively easily preventable, tooth decay remains one of the most common diseases among children, being five times more common than asthma and seven times more common than hay fever [3-5]. A study carried out on a sample of 3000 Italian children showed a prevalence of early childhood caries (ECC) approaching 15% in the age group between 4 and 6 years and highlighted the association between the prevalence of caries in children and the parents' incorrect oral care behaviours [5]. Another study, carried out in Romania in 2022, revealed an increased prevalence of caries in the same age group [6].

Children's oral health status can be influenced by many different factors, like parental knowledge about oral practices and their awareness on the importance of oral hygiene, parental level of education, dental fear or access to educational programs related to oral health. Diet and oral hygiene practices are among the life skills children learn from their parents and/or primary caregivers. Therefore, there is a correlation between the oral health status of children and the knowledge and behaviours of parents, caregivers and older siblings [7]. According to Broadbent et al., socioeconomic status, as well as beliefs about oral health care held by individuals and their parents early in life, are related to oral health in early adulthood [8]. Salama et al. noted the strong link between educational level and oral health literacy, but also emphasized how, despite social status, most parents are still unaware of the importance of prevention. According to their results, 46.7% of children under the age of 5 never visited the dentist, 41.8% were bottle-fed on demand, and only between 8 and 22% of children, depending on family income, had their first dental visit during this time [9]. Hiratsuka found in a sample of Alaska residents that although most parents did not achieve adequate oral hygiene frequency, the odds ratio of children achieving the required frequency of tooth brushing was 49 times greater if their parents were used to brush their teeth at least twice a day [10]. In a Mexican sample, Vallejos-Sanchez et al. pointed out that a better maternal approach to oral health and dental care was associated with a 2.4-fold higher chance of frequent tooth brushing in the child [11]. Improvements in parental knowledge are generally associated with short-term improvement in children's plaque index [12]. Very few studies have been conducted to assess the incidence of dental caries after oral health education. Indeed, there is a need to understand children's and parents' knowledge to develop more effective approaches to promoting oral health. Periodic reminder through educational programs is fundamental to achieve a significant long-term result. A 2016 study on 396 parents and their children aged 3 to 6 years, in which parents' awareness was determined by comparing the parents' perception of their child's oral hygiene with the results of the dental exam, showed that 40.9% of parents did not know the child's dental hygiene level. Awareness was closely related to children's and parents' oral hygiene, education level, and socioeconomic status. Therefore, educational interventions aimed especially at young people, families with low socio-economic status and parents of children with poor oral hygiene are very important first steps in the prevention of dental caries [13].

Dental fear is generally a common problem among patients of all ages, that frequently leads to avoiding or delaying treatment. Estimates are that approximately 6-15% of the population globally suffer from high levels of dental fear and anxiety [14]. Dental fear and anxiety are thought to be maintained through a vicious cycle, demonstrated by Armfield in a

study of 1036 subjects [15]. The study showed that dental fear acts as a determinant of avoiding or postponing dental visits, which has flow-on effects in terms of additional treatment needed and problem-oriented visits. Avoidance of routine dental care leads to a higher incidence of pain which in turn affects anxiety and vice-versa. It is important to note that negative memories of previous experiences at the dentist's office may act as an indirect, possibly even unconscious way in which parents transfer dental anxiety to their children [16]. Smith et al. showed that parents expressed their own negative experiences with dental treatments through words and expressions and also by delaying dental treatment for themselves and their children [17]. Most visits to the dentist are due to tooth pain, followed by tooth decay, while very few parents bring their children for routine check-up [18]. In a study led by Sakai et al., 58% of parents and 41% of children had never been to the dentist [19].

Dental health education is fundamental in the prevention of dental caries in children, with the aim of changing the knowledge, attitudes and behaviours of the patient and parents. However, the child's ability to assimilate and imitate the good and bad habits of adults cannot be ignored [20]. As highlighted by the WHO, oral health education and community involvement are essential to prevent caries in early childhood, especially in low- and middle-income countries. The family is the child's primary source of learning about oral health and risk factors. WHO suggests improving oral health awareness and CTC prevention among parents through appropriate communication and provision of sound information on prevention and treatment [21]. Evidence suggests the effectiveness of behavioural therapies against CTC when used at individual and family level [22]. Motivational interviewing is a promising approach to induce positive changes in parents' oral health knowledge and child behavioural outcomes. Outcomes are improved when delivered in a patient-centred environment rather than the potentially stressful and distracting environment of a busy dental clinic [23].

Aim and objectives

The objective of this paper is to identify the gaps in parental knowledge regarding children's oral hygiene and to highlight the influence that variables such as the parent's gender, level of education or fear of the dentist have on their knowledge about dental caries, tooth eruption and oral health habits. Awareness of this topic can indicate to the pedodontist and other professionals in the field of dental medicine, at what level to educate and intervene to improve the prevention of dental caries.

MATERIAL AND METHODS

The present paper details an analytical cross-sectional study carried out on a target population represented by parents of children aged between 0 and 6 years. Data collection was done by completion of a questionnaire by the parents of patients treated in the Clinic of Pediatric Dentistry from the Faculty of Dental Medicine of "Victor Babeş" University of Medicine and Pharmacy, Timişoara, during the period October-December 2023. The questionnaire items were translated from the study published by Hazal Deniz Köse et al. [24], and used with the consent of the authors. The confidentiality of personal data was respected according to the GDPR, and the respondents gave their written consent to participate in the study. The inclusion criterion was the child's age between 0 and 6 years.

The questionnaire consists of 33 questions, divided into 6 categories. The first part of the questionnaire consists of questions related to demographic information, such as the gender of the parents, the gender of the child, the age of the parents, the age of the child and the level of education of the parents. The second part includes questions about attitude and

behaviour regarding dental visits, such as the time of the child's first visit to the dentist, the reason for the visit, and the dental fear of both the parents and the child. The third part includes questions about the child's diet, such as consumption of dairy products, fruit juices, carbonated drinks and sweets. The fourth part asks questions that test the parents' knowledge about tooth eruption, such as the number of temporary teeth, the number of permanent teeth, the first temporary tooth and the first permanent tooth that erupts, and the fifth and sixth parts include questions about tooth decay and oral hygiene, such as how often you change your toothbrush or when you should start brushing.

A total of 50 questionnaires were completed by parents. Collected data were entered into an Excel spreadsheet and analysed using IBM SPSS (version 29) software. The following research hypotheses were formulated:

1. There are significant differences between parents' level of knowledge about dental caries and eruption, depending on their level of education.
2. There are significant differences between parents' level of knowledge about dental caries and eruption, depending on the presence or absence of the parent's fear of the dentist.

The research hypotheses were verified using the Chi-square independence test at the level of statistical significance $p<0.05$.

RESULTS

The age distribution of the 50 respondents to the questionnaire is: parents under 20 years old - 10%, between 20-40 years old - 58%, and over 40 years old - 32%. The gender distribution of the respondents is: female - 62%, male -38%. Regarding the level of education, 2% of parents who responded to the questionnaire are secondary school graduates, 48% of parents are high school graduates, 16% of parents are post-secondary school graduates, and 34% of parents have university degrees.

According to the answers in the questionnaire related to dental visits, all parents (100%) declared that they had been to the dentist before, while in case of the children 86% have had their first dental visit prior to the study and 14% were visiting the dentist for the first time. The reason for visiting the dentist was in 60% of the cases dental caries, 10% pain, 8% tooth mobility and 22% routine visit.

The level of parental knowledge about the total number of permanent and temporary teeth and their eruption is the following: 61.3% of mothers and 63.2% of fathers answered correctly, 9.7% of mothers and 5.3 % of fathers answered incorrectly, and 29% of mothers and 31.6% of fathers stated that they did not know. Regarding the parent's level of knowledge on this topic, no statistically significant differences were identified between the two sexes ($p=0.853$), between different levels of education ($p=0.628$), and also the absence or presence of parents' fear of the dentist and their level of knowledge are not correlated ($p=0.723$), therefore the two research hypotheses are not confirmed.

Concerning dental fear, 16% of the parents in our study were reported to be afraid of the dentist. The study revealed that in 14% (n=7) of the study group, fear of the dentist was present in both parents and children and in 2% (n=1) fear of the dentist was present in the parent, but not to the child. In 4% (n=2) fear of the dentist was absent in the parent and present in the child, and in 80% (n=40) fear of the dentist was absent in both the child and the parent. These information are summarized in Table 1. The differences between dental fear of parents and their children proved to be statistically significant according to the chi-square test ($p<0.001$).

Table 1. The parent's dental anxiety related to the child's dental anxiety

Dental anxiety of the parent	Child dental anxiety		Total
	Present	*absent*	
present	7 (14%)	1 (2%)	8 (16%)
absent	2 (4%)	40 (80%)	42 (84%)

Parents' knowledge of dental caries and oral health habits are as follows: the majority of mothers (83.9%) and fathers (84.2%) do not consider dental caries to be contagious diseases, and statistical differences are again not significant between sexes (p =0.975). Over 90% of parents know that decayed temporary teeth need to be treated and that the toothbrush should be changed between 0-3 months. A percentage of 32.3% of mothers and 47.4% of fathers consider tooth brushing sufficient to prevent dental caries. Moreover, 53.2% of mothers and 47.4% of fathers do not know the moment when they should start brushing their child's teeth. When asked about the cause of dental caries, 44% of parents consider food and drinks, 12% consider dental plaque and tartar, 10% of parents attribute dental caries to genetic causes and 12% to bacteria and viruses.

Regarding children's nutrition habits, the questions focused on the frequency of dairy, sugar and carbonated drinks consumption. The results are summarised in Figure 1.

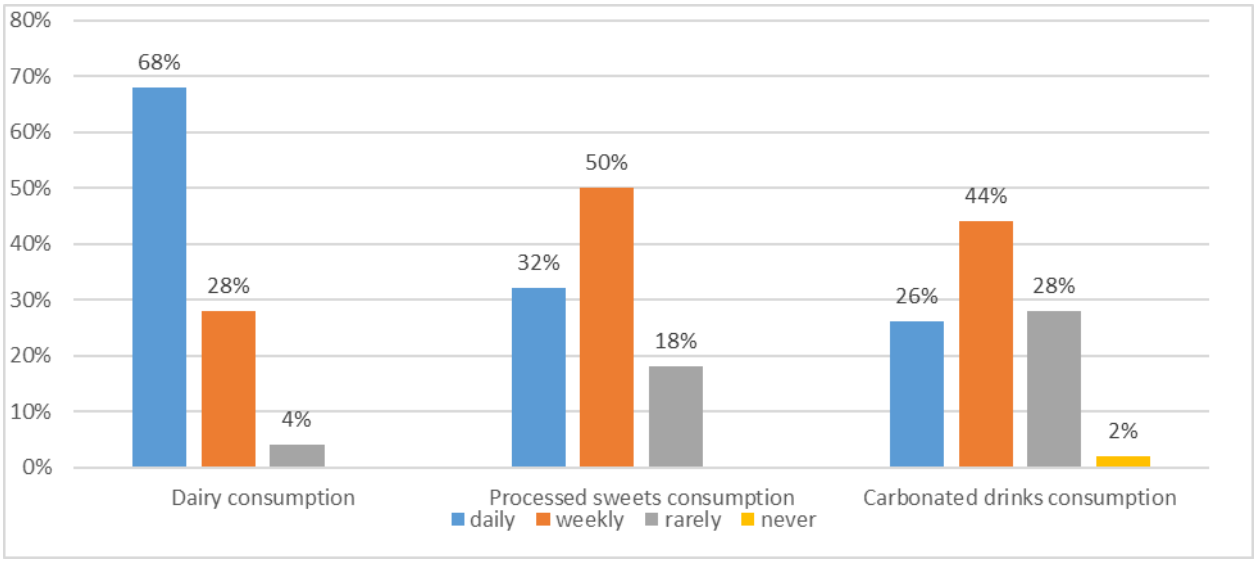

Figure 1. Chart of the nutrition habits in preschool children

DISCUSSIONS

Oral health behaviours that begin in childhood continue to have an impact into adulthood. Given the influence that parents have on their children, it is important to examine parents' attitudes toward factors that influence children's oral health. This study provides important data on parental knowledge of their children's oral health.

