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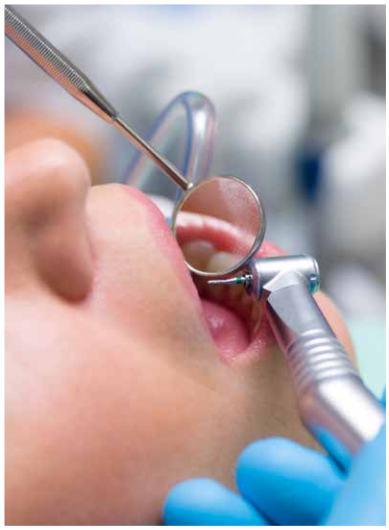

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editorial

Dra. Cristina Meniz García
Director *Científica Dental*

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Dear colleagues and readers of Científica Dental,

This is the sixth consecutive year in which this special supplement in English of Científica Dental appears. This edition includes the best work published in 2019 in the categories of best scientific article, best case study and best publication by new author. Six works are presented which are the finalists in these categories. The subject-matter of the works is up-to-date and varied. Our readers can access them free of charge in the website www.cientificadental.es.

In the exceptional circumstances we are living through, in which online communication forms part of our daily lives, Científica Dental wishes to be present contributing to the knowledge of our readers. For this reason we hope the edition is of interest to you.

Finally we would like to thank our authors for the great quality of the work they have presented, and also the publishers and copy editors whose work is essential for the production of each edition of this journal, and of course our readers for whom this work is intended.

Hoping life returns to normal soon, we wish you a happy summer.

Dra. Cristina Meniz García

Dra. Isabel Leco Berrocal

Original article

Antiseptic Capacity of 0.05% Chlorhexidine Digluconate and 0.05% Cetylpyridinium Chloride. A Prospective and Microbiological Clinical Study

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ABSTRACT

Introduction: The aim of this study was to evaluate the clinical and microbiological efficacy of an oral rinse (colutory) containing 0.05% chlorhexidine digluconate (CHX) and 0.05% cetylpyridinium chloride (CPC) when compared to another rinse without antiseptic properties, used as adjuvants to oral hygiene methods.

Material and methods: Using spectrophotometry, a microbiological study was conducted to evaluate the capacity of each rinse to inhibit the formation and adhesion of Streptococcus oralis bacterial biofilm, followed by a randomized and double-blind clinical trial conducted on a sample of 48 patients randomly assigned to either rinse.

- Oral Rinse A: 0.05% CHX, 0.05% CPC and 0.14% zinc lactate
- Oral Rinse B: 0.10% permethol and 0.50% provitamin B5.

The plaque index (PI), modified gingival index (MGI), and sulcus bleeding index (SBI) were evaluated at one and three months.

Results: The 0.05% CHX and 0.05% CPC-based mouth rinse showed a high capacity to inhibit formation (P=0.013) and adhesion (P=0.001) of bacterial biofilm. Statistically significant differences in inter-group PI were observed at three months of observation (P<0.001). Differences in the MGI were also observed at one month (P=0.034) and three months of observation (P<0.001); and in the SBI at one month (P=0.004) and at three months of observation (P=0.002).

Conclusions: The 0.05% CHX and 0.05% CPC-based colutory

KEYWORDS

Chlorhexidine gluconate; Oral mouth rinse; Cetylpyridinium chloride; Gingivitis; Dental plaque.

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INTRODUCTION

In recent years, molecular characterization of oral microbiota has succeeded in detecting 700 bacterial species or biotypes capable of colonizing the tissues of the oral cavity. However, a healthy individual is home to approximately 150 to 200 different bacterial species, of which between 10 to 30 have the capacity to cause periodontal disease (PD)[1]. Subgingival bacterial counts indicate that a healthy individual hosts 103 colony-forming units (CFUs), while in individuals with established PD this may amount to 108 CFUs[2]. These types of infections are responsible for causing damage to supporting tissues[3-]). Periodontal pathologies are characterized by their high prevalence. Epidemiological studies indicate that between 5 and 20% of the population suffers from advanced forms of periodontitis[6,7]. Periodontal disease etiopathogenesis is strongly associated with the formation of dental plaque. Dental plaque is a complex form of polymicrobial biofilm, a process which begins with the establishment, fixation, and growth of primary colonizing tooth bacteria, such as Streptococcus oralis.

Longitudinal clinical trials have shown that proper control of bacterial plaque prevents periodontitis, and that the lack of proper oral hygiene is accompanied by an increase in bacterial plaque and the onset of such pathology[8-10]. Numerous authors emphasize the importance of oral hygiene practices in preventing the formation of bacterial biofilm[11], as well as the use of oral antiseptics as adjuvants to such techniques[12].

Chlorhexidine digluconate (CHX) is the most widely used antiseptic agent today. It has been shown to be effective in preventing bacterial plaque formation and gingival inflammation[13,14]. The lack of controlled clinical studies evaluating the antiseptic capacity of 0.05% CHX and 0.05% cetylpyridinium chloride (CPC) to reduce or prevent the onset of disease in patients without PD clearly indicated the need for a prospective and microbiological clinical study to determine its effectiveness.

MATERIAL AND METHODS

MICROBIOLOGICAL STUDY

Study Design

The ability of two oral rinses to inhibit adhesion and formation of bacterial biofilm in vitro was analyzed:

- A: 0.05% CHX, 0.05% CPC and 0.14% zinc lactate (CN 323923.3. Halita®, Dentaid, Cerdanyola, Barcelona, Spain), and
- B: 0.10% Permethol and 0.50% Provitamin B5 (CN 350447.8. Parogencyl®, Procter & Gamble, Cincinnati, OH, USA).

Streptococcus oralis is a primary colonizer of tooth enamel and the cellular base on which future dental plaque forms. The adhesion and formation of bacterial biofilm was determined and quantified using spectrophotometric methodology. Polystyrene microtiter plates with 96 wells were used (Masterlab S.L., Madrid, Spain), in which a 175µl bacterial inoculum of S. oralis (obtained from an earlier study[15] suspended in trypticase soy broth was placed (specifically, TSB 150µl broth + 25µl of bacterial suspension adjusted to 0.5 McFarland density), then 25µl of the designated rinse was added to each of the wells.

Ability to inhibit bacterial biofilm formation

In this trial, each rinse under study (25µl) was added in serial dilutions ranging from 1/16 to 1 (undiluted) as a supernatant (25µl of rinse) to the bacterial inoculum (25µl of bacterial suspension in sterile saline solution) and 150µl of culture broth in the microtiter plate wells.

Ability to inhibit the adhesion of bacterial biofilm

For this test, each rinse was placed in the wells (25µl in dilutions ranging from 1/16 to 1) in advance while maintaining one minute contact with the surface of the plate by means of a microtiter plate mixer, decanted, and then the strain of S. oralis (150µl growth medium + 25µl bacterial inoculum) was inserted.

For the two tests in question, following 24 hours of incubation at 37°C, the content of the wells was remo-

ved by decanting, and the plates were washed with sterile distilled water. The plates were dried at room temperature for 30 minutes and then each well was filled with 200µl of crystal violet dye (25%). After 5 minutes, the excess dye was removed by decanting, and the plate was washed again. After 30 minutes, 200ml of hydrochloric acid (25%) was added to the wells, and after 1 minute, the optical density (OD) of the bacterial biofilm that had adhered to the walls of the well was measured with a spectrophotometer (Labsystems Multiskan, Helsinki, Finland) at 450 nm. The tests were repeated four times, and the average readings of the ODs obtained, +/- their standard deviations, were used for comparison. Likewise, in each plate and test performed, the biofilm formed by S. oralis was measured via spectrophotometry in a series of eight inoculum wells without a rinse (basal biofilm), and in another series of wells the optical density obtained with broth without inoculum was measured (negative control).

Taking the spectrophotometric measures of absorbance obtained at 450nm, four values or cut-off points were established to evaluate the ability of the oral rinses to inhibit bacterial biofilm:

- No biofilm formation: OD: 0-0.059 to 450 nm.
- Weak biofilm formation: OD: 0.060-0.150 to 450 nm.
- Moderate biofilm formation: OD: 0.151-0.250 to 450 nm.
- High biofilm formation: OD>0.250 to 450 nm.

CLINICAL STUDY: Study Design

A clinical, randomized, double-blind trial was conducted on a sample of 48 patients. A 3-month observation period was set up during which reviews were scheduled following one and three months after patients joined the study. The study was conducted in accordance with the ethical principles set out in the Helsinki Declaration, following the guidelines of Good Clinical Practice. The study was carried out at the Alfonso X el Sabio University Dental Clinic in Madrid between June and July 2017. An informed consent form was drafted which was evaluated by the Ethics Committee of the "Gómez Ulla" Hospital Central de la Defensa in Madrid. Each patient was randomly assigned (Epidata version 3.1, PAHO/WHO, A Coruña, Spain) to one of the oral rinses:

- A: 0.05% CHX, 0.05% CPC and 0.14% zinc lactate (CN 323923.3. Halita®, Dentaid, Cerdanyola, Barcelona, Spain), and
- B: 0.10% Permethol and 0.50% Provitamin B5 (CN 350447.8. Parogencyl®, Procter & Gamble, Cincinnati, OH, USA).

Selection Criteria

The study inclusion criteria consisted of patients over the age of 18 who had more than 20 testable teeth. The study exclusion criteria consisted of: loss of bone insertion greater than 1/3 of root length, presence of periodontal sacks equal to or greater than 4 mm, individuals undergoing orthodontic treatment or periodontal treatment in the last 3 months, individuals being treated with antibiotics or corticosteroids in the last month, hypersensitivity to any of the study components, smokers with a consumption level greater than 10 cigarettes/day, pregnant or nursing women, patients with Sjogren's syndrome and patients with systemic diseases.

Clinical Procedure

The following clinical indices were analyzed: bacterial plaque index (PI)[16] to evaluate the antiplaque property of the rinses, and the modified gingival index (MGI)[17] and sulcus bleeding index (SBI)[18] to analyze the degree of gingival inflammation. The extrinsic stain index (SI)[19] was included to record possible dyschromia derived from the rinses.

After evaluating PI, MGI, SBI and SI during the initial visit, mechanical removal bacterial plaque was performed using ultrasound (SONICflex quick 2008 L, KaVo®, Benelux, France) and prophylaxis paste (Mira Clean®, Hager & Werken, Duisburg, Germany) employing low-speed rotary instruments (GENTLEPOWER LUX 20 LP, KaVo®, Benelux, France). Each patient was given a kit with oral hygiene products consisting of toothpaste

(CN 150331.2. Sodium fluoride (1450 ppm ion fluoride), vitamin E and xylitol (Dentaid, Cerdanyola, Spain); an intermediate hardness toothbrush (CN 154054.6. (Dentaid, Cerdanyola, Spain); dental floss (CN 332890.6 Dentaid, Cerdanyola, Spain); and the randomly assigned oral rinse (A or B). Patients were also instructed in oral hygiene techniques in order to homogenize both oral hygiene techniques and the products used. After using the oral rinse, volunteers were instructed to refrain from any additional rinsing and eating any food for the following 30 minutes. They were also instructed to avoid using any other method or means of oral hygiene.

The PI, MGI, SBI and SI were measured during the visits at one and three months.

The information obtained from each patient was logged and archived in a dossier in conformity with Organic Law 15/1999 on the Protection of Personal Data.

STATISTICAL ANALYSIS

As measures of central tendency, the arithmetic mean (M) and standard deviation (SD), or the median (θ) and interquartile range (IQR) were used.

Mann Whitney's U-test was used. In all cases, a $p<0.05$ value was taken as the cutoff value for statistical significance. SPSS® v15 software (Microsoft Inc., Redmond, WA, USA) was used as the statistical application.

RESULTS

MICROBIOLOGICAL STUDY

Ability to inhibit bacterial biofilm formation

Oral rinse A showed a greater ability to inhibit the formation of bacterial biofilm (P=0.013), than did oral rinse B (P=0.280) (Figure 1).

Ability to inhibit the adhesion of bacterial biofilm

Both oral rinse A (P=0.001) and B (P=0.001) were shown to be effective in inhibiting the adhesion of bacterial biofilm (Figure 2).

CLINICAL STUDY

The average age of the study subjects was 36.4 with a standard deviation of 10.5; the minimum age was 20 and the maximum 57. Group assignment was conducted randomly and properly weighted for gender (P=0.303); however, statistically significant differences by age (P=0.031) were observed, which were considered clinically irrelevant. In the case of group B there was one volunteer who left the study after one month of observation.

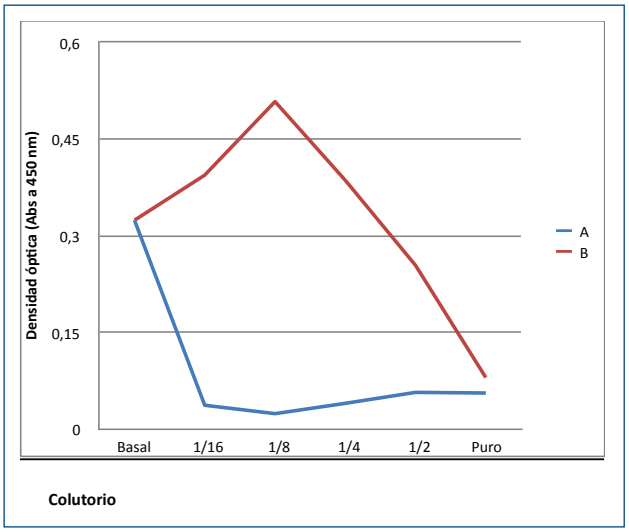

Figure 1. Ability to inhibit the formation of bacterial biofilm.

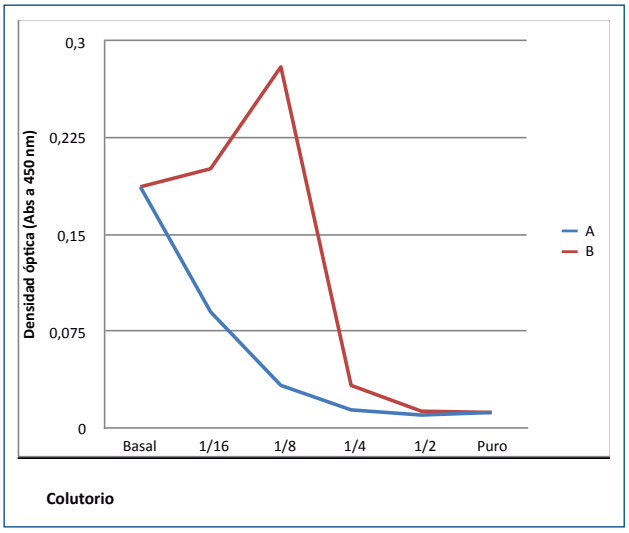

Figure 2. Ability to inhibit the adhesion of bacterial biofilm

No statistically significant differences were found in the variables collected in the medical (P=0.261) or dental history of the two groups (P=0.360).

The median PI value of Group A was reduced from an initial value of 2.5(1) to 2(1) at 30 days and to 1(0) at 90 days, while the median PI value of Group B was reduced from an initial value of 2(1.75) to 2(1) at 30 days and to 2(0) at 90 days. No statistically significant differences in initial PI (P=0.095) were observed, nor in the PI at one month of observation (P=0.205). However, differences between the two groups (P<0.001) were observed at three months (Table 1). Also, there were differences in the percentage of PI reduction between the two groups at one month (P=0.026) and at three months (P<0.001) (Table 2).

The median value of MGI for Group A was unchanged during the observation period, 1(1) while the median value of MGI for Group B was reduced at one month to 1(1) from the initial value of 2(1) and increased to 2(1) at three months. No statistically significant differences were observed in the initial MGI (P=0.269). However, differences were observed at one (P=0.034) and three months between the two groups (P<0.001) (Table 3). There was no difference in the percentage of MGI reduction at one month (P=0.180); however, differences were observed between the two groups at three months (P=0.021) (Table 4).

The median SBI value for Group A was reduced from an initial value of 1(1) to 0(0) at 30 and 90 days, while the median value for Group B was reduced from an initial value of 1(2)to 0(1)at 30 and 90 days. No statistically significant differences were observed in the initial SBI (P=0.556); however, differences between the two groups were observed at one (P=0.004) and three months (P=0.002) (Table 5).

