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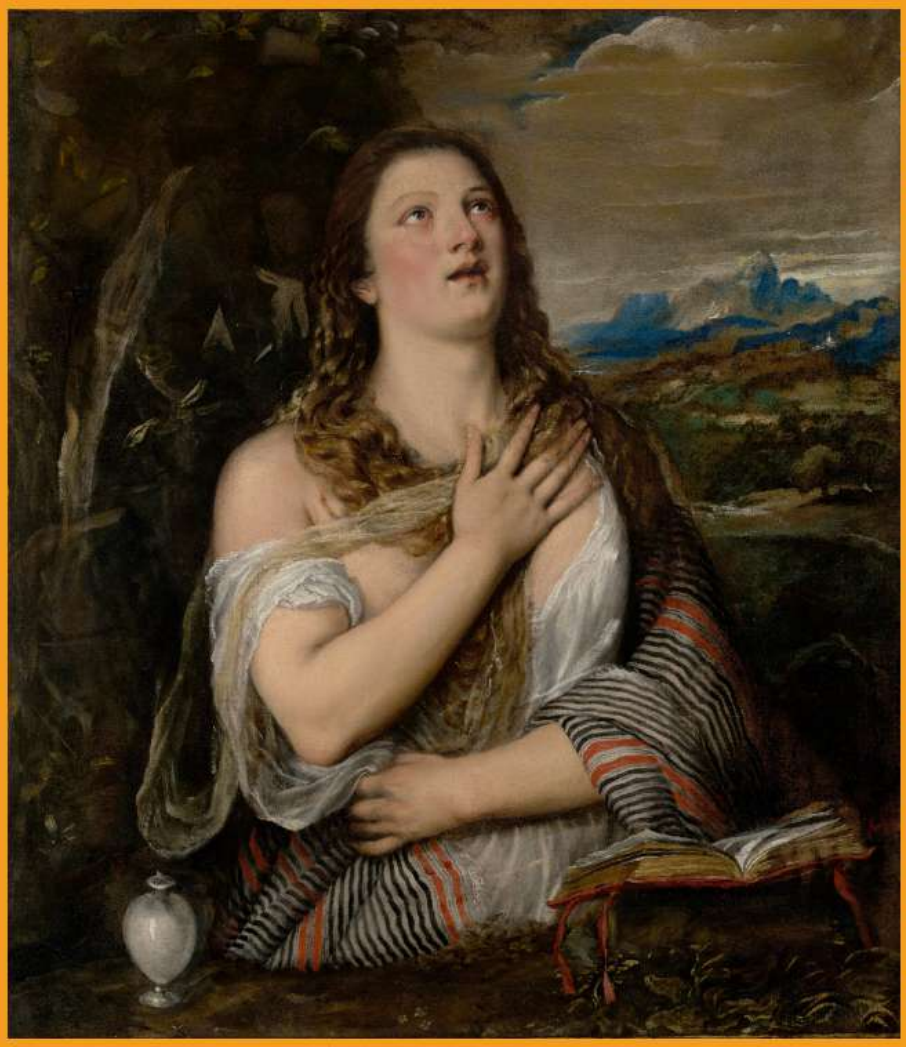

Titian (Tiziano Vecellio), The Penitent Magdalene (1555–1565), Oil on canvas, The J. Paul Getty Museum, Los Angeles, 56.PA.1

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Observational Study

MANAGEMENT OF POST-SURGICAL PAIN AND POSTURAL DYSFUNCTION THROUGH FOCUSED MECHANO-ACOUSTIC VIBRATIONS: A PILOT OBSERVATIONAL STUDY

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ABSTRACT

Nowadays there is a progressive increase in surgical interventions in the fields of cardiology and oncology. This situation increasingly involves the need to identify strategies for managing complications that may affect patients in the post-surgical period, during the rehabilitation phase. Among the symptoms most frequently encountered in this context are pain and postural dysfunction, for which a decisive support could derive from the application of Focused Mechano-Acoustic Vibrations (FMAVs) therapy. In this pilot observational study, 20 patients (12 women and 8 men; average age of 48 years) who underwent cardiac or oncological surgery were observed during the execution of a FMAVs treatment protocol applied in the post-operative period. Patients were evaluated at the beginning and at the end of the protocol through the Numeric Pain Rating Scale (NPRS) and the computerized postural analysis for the calculation of the Postural Biometric Index (PBI), that quantifies postural dysfunctions. All patients were treated with 8 biweekly sessions of FMAVs applied on specific Myofascial Trigger Points (MTrPs). At the end of the protocol, significant reductions of 26.4% for pain detected by NPRS and 17.9% for postural dysfunction detected by PBI were observed. Treatment with FMAVs can determine improvements in pain and postural dysfunction in cardiac and oncological patients subjected to surgery. This preliminary study lays the foundation for further in-depth research on the topic.

KEYWORDS: *Vibrations, post-surgical pain, posture, physical therapy modalities, musculoskeletal rehabilitation*

INTRODUCTION

Recently, surgical procedures in the oncology and cardiology fields have reached a very high diffusion in the general population; in fact, it is estimated that, to date, approximately 1.5 million cardiac surgery interventions and 9 million oncological surgeries are conducted every year in the world, with values constantly increasing (1,2). Since cardiac and oncology surgery often involves invasive procedures, a multitude of negative outcomes can frequently be observed, both

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in the short and long term. In particular, invasive surgical interventions often lead to the onset of depressive states (3,4), pain and reduction of musculoskeletal functionality in patients (5-7). At the musculoskeletal level, this translates into the onset of muscle and joint pain, as well as the appearance of significant postural alterations (8). Since posture can be defined as the spinal cord reflex manifestation of convergences and facilitation, secondary to cortical expressiveness (9), such changes in the postural alignment of patients may be due to information that are aberrant with respect to that which are naturally at the basis of the construction of the posture. This aberrant information may depend on many factors intrinsic to surgical techniques, which can lead to inevitable iatrogenic lesions of muscle-tendon portions (10), as well as to reconstructive techniques involving the musculoskeletal system and soft tissues (11).

Given the spread of these post-surgical complications, it is essential in the clinical setting to identify strategies to contain the various symptoms that may be encountered.

Among the post-surgical rehabilitation strategies most frequently found in the literature are, for example, physical exercise, breathing exercises or manual therapy, although the efficacy of these treatments is still unclear and is often based on personal experiences and anecdotes (12-14).

A new approach that could prove useful in the delicate area of post-surgical management could be represented by non-invasive instrumental therapies, such as Focused Mechano-Acoustic Vibrations (FMAVs). This therapeutic approach is based on the use of focused vibrations determined by variations in air pressure, produced by a turbine, inside plastic cups appropriately positioned on the patient's muscles receiving stimulation (15). The technique is completely non-invasive and allows, by varying the frequency of the administered vibration, to obtain modulatory effects on basal tone of the stimulated muscles (15,16). The therapeutic effects of this approach have been observed in many fields, such as geriatrics (17), orthopedics (18), neurology (19), sports medicine (20), urology (21), regenerative medicine (22) and aesthetic medicine (23).

Therefore, in light of the considerations made, in this study we observed the effects possibly induced by treatment with FMAVs in a post-surgical rehabilitation context of cardiac and oncological patients.

MATERIALS AND METHODS

This research is a pilot retrospective analytical observational study carried out at the Gemelli Molise Hospital (Campobasso, Italy), in cooperation with the Ce.Fi.R.R. (Center for Physiotherapy, Rehabilitation and Re-Education) staff from January to June 2023.

All the procedures applied comply with the national safety regulations and the protocol is accessible to anyone who does not highlight specific contraindications during the initial clinical evaluation necessary for all patients who access the hospital. The main major contraindications to access the protocol are pregnancy, epilepsy, electrical implants, infections and tuberculosis. The protocol is not an experimental practice, since it applies the same procedures used at the study facility for all patients who do not present the above-mentioned contraindications. This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Written informed consent was obtained at enrolment from participants who were willing and able. Furthermore, the Ce.Fi.R.R., as the institution in charge for carrying out the study through part of its staff, owns the ISO 9001:2015 certification for the realization of "Clinical observational studies in the rehabilitation field" (Certificate from the Italian Accreditation Body "Accredia" n. IT15/0304). Due to these considerations and the lack of incontrovertible national legislation regarding the need for the submission of retrospective and/or non-pharmacological observational studies to an ethics committee (24), normal ethics committee clearance was not required (25).