In this study, 84% of the children were visiting the dentist for the first time compared to 18% of the children in the study group published by Köse et al (24). Furthermore, the percentage of parents who believe that other diseases can be caused by tooth decay is much lower in our study (62%) compared to that in the study published by Wyne et al. (98%) [25].

Also, more than 80% of the participants did not consider dental caries to be a contagious disease. In the study by Saied Moallemi et al., approximately 75% of mothers believe that temporary teeth should be treated if they are affected by caries [26]. In the present study, the majority of participants stated that temporary teeth should be treated if necessary, approximately 71% of mothers. After the eruption of the first tooth, tooth brushing should

begin. In Jain et al.'s study, the correct response rate for when to start brushing was 21% [27]. The proportion of correct answers in our study was only 24%. The incorrect answer given by most parents reflects a serious concern for the oral health of children and for development of early childhood caries. On the other hand, the percentage of parents who knew it was necessary to change the toothbrush every three months was much lower in the study of Jain et al [27] - (52%), compared to our study (92%). Parents' answers regarding dental caries and oral health habits did not show a statistically significant difference according to gender, level of education, fear of the dentist or parents' previous knowledge and attitudes about oral health, these conclusions also being reported in the study published by Köse et al [24].

The present study had some limitations, like the small sample size, with only 50 parents who met the study criteria agreeing to complete the questionnaire, and the low sociodemographic diversity since the study was conducted in a single university clinic.

CONCLUSIONS

The study showed that the parent's gender, level of education and fear of the dentist do not influence their knowledge about dental caries, eruption of temporary teeth, eruption of permanent teeth and oral health. However, there seems to be a correlation between the dental fear of the parent and that of the children, and also between oral hygiene practices of parents and their children.

Conflicts of Interest

The authors declare no conflict of interest.

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Effects of Acidic Beverages on Teenagers Dental Enamel – A literature review

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Abstract

1.Background/Objectives: This review article explores the significant relationship between dietary choices, particularly the consumption of acidic and sugary beverages, and oral health outcomes. Understanding the impact of these dietary factors is essential for developing preventive strategies and promoting healthier habits. 2.Methods: A comprehensive analysis of recent studies was conducted to evaluate the effects of acidic and sugary beverages on dental health, focusing on dental erosion, caries development, and changes in salivary ph. Additionally, the role of marketing strategies in influencing consumer behavior was examined. 3.Results: Findings indicate that frequent consumption of acidic beverages leads to enamel erosion and contributes to caries formation. Public health initiatives aimed at educating individuals about healthier dietary choices play a crucial role in mitigating these effects. Furthermore, marketing strategies significantly influence beverage consumption patterns, highlighting the need for targeted interventions. 4.Conclusion: The evidence underscores the necessity of preventive measures, including dietary counseling and improved oral hygiene practices, to reduce the adverse effects of acidic and sugary beverages. Further research is needed to explore the long-term implications of dietary habits on oral health and to develop effective intervention strategies.

Keywords: oral health, acidic beverages, sugary drinks, dental erosion, salivary pH, preventive measures

INTRODUCTION

Teenagers' oral health problems today are closely linked to their dietary choices, particularly the consumption of food and beverages. Research shows that diet and oral health are interconnected in numerous ways [1,2]. Many adolescents are consuming high levels of sugar found in soft drinks and carbonated drinks, and inadequate dental hygiene further exacerbates their oral health issues.

Dental caries remains the leading cause of disease in both developed and developing countries [1]. The etiology of dental caries is multifactorial, influenced by socio-economic factors, behaviour, genetics, oral pH control, bacterial colonization and adhesion, the physicochemical properties of teeth, time, carbohydrate intake, and lifestyle [1,2,3]. Acidic foods and drinks, characterized by low pH levels, play a critical role in the development of dental erosion [1]. However, it is important to note that the pH of a food substance alone is not sufficient to cause erosion [1].

During the COVID-19 pandemic, there was a notable increase in the consumption of carbonated drinks among children, leading to a rise in the DMFT (Decayed, Missing, and Filled Teeth) index. The first carbonated beverages emerged in the latter half of the nineteenth century. Today, carbonated drinks based on fruit syrups are widely popular due to their refreshing taste [1,4,5]. Changes began in the 1890s, when industries developed beverage-based alternatives to cola extracts, initially thought to have medicinal properties [1,6]. The proliferation of manufacturing companies has made these beverages readily available, raising significant concerns about their cariogenic and erosive characteristics [7,8].

Research has highlighted certain foods and beverages with high acidity levels, such as fruits, fruit juices, alcoholic beverages, and carbonated drinks, as well as the timing of their consumption—whether during main meals or as snacks [9]. If left unaddressed, enamel erosion can lead to dentinal hypersensitivity and pain [10,11]. Dental erosion affects both primary and permanent dentition [12].

The consumption of soft drinks leads to a reduction in salivary pH [13]. A pH of 5.5 is recognized as the "critical pH" for enamel dissolution, while the critical pH for dentin is 6.8 [14]. Carbonated drinks exhibit extrinsic acidity, with pH values as low as 2.5 due to the carbonic acid formed when CO2 is added, alongside other acids like citric, phosphoric, and tartaric acids [8,15,16]. Factors such as the type and quantity of acids present, the buffering capacity, and the drink's temperature all contribute to its enamel-dissolving potential [17,18, 19]. Additionally, organic acids produced by the fermentation of sugar in beverages by oral microorganisms in plaque further contribute to demineralization and caries. The unique characteristics of dental enamel differ at both the macro- and micro-structural levels [20,21].

Thus, analyzing the mechanisms of enamel erosion requires a microscopic perspective [22,23]. The erosive power of these drinks has been studied chemically using Fourier infrared spectroscopy (micro FTIR) [24,25]. This review aims to assess findings from the past 10 years in comparison with current data to evaluate the evolution of teenage carbonated beverages consumption and its effects.

Frequent consumption of carbonated beverages among adolescents leads to a significant reduction in salivary and oral pH, resulting in increased enamel erosion and a higher risk of dental caries.

Aim and objectives

The main objective of this study is to evaluate the effects of carbonated drinks on the dental enamel of adolescents. Specifically, the study aims to analyze changes in pH and acid concentrations in carbonated beverages, assess the impact of these beverages on the integrity

of dental enamel, and identify correlations between the frequency of carbonated drink consumption and the severity of dental enamel deterioration.

MATERIAL AND METHODS

PubMed, Scopus, and Web of Science were searched for papers relevant to our topic, covering the period from January 1, 2012, to January 31, 2022, with a restriction to English-language publications. The search strategy utilized a combination of keywords aligned with our investigation's primary objective: studying the relationship between acidic drinks consumption and teenagers' oral health.

Eligibility Criteria

The inclusion criteria were as follows: (1) participants must be teenagers; (2) studies should be human in vivo or in vitro research; (3) publications must be in English; (4) only open access studies were considered; (5) articles and reviews needed to be published no later than 2012; (6) randomized clinical trials were included; (7) research must focus on the effects of carbonated drinks on dental enamel.

The exclusion criteria included: (1) animal studies; (2) publications in languages other than English; (3) non-open access studies; and (4) case reports/series, reviews, editorials, and book chapters published after 2012.

The review followed the PICOS criteria:

- **Participants:** Teeth from teenagers were included, both in vivo and in vitro.
- **Interventions:** Significant consumption of any acidic beverages.
- **Comparisons:** No significant consumption of any acidic beverages.
- **Outcomes:** Damage to dental enamel.

Study: Clinical trials on human teeth, encompassing both in vivo and in vitro studies.

RESULTS

The initial search provided a total of 350 items (PubMed n = 130, Scopus n = 120, WOS n = 100), and after removing 180 duplicates, 170 articles remained. A total of 156 articles progressed to the screening phase, when an additional 118 were excluded for lack of relevant data. Other 38 items were excluded for the following reasons: 22 due to lack of free full text, 3 involving animal studies, and 13 deemed off-topic, resulting in 20 records that met the eligibility criteria for inclusion. Of these, 4 were in vivo studies (Table 1), 4 were in vitro studies (Table 2), and 12 were reviews (Table 3). A PRISMA chart was included to visually summarize the process of selecting studies, ensuring transparency and reproducibility in the systematic review process (Figure.1) [26].

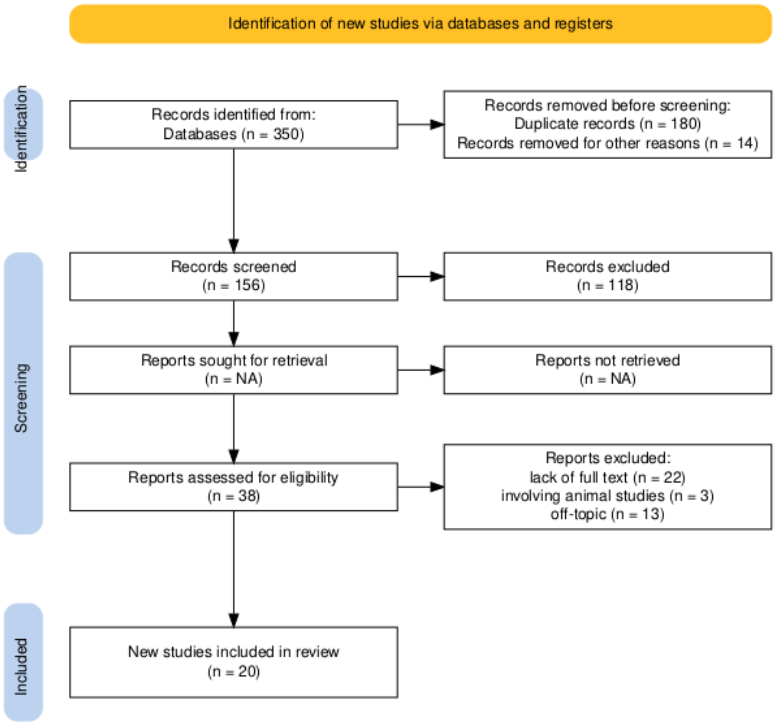

Figure 1. PRISMA flowchart of study selection

Table 1. Selected articles that included in vivo studies

Study	Year of publication	Focus of the Investigation	Type of Study	Sample Size	Results
Pachori et al. [3]	2018	Effects of foods and beverages on salivary pH	Clinical study measuring salivary pH	50	Various foods and beverages significantly changed salivary pH, with acidic foods lowering it notably.
Hadilou et al. [4]	2022	Impact of sugary and acidic beverages on dental caries	Cross-sectional study using DMFT index	5.006	Increased DMFT dex linked to frequent consumption of sugary and acidic beverages.
Al-Zwaylif et al. [8]	2018	Dietary acids and their effect on tooth wear	Clinical study measuring tooth wear	5,586	Strong correlation between dietary acid intake and increased tooth wear.
Hans et al. [12]	2016	Sugary beverages and their impact on salivary pH	Clinical study assessing salivary pH	120	Significant drop in salivary pH after sugary beverage consumption, affecting enamel demineralization.