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Differences in the percentage of SI reduction between the two groups at one (P=0.026) and three months (P<0.001) were also observed. No differences were observed in the percentage reduction of SI between the two groups at one month (P=0.053). However, there differences did arise between the two at 3 months (P=0.026) (Table 6). The SI did not show dyschromia attributable to exposure to the oral rinses during the observation period.

Table 1. Bacterial Plaque Index (PI).

ORAL RINSE			INITIAL VISIT	FIRST MONTH	THIRD MONTH
A	N	Valid	24	24	24
		Lost	0	0	0
	Percentile	25	2.00	1.00	1.00
		50	2.50	2.00	1.00
		75	3.00	2.00	1.00
B	N	Valid	24	23	23
		Lost	0	1	1
	Percentile	25	1.25	1.00	2.00
		50	2.00	2.00	2.00
		75	3.00	2.00	2.00
p			0.095	0.205	<0.001

Table 2. Percentage reduction in the bacterial plaque index (PI).

ORAL RINSE A			ORAL RINSE B		
	IP Variation	Frequency (valid percentage)	IP Variation	Frequency (valid percentage)	Sig. bilateral
FIRST MONTH	Increase 1 point	-	Increase 1 point	2 (8.7%)	
	It stays	5 (20.8%)	It stays	13 (56.5%)	
	Reduce 1 point	14 (58.3%)	Reduce 1 point	7 (30.4%)	
	Reduce 2 points	5 (20.8%)	Reduce 2 points	1 (4.3%)	0.026
	Total	24 (100%)	Total	23 (100%)	
	Lost System		Lost System	1	
	Total	24	Total	23 (100%)	
THIRD MONTH	Increase 1 point	-	Increase 1 point	6 (26.1%)	
	It stays	1 (4.2%)	It stays	11 (47.8%)	
	Reduce 1 point	13 (54.2%)	Reduce 1 point	5 (21.7%)	
	Reduce 2 points	9 (37.5%)	Reduce 2 points	1 (4.2%)	<0.001
	Reduce 3 points	1 (4.2%)	Reduce 3 points	-	
	Total	24 (100%)	Total 23 (100%)		
	Lost System		Lost System	1	
	Total		Total	24	

Table 3. Modified gingival index (MGI).

ORAL RINSE			INITIAL VISIT	FIRST MONTH	THIRD MONTH
A	N	Valid	24	24	24
		Lost	0	0	0
	Percentile	25	2.00	1.00	1.00
		50	2.50	2.00	1.00
		75	3.00	2.00	1.00
B	N	Valid	24	23	23
		Lost	0	1	1
	Percentile	25	1.00	1.00	1.00
		50	2.00	1.00	2.00
		75	2.00	2.00	2.00
P			0.269	0.034	<0.001

No adverse effects were observed in any of the groups during the observation period.

DISCUSSION

The objective of this study was to compare the clinical and microbiological efficacy of 0.05% CHX and 0.05% CPC as an adjuvant agent for oral hygiene methods with respect to a control rinse without antiseptic properties. The clinical efficacy and adverse effects of CHX-based oral antiseptics are associated with their concentration: starting at 0.2% their clinical efficacy no longer increases, but the occurrence of adverse effects does[20,21], while a concentration of less than 0.05% is insufficient to be effective. Long-term clinical studies highlight the clinical efficacy of CHX 0.12% in reducing PI and Gingival Index (GI) between 36.1 to 60.9% and 29.1 to 37.2% respectively[22,23]. These results differ from those obtained in our study because they do not involve manual hygiene techniques, employ lower sensitivity clinical indices, and do not include CPC in the composition of the antiseptic agent.

CPC exerts synergistic action in combination with CHX, performing its action at the level of the bacterial cell membrane and thereby causing a disruption in cell metabolism, inhibition of cell growth, and cell death[24]. The incorporation of CPC into CHX antiseptics has served to reduce its effective concentration and the occurrence of adverse effects without diminishing clinical efficacy[20]. Santos et al. (2004) evaluated the clinical and microbiological activity of an antiseptic based on 0.05% CHX and 0.05% CPC, observing a

Table 4. Percentage reduction in the Modified Gingival Index (MGI).

	ORAL RINSE A		ORAL RINSE B		
	IGM Variation	Frequency (valid percentage)	IGM Variation	Frequency (valid percentage)	Sig. bilateral
FIRST MONTH	Increase 1 point	-	Increase 1 point	-	0.180
	It stays	9 (37.5%)	It stays	15 (65.2%)	
	Reduce 1 point	13 (54.2%)	Reduce 1 point	6 (26.1%)	
	Reduce 2 points	2 (8.3%)	Reduce 2 points	2 (8.7%)	
	Total	24 (100%)	Total	23 (100%)	
	Lost System		Lost System	1	
	Total		Total	24	
THIRD MONTH	Increase 1 point	-	Increase 1 point	5 (21.7%)	0.021
	It stays	10 (41.7%)	It stays	13 (56.5%)	
	Reduce 1 point	10 (41.7%)	Reduce 1 point	5 (21.7%)	
	Reduce 2 points	4 (16.7%)	Reduce 2 points	-	
	Reduce 3 points	-	Reduce 3 points	-	
	Total	24 (100%)	Total	23 (100%)	
	Lost System		Lost System	1	
	Total		Total	24	

Table 5. Sulcus Bleeding Index (SBI).

ORAL RINSE			INITIAL VISIT	FIRST MONTH	THIRD MONTH
A	N	Valid	24	24	24
		Lost	0	0	0
	Percentiles	25	0.00	0.00	0.00
		50	1.00	0.00	0.00
		75	1.00	0.00	0.00
B	N	Valid	24	23	23
		Lost	0	1	1
	Percentiles	25	0.00	0.00	0.00
		50	1.00	0.00	0.00
		75	2.00	1.00	1.00
P			0.556	0.004	0.002

Table 6. Percentage reduction in Sulcus Bleeding Index (SBI).

ORAL RINSE A			ORAL RINSE B		
	SBI Variation	Frequency (valid percentage)	SBI Variation	Frequency (valid percentage)	Sig bilateral
FIRST MONTH	1-point increase	-	1-point increase	1 (4.3%)	
	No change	9 (37.5%)	No change	14 (60.9%)	
	1-point Decrease	13 (54.2%)	1-point Decrease	3 (13%)	
	2-point Decrease	2 (8.3%)	2-point Decrease	5 (21.7%)	0.026
	Total	24 (100%)	Total	23 (100%)	
	Sample Loss		Sample Loss	1	
	Total		Total	24	
THIRD MONTH	1-point increase	1 (4.3%)	1-point increase	4 (17.5%)	
	No change	9 (37.5%)	No change	11 (47.8%)	
	1-point Decrease	12 (50%)	1-point Decrease	5 (21.7%)	
	2-point Decrease	2 (8.3%)	2-point Decrease	3 (13%)	<0.001
	Reduce 3 points	-	Reduce 3 points	-	
	Total	24 (100%)	Total	23 (100%)	
	Sample Loss		Sample Loss	1	
	Total		Total	24	

percentage reduction in PI and GI of 40.8% and 29.4% respectively[25]. These results contrast with those observed in patients assigned to study group A, who reduced their PI by 95.9% and MGI by 58.4% at the three-month mark. These differences are attributed to discrepancies in the observation period, the use of lower sensitivity clinical indices and differences in the sample selection criteria.

CONCLUSIONS

A solution of Chlorhexidine digluconate-based antiseptic at 0.05% and 0.05% cetylpyridinium chloride has demonstrated its clinical and microbiological efficacy by reducing bacterial plaque and gingivitis.

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Original Article

Survey of the Potential Association of Childhood Sleep Disorders with Sleep Bruxism

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ABSTRACT

Objective: Conduct a pilot study of the association between parent-reported sleep bruxism (SB) and sleep disorders in children.

Material and methods: The presence of nocturnal tooth grinding or noise during sleep, clinical variables relating to potential temporomandibular disorders, and various behaviors observed during sleep were evaluated along the previously validated Sleep Disturbance Scale for Children (SDSC) developed by O Bruni et al. Data for the study were collected using a Likert-type rating scale questionnaire given to 43 parents accompanying their children to a pediatric dentistry clinic in the Community of Madrid.

Results: Parent-reported SB in children showed a higher positive correlation with sleep disorders (60%) when compared to levels in children whose parents did not report any presence of SB (40%); a statistically significant result (p=0.000). Among the various sleep disorders evaluated, the two showing an association with reported sleep bruxism were sleep-wake transition disorders (p=0.00) and respiratory sleep disorders (p=0.01)

Conclusions: Some sleep disorders in children may be associated with the presence of sleep bruxism.

KEYWORDS

Bruxism; Sleep bruxism; Childhood sleep disorders; Sleep.

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INTRODUCTION

The definition of sleep bruxism varies in the professional literature[1-5]. An international consensus of experts on the subject define SB as: "A repetitive jaw-muscle activity characterized by clenching or grinding of the teeth and/or by bracing or thrusting of the mandible". Bruxism has two distinct circadian manifestations: it can occur during sleep (indicated as sleep bruxism) or during wakefulness (indicated as awake bruxism)[3].

Estimating the prevalence of this behavioral alteration is made more difficult by variance in the strategies used for diagnosis and the type of study population. According to a number of researchers, its prevalence is higher during childhood and decreases with age[6].

Following a systematic review of parent-reported SB through the use of questionnaires found its prevalence among children aged 2 to 12 y/o could range anywhere from 3.5 to 40.6%[7].

The etiology of sleep bruxism (SB) is multifactorial. Peripheral or morphological factors, such as occlusal interference, have been considered to be the main factors causing bruxism. However, today the evidence is less convincing[5,8-10]. Currently, the focus of research concerns the core contributing factors, which may be physiological and/or psychological; namely, sleep architecture, psychosocial factors, trauma, diseases that alter the central nervous system, and the effects of certain drugs[8-9].

Sleep disturbances are reported in 25-40% of preschool and school-age children. SB may be comorbid with alterations in sleep architecture and form part of a sleep transition stage called micro-arousals, in which sudden changes in sleep depth occur and the individual transitions to a lighter sleep stage. This sleep stage in this case is accompanied by sudden body movements, increased heart rate, respiratory changes, peripheral vasoconstrictions, and increased muscle activity. Sleep bruxism manifests as an intensification in the frequency and strength of natural orofacial activity during sleep, referred to as rhythmic masticatory muscle activity (RMMA)[6,8,11-15].

The use of retrospective questionnaires in this study provides information that supports an additional field of research centering on the etiopatogenia of childhood SB, which would help establish protocols for the prevention and management of this behavioral alteration. Consequently, the objective of this study was to examine the association between parent-reported sleep bruxism and various sleep disorders in children.

MATERIALS AND METHODS

An observational, descriptive cross-sectional pilot study was conducted at a pediatric dentistry clinic following approval by the ethics committee and with the informed consent of the child's parent or guardian. The sample consisted of 43 children aged 6-12 who met the selection criteria. Participation in the study was voluntary, and the privacy and confidentiality of the data obtained during the study was safeguarded at all times in conformity with the terms established under Spanish data protection legislation (Organic Law 15/1999).

The questionnaire collected data on patient affiliation, age and gender, general health status, clinical data related to temporomandibular disorders (such as headaches in the temporomandibular region), the presence of joint noises or clicking, and limitations in jaw aperture[16]. Based on parental reports, the presence of potential sleep bruxism was assessed according to the Lobbezoo et al. diagnostic classification scheme[3]. Lastly, parents or guardians responded to questions on the Sleep Disturbance Scale for Children (SDSC) (O. Bruni et al.)[17], designed to identify sleep disorders in children (Figure 1). The scale was used to investigate the occurrence of sleep disorders over the prior six months. It contains 26 items designed to assess six types of behavioral sleep disorders, including: Disorders of Initiating and Maintaining Sleep (DIMS), Respiratory Sleep Disorders (RSD), Disorders of Arousal (DOA), Sleep-Wake Transition Disorders (SWTD), Excessive Sleepiness (ES) and Night Sweats (Sleep Hyperhidrosis, SHY)[17-19].

A. BRUNI SLEEP DISTURBANCE SCALE FOR CHILDREN (SDSC)

This questionnaire will allow your doctor to gain a better understanding of your child's sleep-wake ratio and of any potential problems in their sleep behavior. Try to answer all questions. Consider each question in terms of only the last 6 months in your child's sleep behavior. Please answer each question by circling or crossing out the numerical score you assign.

Name: _____ **Age:** _____ **Date:** _____

1. How many hours does your child manage to sleep most nights?	1 9-11 hours	2 8-9 hours	3 7-8 hours	4 5-7 hours	5 Less than 5 hours
2. How long after going to bed does your child usually fall asleep?	1 Less than 15'	2 15-30'	3 30-45'	4 45-60'	5 Less than 60'

					5 siempre (diario)
					4 Often (3 to 5 times per week)
					3 Sometimes (1 or 2 times per week)
					2 Occasionally (once or twice a month or less)
					1 Never
3. The child goes to bed in a bad mood	1	2	3	4	5
4. The child has difficulty falling asleep at night	1	2	3	4	5
5. The child feels anxiety or is afraid of falling asleep	1	2	3	4	5
6. The child is startled or parts of their body jerk when falling asleep	1	2	3	4	5
7. The child engages in repetitive movements, such as head-rolling to fall asleep	1	2	3	4	5
8. The child lives out dream sequences when falling asleep	1	2	3	4	5
9. The child sweats profusely while falling asleep	1	2	3	4	5
10. The child wakes up more than twice at night	1	2	3	4	5
11. After waking up at night, the child has difficulty falling asleep again	1	2	3	4	5
12. The child experiences frequent leg contractions or jerking while sleeping, or often changes position at night, or kicks the bed sheets	1	2	3	4	5
13. The child experiences difficulty in breathing during the night	1	2	3	4	5
14. The child gasps for breath or is unable to breathe during sleep	1	2	3	4	5
15. The child snores	1	2	3	4	5
16. The child sweats profusely at night	1	2	3	4	5
17. You have observed your child to sleepwalk	1	2	3	4	5
18. You have observed your child to sleep-talk	1	2	3	4	5
19. The child grinds their teeth during sleep	1	2	3	4	5
20. The child wakes from dreams screaming or confused	1	2	3	4	5
21. The child has nightmares they do not remember the next day	1	2	3	4	5
22. The child is difficult to wake up in the mornings	1	2	3	4	5
23. The child wakes up feeling tired in the morning	1	2	3	4	5
24. The child feels unable to move when waking up in the morning	1	2	3	4	5
25. The child experiences daytime sleepiness	1	2	3	4	5
26. The child suddenly falls asleep at inappropriate moments	1	2	3	4	5
Difficulty initiating or remaining asleep (add up scores for items 1,2,3,4,5,10,11)					
Respiratory sleep disorders (add up scores for items 13,14,15)					
Awakening disorders (add up scores for items 17,20,21)					
Sleep-wake transition disorders (add up scores for items 6,7,8,12,18,19)					
Excessive sleepiness disorders (add up scores for items 22,23,24,25,26)					
Sleep hyperhidrosis (add up scores for items 9,16)					
Total score (add up scores for items for all 6 factors)					

Figure 1. O. Bruni et al.[17] Sleep Disturbance Scale for Children (SDSC).

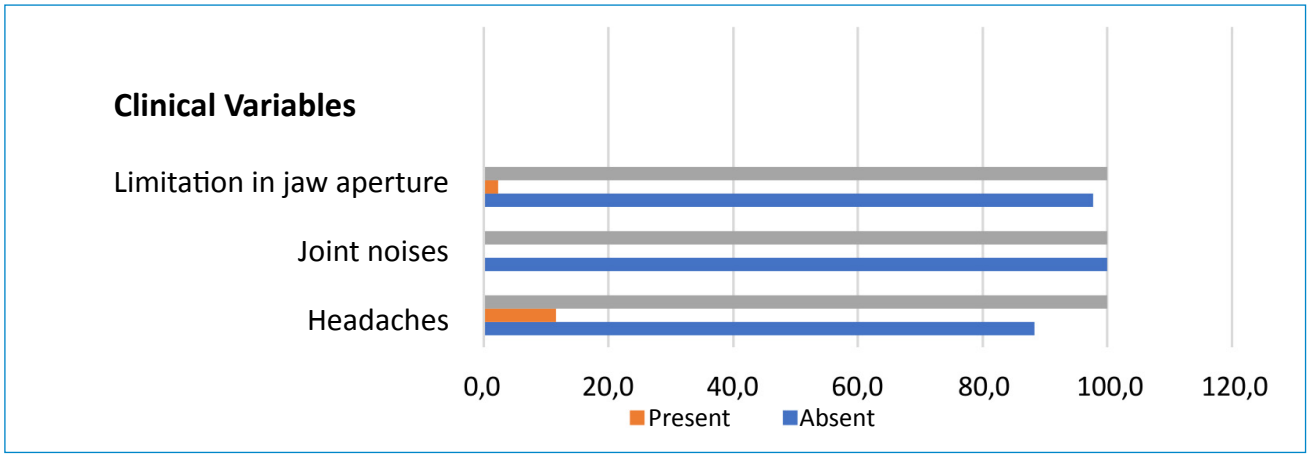

Figure 2. Clinical variables related to temporomandibular disorders.