A total of 20 patients (12 women and 8 men; Caucasian ethnicity; average age of 48 years) were observed within the Gemelli Molise Hospital (Campobasso, Italy).

All patients observed had a history of surgery for cardiac or tumor pathology and underwent surgery no more than two months before the start of the treatment protocol. The therapeutic protocol was prescribed by specialist doctors after careful evaluations of the patient's general health status and the possibility and convenience of intervening on his/her post-surgical pain and postural alteration in a minimally invasive way through a complementary approach.

To assess the musculoskeletal health status of patients before (T0) and after (T1) the therapeutic protocol, a routine evaluation of the patients was carried out using 2 diagnostic tools:

- Numeric Pain Rating Scale (NPRS): it is one of the most common tools for measuring the pain subjectively perceived by patients. It is a derivate of the Visual-Analogue Scale (VAS) divided into ten levels, usually distributed equidistant on a 10 cm long strip, which correspond to the level of pain perceived by the patient at the time of the evaluation, where 0 is the total absence of pain and 10 is the maximum level of pain imaginable and/or ever experienced by the patient (26). This scale is reliable, effective and easy to apply even in the presence of dysfunctions of the general musculoskeletal system (26). In the case of the present study, patients were asked to

express a value from 0 to 10 corresponding to the maximum level of pain perceived at the site of the body which was more painful for them following the surgery;

- Postural Biometric Index (PBI): this is an index calculated by the proprietary software of the Milletrix 3.0 platform (Diasu Health Technologies, Rome, Italy) on the basis of a stabilometric evaluation carried out using the same device (9). This index takes into account the parameters of Center of Pressure, Symmetry of Bipodalic Load, Symmetry of Retro-Forefoot Load, Angle of Centers of Pressure, Podalic Angle, Location of Maximum Pressure Point, Symmetry of Support Surface and Center of Gravity Deviation - Center of Pressure (9). These parameters are then correlated to obtain an index that quantifies the postural state of the patient (9). The PBI value is considered healthy from 0 to 10 and dysfunctional if >10.

The observed patients were subjected to a protocol consisting of the application of FMAVs 2 times a week for 4 weeks, for a total of 8 sessions lasting approximately 20 minutes each, performed on an outpatient basis. FMAVs therapy was administered using the Vibration Sound System (ViSS) (Vissman Europe S.r.l., Rome, Italy), through a vibrating handpiece guided by the therapist. The handpiece was positioned on multiple body areas in which palpable Myofascial Trigger Points (MTrPs) were located. The presence of MTrPs was assessed by the therapist before each session, through a palpatory examination of the patient's body aimed at identifying the most dysfunctional MTrPs (i.e. more painful to palpation or capable of evoking radiated symptoms). When a potential MTrP was manually detected, the therapist performed a functional evaluation of the range of motion of the district where the MTrP was located; if the range of motion of the suspect district resulted reduced compared to the contralateral one, the palpated MTrP was considered in need of stimulation. Each dysfunctional point was stimulated for a time variable from 3 to 5 minutes until the total 20 minutes of treatment per session were reached. The stimulation frequency was set at 120 Hz.

Given the relatively small size of the observed group of patients, the data collected at time T0 and T1 were processed through the application of a non-parametric Wilcoxon signed-rank test. Data analysis was performed through the Statistics Kingdom open online calculator software (https://www.statskingdom.com, Melbourne, Australia). The observed changes were considered significant for p values < 0.05).

RESULTS

At the end of the therapeutic protocol, it was observed that both the NPRS and PBI values have varied in response to the FMAVs treatment.

In particular, the NPRS variable showed a significant reduction ($p < 0.01$) between times T0 and T1, equal to an average percentage variation of -26.4%, going from a mean value of 6.5 ± 1.6 to 4.7 ± 1.7 (Fig.1).

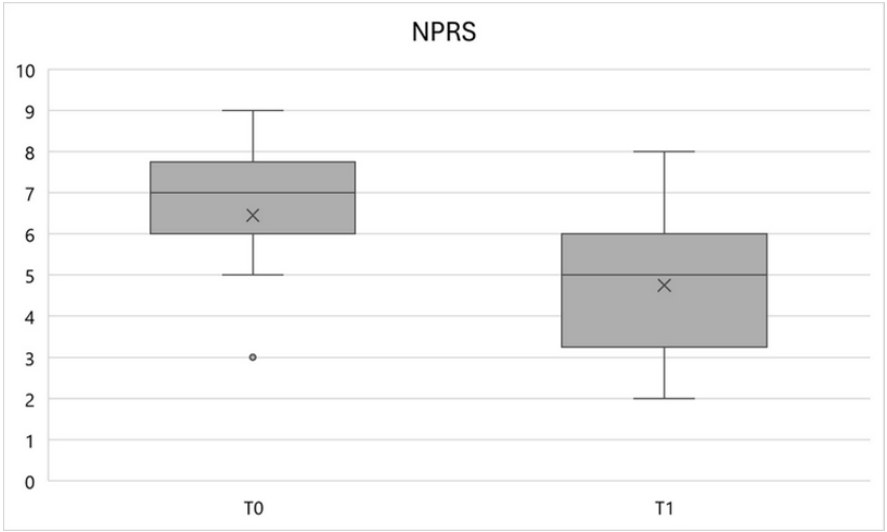

Fig. 1. *Box plots of NPRS values at times T0 and T1.*

Similarly, the PBI variable underwent a significant reduction ($p < 0.01$) between times T0 and T1, equal to a percentage variation of -17.9%, going from an average value of 13.7 ± 3.1 to 11.2 ± 3 (Fig.2).

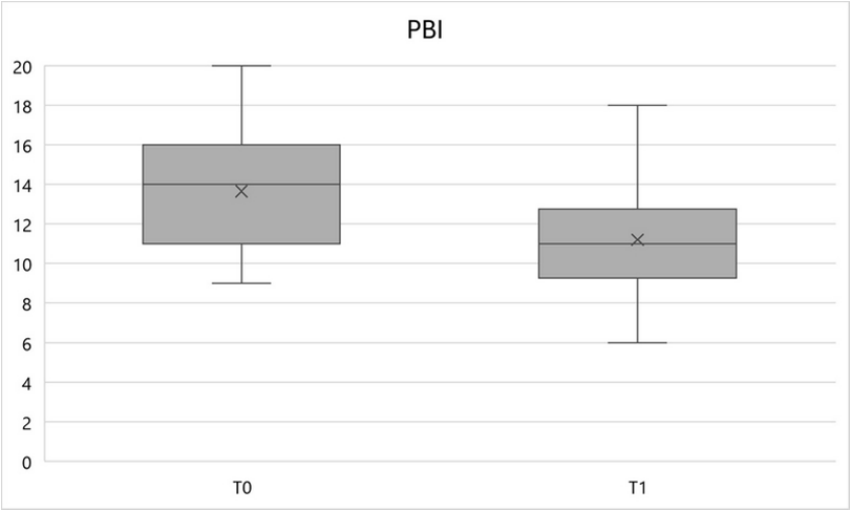

Fig. 2. *Box plots of PBI values at times T0 and T1.*

DISCUSSION

The present pilot analytical retrospective observational study has highlighted how the application of a protocol of 8 FMAVs sessions for a period of 4 weeks is able to induce a reduction in pain, detected with the NPRS scale, and postural dysfunction, detected with the PBI calculation, in post-surgical cardiac and oncological patients.

These results appear consistent with what has already been observed in the literature regarding the efficacy of FMAVs in multiple clinical areas of rehabilitation interest (15-22).

Multiple studies in literature have highlighted how vibration therapies are able to reduce musculoskeletal pain, both when applied to the whole body (27,28) and in the case of localized application (29,30). The mechanisms by which this pain reduction occurs are still a matter of debate. It is believed that a major influence on the analgesic capabilities of vibrations is to be attributed to the stimulation of the Pacinian corpuscles, which can determine the reduction or increase in perceived pain depending on the frequency and amplitude of the vibrations applied locally to the painful areas (31). It is believed that the pain modulating activity induced by vibrations is primarily attributable to Aβ-fibers activation, as well as to the activation of the limbic system, to the reduced local expression of TRPV1 and calcitonin and to the release of oxytocin (32). On the contrary, it would seem that the inflammatory aspect of pain is less influenced by vibrational stimulations, which do not seem to be able to induce significant releases of cortisol or opioid neuropeptides in the stimulated tissues (32). In any case, the vibrational frequency appears to be a more influential parameter than the stimulation intensity in determining the analgesic potential of vibrations, which is best expressed in a range between 100 and 250 Hz (32). This last consideration appears consistent with what has already been observed regarding the optimal ranges of stimulation using FMAVs, according to which frequencies between 100 and 300 Hz express the greatest potential for modulating pain and muscle tone (15), with frequencies in the range 100-120 Hz appearing to be the most effective in relaxing muscles in a state of increased tension (15). Considering that the application in this study was performed with a frequency of 120 Hz on various MTrPs identified in the patients, it is possible that the stimulation simultaneously reduced local pain and the state of tension of the treated muscles, inducing a combined effect of reduction of perceived musculoskeletal pain.