Table 2. Selected articles that included in vitro studies

Study	Year of Publication	Focus of Investigation	Type of study	Sample Size	Results
Gondivkar et al.) [7]	2018	Erosive potential of soft drinks and fruit juices	In vitro study measuring enamel dissolution	21	High erosive potential observed in soft drinks and packaged fruit juices.
Morgado et al. [13]	2022	Impact of still and carbonated waters on dental erosion	In vitro analysis of enamel	105	Both still and carbonated waters affected dental erosion based on pH levels, with carbonated water posing higher risk.
Charpe MP et al. [20]	2019	Erosive potential of carbonated beverages on teeth	In vitro study examining enamel solubility	15	Significant increase in enamel solubility due to exposure to carbonated beverages.

Seredin et al. [21]	2022	Use of nanocrystalline hydroxyapatite for enamel protection	Laboratory study using nanocrystalline hydroxyapatite	50	Promising results for nanocrystalline hydroxyapatite in protecting enamel against acid-induced erosion.

Table 3. Selected review-type articles

Study	Year of Publication	Focus of Investigation	Type of Study	Sample Size	Results
Scardina & Messina [2]	2012	Relationship between diet and oral health	Literature review of clinical and epidemiological studies	N/A	Emphasized the role of a balanced diet in maintaining good oral health and preventing diseases.
Elmore B. [5]	2012	Beverage industry influence on public health	Policy analysis	N/A	Discussed the beverage industry's impact on public health and consumption patterns.
Johansson et al. [27]	2017	Increasing concern over dental erosion due to beverage consumption	Literature review	26	Linked growing dental erosion concerns with rising soft drink and juice consumption.
Kregiel D. [14]	2015	Health risks associated with soft drinks	Literature review on health risks	N/A	Highlighted microbial contamination and erosive impacts of soft drinks on dental enamel.
Barbour & Lussi [16]	2014	Nutrition and environmental factors contributing to dental erosion	Comprehensive review	N/A	Discussed how nutrition and environmental factors contribute to dental erosion.
Davari et al. [9]	2013	Review of dentin hypersensitivity and dietary factors	Literature review	N/A	Noted that acidic foods and drinks exacerbate dentin hypersensitivity through enamel erosion.
Buzalaf et al. [17]	2012	Role of saliva in protecting against dental erosion	Literature review	N/A	Emphasized saliva's protective role against dental erosion and the impact of acidic beverages.
Alcântara et al. [10]	2018	Lifestyle factors and cervical dentin hypersensitivity	Questionnaire-based clinical study	308	Identified a link between acidic diets and cervical dentin hypersensitivity symptoms.

The studies collectively highlight that acidic and sugary beverages significantly lower salivary pH, increasing the risk of enamel demineralization and dental caries. Frequent consumption of these beverages is consistently linked to higher DMFT scores, indicating greater tooth decay. Dietary acids, soft drinks, fruit juices, and carbonated beverages show strong erosive potential, contributing to enamel wear and dissolution.

DISCUSSIONS

The studies included in this review demonstrate a clear connection between dietary choices, particularly the consumption of acidic and sugary beverages, and oral health outcomes. The findings consistently highlight that:

Dietary Influence on Oral Health: The relationship between diet and oral health is multifaceted, with evidence indicating that acidic foods and beverages can lead to dental erosion and increase the risk of caries. Studies such as those by Pachori et al. (2018), in their

article "Effects of Foods and Beverages on Salivary pH," and Hadilou et al. (2022), in "Impact of Sugary and Acidic Beverages on Dental Caries," emphasize the need for increased awareness regarding the erosive potential of common dietary choices among adults.

Salivary pH and Erosion Risk: The importance of salivary pH as a protective factor against dental erosion is reinforced by multiple studies. The findings of Hans et al. (2016) in "Sugary Beverages and Their Impact on Salivary pH" suggest that frequent consumption of acidic beverages significantly lowers salivary pH, which can contribute to enamel demineralization and subsequent dental issues.

Impact of Beverage Marketing: Marketing strategies employed by beverage companies, as explored by Huse et al. (2022) in "Coca-Cola's Marketing Strategies and Soft Drink Consumption," play a significant role in shaping consumer behavior. The increasing consumption of sugary drinks, often marketed as refreshment, highlights the necessity for public health interventions aimed at reducing their intake to mitigate the associated oral health risks.

Preventive Measures and Interventions: There is a growing recognition of the need for preventive measures, including dietary counseling and education on oral hygiene practices, to minimize the impact of harmful dietary choices on dental health. The findings of Buzalaf et al. (2012) in "Role of Saliva in Protecting Against Dental Erosion" underscore the critical role of saliva in protecting against erosion, suggesting that maintaining salivary flow should be a focus of preventive strategies.

Future Research Directions: The literature indicates a significant gap in longitudinal studies that explore the long-term effects of dietary choices on oral health. Future research should aim to investigate the cumulative effects of dietary habits over time and identify effective interventions that can promote better oral health outcomes in diverse populations.

Enamel, despite being the hardest tissue in the body, remains susceptible to chemical exposure from substances found in sodas and other beverages [33]. Two key parameters for evaluating the damage caused by the acids in carbonated drinks are the roughness and hardness of the enamel surface. Research has indicated that increased roughness often represents the initial stages of enamel erosion [34]. Daily consumption of carbonated drinks significantly heightens the risk of tooth erosion [12, 40, 41]. Alarmingly, these beverages, now ubiquitous in modern society, frequently replace water as a primary source of hydration [33].

Dental issues rank among the most prevalent health concerns among young people [32]. The most commonly consumed acidic beverages include soft drinks and fruit juices [33]. Certain studies have shown that poor nutrition during childhood leads to carious surfaces on teeth [31]. These studies employed targeted maximum likelihood estimation to effectively address modeling challenges associated with longitudinal data in pediatric research [31,35,36]. Additionally, some in vivo studies have investigated the prevalence of dental caries in adolescents, attributing findings to inadequate oral hygiene and poor dietary habits [32].

Various factors influencing the erosive potential of different carbonated beverages and fruit juices have been explored [8]. The erosive potential of a beverage is notably impacted by its mineral content and its capacity to chelate calcium from foods and beverages [34]. Consequently, erosion is not solely determined by the pH of carbonated drinks, which is primarily influenced by the content of carbonic acid in dissolved carbon dioxide [24]. Daily consumption of soft drinks has been associated with dental deterioration, and drinking these beverages with meals correlates with both mild and severe tooth decay [9].

Saliva plays a critical role in physiological conditions, providing buffering capacity and forming a protective barrier that minimizes direct contact between enamel and acidic drinks, thus shielding teeth from acid attacks [8]. The rising consumption of carbonated drinks among children and adolescents contributes to increased dental erosion and caries [1,

9]. The issue of enamel erosion is particularly concerning for deciduous teeth [39]. Categories such as sports and energy drinks, fruit juices, and carbonated soft drinks rank among the most acidic beverages, significantly diminishing enamel surface hardness due to mineral loss. Participation in sports has been closely linked to erosive injuries, with dietary needs associated with various physical activities emerging as strong predictors of these injuries among teenagers [1, 22].

CONCLUSIONS

In conclusion, the evidence presented in this review underscores the significant impact that dietary choices, particularly the consumption of acidic and sugary beverages, have on oral health. The studies collectively emphasize the urgent need for public health initiatives focused on educating individuals about the potential risks associated with their dietary habits. Key takeaways from the research highlight the critical role of salivary pH and its relationship to dietary intake, with acidic beverages posing a notable risk to dental health. Additionally, the review calls for targeted marketing regulations and health campaigns aimed at reducing the consumption of erosive beverages. Preventive strategies, such as dietary modifications and improved oral hygiene practices, are also highlighted as essential measures to mitigate the risks of dental erosion and caries. Ongoing research remains crucial in further understanding the complex interactions between diet and oral health, paving the way for innovative preventive measures and therapeutic interventions that can improve oral health outcomes for individuals of all ages.

Conflicts of Interest

The authors declare no conflict of interest.

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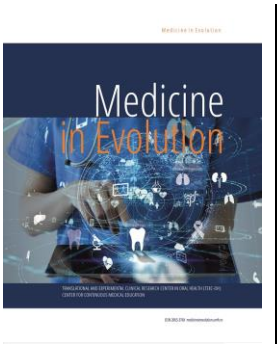
The Association Between Fisetin and Rutin Triggers an Enhanced Cytotoxicity in A431 and A375 Skin Cancer Cells



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Abstract

Background: Skin cancer is a public health problem and conventional treatments lead to multiple limitations that affect patients' well-being. Fisetin and rutin are two phytocompounds that have demonstrated versatile biological properties, including anticancer effects. Methods: A431 and A375 cells were used to evaluate the two compounds and their associative treatment. For investigation, after 24 hours of treatment, cell viability was assessed by MTT technique and cell morphology was analyzed. Results: The results indicated that the associative treatment is more potent compared to the individual treatment of the agents, producing a dose-dependent decrease in cell viability and enhancing cell dimorphologies with increasing the concentration. Conclusion: Associative treatment represents a promising approach as an alternative for skin cancer, exerting a superior effect compared to individual treatment. However, future research directions should be directed towards elucidating the mechanism of action of the FIS+RUT treatment, assessing the impact in 3D experimental models, and verifying the efficacy by incorporation into different nanoformulations.

Keywords: fisetin, rutin, skin cancer, melanoma, in vitro

INTRODUCTION

Skin cancer is among the most common cancers in the United States and can be broadly categorized into melanoma or nonmelanoma skin cancer. Recent studies have shown an alarming increase in cases in recent decades, but nevertheless the exact incidence is difficult to detect due the under-reporting. The treatment strategies are varied and include surgical excision, cryotherapy, chemotherapy or immunotherapy, but the current options are considered a global health problem which affects the well-being of cancer patients due to a number of disadvantages [1,2]. In these aspects, botanical compounds have shown to be promising agents for the prevention and alternative treatment of skin cancers and melanomas, possessing versatile biological activities that make them the subject of numerous research studies [3,4]. Furthermore, it was noted that phytocompounds offer the advantage of a non-toxic profile and a pleiotropic mechanism of action [5]. Medicinal phytochemical compounds are found in a multitude of sources (e.g. plant, marine, microbial) and have been found to include chemo-preventive abilities that have been suggested to be closely related to antioxidant properties. Since it has been realized that natural products may have potential in the symptomatic treatment of cancers and in addition may reduce the adverse effects produced by anticancer therapy, there is an increasing rate of self-medication represented by the oncology patient population who choose botanical agents due to their safety and efficacy [6].