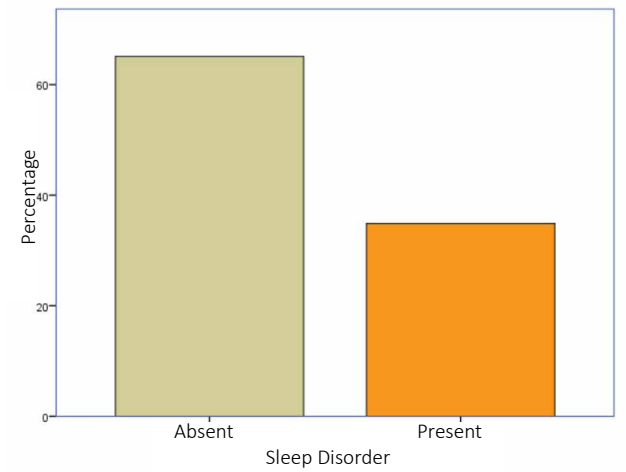

Figure 3. Assessment of sleep disorders on the SDSC scale.

bruxism is a multifactorial disorder, two secondary variables were also evaluated that are evidentially related to the etiology of SB and which we believe could be present in our study population, such as passive smoking and the occurrence of parental SB.

The SPSS application for Windows (v20) was employed to conduct the statistical analysis, split into an initial descriptive analysis and an inferential statistical analysis, where 2 x 2 contingency tables were created to cross-tabulate the qualitative variables using the CROSSTABS function in SPSS. A chi square test and Fisher's Exact Test were used to gauge the independence or dependence between variables. The Phi coefficient was used to measure the strength of the association between the two binary variables, with $p<0.05$ taken as the minimum measure for statistical significance.

RESULTS

In terms of the traits of the sample population, the mean age was 9 y/o, 69.8% female and 30.2% male.

The frequency of parent-reported sleep bruxism was 25.6% among all parents. The frequency of clinical variables related to temporomandibular disorders was higher in the case of headaches (11.6%), followed by limitation in jaw aperture (2.3%), with joint noise or audible clicking not reported by any participants (Figure 2).

Regarding assessment of sleep disorder, 34.9% had a score indicative of a sleep disorder (Figure 3). The most common disorders in the study population were sleep-wake transition disorders (53.5%), followed by sleep onset and maintenance disorders (44.2%). Respiratory sleep disorders (39.5%) were less commonly present, followed by excessive sleepiness disorders (34.9%), sleep hyperhidrosis (32.6%) and waking disorder in only (25.6%) of cases (Figure 4).

With regard to inferential analysis, the association between potential parent-reported SB and the presence of sleep disorders was statistically significant (p=0.000). However, the strength of association was measured using the Phi coefficient, with results of 5.77 being indicative

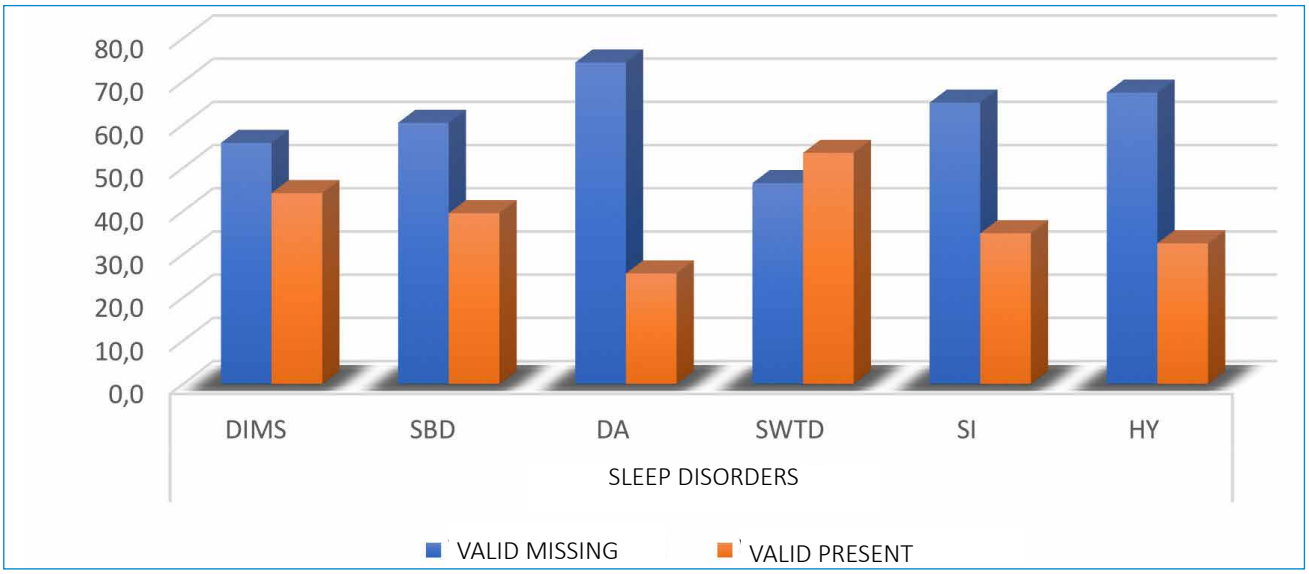

Figure 4. Evaluation of various sleep disorders on the SDSC scale.

of a moderate association. Regarding the association of SB and the various sleep disorders evaluated, only the association of sleep-wake transition disorders and respiratory sleep disorders were found to be statistically significant in both cases (p=0.00 and p=0.01, respectively). The strength of the association measured with the phi coefficient with respect to respiratory sleep disorders was 3.98, indicating a weak association, and 5.47 in the case of sleep-wake transition disorders, indicating a moderate association (Figure 5).

With respect to the secondary variables evaluated, measures of passive smoking and sleep bruxism in parents were low in frequency and their association with SB was not significant.

DISCUSSION

Given the studies finding that SB episodes can be associated with micro-arousal in 86% of cases[6,8], SB can be comorbid with poor sleep quality, manifesting itself as an intensification of orofacial activity (RMMA) in terms of frequency and strength during sleep, falling within the scope of pathology.

Regarding the association between the presence of sleep disorders and parent-reported SB, in his study on the prevalence and risk factors of SB in infant population, Ferreyra obtained statistically significant results ($p<0.01$) involving children with sleep disorders[20]. In a systematic review evaluating the risk factors associated with SB, Clastroflorio et al. found that children with sleep disorders were more likely to have SB[21].These results are considered similar to those obtained in our study, showing a statistically significant relationship between sleep disorders and parent-reported potential SB.

Regarding the evaluation of various sleep disorders using the SDSC scale and their association with SB, while no studies were found that use the same scale to assess various sleep disorders in child populations, certain sleep behaviors relating to each disorder on the scale can be compared to different studies. This study found a significant association between SB and sleep-wake transition disorders and respiratory sleep disorders. Similarly, Restrepo et al.[14] used the child sleep habit questionnaire (CSHQ) and observed that sleep anxiety and sleep breathing disorders increased with the frequency of parent-reported SB in a statistically significant manner ($p<0.05$). Tachibana et al.[22] mention in their study that sleep bruxism shows direct correlations with child sleep behaviors described as “moves a lot during sleep”, “sleeps with mouth open”, and “snores heavily”. Such sleep behaviors are

Inferential Statistics			Sleep Bruxism				Total	Test
	Sleep Disorder		Presence		Absence			
	DIMS (Disorders of Initiating and Maintaining Sleep)		N	%	N	%	N	
		Presence	7	63.6	12	37.5	19	F=0.17
		Absence	4	36.4	20	62.5	24	P>0.05
	SBD (Respiratory Sleep Disorders)	Presence	8	72.7	9	28.1	17	F=0.43
		Absence	3	27.3	23	71.9	26	P<0.05
								C. Phi =3.98
	DOA (Disorders of Arousal)	Presence	4	36.4	7	21.9	11	F= 0.43
		Absence	7	63.6	25	78.1	32	P>0.05
	SWTD (Sleep–Wake Transition Disorder)	Presence	11	100	12	37.5	23	F=0.00
		Absence	0	0.0	20	62.5	20	P<0.05
								C. Phi =5.47
	ES (Excessive Sleepiness)	Presence	3	27.3	12	37.5	15	F=0.71
		Absence	8	72.7	20	62.5	28	P>0.05
	SHY (Sleep Hyperhidrosis)	Presence	6	54.5	8	25.0	14	F=0.13
		Absence	5	45.5	24	75.0	29	P>0.05
		Total	11		32			

The value shown for (F) corresponds to Fisher's Exact Test.

Figure 5. Association of parent-reported SB with various sleep disorders.

similar to those found in our study pertaining to sleep-wake transition disorders and hypervigilance (the child startles or jerks parts of their body during sleep) and respiratory sleep disorders, such as difficulty breathing, gasping, and the presence of snoring during sleep.

The interpretation of our study findings is limited by the lack of a definitive diagnosis of SB, which can be only be determined with a polysomnography exam, considered to be the gold standard for sleep bruxism diagnosis. High financial cost, time limitations, and the need for sophisticated technical equipment, together with an unknown laboratory environment and difficulties in its use with children limit its use as a routine diagnosis. Thus, the data obtained in this pilot study allow us to assess the use of other tools employed in clinical situations and propose new lines of research in the etiopatogenia of sleep bruxism in children.

CONCLUSIONS

There exists a statistically significant strength of association between parentally assessed sleep disorders and parent-reported sleep bruxism. Behaviors associated with sleep-wake transition disorders and respiratory sleep disorders may also be associated with sleep bruxism in children.

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Clinical case study

Periodontal Implications of Cannabis Abuse. Review and Clinical

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ABSTRACT

Cannabis abuse, especially in its most common form, marijuana, has commonly been associated with poor oral hygiene for many years. Cannabis addicts tend to have higher levels of plaque, xerostomy and cavities. However, few publications link marijuana to periodontal disease, except for isolated clinical cases. This article reviews the literature on the subject and presents three clinical cases of habitual marijuana smoking patients with periodontitis.

KEYWORDS

Periodontal disease; Periodontitis; Necrotizing periodontitis; Necrotizing gingivitis; Cannabis; Marijuana; Drugs.

INTRODUCTION

Cannabis is one of the most highly used recreational illicit drugs[1,2]. It contains a family of chemicals called cannabinoids, some of which are psychoactive. Although it seems to possess potentially beneficial effects, as cannabinoids attenuate the production of some inflammatory mediators[3], non-medical use can cause adverse side effects on both general health (including the oral cavity) and mental health, especially when consumed regularly and for long periods of time.

Cannabis for consumption is derived from the Cannabis sativa plant. The plant contains over 400 compounds, including 60 types of cannabinoids. Cannabinoids are a heterogeneous family of molecules which act on cannabinoid cell receptors, the principal one being the delta-9-tetrahydrocannabinol (THC) cannabinoid. The three main forms of cannabis are marijuana, hashish, and hash oil[1].

Smoking marijuana is the most common and efficient way to consume cannabis. When smoked, approximately 50% of the THC is absorbed through the lungs and enters the bloodstream. From there it enters the brain in a matter of seconds. The results from the latest epidemiological study from the Spanish Observatory on Drugs and Drug Addiction (EDADES: Survey of Alcohol and Drug Abuse in Spain, conducted in 2015)(4) shows that 31.5% of the Spanish population aged between 15 and 64 has used cannabis at some time, 9.5 per cent in the last year, 7.3 per cent in the last month, and 2.1 per cent on a daily basis during the last month. The demographic with the highest rate of abuse consists of young males under the age of 25, who on average smoke three joints of marijuana a day.

One major social concern is that the onset of cannabis use normally occurs during adolescence. The earlier in life young people start using marijuana, the more likely they are to become regular users or end up developing a dependency. Teenagers start experimenting with cannabis on average at the age of 18. In addition, the Survey on Drug Abuse in Spanish Secondary Education (ESTUDES, 2014-2015, involving students aged 14 to 18)[5] found that 29.1% admit to having smoked cannabis at some time, 18.6% in the last month, and 1.8% daily. In addition, of those who smoke it daily, 13.8% have substance abuse issues (3 joints per day, according to the Survey), with the negative consequences that this implies.

The negative effects of cannabis use affect almost all systems in the body, as well as overall user health[1,6]. With respect to the cardiovascular system, dose-dependent tachycardia and generalized vasodilation occur. This increase in heart rate causes an increase in heart work and increased oxygen demand, which can lead to cardiac ischemia. In addition, as the ingestion method is via deep inhalation, a very high concentration of carboxyhemoglobin is absorbed from carbon monoxide, which reduces oxygen levels in the heart.

The effects of cannabis use on the respiratory system are mainly associated with long-term abuse of marijuana. A marijuana cigarette (rolled joint) contains the same substances as would regular tobacco, except nicotine. This includes carbon monoxide, bronchial irritants, tar, and higher levels of other carcinogens. Regular marijuana smokers have a higher prevalence of bronchitis and emphysema than nonsmokers. In addition, it is very important to note that the long-term consumption of 3-4 marijuana cigarettes is equivalent to smoking 20 cigarettes a day, or more[1]. This difference stems from the deep inhalation use pattern and the absence of any filter. Three times more tar is absorbed through deep inhalation than is the case with normal cigarettes.

THC, on the other hand, has an immunosuppressive effect on macrophages, natural-killer cells and B and T lymphocytes, which causes a reduction in host resistance to infections, and also increases the secretion of proinflammatory cytokines, such as IL-1[6].

For some years now, it has been often reported that regular cannabis users have worse oral health than do non-smokers, with a higher presence of cavities, especially cervical, higher rates of missing teeth and levels of plaque. One of the most significant effects of cannabis is xerostomy, which can increase the risk of cavities[6-8]. So-called cannabinoid hyperemesis is also

typical of cannabis abuse, characterized by frequent episodes of vomiting. This can cause acid erosion of dental enamel[9]. There has been little scientific evidence linking periodontal disease to cannabis addiction; there is only a handful of clinical case studies, one experimental study in rats and, in recent years, several epidemiological studies.

The first references found in the literature on this subject were published by Darling and Arendorf in 1992 and 1993[7,8]. These authors observed how their cannabis smoking patients had painful, "fire-red" gingivitis with associated white patches, as well as diffuse gingival hyperplasia with concurrent alveolar bone loss. So-called cannabis stomatitis has also been described in the literature, characterized by a number of changes in the oral epithelium, including oral mucosa leukoedema and hyperkeratosis[6], which can evolve into leukoplakia and subsequently progress to oral cancer[8]. In an experimental 2011 study of periodontitis in 30 rats, Nogueira-Filho and et al.[3] demonstrated a statistically significant increased loss of bone support and bone density in the jaw in the experimental group (15 rats subjected to daily inhalations of cannabis for one month).

Cannabis use is more common at an early age, most consumers drop the habit relatively early when they reach adulthood[10]. However, individuals who continue to smoke cannabis at the age of 30 are classified as "long-term" users, and may be at risk of developing what is known as amotivational syndrome[11], characterized by general apathy, emotional withdrawal, and lack of fluidity and spontaneity in conversation[2]. In addition, the subjects do not usually take proper care of personal hygiene or appearance, including oral hygiene, nutrition, and general health. In these cases, dental and periodontal disease may occu [9]. Another factor to bear in mind that favors the development of periodontitis among cannabis addicts is deficient nutrition. Such individuals tend to have poor eating habits, with an erratic and irregular meal pattern along with a below-normal body mass index[9].

Given the limited information regarding the association of marijuana abuse and the presence of periodontal pathologies, we wish to present three clinical cases of habitual marijuana smokers who suffered from necrotizing periodontitis.