With regard to the aspect of postural improvement, more and more evidence can be collected in literature regarding the influence of vibrations, especially focal ones, in improving the parameters of postural stability and efficiency of various types of subjects, both in the pathological (33,34) and sports fields (35,36). It is assumed that the modulation activity of the muscular properties attributable to the FMAVs can determine the improvement of parameters such as strength, resistance, coordination and stability, with positive effects on the postural attitude of the treated subjects. This also appears consistent with what has been experienced in terms of efficacy of FMAVs in the treatment of musculoskeletal and neuromuscular problems, according to a bio-physico-metric approach aimed at improving the postural quality of patients whose pathologies could be linked to the presence of MTrPs (14,37).

Howsoever, it should be highlighted that the average value of postural dysfunction detected through the PBI test at the end of the treatment protocol, although significantly improved, was still slightly higher than the maximum acceptable value of 10 (9). Taking into account the positive trend of the PBI value detected in our study, this observation indicates that a FMAVs protocol could probably require more time or more frequent sessions to normalize the posture of post-surgical patients, while inducing a reduction in pain to levels below appreciable algesia more rapidly.

Although the results of this study appear encouraging, some limitations of this research must be highlighted. First of all, the study sample is relatively small and not sufficiently homogeneous. This is due to the observational nature of the study, which did not allow for the implementation of strict sample selection procedures, being able to consider only patients who had a similar, but not identical, clinical history and who had undertaken the same treatment protocol in the post-surgical period. Furthermore, for the same reasons, it was not possible to effectively configure a follow-up period or an adequate control group. Nonetheless, the observational setting of the study allowed for the evaluation of the effects of FMAVs directly in the operational field, in a more real clinical context, configuring this research as a pilot for possible experimental studies on the same topic, which could include a larger sample, a control group and a follow-up period, in order to confirm or deny the positive effects of FMAVs observed in this study.

CONCLUSIONS

This pilot observational study demonstrates how the application of a 4-week FMAVs protocol in post-surgical patients of the cardiac or oncological type is able to produce a significant improvement in pain and postural dysfunction that occur after the surgery. Since the identification of new therapeutic strategies capable of speeding up the recovery of patients of this type could improve the quality of life of the patients themselves and optimize health resources by making the terms of post-surgical hospitalization more efficient, it could be interesting to investigate more extensively on FMAVs in this therapeutic-rehabilitative context.

Conflict of interest

The authors declare that they have no conflict of interest.

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Original Article

COMPARISON OF IALUNVANCE COMPLEX AND CHLORHEXIDINE IN PERIODONTITIS TREATMENT: A PROSPECTIVE CLINICAL STUDY

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ABSTRACT

Aim: The aim of this study was to evaluate and compare the efficacy of Chlorhexidine and Ialunvance Complex (Euchlorine) as supportive therapies to Full Mouth Disinfection (FMD) in patients with periodontitis, focusing on Plaque Index (PI), Bleeding on Probing (BoP), Probing Pocket Depth (PPD), and patient satisfaction. *Materials and methods:* 92 affected by periodontitis and subjected to FMD were divided into two groups receiving either Chlorhexidine or Ialunvance Complex (Euchlorine) rinses post-disinfection. Clinical parameters, including PI, BoP, and PPD, were recorded at baseline and after six months to evaluate the effectiveness of each treatment. Patient satisfaction was assessed by a questionnaire grading items including perceived enjoyment, comfort, and overall acceptance of the treatment. *Results:* Both treatments significantly reduced PI and PPD, proving their effectiveness in periodontitis management. No significant differences were found between the two groups in these parameters ($p > 0.05$). Ialunvance Complex e showed a more substantial reduction in BoP than chlorhexidine ($p < 0.05$). In addition, patient satisfaction was higher in the Euchlorine group, with fewer reports of discomfort and better taste perception ($p < 0.01$), suggesting a higher level of acceptance and compliance. *Conclusion:* While Chlorhexidine and Ialunvance Complex (Euchlorine) are both effective in reducing negative clinical parameter values, Euchlorine offers additional advantages, such as higher patient satisfaction and fewer side effects, making it a viable alternative to Chlorhexidine. These results highlight the potential of Ialunvance Complex (Euchlorine) in improving periodontal therapy outcomes.

KEYWORDS: *Chlorhexidine, Periodontitis, Mouthwash, Plaque Index, Periodontal Therapy*

INTRODUCTION

Periodontal and peri-implant diseases are multifactorial conditions, primarily caused by a complex interplay between pathogenic bacteria present in dental biofilm, the host's immune response, and other predisposing factors such as smoking, diabetes, and genetic predisposition (1-5).

Periodontitis results from a chronic inflammatory process in which Gram-negative anaerobic bacteria, notably Porphyromonas gingivalis, Tannerella forsythia, and Treponema denticola, play a central role in triggering and maintaining persistent gingival inflammation. This leads to progressive loss of periodontal attachment and alveolar bone

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resorption (6-8). Clinical manifestations may include gingival bleeding, oedema, gingival recession, dentinal hypersensitivity, and, in more advanced stages, tooth mobility and the formation of periodontal abscesses (9,10).

The therapeutic approach to periodontitis focuses on reducing inflammation, arresting disease progression, and, where feasible, promoting the regeneration of damaged periodontal tissues. This is achieved through both non-surgical and, when necessary, surgical interventions (11-13).

Mouthwashes are an adjunctive tool in the management of periodontitis, providing additional support in both conservative and surgical treatment protocols (14).

Chlorhexidine is a widely utilized antimicrobial agent in dentistry, known for its efficacy in reducing bacterial loads in dental biofilm and periodontal pockets. It is available in various formulations, including 0.12% and 0.20% solutions, as well as 1% gels, which can be employed in both acute treatment phases and long-term maintenance protocols (15,16). Clinical studies have demonstrated that chlorhexidine significantly reduces inflammatory markers such as bleeding on probing and probing depth. However, long-term use of chlorhexidine may lead to side effects, including tooth staining and altered taste perception (17,18).

Ialunvance Complex (Euchlorine), a novel agent in clinical use, comprises hydrogen peroxide, hyaluronic acid, and glycine, offering a synergistic effect through its antimicrobial properties and promotion of tissue healing (19). Euchlorine is utilized in diluted solutions as a mouthwash, particularly as an adjunctive treatment in the acute phases of periodontitis or when deep periodontal pockets are present (20).

Studies have shown that Ialunvance Complex (Euchlorine) effectively reduces bacterial loads and periodontal inflammation, without the side effects typically associated with chlorhexidine. Furthermore, the combined action of hydrogen peroxide, hyaluronic acid, and glycine facilitates the regeneration of damaged tissues and enhances post-surgical healing (21).

Comparative studies indicate that Ialunvance Complex (Euchlorine) provides similar efficacy to chlorhexidine in the management of periodontitis, but with a more favorable safety profile (22).

The aim of this study was to evaluate and compare the efficacy of Chlorhexidine and Ialunvance Complex (Euchlorine) as supportive therapy to Full Mouth Disinfection (FDM) applied in patients affected by periodontitis concerning Plaque Index (PI), Bleeding on Probing (BoP), Periodontal Probing Depth (PPD) and patients' satisfaction according to VAS Scale.

MATERIALS AND METHODS

This prospective observational cohort study was designed to systematically assess the efficacy of Chlorhexidine and Ialunvance Complex (Euchlorine) as adjunctive therapies in Full Mouth Disinfection (FMD) for patients diagnosed with chronic periodontitis. The study's methodology and reporting were conducted in strict adherence to the Strengthening the Reporting of Observational Studies in Epidemiology for Clinical Trials (STROBE-CT) guidelines.

Patient recruitment took place at the Department of Dentistry, IRCCS San Raffaele Hospital, Milan, Italy, between January and September 2023. All procedures performed on the participants were in compliance with the ethical standards established by institutional and national research committees and were consistent with the principles articulated in the 1964 Declaration of Helsinki, including its later revisions. Ethical approval for the study was obtained from the institutional review board under approval number CE/INT/10/2015.