(FIS) and rutin (RUT) are two natural compounds belonging to flavonoid class [7]. FIS is a phytoestrogenic flavonoid distributed in various fruits and vegetables and with numerous biological properties including anti-inflammatory, antioxidant and anticancer effects through anti- invasion, anti-metastatic and apoptosis promoting activities by increasing pro-apoptotic Bax and caspase 3/8. Additionally, it was also noted that FIS modulates different signaling pathways and increases the efficacy of chemotherapeutic agents [5]. RUT presents a diverse spectrum of pharmacological properties, including anti-inflammatory, antioxidant, antibacterial and antimutagenic. Besides, RUT has been shown to minimize photoaging of the skin by enhancing skin density and elasticity through the regulation of extracellular matrix enzymes [8–10]. An important fact is that the natural compound RUT demonstrated its ability in a panel of cancers, including cutaneous melanoma [11]. The skin is the largest organ of the human body which has the role of protection against external factors such as radiation, chemicals, allergens or infections. Alongside the aforementioned abilities in skin cancers and melanoma, flavonoids have also revealed their therapeutic potential for a number of other skin-related conditions (e.g. atopic dermatitis, psoriasis, vitiligo) [12].

Aim and objectives

The aim of the current work was the in vitro assessment of two natural compounds belonging to the flavonoid class, namely FIS and RUT and their association (FIS + RUT), regarding their impact on two distinct 2D cancer cell lines, i.e. the A431 (epidermoid carcinoma) and the A375 (malignant melanoma) cell lines.

MATERIAL AND METHODS

Reagents and Instruments

The tested samples fisetin and rutin and the MTT (3-(4,5-dimethylthiazol2-yl)-2,5-diphenyltetrazolium bromide) kit were obtained from Sigma-Aldrich, Merck KGaA (Darmstadt, Germany). The Dulbecco's Modified Eagle Medium (DMEM) and dimethyl

sulfoxide – DMSO (solvent) were obtained from PAN-Biotech GmbH, Aidenbach, Germany; fetal bovine serum (FBS- 30-2020 ™), the penicillin/streptomycin mixture, and trypsin-EDTA solution were purchased from American Type Culture Collection (ATCC) Manassas, VA, USA. The devices used, Cytation 5 (plate reader) and Lionheart FX (automated microscope) were from BioTek Instruments Inc. (Winooski, VT, USA).

Cell Culture Conditions

The experiments were performed using two different 2D cell lines: A-431 CRL-1555 ™ (epidermoid carcinoma) and A-375 CRL-1619 ™ (malignant melanoma) obtained from ATCC, Manassas, VA, USA. Both cell lines were cultured in the specific growth medium DMEM supplemented with 10% FBS and 1% antibiotic mixture (100 U/mL penicillin/100 µg/mL streptomycin). The cells were maintained in a humidified incubator, at 37°C and 5% CO2. Fisetin and rutin were dissolved to form the stock solution in DMSO. The concentration of DMSO did not exceed 0.5%.

Cell Viability – The MTT Test

The cell viability was evaluated via the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) method to observe the impact of FIS, RUT and FIS+RUT (30, 40 and 50 µM) on A431 and A375 cells. After 24 hours, 100 µL of fresh medium and 10 µL of MTT were inserted to each well and the plates were introduced in the incubator. After 3 hours of incubation, 100 µL of MTT solubilizing solution were added and the plates were maintained for 30 minites at room temperature. The absorbance was read at 570 and 630 nm wavelengths at Cytation 5.

Bright-Field Cell Morphology Evaluation

The impact of the test samples FIS, RUT and FIS+RUT (30, 40 and 50 µM) on A431 and A375 cell morphologies was evaluated by taking representative photos of the control group (untreated cells) and treated cells under brightfield illumination (magnification 20×) using the Lionheart FX automated microscope. The obtained pictures were processed in the Gen5™ Microplate Data Collection and Analysis Software (Version 3.14) - BioTek Instruments Inc. (Winooski, VT, USA).

RESULTS

The impact of FIS, RUT and FIS+RUT Treatment on Cell Viability

In the case of treatment of A431 cells with FIS (Figure 1A), the results obtained indicated that cell viability decreased in a concentration-dependent manner, i.e. treatment with 30 µM FIS reduced cell viability to 40%and the highest concentration tested of 50 µM produced a decline in cell viability to a threshold of 31%. Treatment with RUT in A431 cells (Figure 1B) exhibited a dose dependent reduction in cell viability, reaching at the highest concentration tested (50 µM) a percentage of 64%. The combinatorial treatment between RUT and FIS (Figure 1C) resulted in a decreasing cell viability under the same dose-dependent trend, with the percentages gradually diminishing with increasing dose from 36% (at the lowest concentration of 30 µM) to 26% (at 50 µM).

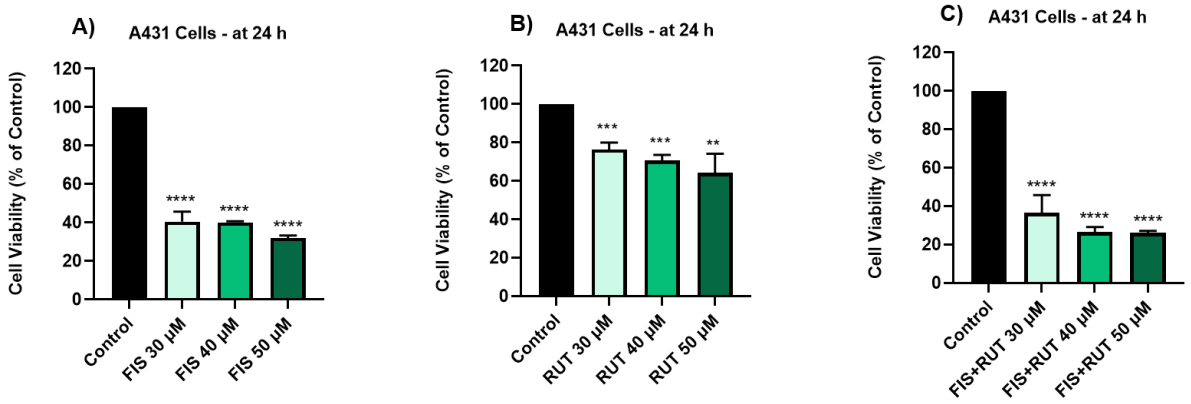

Figure 1. Graphical representation of cell viability percentages 24 hours after treatment of A431 cells with (A) FIS (30, 40, 50 µM), (B) RUT (30, 40, 50 µM), (C) and the combinations between FIS and RUT (30, 40, 50 µM). The results are presented as percentages (%) normalized to control (untreated cells). All data are expressed as mean values ± SD from three independent experiments done in triplicate. For analyzing the statistical differences between the control group - untreated cells and treated groups, the One-way ANOVA test was conducted, followed by the Dunnet's multiple comparison post-test. "*" marks statistical significance (** $p<0.01$; *** $p \leq 0.001$; **** $p \leq 0.0001$).

For A375 cells, the treatment with FIS (Figure 2A) slightly reduced the cell viability concentration-dependently up to 87%, which was observed at the highest concentration examined, i.e. 50 µM; and according to Figure 2B, RUT decreased cell viability up to 91%.The associative treatment of FIS + RUT (Figure 2C) provided for the 30 µM treatment a cell viability of 83%, at the 40 µM treatment the cell viability decreased to 80%, while at the highest concentration of 50 µM the threshold of about 74% was reached.

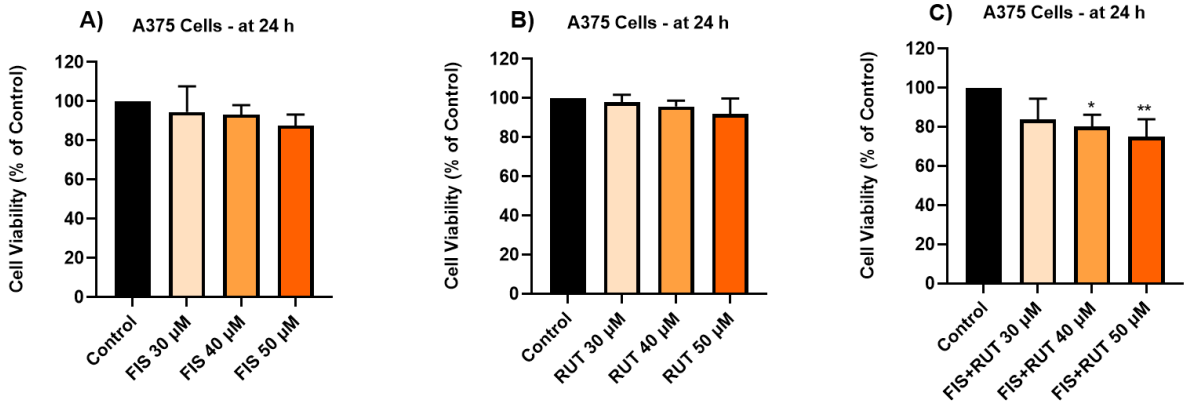

Figure 2. Graphical representation of cell viability percentages 24 hours after treatment of A375 cells with (A) FIS (30, 40, 50 µM), (B) RUT (30, 40, 50 µM), (C) and the combinations between FIS and RUT (30, 40, 50 µM). The results are presented as percentages (%) normalized to control (untreated cells). All data are expressed as mean values ± SD from three independent experiments done in triplicate. For analyzing the statistical differences between the control group - untreated cells and treated groups, the One-way ANOVA test was conducted, followed by the Dunnet's multiple comparison post-test. "*" marks statistical significance (* $p < 0.05$ and ** $p<0.01$).

Analysis of Cellular Morphology

The next step of the investigation of FIS, RUT and FIS+RUT combinatorial treatment after 24 hours of treatment on A431 and A375 cells was to analyze the cell morphology. In the case of A431 cells, as shown in Figure 3, FIS treatment produced a dose-dependent decrease in cell confluency, with the highest concentration of 50 µM showing a massive rounding of the shape and a decrease in size. Application of RUT treatment decreased cell confluence gradually and produced cell rounding at 50 µM, while the combinatorial treatment between

FIS and RUT showed dysmorphologies from the lowest concentration of 30 µM that were accentuated in a dose-dependent manner up to 50 µM where a massive cell rounding, reduced confluence and signs of detachment of cells from the plate were noticed.