CLINICAL CASES

Case 1

A 34-year-old male who came in for a visit complaining of significant gingival-related pain. After taking his medical history, he acknowledged that he smoked eight[8] cannabis joints every day. Complete blood work was requested to rule out other associated pathologies, which showed high levels of C-reactive protein (0.82 mg/dL, < 0.1 mg/dL being the norm), an acute phase protein that indicates systemic inflammation and may be increased in severe cases of periodontal disease.

Upon examination, the patient was found to suffer from necrotizing periodontitis, with ulceration and necrosis of interdental papillae, especially in the lower incisors. A large amount of supra and subgingival calculus was also observed. Areas with necrosis were painful in response to catheterization, and the patient referred to experiencing pain in these locations when eating and brushing (Figure 1).

As periodontal treatment, the patient was instructed in oral hygiene techniques (appropriate tooth brushing plus use of interdental brushes) while stressing the need to eliminate harmful habits, such as tobacco and cannabis smoking. Perio scaling and root planing per quadrant was applied, along with empirical antibiotic treatment (metronidazole 500 mg every 8 hours), in addition to the use of 12% chlorhexidine gel and mouthwash every 12 hours for a month. After one month, his oral hygiene had improved considerably, inflammation and areas of gingival necrosis had disappeared, and response to periodontal catheters was normal. In addition, he had managed to reduce his cannabis intake to one joint per day. It was therefore decided to move the patient to the periodontal maintenance phase, the treatment regime he is currently under (Figure 2).

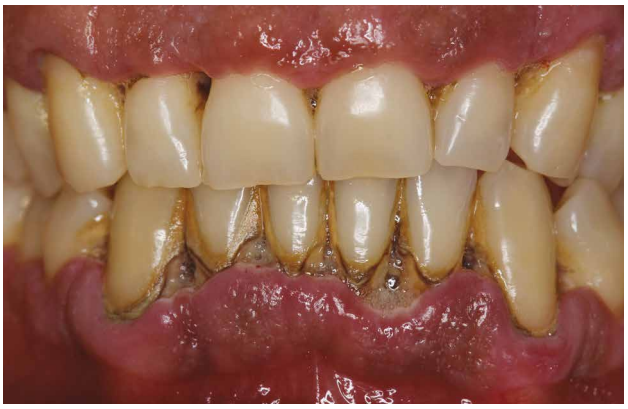

Figure 1. Necrotizing periodontitis, Case 1 patient.

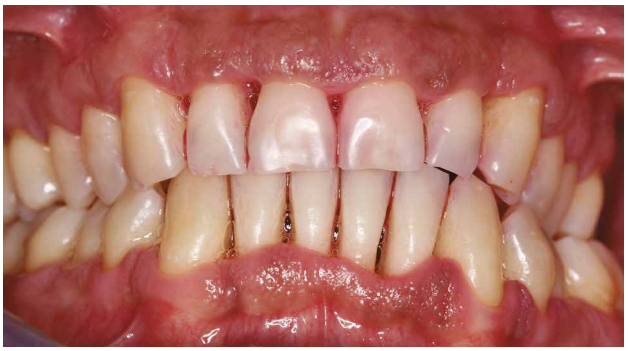

Figure 2. Case 1 patient clinical status upon reexamination following the basic periodontal treatment phase.

Case 2

A 31-year-old male whose motive for consultation was the significant and extensive pain he was experiencing in his gums, which even prevented him from eating (Figure 3 and 4). During anamnesis, he acknowledged that he smoked 2 cannabis joints and 30 tobacco cigarettes a day. A blood test was performed, and the results showed he was positive for the hepatitis C virus; the patient had been unaware of being a carrier until that time.

The patient's diagnosis was chronic, moderate-severe periodontitis, with large regions of necrotizing periodontitis, both in incisors and upper molars. The patient was treated by modifying his oral hygiene habits, Perio scaling and root planing per quadrant and systemic antibiotics, consisting, in this case, in Vibramycin 100 mg every 12 hours due to his liver problems. The patient, however, was unable to change

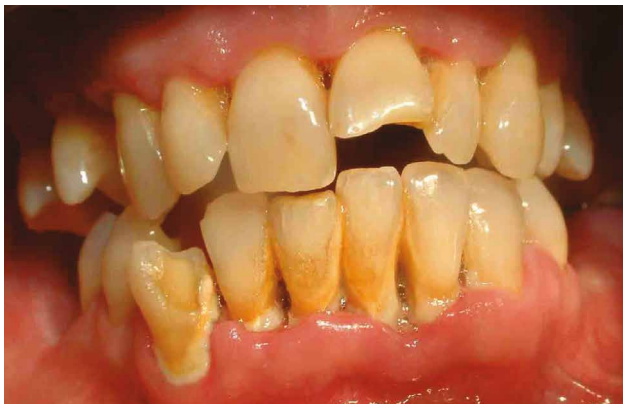

Figure 3. Patient Case 2 periodontal status when he first came in for an appointment. Note the necrosis of gingival papillae in the anterior region.

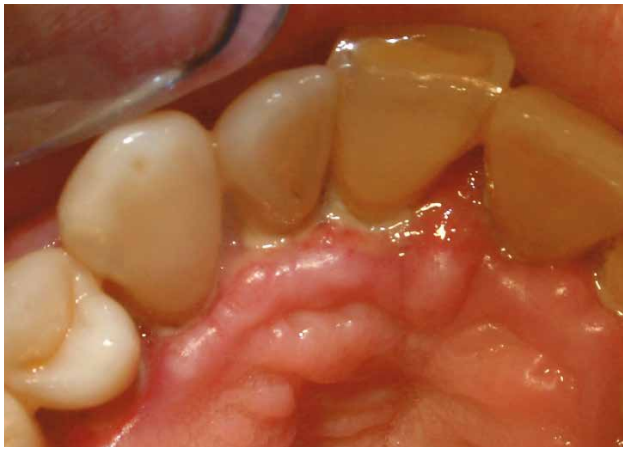

Figure 4. Papillary necrosis and palatine suppuration of the upper teeth in the Case 2 patient prior to treatment.

his habits, nor did we manage to motivate him to do so, and shortly after starting he ceased seeking treatment.

Case 3

A 28-year-old male who visited the clinic accompanied by his mother, apathetic and poorly motivated to improve his oral health. Examination showed he had cavity lesions in almost all his teeth, some already impossible to restore, and the presence of moderate-severe periodontitis, with regions of necrotizing periodontitis (Figure 5).

He acknowledged that he smoked over 30 cigarettes and 2 joints per day. A blood test was ordered to rule out some other systemic pathology, finding that all blood parameters were within normal limits.

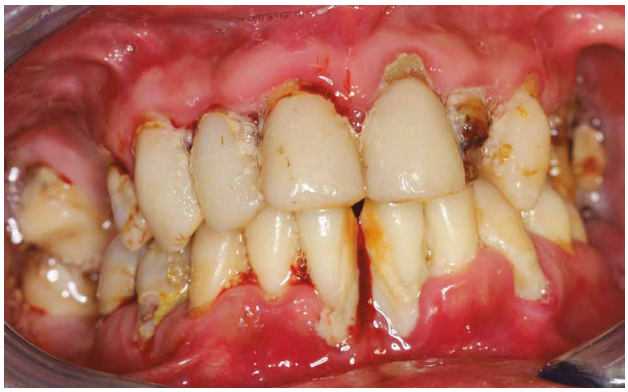

Figure 5. Initial Case 3 patient status, gingival inflammation, suppuration, papillary necrosis, major loss of periodontal insertion in lower incisors, as well as cavities in various teeth can be observed.

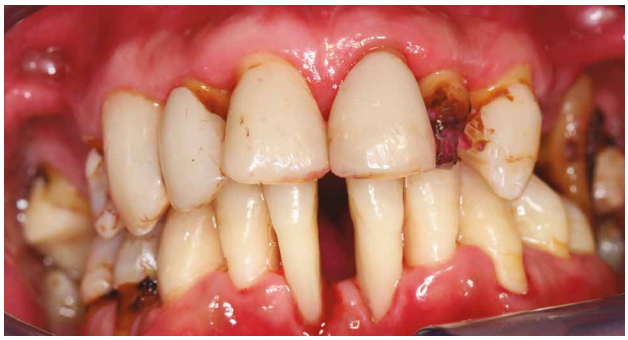

Figure 6. Case 3 patient status following reexamination, showing improved gums, although no restorative treatment had been carried out.

He was encouraged to change his oral hygiene habits. An attempt was made to eliminate or at least reduce his harmful habits. Periodontal treatment consisted in Perio scaling and root planing per quadrant, along with antibiotic treatment (metronidazole 500 mg every 8 hours for a week) and antiseptic (chlorhexidine at 0.12% every 12 hours for a month). In addition, he was advised to undergo restorative treatment consisting of filling cavities and extracting the teeth that were beyond repair. During reexamination following the basic periodontal treatment phase (Figure 6), he was observed to have managed to reduce his smoking habit to 12 cigarettes a day. However, he did not return soon thereafter, and not until a year had passed. At that time, he had not performed the rest of the required treatment.

DISCUSSION

Cannabis use, as highlighted by the surveys by the Spanish Observatory on Drug Use and Addiction, is very common in the population aged 15 to 34. Between 15 and 20% of young people in these age groups admit to having consumed cannabis at some point. In terms of gender, consumption is more widespread in males. Among females, the prevalence is lower, ranging from 2 to 11 points less, depending on the age range. As we have seen, the three cases of necrotizing gingival lesions we present had been observed in males.

Apart from some isolated clinical cases[12,13] and those presented in this paper, there is very little literature on the effects of cannabis use on periodontal health. The few cases described to date may be due to the ethical and legal ramifications involved in this addictive conduct. Also, identifying this use as an exclusive risk factor for periodontal disease is difficult, as there are other predisposing factors that can influence susceptibility to necrotizing periodontitis, such as age, oral hygiene, tobacco use, general health, or combined use with other types of drugs. Above all, it should be borne in mind that cannabis is usually mixed with tobacco in hand-rolled cigarettes in Spain[6], a factor which prevents determination of the precise influence of each component in gingival pathologies. In the case of the patients we discuss, the first patient only smoked cannabis, while the other two were both cannabis and tobacco users.

In 2008, the first longitudinal study attempting to link the use of cannabis to periodontal disease was published[14]. Thomson et al. conducted a longitudinal cohort study of all children born in a New Zealand hospital between 1972 and 1973 which continued until they were 32 years old.

From the time they turned 18, the study classified the 1,037 children into three groups: non-cannabis smokers, moderate cannabis smokers (<40 times/year), and heavy cannabis smokers (>41 times/year). At age 32, they found that cannabis use was a risk factor for periodontitis. Patients with high exposure to cannabis had a 7-fold higher risk of periodontal disease

than those who did not. In addition, the severity of periodontitis was also significantly higher among heavy users after adjusting for tobacco use as a contributing factor. They concluded that smoking cannabis could be an independent risk factor for developing periodontitis, as in the case of tobacco. In addition, it is interesting to note that in New Zealand, cannabis is not habitually mixed with tobacco, so the results of this study eliminate this obfuscating factor. They attributed their findings to exposure to the more than 400 deleterious substances contained in cannabis, some cannabinoids, and others similar to tobacco.

This longitudinal study was prolonged for 5 additional years[15]. Previous subjects were re-evaluated at the age of 38 to see if continued cannabis use over the course of 20 years could worsen their overall health. Various periodontal health, lung function, inflammation, metabolic syndrome, HDL cholesterol, triglycerides and glycosylated hemoglobin parameters were considered. Of all the factors analyzed, only periodontal health was related to the continued use of cannabis, even after controlling for tobacco use, brushing, flossing, and alcohol use as contributing factors. Thus, they serve to confirm that cannabis can be an independent risk factor for periodontal disease.

On the other hand, in 2017 Shariff et al.[16] published a major epidemiological study, part of the U.S. National Health and Nutrition Examination Survey (NHANES) conducted between 2011-2012. Nine hundred eighty (980) men and nine-hundred fifty-eight (958) women aged between 30 and 59 were examined periodontally in six[6] locations per tooth and divided into two groups: cannabis users (>= 1 use per month during the last year), and non-cannabis users. In this representative sample, 27% reported smoking cannabis at least once per month. The findings of the study showed a significant association between cannabis use and worse periodontal condition (greater depths and worse levels of catheter insertion) with respect to non-users. In addition, after adjusting for all significant contributing factors, cannabis users were more likely to suffer from severe periodontitis than were non-users. The most significant contributing factor was tobacco, and once eliminated, the study created a second model that included only participants who had never smoked tobacco. In this case, cannabis users who never smoked tobacco were twice as likely to present worse periodontal health than were non-cannabis users. This led them to corroborate the data from Thomson et al.[14] and Meier et al.[15] and conclude that the use of cannabis is an independent risk factor from tobacco for periodontitis in young adults.

However, there are other studies, such as the one published by López and Baelum[17] in 2009, that do not find a significant relationship between cannabis use and periodontal disease. This work consists of a cross-sectional study of 9,163 students from Santiago de Chile which evaluated these patients periodontally. This study has differences with respect to the prospective study of Thomson et al.[14] in that patients are younger (12-21 years), only periodontal health is evaluated, and in addition the duration of exposure to cannabis was much shorter. Lopez and Baelum[17] suggest that the effect of cannabis on periodontal health may be greater in patients who have used cannabis over a long period of time. In this regard, three patients in our clinical study were all young adults, aged close to 30 years, and heavy users since adolescence. The effects of the drug on their periodontal hygiene may be more severe than in the case of much younger cannabis users where such long-term exposure has not yet occurred. It should also be borne in mind that the persistence over time of this habit makes behavioral modification all the more challenging.

Finally, we wish to emphasize that, although periodontal treatment and hygiene motivation were equally applied in all three patients, we only managed to reduce cannabis use and encourage a lasting motivation to modify behavior associated with proper and suitably periodic periodontal care in the case of the first patient. In contrast, the other two patients clearly suffered from amotivational syndrome, characterized by apathy, deficient social interaction with clinic professionals and complete lack of discipline in terms of plaque control. This made it very difficult for the periodontists and hygienists who cared for the patients to do so.

We can conclude that there is scant yet highly relevant data that show that cannabis users possess deeper periodontal sacks, higher levels of periodontal insertion loss and therefore higher likelihood of severe periodontitis than do non-users. In addition, the use of cannabis in the absence of tobacco use appears to influence periodontal pathology, although the biological mechanisms that link the two processes are unknown. On the other hand, we have seen that this risk factor is time-dependent, since it has been observed that the longer the habit lasts, the greater loss of ensuing periodontal insertion. We believe it necessary, given that there are few publications on periodontal disease and cannabis abuse, that more studies on this subject be conducted, as well as developing dental protocols and guidelines for such patients, similar to those that exist for habitual tobacco users. In addition, dental professionals should be aware of and bear in mind the deleterious effects of cannabis abuse on general, psychological, and oral health. It is advisable to take this risk factor into account when putting together a medical history, consistently inquiring about cannabis use as a conduct with repercussions on oral hygiene. Moreover, in such cases there is greater reason to consider motivation critical to the overall treatment protocol since it is essential to achieving both an improvement in the periodontal health of such patients, as well as in their habitual behavior and consequently their overall physical and emotional health.

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Clinical case

Combined Surgical Approach for Disinfection and Regeneration of Peri-Implant Defects. Three Case Report

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ABSTRACT

Dental implants suffer a high incidence of mucositis and peri-implantitis, which can lead to failure. There are multiple non-surgical and surgical therapeutic approaches for these pathologies, although surgical treatment is indicated for peri-implantitis. Surgery may take the form of access surgery, resective and/or regenerative treatment. In order to achieve biofilm removal and improvement of peri-implant tissues, prior implant decontamination should always be performed. Mechanical, chemical, antibiotic or laser methods may be used to carry out the procedure. This article discusses three clinical cases in which a combined surgical approach was used employing implantoplasty, decontamination with chlorohexidine and orthophosphoric acid, application of local antibiotic (piperacillin/tazobactam) and regeneration via synthetic hydroxyapatite and resorbable membrane, showing favorable clinical outcomes consistent with bibliographical references.

KEYWORDS

Peri-implantitis; Implantoplasty; Piperacillin; Tazobactam; Hydroxyapatite.