Patient Selection

Inclusion Criteria:

- Age ≥ 18 years: All participants had to be adults aged 18 years or older, with no upper age limit, allowing the study to encompass a wide range of adult patients;
- Confirmed diagnosis of chronic periodontitis: Patients were required to have a definitive clinical diagnosis of chronic periodontitis, with criteria such as clinical attachment loss, periodontal pocketing of ≥ 4 mm, and radiographic evidence of alveolar bone loss;
- Good oral hygiene compliance: Participants needed to demonstrate adequate oral hygiene practices, including regular tooth brushing and interdental cleaning, as determined by pre-treatment assessments;
- Commitment to the treatment protocol: Patients were required to show a willingness to comply with the periodontal treatment plan, including both Full Mouth Disinfection and adjunctive therapies, as well as follow-up care;
- Signed informed consent: Participants had to voluntarily agree to participate in the study by signing an informed consent form after being fully informed of the study's objectives, potential risks, and benefits;

- Availability for follow-up visits: Patients were required to commit to attending all scheduled study visits over the course of the follow-up period, ensuring the regular monitoring of clinical outcomes and adherence to the protocol;
- Baseline clinical parameters: Participants were required to have a baseline bleeding on probing (BOP) score of ≥ 30% and probing pocket depths (PPD) ≥ 4 mm in at least 6 sites, ensuring inclusion of patients with moderate to severe periodontitis.

Exclusion Criteria:

- Presence of systemic conditions affecting periodontium: Patients with systemic diseases known to affect periodontal health or healing, such as uncontrolled diabetes mellitus, autoimmune disorders, or osteoporosis, were excluded to eliminate confounding variables;
- Use of medications affecting periodontal status: Patients taking medications that could alter the periodontal condition, such as immunosuppressants, bisphosphonates, or long-term corticosteroids, were excluded;
- Active tobacco use: Patients who were current smokers, or who had quit smoking within the past 12 months, were excluded due to the detrimental impact of smoking on periodontal disease progression and treatment outcomes;
- Known allergies or hypersensitivities: Individuals with documented allergies or adverse reactions to Chlorhexidine, Euchlorine, hydrogen peroxide, hyaluronic acid, glycine, or any components of the treatment agents were excluded;
- Pregnancy or breastfeeding: Women who were pregnant, planning pregnancy during the study period, or breastfeeding were excluded due to hormonal influences on periodontal conditions and the need to avoid potential risks to the fetus or infant;
- Inability to attend scheduled follow-up visits: Patients who could not reliably commit to attending all scheduled follow-up visits within the study protocol's timeline were excluded to maintain consistent monitoring;
- Participation in other periodontal treatment studies: Patients involved in other clinical trials or under any experimental treatments that could interfere with or influence periodontal health were excluded to ensure the integrity of the study's findings.

Patient recruitment phase (T0)

During the first visit, after signing the informed consent and collecting the medical history, each patient underwent Periodontal Screening and Recording (PSR). A systematic examination was performed at six sites around each tooth (distobuccal, mid-buccal, mesiobuccal, distolingual, mid-lingual and mesiolingual) using a UNC-15 probe.

Each site was assigned a numerical code from 0 to 4, with the following interpretations: code 0 was assigned when the probe remained completely visible at the point of maximum probing, indicating gingival health without the presence of tartar or bleeding on probing. Code 1 was assigned when, in addition to probe visibility, bleeding was observed at probing without the presence of tartar. Code 2 was recorded when, in addition to code 1, tartar and/or overflowing margins of restorations were present. Code 3 indicated that the colored portion of the probe was only partially visible at the point of maximum probing, indicative of periodontal pockets between 3.5 and 5.5 mm deep. Code 4 was assigned when the probe was not visible at the point of maximum probing, indicating the presence of periodontal pockets deeper than 5.5 mm.

Patients who showed a code 3 or 4 in one or more sextants were considered positive for screening and were identified as needing further diagnostic investigations, including completion of the periodontal chart and a radiographic examination for a more detailed evaluation of the periodontal status.

BoP and PPD data were extracted from the periodontal chart.

Two-session periodontal treatment (T1)

During the first session, the following was performed:

- PI was measured using an erythrosine-based detector;
- An oral hygiene instruction and motivation session was conducted, which included instruction on proper tooth brushing, interdental hygiene and tongue cleaning;
- Full-mouth disinfection (FMD), including:
- Mechanical and/or manual supra/subgingival debridement was performed using curettes and periodontal tips, with treatment of two hemi-arches;
- During the treatment phases, rinses with Chlorhexidine 0.20% or Ialunvance Complex (Euclorina Gengive, Dompé S.p.A, Milan, Italy) for 2 minutes were performed;

- The periodontal pockets were irrigated with 1% Chlorhexidine gel or Ialunvance Complex, with three applications every 10 minutes;
- The tongue was treated with 1% Chlorhexidine 1% gel or Ialunvance Complex gel (Euclorina Gengive Gel, Dompé S.p.A, Milan, Italy) for 1 minute.

At the end of the first session, the patient was prescribed a home protocol including:

- Rinsing with 0.20% Chlorhexidine mouthwash or Ialunvance Complex;
- Brushing the tongue with 1% Chlorhexidine gel or Ialunvance Complex gel;
- Use of 0.20% Chlorhexidine spray for the tonsillar area.

The patient was instructed to repeat this protocol at least twice a day, integrating it into normal daily home hygiene procedures.

The second session included a new PI measurement using a plaque detector, motivational reinforcement and the same FMD protocol as previously applied.

The home protocol included:

- Rinsing with 0.12% Chlorhexidine mouthwash or Ialunvance Complex;
- Brushing the tongue with 1% Chlorhexidine gel or Ialunvance Complex;
- Use of 0.20% Chlorhexidine spray for the tonsillar area.

The home protocol included the same steps as recommended after the first session. The only variation was that rinses were to be done with Chlorhexidine 0.12% instead of 0.20% or with Ialunvance Complex as described above.

Patient re-evaluation phase (T2)

With the plaque detector, re-evaluation of PI was performed. A new periodontal chart was compiled to evaluate the new BoP and PPD values and compare them with those obtained at T0.

A satisfaction questionnaire about the achieved procedure according to the VAS scale was given to each patient (Table I).

Table I. *Satisfaction questionnaire.*

Question	**Evaluation score**									
	1	2	3	4	5	6	7	8	9	10
What was the degree of discomfort during the treatment?										
What was the degree of pain during treatment?										
Did you benefit from the treatment?										
Would you repeat the treatment?										
Would you recommend the treatment to someone?										

The clinical and collection and evaluation phases were summarized as follows (Table II).

Table II. *Protocol phases.*

	Phase	**Performed procedure**	**Outcomes**
T0	Patient recruitment	PSR; CODE 3 and 4 → Patients included → Periodontal chart and radiographic status.	Through periodontal chart PPD and BoP were recorded.
T1	Two-session periodontal treatment	FMD.	PI before treatment was recorded.
T2	Patients' re-evaluation	Periodontal chart and delivery of satisfaction questionnaire.	PI following treatment was recorded. PPD and BoP were reassessed through the periodontal chart. Patient's satisfaction score was registered.

CLINICAL OUTCOMES

The clinical outcomes were:

- Difference in BoP between T0 and T2. BoP was measured as the percentage of tooth sites where bleeding occurred upon probing out of the total sites examined. It can be represented as: BoP =

(Total number of sites examined/Number of sites with bleeding) ×100. This calculation provided a quantitative assessment of gingival inflammation and was integral in monitoring changes in periodontal health over time.

- Difference in PPD between T0 and T2. The average PPD per patient was calculated by averaging the measurements taken at multiple sites around each tooth. PPD= (Number of measured pockets/Sum of depths of all measured pockets).
- Difference in PI between T0 and T2. The Plaque Index was determined by visually assessing the amount of plaque present on tooth surfaces using a scoring system ranging from 0 to 100 per tooth surface. The formula used to calculate the PI score for each patient was: Plaque Index (PI)= (Total number of teeth assessed/Total number of teeth with visible plaque) ×100.
- Patient satisfaction level. To assess the overall degree of patient satisfaction using the questionnaire described above, the average score for each question was calculated. The total sum of the scores assigned by all patients for each question was calculated, and then the average of these sums was determined to obtain an overall average patient satisfaction score.