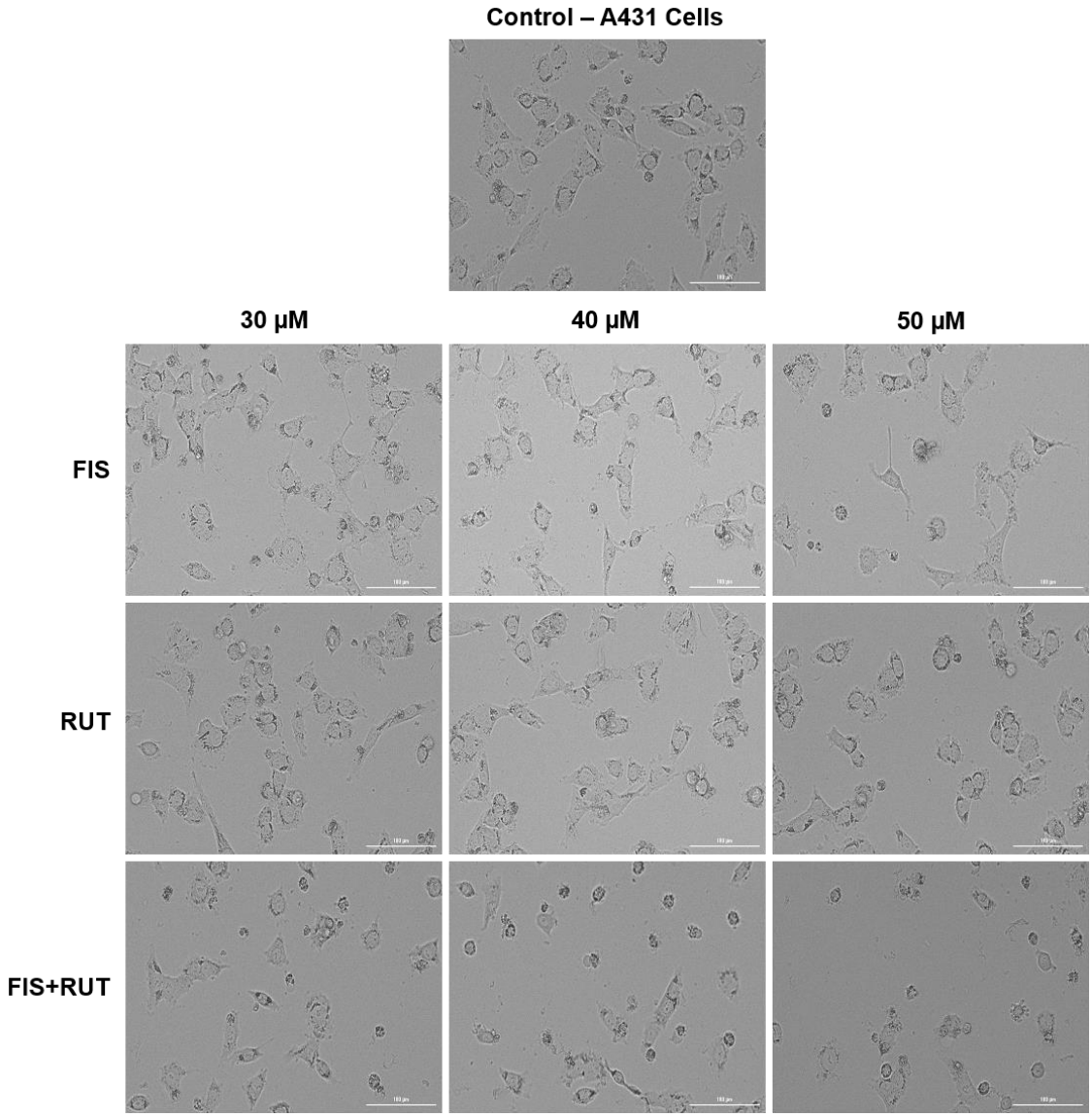

Figure 3. Representative images illustrating the morphological changes observed at 24 h of treatment of A431 cells with FIS (30, 40, 50 µM), RUT (30, 40, 50 µM) combinations between FIS + RUT (30, 40, 50 µM), The pictures were taken at a magnification of 20×, and the scale bar indicates 100 µm

For A375 cells (Figure 4), the 24 h treatment with FIS and RUT did not induce significant changes in cell morphology. In contrast, upon application of the combinatorial treatment between FIS and RUT, at the highest tested concentration of 50 µM, slight signs of detachment of the cells from the plate and a reduction in confluency could be observed.

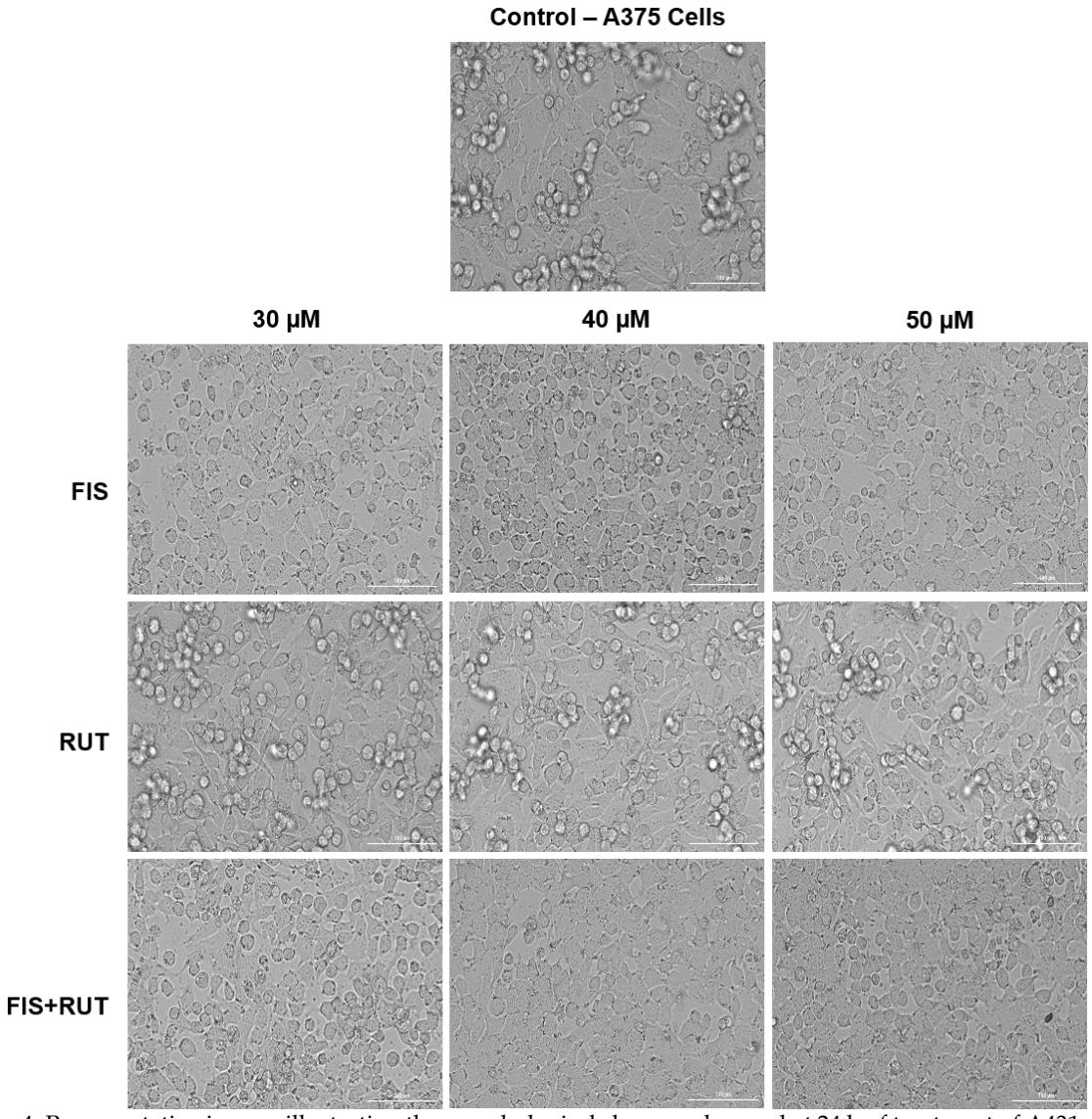

Figure 4. Representative images illustrating the morphological changes observed at 24 h of treatment of A431 cells with FIS (30, 40, 50 µM), RUT (30, 40, 50 µM) combinations between FIS + RUT (30, 40, 50 µM), The pictures were taken at a magnification of 20×, and the scale bar indicates 100 µm

DISCUSSIONS

Skin cancer is one of the most aggressive forms of cancer and is formed by the non-repair of deoxyribonucleic acid in skin cells which leads to mutations and genetic defects. There are certain parameters such as symmetry, color, shape or size that are used to identify skin cancer and to differentiate melanoma from benign skin cancer [13]. Considering the current treatments, there are several limitations among which the most recognized include toxic effects, high costs and resistance to treatment [2] . Phytochemicals are biologically active products that are derived from plants, and in recent decades have been found to possess multiple anti-cancer properties that are cost-effective and tolerated. Also, the anticancer activities exerted by herbal compounds are the result of their antioxidant, anti-inflammatory, anti-proliferative and anti-angiogenic properties [14]. Based on these reasons, researchers have turned their attention to finding new approaches or therapeutic alternatives for the management of skin cancers.

The objective of the present study was the evaluation of two natural compounds FIS and RUT, and the associative treatment of FIS+RUT on two distinct cell lines A431 and A375. RUT and FIS were selected on the basis of the specialized literature, that proved that the two flavanoids compounds exhibit potential in the alternative treatment of skin cancers and cutaneous melanomas, expressing anti-proliferative and anti-invasive effects on cancer cells. The concentration range chosen for the investigation was also considered taking into account the results indicated in the scientific literature, in which the two botanical compounds have been reported to display therapeutic effects on cancer cells [5,11]. The results suggested that for both compounds and for the associative treatment, the reduction in cell viability was dose-dependent in A431 cells (which were more strongly impacted by the treatment) and in A375 cells. FIS has been shown to inhibit growth and colony formation in A431 cells. Thus, another study showed that following MTT analysis, FIS (5- 80 μM) acts in a time- and dose-dependent manner and complementarily induces cell apoptosis and G2/M arrest [15]. FIS was also tested for 72 h in A375 cells where at 20 μM it decreased cell viability up to 86.40% [5]. Furthermore, FIS was also explored in combination with other compounds, i.e. aspirin, to check the combinatorial potential in the treatment of A375 cells and the results obtained showed promising results, the therapeutic association between the natural compound and aspirin being more potent compared to individual treatment of the compounds on cancer cells for a period of 72 hours [5]. About RUT was demonstrated to have the capacity to attenuate superoxide production, decrease adhesion and migration of human cancer cells and induce in vitro cytotoxicity in cancer cells [10] In addition, the bioflavonoid RUT modulates multiple signaling pathways among which can be listed NF-κB, PI3K/Akt/mTOR, Nrf2, ERK, JNK, or p38 MAPK [9]. Similarly, one study showed that RUT (1-50 μM) decreases the viability of RMPI-7951 and SK-MEL-28 malignant melanoma cells in a concentration-dependent manner after 24 hours of treatment, reaching at the highest concentration a cell viability of 60% for RPMI-7951 cells and 51.48% for SK-MEL-28 cells [11]. In order to investigate the cytotoxicity, microscopic analysis of cell morphology are crucial tools, providing information about the mechanism of action of the targeted samples and about the type of cell death involved [2]. The results of the cell morphology investigation suggested that the two compounds exert a more pronounced action when combined for both cell lines used in the study. In A431 cells, Pal et. al showed that treatment of cells with FIS significantly decreases the number of colonies compared to untreated cells. In the same study, using Annexin V/PI staining, FIS was observed to induce apoptosis of skin cancer cells [15] . Also, Iftode and colleagues noticed that at the morphologic level, treatment with FIS 20 μM for 72 hours caused a confluency reduction of A375 cells [5]. On the A375 cell line, RUT was further assayed in the dose range 1-75 μM for 24 hours and the data yielded that with increasing dose the cell confluency decreases, and at the highest concentrations cells become rounded and lose adhesion [8].