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INTRODUCTION

Treatment with dental implants is a highly predictable procedure, with survival rates between 94.52% and 96.63%[1]. However, the high frequency of peri-implant mucositis and peri-implantitis has been observed to affect patients. Mucositis is characterized by inflammation of the peri-implant mucosa with no signs of bone loss and affects about 80% of patients and 50% of implants. Peri-implantitis consists of the involvement of hard tissues in addition to the mucosa, and affects between 28 and 56% of patients, as well as between 12 and 40% of implants, according to the 2008 European Peri-implantitis Workshop[2].

There are multiple therapeutic approaches which fall into two main categories: non-surgical and surgical treatment. Non-surgical treatment consists in the removal of biofilm from the peri-implant surface using various means: curettes, ultrasound, abrasive air systems and lasers, which can be accompanied by a variety of disinfection protocols: chlorhexidine, citric acid, minocycline, etc. This treatment is effective for mucositis and the prevention of peri-implantitis but fails to be effective for the latter pathology once established[3,4]. According to the depth of peri-implant defects, various authors recommend a surgical approach, either through access surgery, resective surgery, regenerative treatment, or combined resective-regenerative treatment. Such surgical protocols should be accompanied by disinfection procedures employing chemical treatments or antibiotics. There exists a broad array of antibiotics and combinations thereof suitable for topical application; however, there is no consensus regarding their long-term effectiveness for peri-implantitis suppression[5].

The objective of this study is to assess the effectiveness of a novel combined approach to peri-implantitis treatment using implantoplasty and regenerative techniques accompanied by disinfection with a combination of piperacillin and tazobactam antibiotics.

CLINICAL CASES

Three clinical cases that were handled by the Oral Surgery and Implantology Service at the Virgen de la Paloma Hospital in Madrid for peri-implantitis treatment are described below.

Case 1

A 47-year-old male patient, smoker, no significant medical history, complained of "bleeding during brushing." Inflammation of the peri-implant mucosa in implants at 25 and 26 was observed during intraoral examination. Two years had passed since placement of the implants without any follow-up protocol. During clinical examination, bleeding and suppuration was observed during catheter insertion at probe depths >6 mm. Radiological examination showed the presence of peri-implant bone defects in both implants, with bone loss levels greater than 50% of the implant length at 26 (Figure 1).

Case 2

A 62-year-old female patient, with no significant medical history, complained of looseness in the bridge over implants from 12 to 22. The implants had been placed 5 years earlier. An increased catheter probe depth of >4 mm with bleeding upon implant probing was observed at 22, accompanied by radiological bone loss of >2 mm (Figure 2).

Case 3

A 65-year-old male patient, with no significant medical history, with a single crown implant at 36, complained of food entrapment at 36. Upon intraoral examination,

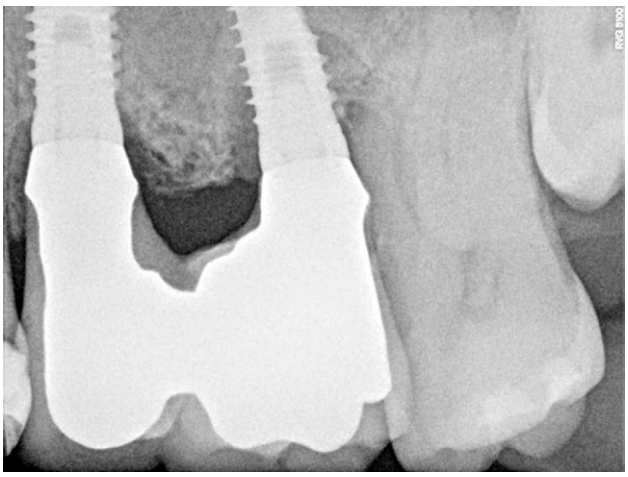

Figure 1. Case 1: Initial periapical x-ray.

clinical screw loosening was detected, with consequent corona mobility, food entrapment and inflammation of the peri-implant mucosa. During periodontal and peri-implant assessment, good periodontal health was determined, while at the implant level at 36 bleeding was observed upon catheterization with probe depth at >4 mm. Radiological examination yielded a diagnosis of peri-implantitis, confirmed by the presence of a peri-implant bone defect of around 3 mm (Figure 3).

In all three cases, the need for peri-implantitis treatment was indicated, using a combined surgical protocol consisting of implantoplasty, chemical and antibiotic decontamination, and regeneration using the Implacure® system (MTD, Switzerland).

Following the signing of informed consent, the first phase of the chosen protocol was carried out, which consisted of irrigation of the peri-implant sulcus with a 100/12.5 mg solution of piperacillin/tazobactam seven days prior to surgery.

The surgery was performed under local anesthesia. Intrasulcular incision was made, with mesial and distal discharges and flap raised to full thickness. The defect type was identified: Class Ic in case 1 (Figure 4), Class Ie in case 2 (Figure 5) and a combination of Class II and Class Ie in case 3 (Figure 6). Curettage of the defect was performed with ultrasound and preshaped curettes, and implantoplasty was performed using coarse, medium, and fine diamond burs included with the Implacure® system (Figure 7-9). Once the surface of the implant had been polished, it was chemically decontaminated by applying a 37% orthophosphoric acid gel combined with 2% chlorhexidine for two minutes, while taking the precaution of protecting the bone with gauze (Figure 10). Again, the surface of the implant was decontaminated by applying a gauze soaked in the piperacillin/tazobactam 100/12.5 mg solution and allowing it to act for one minute (Figure 11).

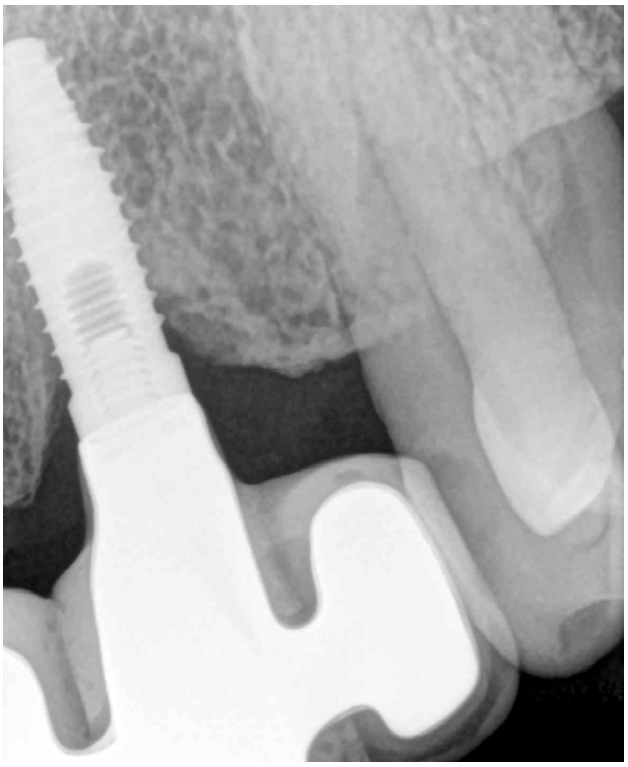

Figure 2. Case 2: Initial periapical x-ray.

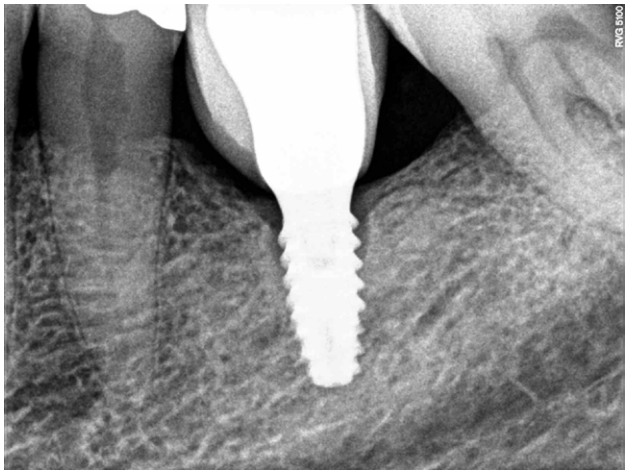

Figure 3. Case 3: Initial periapical x-ray.

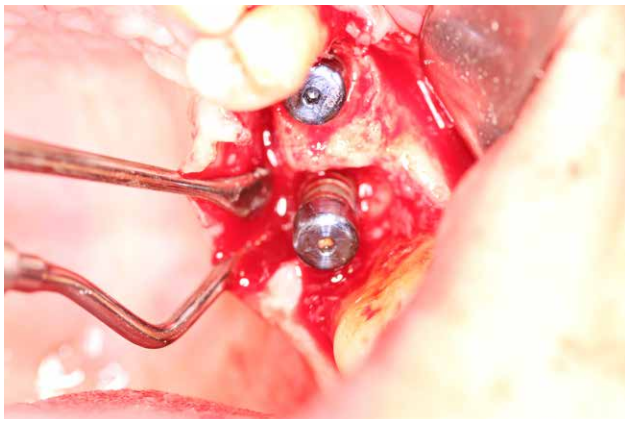

Figure 4. View of the defect after lifting flap in case 1.

Regenerative treatment of the peri-implant defect was then performed. Synthetic hydroxyapatite (Osbone®, Curasan, Germany) was used for this purpose, hydrated with a piperacillin/tazobactam solution, and covered with a collagen resorbable membrane (Osgide®, Curasan, Germany) hydrated with the same combination of antibiotics (Figure 12). Finally, submerged healing was fostered using a tensionless suture.

Clinical and radiological follow-up was carried out at one week, after 15 days, and at one, three and six months. After six months of follow-up, a decrease in catheter insertion depth (Table) and in bone defect at the radiological level was observed (Figure 13-15).

DISCUSSION

There are several therapeutic options for the management of peri-implantitis: using either access surgery or a resective or regenerative procedure, depending on the type of bone defect. In horizontal natural defects, resective treatment by implantoplasty and apical flap displacement is recommended. Regenerative treatment[5,6] is recommended in vertical infra-bony defects and wound dehiscence.

In any event, such surgical procedures must be accompanied by proper disinfection of the defect and the implant surface. Multiple procedures have been proposed for this purpose, including mechanical treatment, use of chemicals and/or antibiotics, or photo-dynamic systems[7]. However, since the objective is to achieve maximum decontamination of the peri-implant substrate, the use of these methods in combination with each other is recommended[8].

Dostie et al.[9] conducted an in vitro study comparing different disinfection methods. Rinsing with a saline solution was performed in all cases, in combination with 1% chlorhexidine, 35% orthophosphoric acid, tetracycline 250 mg, and a mix of cetrimide 0.3 with chlorhexidine 0.1 and EDTA 0.5. Compared to the use of saline solution alone, the bacterial count showed a 33.2% greater reduction when using chlorhexidine (p-0.028); 26.1% more when using orthophosphoric acid ($p<0.05$), and 33.9% more with the application of tetracycline (p-0.027).

However, when analyzing the survival rate of bacteria, a higher percentage of dead cells was observed in the groups treated with chlorhexidine and orthophosphoric acid: 11.8% (p-0.023) and 6.9% (p-0.017) respectively; greater than with the use of saline solution alone. This study shows the clinical results following treatment with a combination of chlorohexidine 2% and 37% ortho-phosphoric acid, showing reductions in the depth of catheter insertion, and no bleeding and suppuration upon probing. These results serve to corroborate the reduction in bacterial load in the peri-implant area.

In addition to chemical decontamination, numerous authors propose the use of intralesional antibiotics. For example, Faggion et al.[10] conducted a meta-analysis in which they observed that mechanical debridement together with topical application of antibiotics achieved greater reductions in the depth of catheterization than mechanical debridement treatment in isolation. (0.49 mm). The second most effective treatment was obtained by the combination of mechanical debridement and PerioChip® (2.5 mg chlorhexidine) (0.4 mm). However, by comparing the combined treatment of debridement together with antibiotics with debridement combined with chlorhexidine, the first group achieved a reduction in the depth of probing averaging 0.262 mm more than the second group.

TABLE. DEPTH OF PRE-SURGICAL CATHETER PROBE AND AT 6 MONTHS AFTER SURGERY.

	Case 1		Case 2		Case 3	
Probe depth (mm)	Baseline	6 months	Baseline	6 months	Baseline	6 months
Vestibular	6	3	5	3	3	2
Palatino	7	4	5	3	3	3
Mesial	7	3	6	4	4	3
Distal	7	3	6	3	4	3

Javed et al.[11] included 10 articles on the use of local or systemic antibiotics in their systematic 2013 review. Of the 10 studies, six administered the following antibiotics locally: tetracycline + doxycycline, minocycline, doxycycline, and tetracycline combined with hydrogen chloride (HCl) fibers. Five of these studies used non-surgical mechanical debridement techniques prior to the application of the antibiotic. In only one of the studies did patients undergo access surgery. Despite the different protocols used, statistically significant reductions in probe depth were observed in the six studies.

These results are consistent with those observed in the clinical cases described in this article, which show reductions in catheter insertion depth of between 1 and 3 mm after 6 months of follow-up.

It is worth taking note of the study conducted by Rams et al.[12], in which samples taken from 120 patients suffering from peri-implantitis were cultivated and analyzed for susceptibility to the following antibiotics: doxycycline 4 mg/l, amoxicillin 8 mg/l, metronidazole 16 mg/l and clindamycin 4 mg/l. Some 46.7% of patients had clindamycin-resistant bacteria, 39.2% were resistant to amoxicillin, 25% to doxycycline, and 21.7% to metronidazole. In addition, a post-hoc analysis showed that 6.7% of patients were home to species resistant to both amoxicillin 8 mg/l and metronidazole

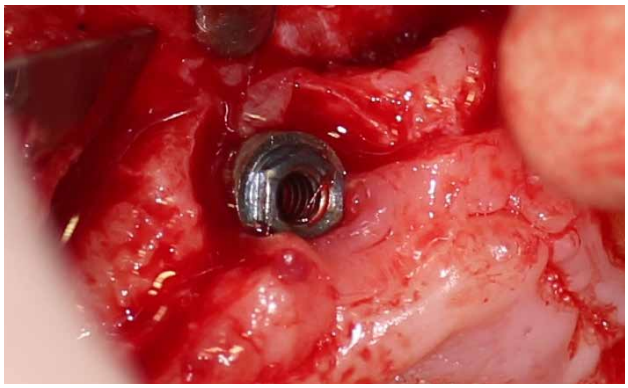

Figure 5. Circumferential defect in case 2.

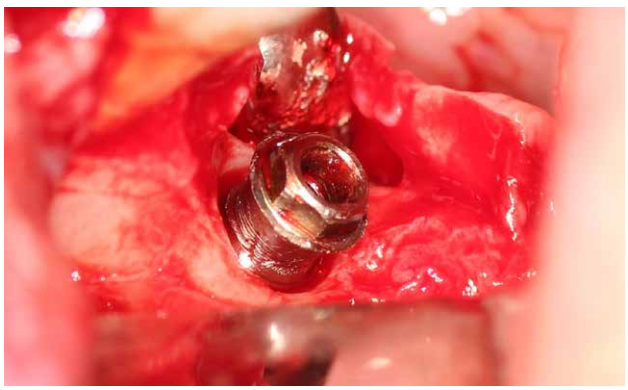

Figure 6. Horizontal and vestibular composite defect in case 3.

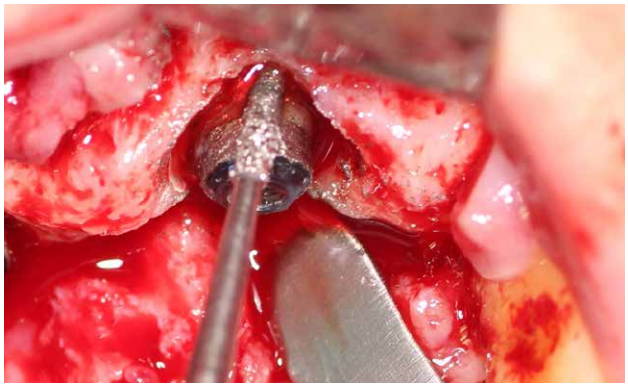

Figure 7. Implantoplasty with coarse-grained drill bit.

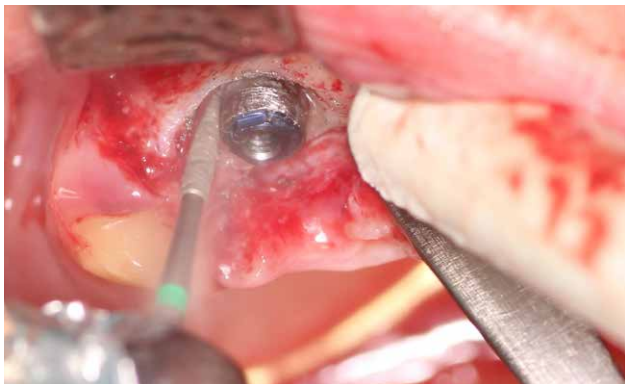

Figure 8. Implantoplasty with medium-grained drill bit.