STATISTICAL ANALYSIS

The statistical analyses were conducted using Python 3.10.6 with the packages math, scipy, statsmodels, and pandas.

The chi-square test or Fisher's exact test was employed to compare the prevalence of Bleeding on Probing (BoP) between T0 and T2 within the same group of patients. The null hypothesis (H0) posited that there was no difference in BoP prevalence between T0 and T2 for both treatment groups.

Paired Student's t-test was utilized to compare the means of Periodontal Probing Depth (PPD) between T0 and T2 within the same group of patients. The null hypothesis stated that there was no difference in the mean PPD between T0 and T2 for both treatment groups.

Paired Student's t-test was used to compare the means of Plaque Index (PI) between T0 and T2 within the same group of patients. The null hypothesis hypothesized that there was no difference in the mean PI between T0 and T2 for both treatment groups.

Independent Student's t-test was performed to compare the means of the differences in BoP, PPD, and PI between patients treated with Chlorhexidine and those treated with Euchlorine at T2. This test assessed whether there were statistically significant differences in the changes of BoP, PPD, and PI between the two treatment groups. The null hypothesis stated that there were no differences in the mean changes of BoP, PPD, and PI between the groups treated with Chlorhexidine and Ialunvance Complex (Euchlorine).

Descriptive analysis calculated the means and standard deviations of patient satisfaction scores for those treated with Chlorhexidine and Euchlorine. Subsequently, an independent Student's t-test was conducted to compare the satisfaction means between the two groups. The null hypothesis (H0) posited that there were no significant differences in satisfaction scores between patients treated with Chlorhexidine and Ialunvance Complex (Euchlorine).

Throughout all analyses, a significance level of $p < 0.05$ was used to determine statistical significance.

Power Analysis/Sample Size/Normality Check

The power analysis was performed using the formula: $n = (Z\alpha/2+Z\beta)2\times\sigma 2\ ES2$, where σ is the estimated standard deviation, Zα/2 and Zβ are critical values for the chosen significance level and power, and delta is the effect size.

In the preliminary assessment, the research team calculated the effect size, power, and significance of the sample size. These metrics collectively provided insights into whether the sample size was adequate for reliable statistical analysis. With a cohort size of 60 participants, an alpha level of 0.05, and an effect size of 0.5, the power analysis indicated a power of 0.78 (1-beta). This suggested a high probability of detecting significant effects if they were present, maintaining a widely accepted balance between Type I and Type II errors in the analysis.

Regarding the power analysis, the study with 90 participants, an alpha level of 0.05, and an effect size of 0.5 yielded a power of 0.78 (1-beta). This ensured a sufficient likelihood of identifying significant effects, maintaining an accepted balance between Type I and Type II errors.

RESULTS

According to inclusion and exclusion criteria 97 patients, of whom 43 were female and 54 were males (mean age = 57.5; 44-71) were selected for the study.

Of these patients, 5 were within the dropout. Of these, 2 did not finish the protocol for health reasons, while the other 3 did not comply with the scheduled recall sessions.

Of the 92 subjects considered, 46 were treated with Chlorhexidine, as many with Euchlorine.

For each clinical outcome, the mean of the results obtained ± the standard deviation was performed. Statistical tests were then employed to assess both the difference in parameters between T0 and T2 and between the examined groups (Euchlorine vs. Chlorhexidine).

Study results were summarized as follows (Table III).

Table III. *Study results summary.*

Parameter	Mean ± SD	p-value
BoP at T0	0.35 ± 0.08	
BoP at T2	0.20 ± 0.05	< 0.001
BoP Euchlorine at T2	0.18 ± 0.04	0.02
BoP Chlorhexidine at T2	0.22 ± 0.06	0.02
PPD at T0	4.5 mm ± 1.0 mm	
PPD at T2	3.0 mm ± 0.8 mm	< 0.001
PPD Euchlorine at T2	2.8 mm ± 0.7 mm	0.03
PPD Chlorhexidine at T2	3.2 mm ± 0.9 mm	0.03
PI at T0	2.5 ± 0.6	
PI at T2	1.2 ± 0.4	< 0.001
PI Euchlorine at T2	1.2 ± 0.3	0.15
PI Chlorhexidine at T2	1.3 ± 0.4	0.15
Patient Satisfaction Euchlorine	4.5 ± 0.5	0.01
Patient Satisfaction Chlorhexidine	3.8 ± 0.7	0.01

Bleeding on Probing

A significant reduction in BoP was observed over the course of the study. At baseline (T0), the mean BoP was 0.35 ± 0.08. By the follow-up assessment (T2), BoP had significantly decreased to 0.20 ± 0.05 ($p < 0.001$), reflecting a substantial improvement in periodontal condition following treatment, with a reduction from 35% to 20% of the evaluated sites.

In comparing the two treatment groups at T2, the Ialunvance Complex group exhibited a mean BoP of 0.18 ± 0.04, while the Chlorhexidine group recorded a BoP of 0.22 ± 0.06. This difference was statistically significant ($p = 0.02$), indicating that the Ialunvance Complex group achieved a greater reduction in BoP compared to the Chlorhexidine group.

Periodontal Probing Depth

A significant reduction in PPD was observed throughout the study. At baseline (T0), the mean PPD was recorded at 4.5 mm ± 1.0 mm. By the follow-up period (T2), the PPD had significantly decreased to 3.0 mm ± 0.8 mm ($p < 0.001$), indicating a substantial improvement in periodontal condition and a marked reduction in probing depth as a result of the treatment.

In comparing the two treatment groups at T2, the Ialunvance Complex group showed a mean PPD of 2.8 mm ± 0.7 mm, while the Chlorhexidine group exhibited a mean PPD of 3.2 mm ± 0.9 mm. This difference was statistically significant ($p = 0.03$), suggesting that Ialunvance Complex was more effective in reducing PPD compared to Chlorhexidine, resulting in improved treatment outcomes.

Plaque Index

A significant reduction in PI was observed over time. At baseline (T0), the mean PI was 2.5 ± 0.6, which significantly decreased to 1.2 ± 0.4 at follow-up (T2), with a p-value of less than 0.001. This improvement reflects the effectiveness of the periodontal treatment and the reinforcement of proper home hygiene practices, leading to better plaque control.

When comparing the two treatment groups at T2, the Ialunvance Complex e group recorded a mean PI of 1.2 ± 0.3, while the Chlorhexidine group showed a mean PI of 1.3 ± 0.4. However, the difference between the groups was not statistically significant ($p = 0.15$), indicating that both treatments were equally effective in reducing plaque levels.

Patient satisfaction level

Patient satisfaction levels showed notable differences between the two treatment groups. In the Ialunvance Complex group, the mean satisfaction score was 4.5 ± 0.5, while the Chlorhexidine group had a lower mean score of 3.8 ± 0.7. This difference was statistically significant ($p = 0.01$), indicating higher patient satisfaction with Ialunvance Complex. The improved satisfaction with Ialunvance Complex may be attributed to better taste and fewer instances of mucosal irritation,

factors commonly associated with the use of Chlorhexidine. This suggests that Ialunvance Complex was more favorably received by patients in terms of comfort and overall treatment experience.

Overall, the T0 to T2 difference for the parameters BoP, PPD and PI could be summarized as follows in the figure (Fig.1).