Moreover, an important aspect to investigate concerning the compounds with potential in anticancer therapy is their behavior on healthy cells. In this respect, both FIS and RUT have been evaluated individually in different healthy cell lines (such as HaCaT keratinocyte cells) and the data obtained indicated that the two compounds do not induce cytotoxicity [8]. This selectivity behavior of the two compounds represents an additional advantage, because among the primary limitations of chemotherapy is the lack of specificity on the target, often affecting healthy cells and consequently causing adverse effects to patients by compromising the immune system, chemotherapy having the ability to destroy even immune cells [16]. Combinatorial treatments between two naturally derived agents constitute a potentially effective approach for the treatment of different skin cancers, thus several studies with the objective of evaluating an associative treatment between two phytocompounds presented promising results [17].

The findings of the present work showed that RUT+FIS associative treatment exerted superior effects compared to individual administration of the compounds in skin cancer cells. In view of these aspects, future directions should focus on investigating the mechanism of action underlying the anticancer activity of the two compounds, as well as the association between the two substances; assessing the combinatorial treatment on 3D experimental models; performing a detailed screening of the associative treatment in healthy tissues; and studying the association of FIS+RUT in nanoformulations.

CONCLUSIONS

The results framed that FIS and RUT compounds are promising candidates as an alternative for skin cancer. Additionally, the combinatorial treatment of FIS and RUT demonstrated a stronger effect than individual treatment on A431 and A375 cells which was described by a dose-dependent decrease in cell viability and the induction of cellular dysmorphologies that were intestified with increasing the concentration.

Conflicts of Interest

The authors declare no conflict of interest.

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A Therapeutic Approach in Cardiac Patients to Induce Anesthesia – a Brief Review

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Abstract

1.Background/Objectives: Anesthesia is an important achievement of modern medicine, which ensures the quality of life of patients and also provides additional comfort, safety, and accuracy to specialists. Cardiac disorders are one of the leading causes of morbidity and mortality worldwide. Anesthesia in cardiac patients is intricate and needs careful analysis. This study aims to analyze the anesthetics used in cardiac patients, with a focus on the induced side effects. 2.Methods: The present review analyzed papers retrieved from PubMed, ScienceDirect, and Google Scholar, following the keywords: "general anesthetic", "local anesthetic", "analgesic", "sedative", "side effect" and "cardiac effect". 3.Results: The term opioid-free anesthesia has been introduced around for a while. Lidocaine, ketamine, and dexamethasone are the three popular non-opioid analgesics used in cardiac surgery. The effects of midazolam, etomidate, and dexmedetomidine on the cardiovascular system during the phacoemulsification process using local topical anesthesia are also confirmed. Other studies have shown the cardioprotective benefits of propofol, in addition to anti-inflammatory properties. 4.Conclusion: Cardiac pathology is a constantly evolving problem that requires the involvement of anesthesia, therefore it is essential to know the particularities of anesthetic drugs in the case of these subjects.

Keywords: anesthesia, cardiac disorder, anesthetic drugs, side effects

INTRODUCTION

The introduction of anesthesia in modern medical sciences is considered one of the prominent achievements of the development in the medical field [1]. Anesthesia is a medical status induced by the administration of drugs causing a temporary loss of sensation or awareness. It is usually used for medical procedures and surgeries to prevent pain and discomfort. The first general anesthesia induced by inhaled ether was used during an operation procedure performed by William Morton [1].

Numerous recent studies have investigated the mechanisms behind general anesthesia, highlighting that the various behavioral responses are associated with its specific implications in different brain areas and molecular targets [2,3]. Remarkably, the binding sites of general anesthetics are closely linked to ion channel receptor functional sites. Among the various ion channels, the γ-aminobutyric acid type A (GABAA) subunit receptor is recognized as playing the most crucial role as a functional site for general anesthetics [1,4,5]. Figure 1 presents the classification of the commonly used anesthetic drugs with the induced mechanism and the main representants.

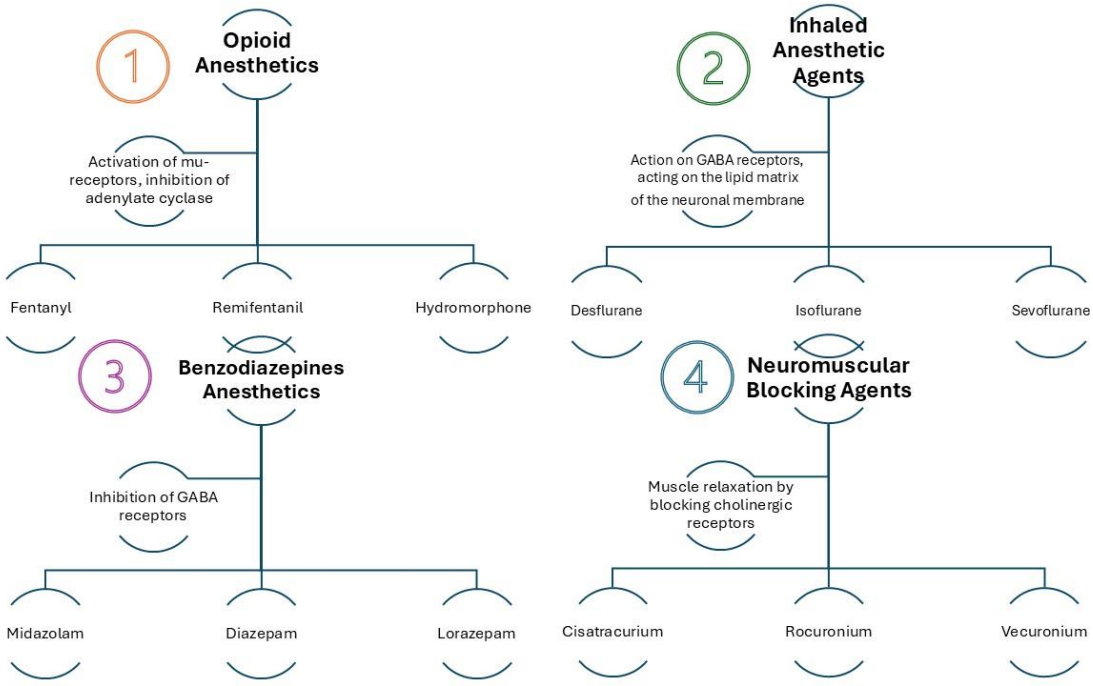

Figure 1. Anesthetic classification, mechanism of action, and representatives

Anesthetic drugs act on the nervous system, circulation, and metabolism, and thus could induce different side effects depending on the type of anesthesia used (general, regional, or local). Most effects are easily manageable and temporary, but some can induce severe disorders, especially in high-risk patients. Opioid drugs remain the most potent medication used to manage severe pain. In the case of these drugs used in acute pain settings, nausea, vomiting, pruritus, and dizziness are well-known adverse effects, which can retard recovery and even induce harm to the patients, especially bradycardia, respiratory depression, and deep sedation [6]. In the case of chronic use, considerable social issues like misuse, abuse, and unintentional deaths from overdoses were noticed [7].

Cardiac disorders are one of the leading causes of morbidity and mortality worldwide. Anesthesia in cardiac patients is intricate, needing the careful analysis of the general

anesthetic's fundamental goals with the requirement to ensure hemodynamic stability, protect organs, and preserve myocardial function.

Aim and objectives

For this reason, the use of anesthetics is challenging, so this study aims to analyse the anesthetics used in cardiac patients, with special emphasis on the induced side effects.

MATERIAL AND METHODS

The present review analyzed published papers retrieved from PubMed, ScienceDirect, and Google Scholar. The relevant research articles published online in English were selected. The searching was carried out by using the following terms or combinations: "general anesthetic", "local anesthetic", "analgesic", "sedative", "side effect" and "cardiac effect". Selected articles were chosen by title, abstract, and text relevance. Their bibliographies were analyzed too for additional references.

ANALGESIA IN HEART SURGERY

Analgesia, numbness, muscle relaxation, and amnesia are all symptoms of the administration of anesthetic drugs, characterized by full-body numbness. There is currently no gold standard method for using anesthesia in the case of heart surgery. For this reason, the anesthesiologist's professional experience and the patient's pathophysiologic state will determine the drug combination employed. Hypnosis, amnesia, analgesia, and muscular relaxation are the most critical components of current procedures that make up general anesthesia. Different factors, such as physiology, the patient's age, co-morbidities, type of operation, and other medical conditions, direct the selection of substances and doses. Both intravenous administration and inhalation are acceptable methods after induction for ensuring the maintenance phase of anesthesia [8]. The frequent reactions observed after anesthetic medication administration are presented in Figure 2.

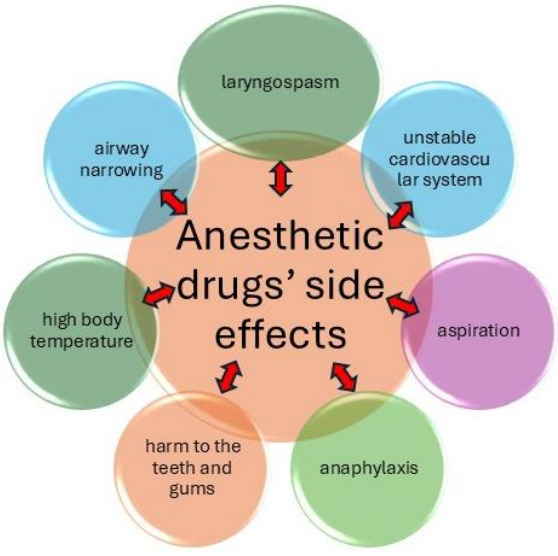

Figure 2. Consequences of general anesthesia

The term opioid-free anesthesia has been introduced around for a while. Lidocaine, ketamine, and dexamethasone are the three most popular non-opioid analgesics used in cardiac surgery. Murphy et al. highlighted that the administration of dexamethasone may reduce morphine consumption and duration of stay in the intensive care unit [9]. Different studies indicated that ketamine could reduce the need for opioids and alleviate pain. Both

non-cardiac and cardiac surgeries have shown that lidocaine can also effectively diminish pain and reduce the need for opioids [10-12].

The effects of midazolam, etomidate, and dexmedetomidine on the cardiovascular system during the phacoemulsification process using local topical anesthesia were followed by researchers. The randomized, double-blind study included 90 subjects treated with phacoemulsification as a candidate for cataract surgery. One group was given 1 μg/kg of dexmedetomidine for 10 min, followed by an infusion of the drug at a rate of 0.5 μg/kg/h. Another group was treated with a gradual intravenous injection of 0.2 mg/kg of midazolam, and the other 2 groups were administrated 0.05 mg/kg of the drug. The sedation levels, their vitals, and any side effects were always monitored. It was observed that all the drugs produced comparable levels of sedation. However, researchers affirmed that in terms of maintaining stable blood pressure and pulse rate, etomidate seemed to be more suitable than the other two drugs [12].

Other studies have shown the cardioprotective benefits of propofol, in addition to anti-inflammatory properties and downregulation in the production of inflammatory mediators. Propofol has diverse anti-inflammatory advantages when used during open-heart surgery, especially before aortic cross-clamp release in the case of patients having elective coronary artery bypass grafting surgery. At the myocardium level, it can downregulate the effect of lipid peroxides, significantly minimize the probability of an inflammatory reaction as a significant reaction to myocardial reperfusion, and limit the inflammatory cascade [13,14].