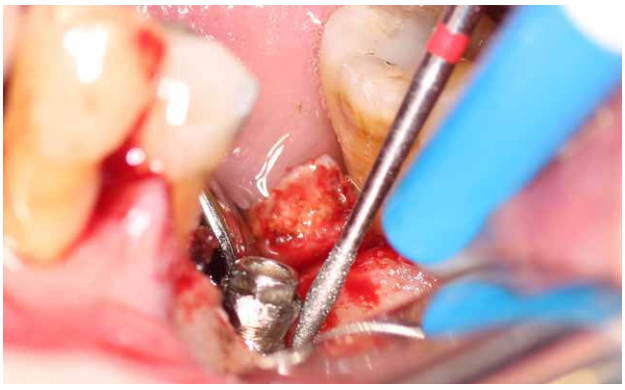

Figure 9. Implantoplasty with medium-grained drill bit.

16 mg/l. Overall, 71.7% of the 120 peri-implantitis patients showed pathogens resistant in vitro to one or more of the antibiotics studied.

Given the enormous antibiotic resistance of bacteria present in peri-implantitis, the protocol described in this article proposes the use of a 100/12.5 mg piperacillin/tazobactam solution. Piperacillin is a broad-spectrum semisynthetic penicillin that exerts its bactericidal activity by inhibiting the synthesis of the cell wall and septum. Tazobactam is a beta-lactam that acts as an inhibitor of numerous 0-lactamases, which often produce resistance to penicillin. Tazobactam extends the antibiotic spectrum of piperacillin to include numerous beta-lactamase-producing bacteria that have acquired resistance to piperacillin alone: aerobic and anaerobic gram-positive and gram-negative bacteria[13]. González-Regueiro et al.[14] published a clinical case treated under the same protocols as those described in this study, using the same antibiotic combination of piperacillin/tazobactam, and observed clinical improvements evidenced by the absence of bleeding and suppuration after three months.

These disinfection procedures manage to reduce the bacterial load on the peri-implant defect, achieving improvements in clinical parameters such as the depth of catheterization or bleeding upon catheterization, as well as improvements in peri-implant natural levels. However, to achieve reosseointegration of the implant, it is essential to employ regenerative techniques.

Daugela et al.[15] carried out a meta-analysis on 18 studies in which various regenerative approaches to peri-implantitis were performed. Upon radiological examination they observed increases in natural levels of 1.97 mm (1.58-2.35 mm) on average, with better results after using submerged healing. Improved results were observed in studies that used material coating membrane (2.12 mm) compared to those in which no membrane (1.86 mm) was used.

The use of autologous bone has shown favorable results in terms of reducing the depth of catheterization, either through its application in isolation or in combination with a resorbable membrane[16].

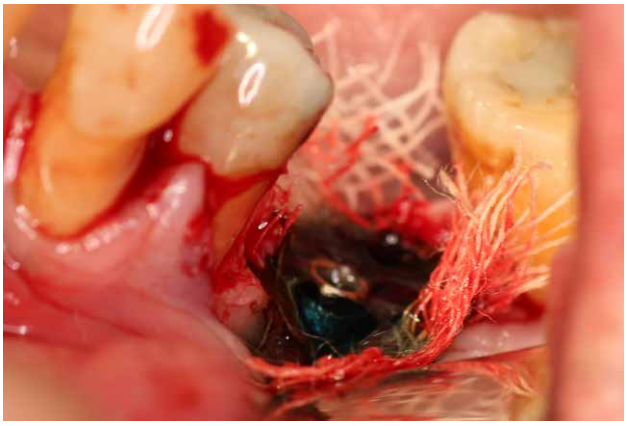

Figure 10. Application of 37% orthophosphoric acid gel and 2% chlorhexidine.

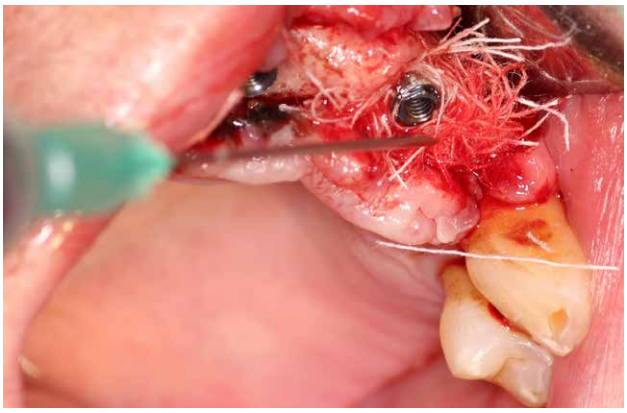

Figure 11. Application of piperacillin/tazobactam to the implant surface.

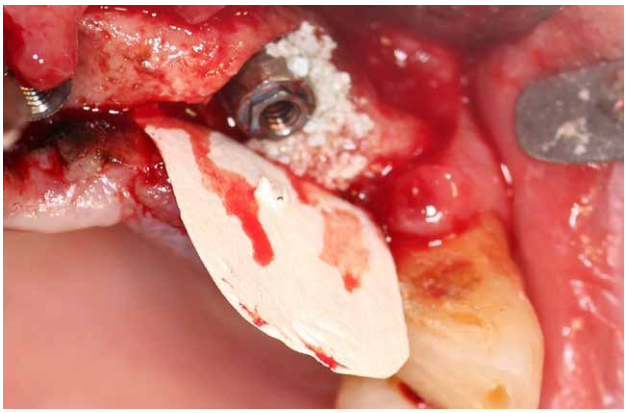

Figure 12. Defect regeneration.

In addition, a number of biomaterials have been proposed as fillers, including the use of titanium granules, which has shown favorable results in filling the peri-implant defect, as well as an increase in implant

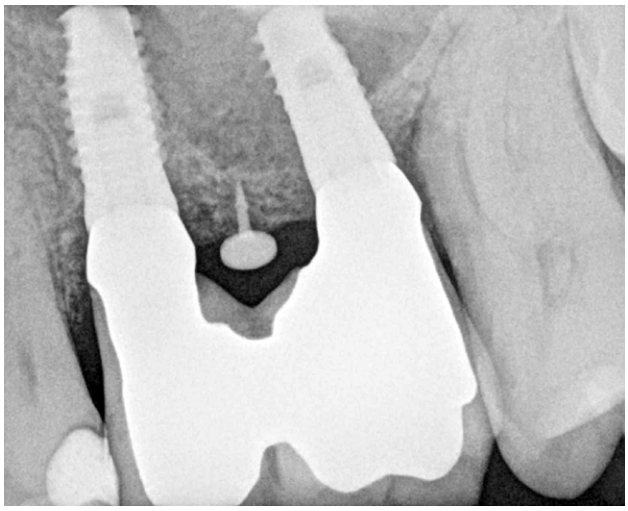

Figure 13. X-ray exam at 6 months of follow-up to case 1.

stability quotient (ISQ) of 1.6 units[17]. The use of bovine xenografts in deep defects has shown reductions in the sound depth of between 2.1 and 3.5 mm[18]. No significant differences have been observed between the use of bovine xenografts or the application of titanium granules, either clinically or upon radiological examination[19].

Roos-Jansaker et al.[20] compared the use of hydroxyapatite alone with the use of membrane-covered hydroxyapatite. After five years of follow-up, significant bone regeneration levels were observed in both groups ($p<0.001$), with mean regeneration levels of 1.3 mm. These positive results are supported by what can be observed in the set of cases used for this study, where regeneration of defects between 2 and 4 mm is observed.

In contrast, Schwarz et al. [21] showed unfavorable results regarding the use of synthetic hydroxyapatite. They compared the use of nanocrystalline hydroxyapatite with the use of BioOss® bovine biomaterial coated with swine resorbable membrane. After four years of follow-up, worse results were observed in the hydroxyapatite group in terms of reductions in probe depth: 1.1-0.3 mm as compared to 2.5-0.9 mm. In addition, only radiological bone defect regeneration was observed at 5 points, compared to 8 points in the BioOss® group. However, the small sample size of the study should

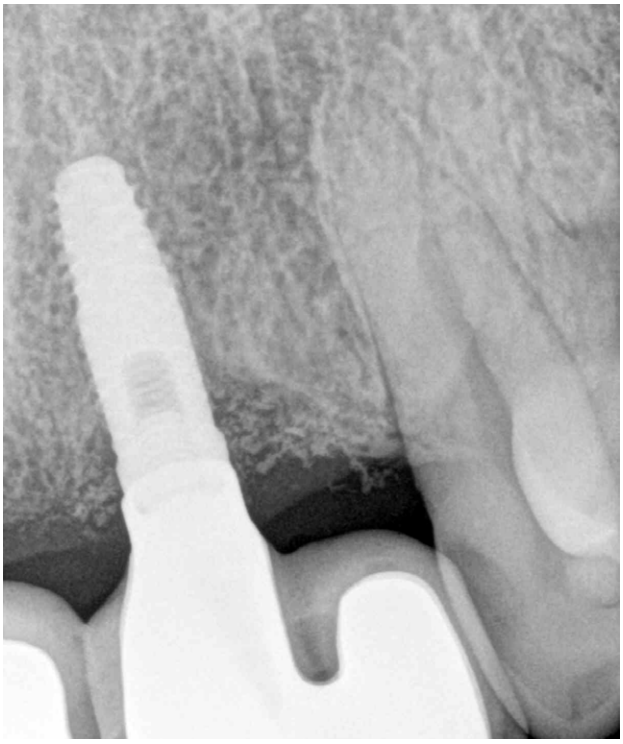

Figure 14. X-ray exam at 6 months of follow-up to case 2.

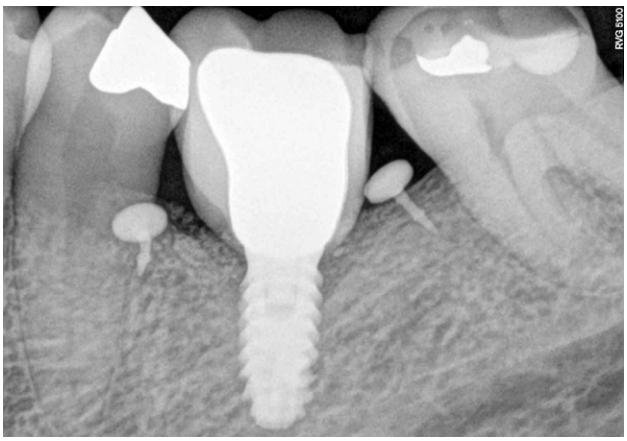

Figure 15. X-ray exam at 6 months of follow-up to case 3.

be considered: only 19 patients in total, as well as the bias of comparing a group in which membraneless biomaterial has been applied with another group in which biomaterial with membrane was used.

Currently, trial use of stem cells and morphogenetic proteins (BMP-2) for the treatment of peri-implantitis in animals is being conducted, with increased regeneration and reosseointegration being observed[22].

CONCLUSION

A combined therapeutic approach shows favorable results at the clinical and radiological levels, coinciding with the outcomes described in the literature.

This new approach constitutes a comprehensive decontamination and regeneration treatment system that shows clinical and radiological improvement after 6 months of follow-up.

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Update

Use of Autogenous Dentin as Graft Material in Oral Surgery

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ABSTRACT

Dimensional changes in alveolar height and width occur after tooth extraction, which leads to reduced function for patients and makes it difficult for professionals to place dental implants. To minimize such bone loss, a variety of grafting materials are used, among which autogenous grafts stand out for their ability to foster osteogenesis, osteoconduction and osteoinduction. The use of dentin as an autogenous graft material appeared in the professional literature for the first time in 2010, demonstrating that this material can be an effective therapeutic alternative to other graft materials, as it fosters osteoconduction and osteoinduction, and leads to new bone formation in 46-87% of the area treated with an autogenous dentin graft 3 months after use. The latest systematic review, published in 2018, concluded that implants placed in regenerated areas where dentin was used as graft material were observed to have survival rates of 97.7% after one year, suggesting this new material can be an effective alternative offering promising results, although further research is needed in this regard.

KEYWORDS

Autogenous dentin; Autologous graft; Demineralized human dentin.

INTRODUCTION

Tooth extractions result in a reduction in alveolar crestal bone dimensions, which varies among individuals and tooth location, and may be greater when such extractions are motivated by periodontal pathology or are owed to the presence of endodontic lesions[1]. This reduction or loss of bone occurs horizontally (width) on the order of 5-7 mm during the first 12 months, and vertically (height), with an average loss of 1.67-2.03 mm during the first 3 months. Loss in width is greater in the vestibular cortical bone, and loss in height is greater in the jaw than in the maxilla[2,3].

Such bone loss entails functional alterations and decreased alveolar volume, with consequent difficulty in retention of prostheses or placement of implants. Therefore, preventative methods have been discussed in the literature, including regenerative procedures for alveolar preservation, or the immediate placement of implants[2-4].

Alveolar ridge preservation techniques were described in 2013 as a procedure which is performed at the time of extraction with the aim of minimizing bone reabsorption and maximizing bone formation in the alveolar ridge[5].

In the last Osteology Consensus Report in 2012, the indications for alveolar preservation were established. On the one hand, the goal is to preserve hard and soft tissue while additionally preserving crestal bone volume to optimize functional and aesthetic outcomes, as well as to ultimately simplify post-extraction and alveolar preservation procedures. To achieve these objectives, various authors recommend seeking to achieve primary wound closure following biomaterial placement by using biomaterials with low reabsorption rates[6].

As for the ideal properties of the biomaterial, its osteoconductive properties are noteworthy; namely, the material's ability to serve as scaffolding for bone regeneration, as well as its ability to foster osteoinduction (ability to promote the recruitment of bone-forming cells), and osteogenesis (ability to induce cells contained in the graft material to promote bone regeneration)[7-11], each type of graft possessing different properties, as shown in Table[8].

Human dentin and bone are mineralized tissues with a similar chemical composition, and once demineralized, their composition is comprised of 95% type I collagen and non-collagen proteins. These proteins include Insulin-like growth factor 1 (IGF-1), insulin growth factor 2 (IGF-2), transforming growth factor-beta (TGF-beta), and bone morphogenetic proteins (BMPs), which are molecules that induce bone formation in several experimental animals (rats, rabbits). For these reasons, the demineralized dentin matrix is defined as an acid-insoluble and bioabsorbable molecule, constituting a bound collagen matrix inducing bone formation[9].

According to several studies[9], human dentin can be classified into three groups according to the degree of demineralization; nondemineralized dentin (calcified dentin), partially demineralized dentin matrix (70% decalcified) and demineralized dentin matrix, the latter being biocompatible and osteoinductive given its similarity to the demineralized bone matrix.

Human dentin is composed of 70% inorganic content with 4 types of calcium phosphates (hydroxyapatite, tricalcium phosphate, octacalcium phosphate and amorphous calcium phosphate), which give the tooth osteoconductive properties, making it a biocompatible graft material. Hydroxyapatite in dentin comes in the form of low crystalline calcium phosphate, which makes it easier to degrade by osteoclasts, thus lending it good osteoconductive properties[10].

Another 20% of its composition is organic, 90% of which is a type I collagen network while 10% is comprised of non-collagenous proteins (osteocalcin, sialoprotein, and phosphoprotein, which are involved in bone calcification) and growth factors (bone morphogenetic proteins: BMPs, LIM and insulin-like growth factor, which give the tooth osteoinductive properties). In vitro studies show that proteins extracted from dentin affect the proliferation and differentiation of osteoprogenitor cells, such as TGF-B and other factors,

Table. Graft types and their properties[8].

Type	Graft	Osteoconduction	Osteoinduction	Osteogenesis	Advantages	Drawbacks
Bone	Autograft	YES	YES	YES	"Gold standard". Best results. Good percentage of bone volume and mineralization	Associated morbidity Limited availability
	Autograft	YES	YES	NO	Available in various formats	Worse results than autogenous bone
Dentin	Autograft	YES	YES	NO	Good compatibility and bone formation	Limited availability
Biomaterials	Bovine hydroxyapatite	YES	YES	NO	Some osteoinductive capacity. Combinable with autogenous bone	Not completely reabsorbed
Ceramic	Tricalcium phosphate	YES	NO	NO	Good biocompatibility. Good bone formation	Not completely reabsorbed
Composites	Various combinations	-	-	-	Allows combining the advantages of each component	

which can influence the development, remodeling, and regeneration of mineralized tissues. The remaining 10% is water[7, 11].