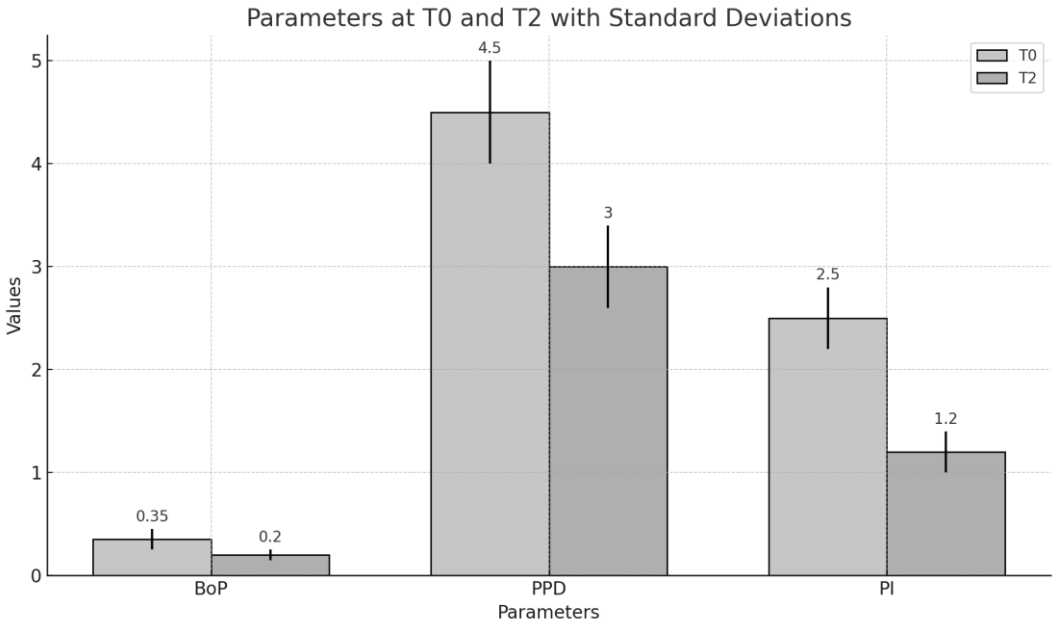

Fig. 1. *Periodontal parameter comparison chart from T0 to T2.*

The bar chart compares three periodontal health parameters (Bleeding on Probing, Periodontal Probing Depth, and Plaque Index) between two time points (T0 and T2), showing improvements across all parameters with standard deviations indicated by vertical error bars.

The Euchlorine versus Chlorhexidine comparison concerning periodontal parameters and patient satisfaction was outlined as follows (Fig.2).

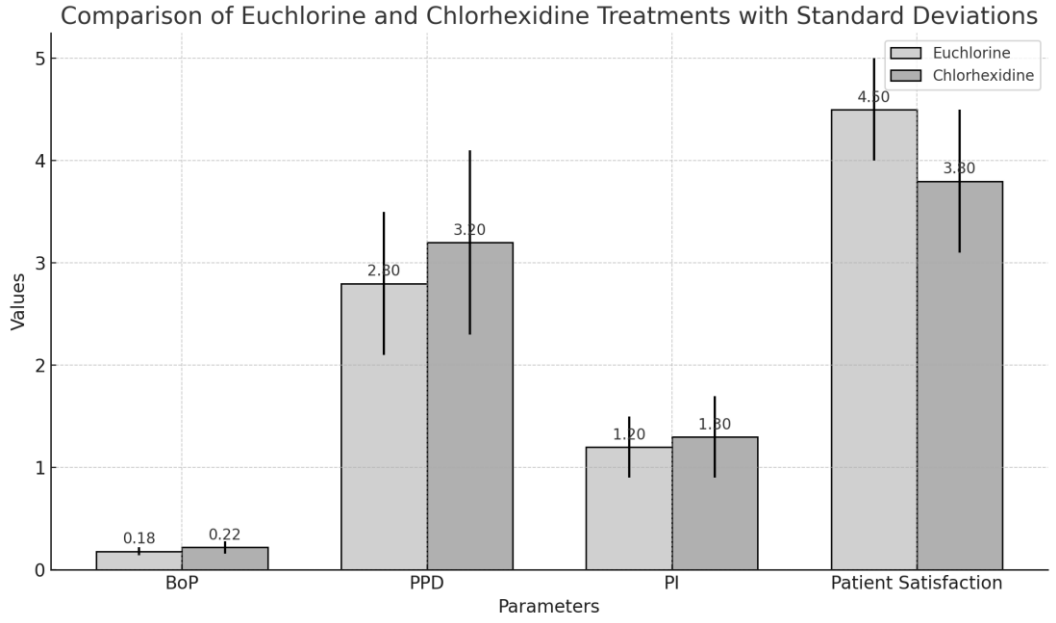

Fig. 2. *Euchlorine versus Chlorhexidine comparison concerning periodontal parameters and patient satisfaction.*

The bars represent the mean values for each parameter, with error bars indicating the standard deviations. Ialunvance Complex is shown in light blue, while Chlorhexidine is shown in light coral. The vertical black lines on each bar represent

the variability (standard deviation) around the mean value, providing insight into the consistency and reliability of each treatment.

DISCUSSION

The aim of this study was to evaluate and compare the efficacy of Chlorhexidine and Ialunvance Complex as supportive therapy to Full Mouth Disinfection applied in patients affected by periodontitis concerning PI, BoP, PPD and patients' satisfaction.

Both Ialunvance Complex and Chlorhexidine showed an effective reduction in plaque levels in Plaque Index results. Gunsolley (2010), in a systematic review evaluating 40 studies on the clinical efficacy of antimicrobial rinses, including Chlorhexidine, concluded that they were effective in controlling plaque and gingival inflammation (23). Kolahi and Soolari (2006), in a systematic review of 25 studies, confirmed the efficacy of Chlorhexidine in reducing plaque when used after brushing and flossing. Our study supports these findings but found no significant differences between Euchlorine and Chlorhexidine in plaque reduction, suggesting that both treatments may be effective (24).

In a randomized controlled trial, Gkatzonis et al. (2018) compared the effectiveness of three different oral rinses, including Chlorhexidine, in post-surgical periodontal patients. The results showed that Chlorhexidine was effective in reducing plaque, but the Ialunvance Complex-containing rinse demonstrated similar efficacy without the side effects associated with Chlorhexidine, such as tooth pigmentation and taste alteration (25). Herrera-Barraza et al. (2014), in a systematic review, analyzed the efficacy of oral rinses in the prevention of plaque and gingival inflammation, confirming that Chlorhexidine is one of the most effective, but also emphasizing the need for alternatives that can reduce long-term side effects (26).

Chen et al. (2019), in their systematic review and meta-analysis, examined oxidative stress-related biomarkers in saliva and gingival crevicular fluid associated with chronic periodontitis. The results indicated that reducing plaque levels can significantly reduce oxidative stress biomarkers, improving gingival health. This supports the importance of effective treatments such as Ialunvance Complex in plaque control (6). Montenegro et al. (2020), in a systematic review on subgingival microbial composition in patients with aggressive and chronic periodontitis, reported that plaque management is essential to prevent inflammation and disease progression. The use of effective antimicrobial agents such as Ialunvance Complex may therefore contribute significantly to the management of periodontal disease (7).

About BoP, as reported by Solderer et al. (2019), in a systematic review on the effectiveness of Chlorhexidine rinses after periodontal or implant operations, Chlorhexidine was found to be effective in controlling gingival bleeding. This study analyzed 15 articles and concluded that Chlorhexidine rinses can significantly reduce post-operative bleeding. However, our study showed that Ialunvance Complex led to a more significant reduction in BoP than Chlorhexidine (16). Herrera-Barraza et al. (2022), in a systematic review that evaluated simple post-extraction complications in 20 studies, suggested that alternative treatments to Chlorhexidine may offer superior benefits in controlling bleeding, thus supporting our results (26). In contrast, Costa et al. (2022) in a cross-sectional study involving 150 patients, found that the use of Chlorhexidine did not show a significant reduction in bleeding compared to other treatments, suggesting that the efficacy of Chlorhexidine may vary depending on the clinical setting and mode of application (27). De Souza et al. (2012), in a clinical trial of 100 patients, observed that the efficacy of Chlorhexidine in reducing gingival bleeding may be influenced by factors such as smoking and the presence of systemic diseases, which may explain the variability in results (28). Jepsen et al. (2015), in a systematic review on primary prevention of peri-implantitis, highlighted that the management of peri-implant mucositis is crucial to prevent bleeding and long-term complications. Their review of 25 studies showed that the use of Chlorhexidine, although effective, may not be sufficient on its own and that alternative approaches, such as Ialunvance Complex, may offer better results in terms of bleeding control (3).

Regarding PPD, the significant reduction in probing depth observed in the present study indicates an improvement in periodontal health. Dreyer et al. (2018), in a systematic review that examined 25 studies on the epidemiology and risk factors of peri-implantitis, highlighted the importance of PPD reduction for the prevention of peri-implant complications (29). Similarly, Salvi and Zitzmann (2014) demonstrated in a systematic review of 30 studies that preventive anti-infective measures, including the use of Chlorhexidine, are effective in reducing PPD and preventing biological implant complications (30). In another systematic review, Schwarz and Ramanauskaite (2022) emphasized that PPD reduction is critical to maintaining the health of peri-implant tissues but also pointed out that alternative treatments and novel antimicrobial agents, such as Ialunvance Complex, may offer additional benefits. Our study suggests that Ialunvance Complex may offer an additional benefit over Chlorhexidine in terms of PPD reduction, supporting the need for further research to confirm these benefits (31). In a clinical study by Gkatzonis et al. (2018), three different oral rinses were compared in patients undergoing periodontal surgery. The results showed that although Chlorhexidine was effective, the

use of Ialunvance Complex led to a more significant reduction in PPD, without the side effects associated with Chlorhexidine, such as tooth pigmentation (25).