Ketamine is another protagonist able to decrease neuronal cell loss in the cortex by stopping apoptosis and excitotoxic damage during cerebral ischemia. The drug has the potential to ensure stable cerebral perfusion pressure through the activation of the sympathetic nervous system and reduces the need for vasoactive medicines after a cardiopulmonary bypass. Other neuroprotective effects of ketamine may be due to its potential to reduce systemic inflammation after surgery [15]. In addition, it can reduce postoperative delirium after heart surgery with a cardiopulmonary bypass graft. Moreover, cardiac surgery is related to an augmented risk of postoperative cognitive dysfunction. Ketamine can protect neurons by lessening inflammation and excitotoxicity observed after cerebral ischemia. It can reduce postoperative cognitive dysfunction one week after heart surgery, a property that may be due to the drug's anti-inflammatory potential [16]. The most common drugs used for anesthesia reasons and their side effects are related in Table 1.

Table 1. Common Anesthesia Drugs and Their Side Effects

Drug's name	Therapeutic effect	Side effects	Reference
Remifentanil	A synthetic opioid short-acting, potent analgesic. In addition to the anesthetic action, it is administered to patients to reduce discomfort during surgery.	fast onset of bradycardia, quick respiratory depression, confusion, blurred vision, dizziness, chest pain and discomfort, faintness or lightheadedness, nervousness, sweating, unusual weakness or tiredness, and headaches.	[17].
Morphine	Opioid pain liberator, it is is given to patients with severe pain not responding to other painkillers.	Reduction of the the cardiac output and pulse rate, depressing the myocardium, chest pain, blurred vision, dizziness, confusion, respiratory depression, nervousness, headaches.	[18].
Isoflurane	A liquid inhalation anesthesia used by vaporizing, acting on the lipid matrix of the neuronal membrane, leading to disruption of neuronal transmission to the brain	Augmentation of potassium levels, lightheadedness, feeling faint, irregular heartbeat, respiratory depression, muscle stiffness, bluish skin, confusion, nail beds, shortness of breath, numbness slips, fingers, hyperthermia, stiffness in the jaw.	[19].

Drug's name	Therapeutic effect	Side effects	Reference
Etomidate	A unique drug used to induce general anesthesia and sedation. It was observed that in healthy subjects, low dosages of the medicine result in few changes to the heart rate (<10%).	Pain at the injection site, postoperative nausea or vomiting, skeletal muscle movements, and adrenocortical suppression.	[20].
Ketamine	Stimulators of all parts of the central nervous system directly or indirectly stimulate a characteristic pattern of augmented voltage, with slow frequency spike discharges alternated with low voltage and fast frequency desynchronized activity. Because of the potential for dose-dependent elevations in blood pressure, and cardiac output, ketamine should be administered with care to patients with cardiovascular problems.	Hallucinations, confusion, extreme fear, unusual thoughts, painful or increased urination, blood in urine, incontinence, bradycardia, lightheadedness, shallow breathing, blurred or double vision, lucidity, nausea, insomnia, loss of appetite, or vomiting, hypertension, tachycardia, arrhythmias.	[21].
Propofol	Intravenous anesthetic which may be safely used for the induction and maintenance of anesthesia throughout most surgical operations.	Breathing, lightheadedness, severe pain, bradycardia or tachycardia, shallow burning, stinging at the injection site, or a mild rash. Prolonged use – propofol infusion syndrome, which can result in death.	[22].
Midazolam	Oral anesthetic medication used for sedation, 5 times more potent than diazepam.	Blurred vision, nausea or vomiting, sweating, decreased ability to swallow (especially at higher doses), body aches, depressed airway reflexes and dizziness, chills, fever, congestion, sore throat, insomnia, irregular heartbeat, disorientation, blue or pale lips, fingernails.	[18].

ANESTHESIA IN CONGENITAL HEART DISEASE

Congenital heart disease (ChD) represents one of the most common birth defects. A study published in 2019 highlighted an overall incidence of ChD of approximately 10/1000 live births worldwide, with atrial septal defect, patent ductus arteriosus, and ventricular septal defect as the three most frequent anomalies [23].

A recent study including 78 cardiac surgical centers from Germany analyzed the congenital cardiac surgery program. Centers included were asked to participate in an online questionnaire to assess their current anesthetic practice. Results showed that 27 German centers had an active program for congenital heart surgery, ensuring more than 3,000 pediatric cardiac surgeries every year. Standard induction agents were etomidate in 26.9%, propofol in 19.2%, a combination of ketamine with benzodiazepines in 19.2%, and barbiturates in 11.5%. Sevoflurane was the most common volatile agent used to induce general anesthesia 81.2%. The intraoperative first-line inotropic medicine was epinephrine, 53.8%, followed by milrinone, 23.1%, and dobutamine 15.4%. Thus, this study showed the diversity of protocols applied in pediatric cardiac anesthesia for patients with ChD exposed to surgery in Germany [24].

OBSTETRIC ANESTHESIA AND HEART DISEASE

Cardiovascular disease is the leading cause of maternal mortality cause in the United States. Epidural catheters are frequently used during labor to reduce pain and can be placed via an epidural, dural puncture epidural, or combined spinal-epidural technique. When an epidural catheter is fixed, usually a test dose of epidural medication is followed to infirm/conform unintentional intrathecal or intravascular placement. A classic test dose consists of 3ml of lidocaine 1.5% or 2.0% with epinephrine 1:200,0000 dilution. In women with

cardiac disease, it is essential to ensure that the risks outweigh the benefits of a traditional test dose. This classic intravascular dose of epinephrine 15mcg in patients with a history of stenotic heart lesions, arrhythmias, or severe aortopathies could be dangerous. In these cases, fentanyl 50–100 mcg can be a more suitable intravascular test dose, the specialist has to ask the patients to report any effects of intravascular opioid administration [24]. In patients with cardiovascular disorders, the intrathecal test dose should also be carefully chosen because high spinal anesthesia has been observed after intrathecal test doses which would be badly tolerated in a woman with cardiovascular disease [25]. Here, lidocaine may be changed to 5ml aliquots of the epidural labor analgesia solution (e.g. 1-2mcg/mL fentanyl with bupivacaine 0.0625% - 0.125%) and assess the patient for intrathecal placement every 5 minutes until the anesthesia is established [26].

CONCLUSIONS

Cardiac pathology is a constantly evolving problem. Therapeutic approaches often require the involvement of both general and partial or local anesthesia, therefore it is essential to know the particularities of anesthetic drugs in the case of these subjects. In heart surgery, etomidate seems to be a good choice in terms of maintaining stable blood pressure and pulse rate. In congenital cardiac pathologies, standard induction agents are etomidate, propofol, and a combination of ketamine with benzodiazepines, and barbiturates. In obstetric cases, it is essential to analyze cardiac pathology and possibly replace standard medication with special drugs, adapted to the patient's needs.

Conflicts of Interest

The authors declare no conflict of interest.

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Recent Advances Regarding the Phytochemical and Therapeutic Uses of Ribes Nigrum Leaves

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Abstract

1.Background/Objectives: This review examines the phytochemical composition and therapeutic effects of Ribes nigrum (blackcurrant). Rich in anthocyanins, flavonoids, polyphenols, and essential fatty acids, it exhibits antioxidant, anti-inflammatory, antimicrobial, and cardioprotective properties, highlighting its medical potential. 2. Methods: A systematic analysis of recent in vitro, in vivo, and clinical studies was conducted to evaluate its pharmacological effects. The review focuses on its role in inflammation reduction, oxidative stress prevention, metabolic regulation, anticancer activity, and antimicrobial defense. Extraction methods and key bioactive compounds were also assessed. 3. Results: Ribes nigrum demonstrates strong anti-inflammatory effects by inhibiting pro-inflammatory cytokines and enzymes. Its antioxidant properties help reduces oxidative stress. Metabolic benefits include cholesterol regulation, improved glucose metabolism, and cardiovascular protection. Studies suggest its potential anticancer effects through apoptosis induction in cancer cells. Additionally, its antimicrobial and antiviral properties support its use in treating infections and maintaining oral health. 4. Conclusion: The findings confirm Ribes nigrum's therapeutic value, supporting its traditional medicinal applications and future pharmaceutical development. Further research is needed to explore its long-term clinical benefits, optimize extraction methods, and develop standardized medicinal formulations.

Keywords: Ribes nigrum, natural compound, blackcurrant, antioxidant, therapeutic effects

INTRODUCTION

Blackcurrant (Ribes nigrum L., Grossulariaceae) is native to Central Europe and North Asia and is found worldwide, including the United States. Recently, researchers have demonstrated various significant pharmacological effects for global health, including anti-inflammatory, antioxidant, and antimicrobial effects. The medical and pharmaceutical properties of blackcurrant are conferred by its constituents, especially delphinidin-3-O-glucoside, delphinidin-3-O-rutinoside, cyanidin-3-O-glucoside, and cyanidin-3-O-rutinoside, as well as flavonols and phenolic acids. Many studies in the specialized literature have been the subject of research on the impact of this natural compound in the medical field [1].

Berries are compounds with nutritional advantages due to their high content of vitamins, minerals, and compounds with antioxidant action. Among them, blackcurrants (Ribes nigrum L.) are appreciated not only for their fruits but also for their leaves. Several publications have reported on blackcurrant leaves, which, due to their rich polyphenol content, are more effective than berries in reducing inflammation and exhibiting antioxidant effects. Other mentions have brought to light the antimicrobial and antiviral effects, equally important for human health [2, 3]. R. nigrum is considered a "super-plant" due to its numerous therapeutic benefits, which are attributed to the phytocompounds it contains. Recent research has demonstrated their ability to treat chronic diseases associated with oxidative stress. The main classes of bioactive compounds in R. nigrum are: phenolic acids, flavonoids, and proanthocyanidins [3]. A group of researchers applied the thin-layer chromatographic method for the quantitative determination of bioactive compounds, including the presence of proanthocyanidins and prodelphinidins [4,5]. Blackcurrant juice and extract, rich in anthocyanins and polyphenolic compounds with anti-inflammatory, antioxidant, and cardioprotective effects, have been demonstrated to exhibit immunostimulatory effects in recent clinical research [6].

Given the multiple phytotherapeutic uses of Ribes nigrum leaves, this review provides an updated perspective on the active compounds and their pharmacological mechanisms, highlighting potential therapeutic applications and future research directions. Figure 1 was created for an overview of the biological properties observed in research on Ribes nigrum L. extracts.