The first known use of dentin as an autogenous graft was in 2010, with Kim et al.[11] being the first authors to describe the procedure by suggesting the use of extracted teeth as graft material, given that they possess suitable physical properties (density, roughness and homogeneity) and chemistry (calcium/phosphate composition similar to human bone in the cortical region). In addition, dentin is a biocompatible material, stimulating the formation of bone tissue, is well-accepted by the host and is capable of integrating completely into the newly formed bone[12, 13].

Concerning the use of human dentin as an autograft for alveolar preservation, one of the techniques described in the literature is to perform an atraumatic extraction, remove the pulp from the tooth extracted with endodontic files, and the enamel and cement using rotary instruments, divide the root into several fragments, and then crush them to obtain a particle size of 0.25-2 mm, which when mixed with blood from the patient's tooth socket is then introduced into the socket under controlled pressure, covering it with a fibrin sponge and a cross stitch[14].

The objective of this study is to examine the current state of dentin use as an autogenous graft in various oral surgery procedures.

LABORATORY ANIMAL STUDIES

A study using demineralized, artificially perforated human dentin matrices in 6 iliac crest defects in sheep, sacrificing 3 sheep at two months and 3 at four months, showed new bone formation at the edges of the demineralized dentin block at 2 months, but not within the material. However, there was bone formation within the dentin block at 4 months, where excellent bone regeneration was observed. This study confirmed that BMP-2 produced better osteoinduction in porous materials than in non-porous materials, as pores measuring 300 micrometers in diameter allowed infiltration of bone-forming cells and osteoclasts. Dentin scaffolding with artificial perforations showed angiogenesis by the formation of new capillaries and development of existing ones, in addition to better diffusion of oxygen and other nutrients[15].

Demineralized human dentin matrix has also been used as graft material in the sockets of 32 rats, performing a

histological, morphometric and immunohistochemical analysis at 3, 7, 14 and 21 days after surgery, resulting in an increase in the expression of vascular endothelial growth factor (VEGF), which is the most important proangiogenic factor in physiological and pathological neovascularization processes[19]. Another study that used demineralized human dentin matrix in the alveoli in 16 rats showed an increase in osteoblast differentiation by producing an increase in BMP-2 and BMP-4 and demonstrated that the matrix acts as scaffolding for osteoblastic differentiation[20]. Along this line, another study conducted in rats comparing human demineralized dentin injection and human demineralized dentin mixed with BMPs demonstrated that the demineralized human dentin matrix accelerated BMP-2 activity, acting as scaffolding for this growth factor and accelerating bone and cartilage formation, suggesting its use as scaffolding material for bone-forming cells[16].

A systematic review of dentin processing methods in tissue bone engineering shows that the demineralization process of dentin increases osteoinduction and decreases antigenicity, this being the motive for using human demineralized dentin matrix in all human and animal studies since 2008, since the demineralization process prevents the denaturalization of proteins in order to preserve growth factors and proteins involved in osteoinduction. In addition, the studies conclude that the ideal particle size to promote bone regeneration is 75-500 micrometers in diameter[17].

HUMAN STUDIES

Dentin as autogenous graft material was described by Kim et al.[11] in 2010, when the team performed extractions of 6 permanent teeth in 6 patients, removing the pulp and cement and then crushing them, converting them into granules and using them as graft material for implant placement. At 3 months, coinciding with the second phase, they performed biopsies on their patients, verifying the reabsorption of almost all dentin and the replacement of new bone in 46-87% of grafted material while detecting a large number of inorganic compounds (hydroxyapatite, tricalcium beta phosphate, amorphous calcium phosphate and octacalcium phosphate), similar in both dentine and bone.

Six years later, Kim et al. published the results of marginal bone loss in 10 implants placed in 5 patients (after having lost one subject who left the study) after having placed an implant in the jaw and the rest in the jawbone. In all patients, dentin implants were placed as graft material, the second phase was performed at 3 months, and at 5 months the definitive prosthesis was placed. Measurements of marginal bone loss in the palatine, vestibular and the width of alveolar crest were compared by first performing initial Cone Beam Computed Tomography (CBCT), a CBCT following implant placement surgery, another CBCT after placement of the prosthesis, and the final one at 5 years. They showed that autogenous dentin appeared to maintain bone volume as periimplantary bone underwent less reabsorption, with 1 mm marginal bone loss at 6 years, and the other four cases suffered no marginal bone loss. However, they concluded their study by highlighting that more studies with larger sample sizes and a longer follow-up period were needed[12]. Valdec et al.[14] described a protocol for an alveolar preservation technique using particulate autogenous dentin, including 4 patients undergoing extraction of anterosuperior teeth, removing the pulp from 3 of them and the endodontic filling in one, removing cement and enamel with high-speed drills, splitting the dentin with a bone grinder and mixing it with the patient's autogenous blood, sealing the socket with a free graft of the palate obtained using a circular scalpel. At 4 months they placed the implant and took a sample for histological analysis (where autogenous dentin can be seen surrounded by vital bone, with the presence of osteoblasts, and without signs of infection or necrosis) in addition to performing a CBCT.

Lee et al.[18] performed extractions of 29 teeth in 9 patients, turning them into blocks or dentin granules, then using them in combination with xenograft, allograft or synthetic bone in 11 locations and uniquely in 2 locations for the placement of 26 implants (24 in

maxilla and 2 in jaw), 9 implants in 3 patients placed simultaneously with performing the graft, and 17 implants in 6 patients after a period of 6-9 months. The histology showed rapid formation and stable bone structure, which coincides with the outcomes reported by other authors, such as Kim et al. There were no complications, such as suture infection or dehiscence, and proper healing resulted. However, it was a heterogeneous study in terms of the type of graft material used, with a short follow-up time, and no pre- and post-regenerative procedure assessments were performed.

Other authors, such as Jeong et al.[19], also used autogenous dentin from extracted teeth, alone or in combination with other materials as graft material for the realization of breast lifts. One hundred (100) implants were placed in 51 patients, immediately placing 76 implants at the time of the mastopexy, and 24 post-procedure implants. These authors used dentin as a single graft material, or mixed with autogenous bone (tuberosity), synthetic bone, or xenograft (Bio-oss, Biocera). They performed a biopsy 3-6 months after the breast lift procedure on the 27 patients in which only dentin was used as graft material for the placement of 38 implants, and observed dentin tubules, osteoblasts and osteoclasts around the graft material, with adequate bone formation (46-87% at 6 months) thanks to its osteoconductive and osteoinductive properties. An implant survival rate of 78% was obtained, demonstrating that this grafting material could also be suitable for mastopexy.

Autogenous dentin has been used in the form of block grafts for subsequent implant placement. Kim et al.[20] placed 14 implants simultaneously with the block grafts and 15 following them. In the later histological analysis, the union of implant and gum, osteocytes embedded in the matrix of demineralized dentin, and osteoclasts reabsorbing the matrix were observed, as well as the formation of new osteoid tissue and vascular invasion within the fibrous tissue. These authors recommended that, in the use of autogenous dentin in the form of blocks, better results can be obtained when used in association with some biomaterial in the form of granules. They also published a report on a series of 15 cases in which 23 implants were placed in molars, in 1 patient in the form of a block, and in the rest in the form of granules. A 31-month follow-up was carried out. They performed biopsies at 2 months during the second phase and 4 months after placement of the autogenous dentin, detecting areas of osteoconduction at 2 months through the direct binding of the bone formation zones, as well as regions of fibrous and bone tissue being introduced into the region of reabsorption of the graft material. At 4 months, the graft material was replaced with neoformed bone, detecting dense, well-vascularized tissue, while concluding that, although autogenous dentin showed rapid healing and closure and did not induce immune reactions, more studies were needed to evaluate this material over the long term[21].

Comparing the use of autogenous dentin as a single graft material with the use of bovine xenograft as a single graft material to assess differences between them, Pang et al.[22] published a randomized clinical trial in which they placed 21 implants while performing regeneration with autogenous dentin, and 12 implants in which they performed bone regeneration with bovine xenograft (Bio-oss) for the regeneration of vertical defects in the vestibular bone. They performed the regeneration procedure within 2-4 weeks of extraction, and at 6 months performed a biopsy in both groups. Proper healing occurred in both groups without postoperative infection or suture dehiscence. There were no statistically significant differences in vertical bone gain or primary stability of implants. In histological analysis, the percentage of new bone formed, as well as the percentage of residual grafted material, were similar in both groups.

Kabir et al.[23] published a clinical case study in which, following the extraction of the third upper right molar, the researchers pulverized it and used it as a graft material in the post-extraction socket to assess alveolar preservation, performing clinical and radiographic controls at the time of extraction and at 3 and 12 months, showing replacement of the demineralized dentin matrix with new bone tissue. The Micro

Computed Tomography (micro-CT) scan showed new bone with trabecular structure at 12 months without remnants of dentin matrix, thus suggesting this material as a possible autogenous graft for other types of procedure apart from breast lifts or placement of dental implants.

In 2018, Gual-Vaqués et al.[24] published a systematic review of 6 studies on humans analyzing implant stability using the Implant Stability Quotient Index (ISQ). Complications arose, with suture dehiscence being the most common, affecting 29.1% of the cases, and less frequently, hematoma, infection, marginal bone loss (follow-up was performed for only one year). They also record implant survival and failure rates within 6 months of placing the prosthesis, with a 97.7% success rate, analyzing the mineral composition and healing process histologically and histomorphometrically, which suggested dentin is an excellent grafting material, demonstrating new bone formation in 46-87% of locations during a healing period lasting 3-6 months, as well as an abundance of osteoblasts and osteoclasts around the graft material and new bone formation via osteoconduction and osteoinduction processes. This systematic review shows that there are no statistically significant differences between using dentin in granules or blocks, or in using it alone or in combination with other graft materials and shows greater secondary stability than primary stability. The limitations of this systematic review lie in the fact that there are few studies in this regard and in the small sample size analyzed. In addition, there is great variability among the studies (different locations, anatomical considerations, different evaluation methods, different types of surgery), such that more long-term studies are needed with uniform study variables and comprising a larger sample size.

In 2018, Schwarz et al.[25] published a prospective clinical study in which they performed alveolar crest augmentation techniques on 30 patients, using block-shaped autogenous root dentin in 15 cases, and blocks of autogenous bone obtained from the ascending branch in the other 15. In patients where dentin is used as graft material, it was obtained from retained third molars which were extracted and then, by removing the crown and root cement, a root fragment with dentin and pulp was obtained. Autogenous bone blocks were obtained from the retromolar region in the external oblique ridge by combining rotating and piezoelectric tools. Measurements of the alveolar crest were performed before and after the regenerative procedure, and upon revisit for the placement of dental implants at 26 weeks. There was an increase of 5.53 mm in patients where autogenous dentin was used, and 3.93 mm in cases where autogenous bone blocks were used, with less reabsorption observed in the first group. In addition, homogeneous integration of both grafts could be clinically and radiographically observed upon patient revisit, which allowed the placement of implants with good primary stability, with the authors concluding that autogenous dentin appears to be a viable alternative as a graft material for bone width regeneration, but that studies with larger sample size and follow-up time are needed.

In 2019, Canto-Díaz et al.[26] published a split pilot study in 6 patients, in which they perform alveolar preservation with autogenous dentin on the research group and allow convention healing to occur in the control group, sealing both alveoli with a collagen membrane. They performed tooth extractions for periodontal motives, root cavities or non-restorable fractures and placed implants at 16 weeks. For preparation of the dentin graft group, they removed the crowns or fillings of any kind using rotating tools, washed the tooth fragments with saline, and crushed them to obtain a particle size of 300-1200 microns, which was then sterilized for 10 minutes with sodium hydroxide and ethanol, and finally washed with saline solution. After placing collagen membranes on both alveoli, they sutured with 5/0 monofilament and performed a postoperative CBCT at 8 and 16 weeks, detecting lower dimensional contraction of the post-extraction socket among the study group than in the control group at 16 weeks following surgery, and stable and homogeneous densiometric values (Hounsfield units) in both groups in the three regions under study (apical, medial and coronal socket regions), thus suggesting that autogenous dentin is suitable as graft material for alveolar preservation.

The latest review of the use of graft material derived from extracted teeth concludes that the ideal particle size is still controversial, although most authors report using particles between 300-1200 microns, while agreeing that dentine is a promising material owing to its osteoconductive and osteoinductive properties stemming from its similarity to bone[27].

CONCLUSIONS

Although the material of choice in regeneration is autogenous bone, human dentin and bone tissue have a similar chemical composition, such that dentin has begun to be used as a regenerative material in oral surgery.

Autogenous dentin possesses the properties of osteoconduction and osteoinduction, which has led to its use in different regenerative procedures in implantology (alveolar preservation, guided bone regeneration, breast lifts), in isolation or in combination with other materials.

Dentin has been shown to yield good results in terms of bone gain and primary implant stability, and even better results when compared to other materials.

However, studies using a larger sample size are needed, especially with a longer follow-up period in order to confirm the long-term stability of this material.

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Bibliographic review

Peri-Implant Soft Tissue Augmentation. Proper Timing and Surgical Procedure for Predictable Surgical Outcomes. A Bibliographic Review

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ABSTRACT

The role that the width of keratinized mucosa (KM) surrounding dental implants plays in the long-term stability of peri-implant tissues remains a topic for debate.

The aim of this review is to evaluate and describe the outcomes of available surgical procedures and the proper timing for augmenting peri-implant soft tissue.

A bibliographic search was conducted on the online PubMed and Medline databases, as well as a manual search for relevant articles comprising the period between 2012 and 2017, selecting for articles dealing with the various surgical procedures performed starting at time B (implant placement).

A total of 10 articles was selected, contrasting them in terms of the moment in time at which the surgical procedure was performed while analyzing the following study variables: keratinized mucosa width, keratinized mucosa thickness, postoperative contraction, surgical timing, and aesthetic outcome and postoperative discomfort.

The conclusion may be drawn that free gingival grafting has been shown to result in the greatest widths of keratinized mucosa. However, there are other materials available that reduce patient morbidity and eliminate the need for a second surgical site, such as a xenogeneic collagen matrix, which can be equally effective and predictable in outcome. Both a xenogeneic collagen matrix and connective tissue grafting offer superior aesthetic results to those achieved with free gingival grafting.

KEYWORDS

Dental implants; Connective tissue graft; Mucograft; Peri-implant keratinized mucosa; Peri-implant soft tissue volume; Increased soft tissue.

INTRODUCTION

Long-term successful outcomes in dental implants depend not only on osseointegration of the implants in the surrounding bone tissue, but also on preserving the health and integrity of the surrounding soft tissues.

The soft tissue surrounding the teeth is subdivided into keratinized mucosa (KM) and immobile keratinized mucosa (attached mucosa, (AM)) separated by the mucogingival junction. However, in implantology, peri-implant soft tissues are unevenly dealt with[1,2]. The structure and composition of the peri-implant mucosa are organized into a well-keratinized oral sulcus followed by a long binding epithelium and an insertion of connective tissue (Figure).

Despite many similarities, peri-implant tissues differ from the tissue surrounding the teeth in a number of ways, such as the amount of blood supply, the directionality of connective tissue fibers, the amount of fibroblasts and collagen fibers present, the permeability of the binding epithelium, and the presence of a minimum width of keratinized soft tissue attached to the teeth[1-3].

The role that the width of keratinized mucosa (KM) surrounding dental implants plays in the long-term stability of peri-implant tissues remains a topic for debate[4].

Recent systematic reviews conclude that inadequate KM peri-implant width is associated with increased plaque buildup, the presence of inflammation, soft tissue loss and insertion loss[1-7].

Also important for long-term success is the sealing of the circumferential tissues around the implants; namely, the early formation of an effective barrier capable of biologically protecting peri-implant structures, thus preventing bacterial penetration and the progression of marginal bone loss[8].

In line with this view, scientific data and clinical reports seem to indicate that an adequate width of the attached mucosa can facilitate oral hygiene procedures, thus preventing peri-implant inflammation and tissue degradation. Consequently, in order to prevent biological complications and improve long-term prognosis, the condition of soft tissues should be carefully evaluated when planning implant therapy. Knowledge of the appropriate surgical procedure and the most suitable timing for carrying it out appears to be of the utmost clinical significance when considering implant therapy[9].