From the results of the present study, patient satisfaction was significantly higher in the Ialunvance Complex -treated group than in the Chlorhexidine-treated group. James et al. (2017), in a systematic review of 51 randomized clinical trials, pointed out that Chlorhexidine may cause patients discomfort due to unpleasant taste and mucosal irritation (15). From the results of the present study, patient satisfaction was significantly higher in the Ialunvance Complex -treated group than in the Chlorhexidine-treated group. James et al. (2017), in a Cochrane systematic review of 51 randomized clinical trials, pointed out that Chlorhexidine may cause patients discomfort due to unpleasant taste and mucosal irritation (15). Poppolo Deus and Ouanounou (2022), in a literature review of 20 studies, discussed the adverse effects of Chlorhexidine, including mucositis and taste alteration, which may adversely affect patient compliance (32). In a clinical study by Gkatzonis et al. (2018), patient satisfaction was assessed using a structured questionnaire. Patients treated with Ialunvance Complex reported higher overall satisfaction than those treated with Chlorhexidine, citing less discomfort and a better taste experience (25). This is supported by Kolahi and Soolari (2006), who noted that patient acceptance of treatment is crucial for long-term success, and that alternative treatments to Chlorhexidine can improve compliance (24).

Calderini et al. (2013) explored the additional effect of Chlorhexidine-based antiseptics in mechanical periodontal treatment, finding that despite efficacy in controlling inflammation, patient tolerability was lower than with other treatments (33). This reinforces the results of our study, which indicate a higher level of satisfaction with Ialunvance Complex. In another systematic review, Canullo et al. (2020) examined the efficacy of Chlorhexidine in preventing post-operative complications in extractive, periodontal and implant surgery. The results showed that although Chlorhexidine is effective in reducing complications, many patients report side effects that may negatively affect the overall treatment experience (17). This supports the idea that Ialunvance Complex could be a viable alternative with fewer side effects and greater patient acceptance.

Sharma et al. (2019), in a randomized controlled trial, compared the efficacy of Chlorhexidine, hydrogen peroxide and tulsi extract in reducing halitosis. The results showed that although Chlorhexidine was effective, tulsi extract and hydrogen peroxide were better tolerated by patients (22). This suggests that alternative treatments to Chlorhexidine may offer advantages in terms of patient acceptance and comfort, similar to what was observed with Ialunvance Complex in our study. Litwiniuk et al. (2016) explored the use of hyaluronic acid in inflammation and tissue regeneration. Although not directly related to the use of Euchlorine or Chlorhexidine, this study highlighted the importance of finding treatments that are not only effective, but also improve the patient experience during healing (19). Ialunvance Complex, with its fewer side effects, could be a solution in this direction.

Tetè et al. (2021) developed a new Chlorhexidine-based mouthwash with an anti-discoloration system to address one of the most common side effects of Chlorhexidine, namely tooth pigmentation. Although this new product improves the acceptability of Chlorhexidine, our results suggest that Ialunvance Complex could still offer a better overall patient experience without the need for additional modifications (34). Di Petto et al. (2023) emphasized the importance of the dental hygienist's role in the professional maintenance of aesthetic restorations and evaluated the in vitro antimicrobial efficacy of mouthwashes. The results of this study showed that Ialunvance Complex may be an effective option for maintaining oral health in patients with aesthetic restorations, further supporting the use of Ialunvance Complex as an alternative to Chlorhexidine (35).

CONCLUSIONS

Within the limitations of this study, both Euchlorine and Chlorhexidine are effective in reducing plaque, BoP, and PPD, with Ialunvance Complex showing comparable efficacy but with fewer side effects. Patients treated with Ialunvance Complex reported higher satisfaction due to less discomfort and better taste. These findings suggest that Euchlorine is a viable alternative to Chlorhexidine, offering effective periodontal support with improved patient compliance. Further clinical studies may be necessary to confirm the results obtained.

Conflict of interest

The authors declare that they have no conflict of interest.

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Original Article

COMPARISON OF CHLORHEXIDINE AND IALUNVANCE COMPLEX IN THE POST-SURGICAL MANAGEMENT OF PATIENTS FOLLOWING ORAL AND IMPLANT SURGERY: PROSPECTIVE CLINICAL STUDY

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ABSTRACT

Aim: The aim of this prospective clinical study was to compare Chlorhexidine 0.20% and Ialunvance Complex (Euchlorine) in the post-operative management of patients undergoing oral and implant surgery, and to evaluate Placque Index and Bleeding on Probing values according to type of mouthwash, patient age, systemic diseases, smoking and surgical procedure. *Materials and methods:* This study included patients who required oral and implant surgery procedures. Post-operative therapy involved the use of Chlorhexidine 0.20% or Euchlorine mouthwash. The clinical outcomes analyzed were Plaque Index and Bleeding on Probing. These parameters were measured immediately before surgery, seven and 30 days after the surgical procedure. The study assessed the influence of type of mouthwash, patient age, systemic diseases, smoking habits and surgical procedure performed on the analysed parameters. *Results:* The t-test analysis revealed that Bleeding on Probing was significantly higher after third molar extractions, in females, and in smokers, with Euchlorine mouthwash showing significant improvement over Chlorhexidine. The Plaque Index was significantly higher following full-arch implant-prosthetic rehabilitations, but showed no significant differences between genders, smokers, and the type of mouthwash used ($p > 0.5$). Systemic diseases did not significantly affect either Bleeding on Probing or Plaque Index. *Conclusion:* Ialuvance Complex mouthwash is more effective than Chlorhexidine 0.20% in reducing Bleeding on Probing. The Plaque Index was higher in full-arch implant-prosthetic rehabilitations but was not influenced by gender, smoking, or mouthwash type. Systemic diseases did not affect Bleeding on Probing or Plaque Index. Further studies are needed to confirm these findings.

KEYWORDS: *Oral Hygiene, Mouthwashes, Oral Surgery, Dental Implants, Chlorhexidine*

INTRODUCTION

Recent developments in dental practice have led to a growing interest in optimizing post-operative protocols for oral surgery and implant procedures (1,2).

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Avulsions of dental elements, as well as implant placement, could be marred by phenomena of infectious origin that could cause the following complications: local infections, alveolitis, failure of osseointegration due to bacterial proliferation, peri-implantitis, cellulitis and osteomyelitis (3-5).

Among the most frequently used protocols, the use of mouthrinses has attracted considerable attention due to their crucial role in promoting tissue healing and preventing the risk of infection by reducing intra-oral bacterial load (6,7).

In the context of post-operative oral hygiene, chemical plaque control could represent a valuable support to the extent that the patient, due to pain and oedema, is unable to remove supragingival biofilm by the sole use of mechanical devices (8).

In the current scenario, mouthwashes based on Chlorhexidine (CHX) and Ialunvance Complex (Euchlorine) could be considered as reference antiseptic agents (9-11).

Chlorhexidine is a cationic bis-biguanide, i.e. a class of compounds that are chemically related and known for their bactericidal properties (12). The antimicrobial effect of CHX is dose-dependent: at low concentration levels (0.02%-0.06%), a bacteriostatic action is obtained, conversely, at higher concentrations (> 0.12%), bactericidal (13,14).

The use of CHX in oral surgery could be crucial in preventing the accumulation of biofilm and accelerating the wound healing process, as well as in implant surgery as an antiseptic against bacteria responsible for peri-implant disease (15-17).

Ialunvance Complex (Euchlorine), considered as a possible alternative to CHX, consists of three main substances: Hydrogen Peroxide (H2O2), Hyaluronic Acid (HA) and Glycine.

Concerning H2O2, the main mechanism associated with it is its ability to neutralize volatile sulphury compounds (VSC), which are volatile sulphury compounds related to halitosis problems (18,19).

Another property of this chemical compound, when applied at a percentage between 0.5 and 3%, is its anti-inflammatory action. During wound healing, hydrogen peroxide induces chemotaxis and the adhesion of antibodies such as macrophages and neutrophils, which, through the release of proteases and elastases, determine the bactericidal activity of the solution (20).

In addition, H2O2 promotes the migration of keratinocytes to the surgical site, which promotes epithelial healing (21,22).