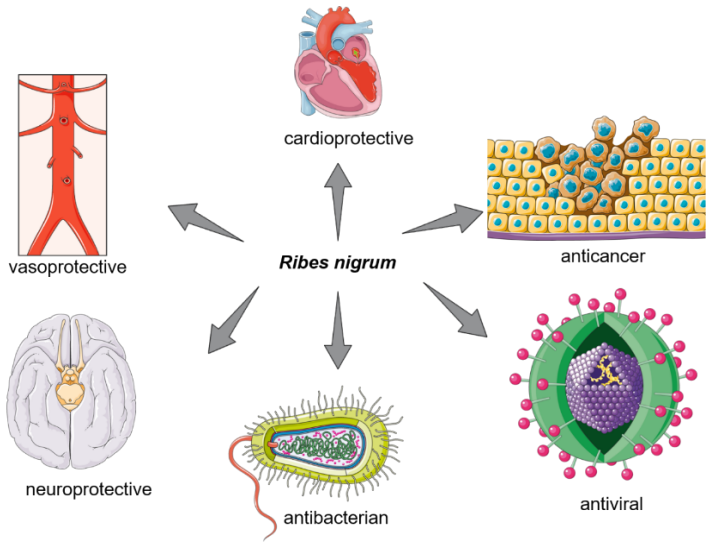

Figure 1. General presentation of the biological properties observed in specialized studies for Ribes nigrum L. The figure was made using SMART-SERVIER

GENERAL ASPECTS OF THE PHYTOCHEMICAL COMPOSITION OF RIBES NIGRUM L.

R. nigrum has been used since ancient times as a traditional botanical medicine in various cardiovascular pathologies, hypertension, and hepatitis due to its high content of anthocyanidins, flavonoids (which give the fruit its intense black color), and polysaccharides [1]. The fruits of the plant have a vitaminizing, remineralizing action, being recommended in cases of overwork, convalescence, anemic states, and iron deficiency, having positive effects on sports performance by reducing free radicals that cause fatigue [2, 3]. Equally important are studies demonstrating improved cognitive performance [4]. In the composition of the R. nigrum species, a large amount of vitamin C was also identified, 3-4 times higher concentration than in oranges, which contributes to support the immune system, maintains the health of bones, teeth, cartilage, blood vessel walls and plays a role in protecting cells from oxidative stress, fatty acids have also been identified, including linoleic acid (omega 6), a polyunsaturated acid with a role in maintaining optimal cell function, gamma-linolenic acid (GLA), a derivative of linoleic acid, with anti-inflammatory role and α-linoleic acid (omega 3), a well-known cardiovascular and neuroprotective [5].

Volatile compounds with anti-inflammatory, antimicrobial, antifungal, and respiratory tract decongestant properties have been detected in R. nigrum leaves. The most important aromatic compounds identified were α-pinene (a monoterpene responsible for the pine odor, with anti-inflammatory and antioxidant properties), linalool, β-pinene (with an anti-inflammatory effect), and limonene (responsible for the citrus odor, with an antimicrobial effect [11]. A 2015 study by Sasaki, based on a phytochemical analysis of R. nigrum leaves, identified lignoid compounds. Out of the 8 lignoids isolated, 6 exhibited antioxidant activity [6]. Another group of researchers identified phenolic acids (p-coumaric acid, caffeic acid, ferulic acid, gallic acid, ellagic acid, p-coumaric acid, caffeic acid, ferulic acid, gallic acid, ellagic acid) by methanolic acetic acid extraction using the HPLC technique [7]. Because evaluation of extracts and active compounds has been and is a topical subject, another paper regarding the chemical composition of plant products identifies the main flavonoids and phenolic acids in R. nigrum leaves: quercetin (the main compound), isoquercetin, campherol, myricetin, myricetin, isoramnetin, quercetol, with multiple therapeutic properties, among which we mention the antioxidant, anti-free radicals, reacting with superoxide anions [8].

Aim of the study

This study aims to discuss the phytochemical composition and biological effects of Ribes nigrum leaves, highlighting their potential therapeutic applications.

MATERIAL AND METHODS

This review was conducted through a systematic analysis of scientific literature on Ribes nigrum, focusing on its phytochemical composition and pharmacological properties. Relevant studies, including in vitro, in vivo, and clinical research, were collected from reputable scientific databases such as PubMed, Scopus, ScienceDirect, and Google Scholar. The selection criteria prioritized peer-reviewed articles that explored the anti-inflammatory, antioxidant, metabolic, anticancer, antimicrobial, and dermatological effects of R. nigrum. The searching was carried out using the following terms or combinations: Ribes nigrum, natural compound, blackcurrant, antioxidant, therapeutic effects.

RESULTS

Anti-inflammatory effect

Anti-inflammatory properties have been demonstrated in numerous studies by the inhibition of enzymes and molecules involved in inflammatory processes, such as cyclooxygenase (COX) and pro-inflammatory cytokines (TNF-α, IL-1, and IL-6). In this sense, a study showed reduced levels of these genes in ovariectomized (OVX) rats fed a regular diet or a diet supplemented with 3% blackcurrant extract (CaNZac-35), compared to the group fed a regular diet for three months [9]. Another study by Garbacki, N. studied the anti-inflammatory effects of proanthocyanidins from Ribes nigrum L. were evaluated using carrageenan-induced paw edema and carrageenan-induced pleurisy in laboratory rats, and the results indicated that pretreatment with proanthocyanidins reduced carrageenan-induced paw edema in a dose- and time-dependent manner and also proanthocyanidins inhibited carrageenan-induced pleurisy in a concentration-dependent manner [10]. Due to the rich content of fatty acids, with a role in reducing inflammation and relieving muscle and joint pain, it was concluded that the anti-inflammatory activity is similar to that of indomethacin/niflumic acid [11]. It has been shown that an extract of R. nigrum, under the trade name of "Currantex 30" reduces inflammation of stimulated human pulmonary epithelial cells and suppresses secretion of CCL11, a chemokine responsible for triggering allergic asthma [12]. Another paper indicates the beneficial effects for the inflammated respiratory tract, the study being carried out using 4 concentrated macerates, extracted with alcohol-glycerol-water solution in equal parts, from different plants, including R. nigrum, of which 5-15 drops/day were administered [13].

Anti-oxidant effect

Numerous studies have been performed that have highlighted the antioxidant potential of R. nigrum [14,15]. Free radicals, caused by radiation, environmental pollution, smoking, and chemicals, can damage cells and accelerate the aging process, as well as contribute to the development of chronic diseases. In a in vivo study, R. nigrum extract was shown to reduce inflammation and improve the activity of antioxidant enzymes such as superoxide dismutase (SOD) and catalase [16]. Above all, the compounds in blackcurrant fruits and leaves are recognized for their preventive and therapeutic properties, with HPLC analyses demonstrating that they comprise various polyphenols and anthocyanins that serve antioxidant activity. [16]

Metabolic activity

In addition to its anti-inflammatory and antioxidant properties, blackcurrant may help improve the immune system, protect cardiovascular health, and improve eye health [5,9,17]. In vivo metabolic activity in laboratory animals showed a decrease in body mass, a hypotensive and cardiodepressant effect on blood pressure, and a hypoglycemic effect by lowering postprandial glycemia [18]. A recent study evaluates the effects on cellular CaCo-2 gene proteins and shows increased cholesterol transport through enterocytes, with a hypocholesterolemic role [18,19].

Blackcurrant extract has been shown to have a vasculoprotective effect on blood vessels on laboratory animals included in a study [17]. Investigations indicated that Ribes nigrum may improve endothelial function and reduce the risk of cardiovascular disease. Anthocyanins and other bioactive substances in R. nigrum have been associated with lower blood pressure and improved blood circulation [20]. Another group of researchers has shown an in vitro hypoglycemic effect. In this regard, it has been mentioned that berries have beneficial effects on postprandial glucose metabolism that have been linked to the presence of polyphenolic compounds derived from berries [21].

Anti-cancer effects

Bishayee et al. studied the induction of apoptosis and/or inhibition of proliferation in different types of cancer, demonstrating the antitumor effect of R. nigrum extract on hepatocellular carcinoma cells [22]. Also, numerous studies on R. nigrum extracts have demonstrated significant antitumor activity, suggesting their future use as adjuvants in the treatment of cancers for increased efficacy and reduced side effects [23]. Using a 45% (v/v) ethanolic solution on mice, another work showed that after administration of black currant extract, the development of Ehlich carcinoma was delayed by 45% [22,23]. Valuable information was also evidenced on gastric cancer, where black currant extract demonstrated anticancer potential by the potential to induce apoptosis, programmed cell death [23].

Activities on the skin and mucous membranes

The components of the terpene family, including terpinen-4-ol, terpinolenol, spatulenol, and caryophyllene oxide, are primarily found in blackcurrant extracts. These volatile compounds are responsible for the anti-inflammatory effect on the mucous membranes of the respiratory tract and have beneficial effects in conditions such as rhinitis, rhinopharyngitis, colds, sinusitis, and bronchitis [24].

The anti-inflammatory effects of these compounds could also be relevant in inflammation induced by external factors such as UV radiation, which causes inflammation of the epidermis and stimulates the production of inflammatory cytokines. In one study, CAPS administration (0.2% and 1% R. nigrum powder, respectively) reduced UV-induced skin dehydration and prevented atopic dermatitis in NC/Nga mice [25]. Kendir Gon et al. used male albino mice and rats as experimental models, and they focused on investigating the effect of administering 1% R. nigrum extract added to Fitocream ointment for 15 days, demonstrating a beneficial effect on wound healing [26]. In vitro, due to its high content of vitamin A, β-carotene, and zeaxanthin, R. nigrum maintains the health and integrity of mucous membranes and is successfully used in ophthalmologic disorders [27]. It also increases levels of collagen, elastin, and hyaluronic acid in the skin, having an anti-aging effect [28]. A recent in vitro study on fibroblasts (BJ cells) and normal human keratinocytes (HaCaT) demonstrates the beneficial role of R. nigrum extract on the skin by inhibiting collagen degradation. It also has a beneficial effect on the respiratory tract mucosa and has been successfully used in the treatment of viral and bacterial infections of the upper respiratory tract. A recent in vitro study on fibroblasts (BJ cells) and normal human keratinocytes (HaCaT) demonstrates the beneficial role of R. nigrum extract on the skin by inhibiting collagen degradation [29].

Antimicrobial and antiviral activity

Extracts of R. nigrum have demonstrated antimicrobial effects against pathogenic bacteria such as Staphylococcus aureus and Escherichia coli, thus suggesting its potential use in treatments for mild infections or as an adjunct in oral hygiene. As a major result, the bactericidal effect of blackcurrant juice against bacteria responsible for the development of caries, periodontosis, and endodontic infections was discovered, thus demonstrating its efficacy also for the dental sphere [30].

Concerning antiviral functions, a group of researchers have studied antiviral activity using mice as an experimental model, administered an aqueous extract 10 mg/ml (LADANIA 067), and observed dose-dependent reduction in virus titers (anti-influenza virus) [26]. In vitro results of a studie highlighted antibacterial and antiviral activity against a broad spectrum of common germs. Antiviral activity has also been demonstrated in herpes virus infectious diseases by inhibition of herpes virus replication in cells due to inhibition of protein synthesis [31, 32]. In complementary, 9 out of 10 extracts of blackcurrant studied had an antibacterial effect against the bacterium Listeria monocytogenes [31, 32].

CONCLUSIONS

In conclusion to this comprehensive overview of Ribes nigrum leaves, these botanical compounds demonstrate a wide range of biological effects, including cardioprotective, antioxidant, anti-inflammatory, antidiabetic, and antibacterial properties, which lead to further advanced studies on the mechanisms underlying these actions. As future research directions, in vitro studies on various cancer cell lines could also provide discoveries in the oncological field.

Conflicts of Interest

The authors declare no conflict of interest.

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