Two methods for augmenting peri-implant soft tissue can be distinguished[1,2]:

1. Augmented KM *width*: apical replacement flaps (in combination with free gingival (FGG), allogeneic, or xenogeneic grafts).
2. Augmented KM *thickness*: subepithelial connective grafts, other soft tissue replacement grafts (xenogeneic, allogeneic).

In terms of optimal timing, four different loading protocols for carrying out an augment in the width or thickness of the soft tissues around implants can be distinguished[1,2]:

a. Prior to implant placement.

b. During implant placement.

c. During second surgery (2nd phase).

d. After the implant is osseointegrated, uncovered, and definitively loaded.

The aim of this study is to review the literature on the available surgical procedures and the proper moment in time at which to carry out an augment of peri-implant soft tissues in order to make the outcome predictable.

A total of 10 articles, listed in Table 1, were included.

Our review centered on describing the various augmentation procedures in use only once the implant has been placed; namely, procedures b, c, and d.

KERATINIZED MUCOSA (KM)

Whether or not there is a need for surgical intervention to augment the keratinized tissue surrounding implants in patients with reduced or insufficient tissue width remains controversial in the literature[10].

On the one hand, several studies suggest that the absence of KM in implants may favor peri-implant inflammation and recession. However, others find that there is insufficient evidence regarding the influence of KM width on the survival rate of KM implants and future recession[4].

Regardless of medical opinion, although the absence of KM tissue may not justify surgery, in situations where there is discomfort during brushing, poor control of bacterial plaque, or persistent inflammation or aesthetic alteration, the performance of soft tissue augmentation procedures around the implants may be advisable for restoring health and peri-implant aesthetics.

Various surgical procedures and materials have been proposed to increase the amount of soft tissue around dental implants[11].

Surgical procedures for increasing the width of keratinized tissue can be divided into free grafting procedures, bilamellar procedures, use of an autograft, xenograft, or allograft along with a replacement flap, or flap/vestibuloplasty (VP) procedures. The results of the studies included are listed in Table 2.

Time b: During the placement of implants.

Bruschi et al.[12] describe an apically repositioned partial-thickness flap (APPTF) procedure performed on patients who were to be treated with implants with the aim of increasing KM width. They reported a gain of 5.03 mm at one year and 5.14 mm at four years.

Time c: Coinciding with second surgery (2nd phase)

In the study comparing the use of a xenogeneic collagen matrix (XCM) with a free gingival graft (FGG), a gain of 7.76 mm was observed with the FGG. Higher gains were obtained with FGG (7.76 mm) when compared to the XCM group (6.51 mm)[13].

In the case of connective tissue grafting (CTG), gains of 0.90 mm were observed. No statistically significant differences were found between the use of XCM (1.2 mm) and CTG (0.9 mm) procedures in the Cairo et al. study[14].

Time d: After the implant has been osseointegrated, uncovered, and definitively loaded.

In the articles reviewed, KM gains between 2.36 and 4.05 mm were seen to be obtained using the FGG protocol. (15-16) Statistically significant differences were obtained in favor of FGG (2.36 mm) with respect to VP (1.15 mm). (15) With respect to the CTG protocol, KM width gain values ranging from 1.7 to 2.33 mm were observed[1,17].

The data obtained by Zucchelli et al.[18] resulted in a gain of 0.57 mm when using coronal flap repositioning (CFR+CTG).

Lorenzo et al.[11] observed KM width gains of 2.3 mm with the use of XCM. Comparing the outcome with the CTG and XCM procedure shows that there are no statistically significant differences between the two[11,19].

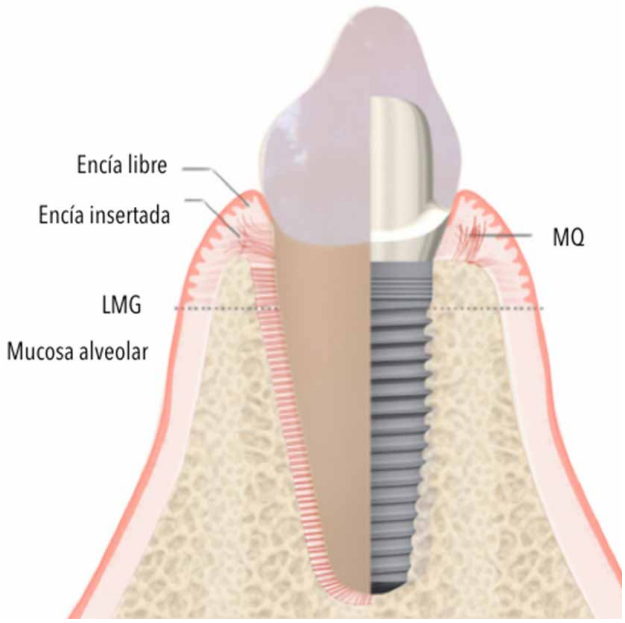

Figure. Cutaway view of the soft tissues around teeth and implants.

Table 1. Articles covered by the review.

Author /Year	Surgical Timing	n (number of implants) / Study group	Aim of Treatment	Surgical Procedure
Zucchelli et al. 2013[18]	D	20	Width - Thickness	CFR+CTG
Bruschi et al. 2014[12]	B	131	Width	APPTF
Lorenzo et al. 2012C[11]	D	24 Grupo control: CRA (EP)+ ITC (12) Grupo test: CRA (EP)+ MCX (12)	Width	APPTF+CTG APPTF+XCM
Schmitt et al. 2015[13]	C	176 Grupo control: VP+IGL (74) Grupo2: VP+MCX (102)	Width	VP+FGG VP+XCM
Roccuzzo et al. 2014[17]	D	16	Treat recession (width)	CTG
Baseman et al. 2012[15]	D	64 Grupo 1: CRA+IGL (32) Grupo 2: VP (32)	Width	APPTF+FGG VP
Puisys et al. 2015[21]	B	40	Thickness	ADM
Cairo et al. 2017[14]	C	60 Grupo control: ITC (30) Grupo test: MCX (30)	Width - Thickness	CTG XCM
Buyukozdemir et al. 2015[16]	D	60 Grupo1: Cantidad insuf de MQ —> IGL (20) Grupo2:Cantidad insuf de MQ —> mant. periodontal (20) Grupo 3:Cantidad suficiente de MQ	Width	FGG
Zeltner et al. 2017[19]	C	20 Grupo control: ITC (10) Grupo test: MCX (10)	Thickness	CTG XCM

LEGEND: *B: During implant placement; C: during second surgery phase; D: after the implant is osseointegrated, uncovered, and definitively loaded; CFR: Coronal flap replacement; CTG: Connective tissue graft; APPTF: Apically positioned partial thickness flap; XCM: Xenogeneic collagen matrix; VP: Vestibuloplasty; FGG: Free gingival graft; ADM: Acellular dermal matrix; KM: Keratinized mucosa.*

SOFT TISSUE THICKNESS (VOLUME)

To date, there exists no broad consensus regarding the amount of soft tissue volume functionally required on the vestibular face of dental implants. However, it can fairly be said that the amount of soft tissue volume will influence the aesthetic outcome and may even partially compensate for the lack of bone in the vestibular area.

The critical thickness for soft tissue on the oral side of dental implants has been shown to be <2 mm. However, as of today this parameter has not yet been evaluated three-dimensionally nor in a long-term clinical study.)

In the case of volume deficiency on the oral side of dental implants, soft tissue augmentation surgery has been considered an integral part of implant therapy. Assessment of the need for soft tissue augmentation is based on mucosal biotype and aesthetic expectations[3].

Fine peri-implant tissues are more prone to recession and are associated with increased marginal bone loss, suggesting the advantage of having a minimum of oral soft tissue thickness to prevent peri-implant tissue discoloration and bone loss[19].

Table 2. KM gain outcomes (in mm), and follow-up time of the studies included in the review.

Author/Year	KM Width Gain		Follow-up time
Zucchelli et al. 2013[18]	CRC+CTG: 0.57 mm		1 year
Bruschi et al. 2014[12]	APPTF: 5.03 mm	5.14 mm	1-4 years
Lorenzo et al. 2012[11]	CTG: 2.33 mm	XCM: 2.3 mm	6 months
Schmitt et al. 2015[13]	FGG: 7.76 mm	XCM: 6.51 mm	1 year
Roccuzzo et al. 2014[17]	CTG: 1.7 mm		1 year
Basegmez et al. 2012[15]	FGG: 2.36	VP: 1.15 mm	1 year
Cairo et al. 2017[14]	CTG: 0.9 mm	XCM: 1.2 mm	6 months
Buyukozdemir et al. 2015[16]	FGG: 4.05 mm		6 months

LEGEND: *KM: Keratinized mucosa; CRC: Coronal replacement flap; CTG: Connective tissue graft; APPTF: Partial thickness apical replenishment flap; XCM: Xenogeneic collagen matrix; FGG: Free gingival graft; VP: Vestibuloplasty.*

Soft tissue grafting contributes to over 40% of final peri-implant volume, results in better aesthetics, more stable oral soft tissue dimensions in combination with immediate implants and may favor more stable marginal bone levels around implants[19, 20].

Autogenous soft tissue grafts taken from the palate (free gingival and subepithelial connective tissue grafts) remain the gold standard for achieving an increase in soft tissue volume around implants. However, this type of procedure involves the need for a second surgical wound, as well as requiring longer healing time, and therefore exhibits greater patient morbidity. This, in addition to the limited availability of tissue, is one of the principal drawbacks to this type of procedure. Hence, alternative materials have emerged, such as the acellular dermal matrix (ADM) or the xenogeneic collagen matrix[21]. The study results are listed in Table 3.

Time b: During implant placement

Puisys et al.[21] observed a soft tissue volume gain of 2.21 mm when using ADM at 3 months.

Time c: At time of second surgery (phase 2)

In the case of CTG procedures, average volume gain ranged from 0.79 to 1.2 mm. As for XCM, the values obtained were between 0.77-0.9 mm[14.19].

While in the Cairo et al. study (14) statistically significant differences were found in favor of the CTG (1.2 mm) compared to XCM (0.9 mm), Zeltner et al. (19) found no differences in volume gain between the two groups (CTG 0.79 mm; XCM 0.77 mm).

Time d: After the implant is osseointegrated, discovered, and finally loaded

Zucchelli et al.[18] achieved a soft tissue volume gain of 1.54 mm at one year by using CRC+CTG.

OTHER FACTORS

Postoperative Contraction

The results of the studies included are listed in Table 4. A reduction in tissue volume of 0.33 mm was observed

Table 3. KM gain outcomes (in mm), and follow-up time of the studies included in the review.

Author/Year	KM Thickness Gain		Follow-up Time
Zucchelli et al. 2013[18]	CRC+CTG: 1.54 mm		1 year
Cairo et al. 2017[14]	CTG: 1.2 mm	XCM: 0.9 mm S	6 months
Puisys et al. 2015[21]	ADM: 2.21 ± 0.85 mm		3 months
Zeltner et al. 2017[19]	CTG: 0.79 mm	XCM: 0.77 mm NS	3 months

LEGEND: *KM: Keratinized mucosa; CRC: Coronal replacement flap; CTG: Connective tissue graft; XCM: Xenogeneic collagen matrix; ADM: Acellular dermal matrix; S: Statistically significant; NS: Not significant.*

Table 4. Postoperative contraction results expressed in mm%, time and statistical significance.

Author/Year	Postoperative Contraction		Follow-up Time	Statistical significance
Zucchelli et al. 2013[18]	3.07%		1 year	S
Lorenzo et al. 2012[11]	CTG: 0.33 mm.	XCM: 0.2 mm	6 months	NS
Basegmez et al. 2012[15]	FGG: 2 mm.	VP: 3.06 mm	1 year	S

LEGEND: *CTG: Connective tissue grafting; XCM: Xenogeneic collagen matrix; VP: Vestibuloplasty; FGG: Free gingival graft; S: Statistically significant; NS: Not significant.*

Table 5. Duration of surgery (in min) and statistical significance.

Author/Year	Duration of Surgery		Statistical significance
Lorenzo et al. 2012[11]	CTG: 46.25 min	XCM: 32.50 min	S
Schmitt et al. 2015[13]	FGG: 84.33 min	XCM: 65.11 min	S
Cairo et al. 2017[14]	CTG: 51.7 min	XCM: 35.5 min	S

LEGEND: *CTG: Connective tissue grafting; XCM: Xenogeneic collagen matrix; FGG: Free gingival graft. S: Statistically significant; NS: Not significant.*

Table 6. Aesthetic appearance results and postoperative pain and discomfort.

Author/Year	Group	Aesthetics		Pain and discomfort	
Zucchelli et al. 2013[18]	CRC+CTG	Patient	Clinical	-	
		VAS (0-10) S Initial: 3.80 Final: 8.00	-		
Lorenzo et al. 2012[11]	CTG XCM	-	Comparative photographs	VAS (0-10) 10 days: <3 CTG/<3 XCM 30 days: <1 CTG/0 XCM	Anti-inflammatory medication: CTG: 8 tablets XCM: 5 tablets
Schmitt et al. 2015[13]	FGG XCM	-	FGG < XCM in texture and color	-	
Roccuzzo et al. 2014[17]	CTG	VAS (0-10) S Initial: 3.60 Final: 8.50	-	-	
Cairo et al. 2017[14]	CTG XCM	-		VAS (0-100) S CTG: 37 XCM: 13	Anti-inflammatory medication: S CTG: 3.9 tablets XCM: 2.2 tablets

LEGEND: *CRC: Coronal replacement flap; CTG: Connective tissue graft; VAS: Visual analog scale; APPTF: Partial thickness apical replenishment flap; XCM: Xenogeneic collagen matrix; FGG: Free gingival graft; VP: Vestibuloplasty; ADM: Acellular dermal matrix; -: not measured in the study; S: Statistically significant.*

at 6 months using CTG as compared to 0.2 mm using XCM, the results not being statistically significant[11].

Zucchelli et al. (18) report a contraction of 3.07% at one year using the CRC+CTG procedure. For their part, Basegmez et al. (15) report a statistically significant difference between contraction when using FGG compared to VP, FGG being lower (2 mm) with respect to VP (3.06 mm).

Duration of Surgery

The results from the studies under review are listed in Table 5. The revised studies describe a surgical duration ranging from highest to lowest of: FGG (84.33 min), CTG (46.25-51.7 min) and XCM (32.50-65.11 min), the latter being lower in a statistically significant manner when compared to the first two. (11,13,18)

Aesthetics

The results from the studies under review are listed in Table 6. Two of the studies report patient aesthetic perception using the visual analog scale of 0-10 (VAS), obtaining values between 8 and 8.5 for CTG (17,18). Lorenzo et al. do not find statistically significant differences in terms of coloration and aesthetics between CTG and XCM[11].

Significant differences in both coloration and texture were detected when comparing FGG to XCM, which showed no differences with respect to adjacent areas[13].

Pain and Discomfort

In contrast, no statistically significant differences in pain and the amount of anti-inflammatory medication needed were found when comparing CTG with

XCM[11].Cairo et al.[14] did report statistically significant differences, both in the amount of pain and anti-inflammatory medication required.

CONCLUSIONS

Bearing in mind the limitations of any bibliographic review and the heterogeneity of the data, we may conclude that:

1. Optimal soft tissue sealing protects and preserves the underlying bone and is necessary to creating the emergency profile and biological peri-implant width.
2. The performance of soft tissue augmentation procedures around implants is recommended in cases of discomfort when brushing, poor bacterial plaque control, persistent inflammation, or aesthetic alterations.
3. Fine biotypes are more prone to recession and are associated with increased marginal bone loss; consequently, it is advisable to have a minimum thickness of oral soft tissue to prevent tissue discoloration and peri-implant bone loss.
4. Free gingival grafting has been shown to obtain the widest widths in keratinized mucosa when performed both during the second surgical phase and after osseointegration and functional loading of the implant.
5. CM as an alternative to the use of connective tissue grafts could be equally effective and predictable for increasing the width and thickness of keratinized mucosa, is associated with less patient morbidity, and yields similar results in terms of postoperative contraction.
6. Connective tissue grafts and use of a xenogeneic collagen matrix offer aesthetic results equal to or better than a free gingival graft.

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