HA, a member of the glincosaminoglycan family, plays a significant role in tissue regeneration by promoting the development of granulation tissue; it also has an inflammatory effect and inhibits biofilm growth. Because its constituent molecules penetrate oral mucous membranes allowing a long-lasting effect, it is present at all stages of the wound healing process (23,24).

Glycine is the smallest non-essential amino acid and consists of a carbon molecule linked to an amine group and a carboxyl group. Due to its small size, it is able to form helices in proteins and act as an extracellular signaling molecule. Recently, in a study by T. Schaumann et al., it was shown that the amino acid glycine possesses anti-inflammatory and immunomodulatory properties in oral tissues and acts both by reducing the inflammatory state and by inhibiting macrophages and preventing the formation of free radicals (25,26).

The aim of this prospective clinical study was to compare Chlorhexidine 0.20% and Euchlorine in the post-operative management of patients undergoing oral and implant surgery, and to evaluate Placque Index (PI) and Bleeding on Probing (BoP) values according to type of mouthwash used, patient age, systemic diseases, smoking and surgical procedure.

MATERIALS AND METHODS

The current prospective clinical trial has been undertaken to systematically explore the efficacy of Chlorhexidine and Ialunvance Complex (Euchlorine) as post-surgical interventions. The methodology and reporting of this study followed the Strengthening the Reporting of Observational Studies in Epidemiology for Clinical Trials (STROBE-CT) guidelines.

Participants were recruited from the Department of Dentistry at San Raffaele Hospital in Milan, Italy, between January and September 2023. All procedures conducted on the enrolled patients adhered to ethical standards set by institutional and national research committees, as well as the principles outlined in the 1964 Declaration of Helsinki and its subsequent amendments. The study received approval from the ethics committee under approval number 190/INT/2021.

Partecipants

Inclusion criteria:

- Age > 18 years old;
- Patients subjected to implant or extractive surgery procedures;
- Subjects who were eligible for immediate loading and did not require regenerative surgical procedures for dental implant placement;

- Smokers;
- Affected by balanced systemic diseases.

Exclusion criteria:

- Absolute contraindications to implant-prosthetic rehabilitation or extractive procedures;
- Allergy to the tested substances;
- Inability to adhere to monitoring checks and professional hygiene maintenance protocols planned during the follow-up;
- Involvement in concurrent clinical trials that could interfere with the present protocol.

Surgical procedures

- Extraction of single extruded tooth
- Extraction of third molar in partial bone impaction;
- Extraction of third molar in total bone impaction;
- Placement of single immediate load dental implant;
- Placement of axial dental implants supporting immediate load bridges;
- Placement of axial dental implants supporting full-arch immediate load prostheses.

The surgical procedures were performed by three oral surgeons with at least 5 years of professional experience.

Antibiotic therapy (amoxicillin and clavulanic acid 1 g or clarithromycin 1 g in case of allergy, twice daily for 6 days after surgery) was prescribed and had to be taken from the day before surgery. Analgesic therapy (non-steroidal anti-inflammatory drugs, as needed) were provided for each patient. Chlorhexidine 0.20% or Ialunvance Complex (Euchlorine) (Fig.1) mouthwash were prescribed. The rinses had been done with 10 ml solution for about 1 minute each, twice a day for one week. An ultrasoft-bristled surgical toothbrush was recommended for the first three days after surgery, taking care not to brush the surgical area. Smoking patients were advised to abstain from smoking for 48 hours after the procedure.

Composition Aqua, hydrogen peroxide, PEG-40 hydrogenated castor oil, xanthan gum, VP/dimethiconylacrylate/polycarbamyl polyglycol ester, glycine, sodium hyaluronate, sodium saccharin, aroma, oxyquinoline sulfate, limonene, phenoxyethanol, caprylyl glycol, hexylene glycol.

Fig. 1. *Ialuvance Complex (Euclorina Gengive, Dompé S.p.A, Milan, Italy).*

Data collection and clinical outcomes

The clinical outcomes analysed were PI and BoP, recorded by two dental hygienists. The considered indices were initially measured at time 0 (T0), i.e. the day of the surgical procedure immediately prior to commencement; subsequently, they were detected at the following post-surgical stages:

- Time 1 (T1) = seven days after surgery, at the same time as suture removal;
- Time 2 (T2) = 30 days after the surgical procedure.

For each procedure, the PI and BoP parameters were measured at relevant sites according to the following chart (Table I).

Table I. *Recording sites of PI and BoP parameters according to type of surgical procedure performed.*

Surgical procedure	Recording sites
Extraction of single extruded tooth	Adjacent tooth/teeth
Extraction of third molar in partial bone impaction	Adjacent tooth (upper or lower second molar)
Extraction of third molar in total bone impaction	Adjacent tooth (upper or lower second molar)
Placement of single immediate load dental implant	Adjacent tooth/teeth
Placement of axial dental implants supporting immediate load bridges	Adjacent tooth/teeth and dental implants placed
Placement of axial dental implants supporting full-arch immediate load prostheses	Dental implants placed

PI

An erythrosine-based plaque detector was used to highlight surfaces prone to bacterial biofilm. The Williams periodontal probe was inserted into the gingival sulcus at the buccal, lingual/palatal, mesial and distal points.

Each surface was evaluated and ranked according to the amount of plaque present using a four-point scale:

- 0: Absence of plaque;
- 1: Slight plaque deposit perceptible only by passing the probe over the gingival margin;
- 2: Moderate plaque accumulation visible on objective examination;
- 3: Abundant plaque accumulation within the gingival sulcus and on the tooth surface.

The sum of all scores obtained was divided by the number of surfaces analysed and multiplied by 100 to obtain the percentage. Based on the score obtained, a diagnosis was made:

- 0-10%: Good oral hygiene;
- 10-20%: Moderate amount of plaque;
- 20-30%: High amount of plaque;
- 30%: High amount of plaque.

BoP

The Williams periodontal probe was inserted into the gingival sulcus at the mesial, medial, distal vestibular and lingual/palatal points. A force of 0.2 to 0.6 Newton was applied (28). Each probing point was given a score of 0 for no bleeding and 1 for no bleeding. The following formula was applied to calculate the BoP percentage: BoP (%) = (Number of positive bleeding sites/Total number of sites probed) x 100.

The reference values for diagnostic purposes were as follows:

- 0-10%: Good gingival health;
- 10-25%: Mild gingivitis;
- 25-50%: Moderate gingivitis;
- 50%: Severe gingivitis.

STATISTICAL ANALYSIS

The statistical analysis was conducted using Python 3.10.6 and the following packages: math, scipy, statsmodels, and pandas. Initially, a two-sample t-test was performed to assess differences in independent variables (Plaque Index and Bleeding on Probing) based on factors such as type of surgery, mouthwash usage, gender, systemic diseases, and smoking habits. For this analysis, systemic diseases and smoking behavior were one-hot encoded and treated as binary variables, distinguishing patients with or without any systemic disease or smoking habits. We computed effect size using Cohen's D. Normality and equality of variance of the independent variables were assessed using the Shapiro-Wilk test and Levene's test, respectively. The null hypothesis tested was that the two independent samples (Patients treated with Euclorin vs. subjects treated with Chlorhexidine) have identical average values. Throughout all analyses, p-values < 0.05 were deemed statistically significant.

To examine changes over time while considering within-subject correlations, repeated measures ANOVA (Analysis of Variance) with type II sum of squares was employed. This statistical method compares means of a variable across different time points and determines whether there are statistically significant differences over time. With type II sum of squares, each term's contribution to the sum of squares is calculated after adjusting for other terms in the model, independent of their order. The results of this analysis were evaluated using effect size, specifically partial eta squared, a variant of the eta squared effect size measure commonly used in ANOVA. Both eta squared and partial eta squared

quantify the proportion of variance explained by a particular independent variable in the total variance of the dependent variable.

Power Analysis/Sample Size/Normality Check

Power analysis on the sample size was performed using the following formula: $n = (Z\alpha/2+Z\beta)2\times\sigma 2\ ES2$, where σ is the estimated standard deviation, Zα/2 and Zβ are critical values for the chosen significance level and power, and delta is the effect size.

In our preliminary analysis, we have calculated the effect size, power, and significance of the sample size. These metrics collectively provide insights into whether the sample size is sufficiently large to support reliable statistical analysis. With a sample size of 60 participants, a significance level (alpha) of 0.05, and an effect size of 0.5, our power analysis indicates a power of 0.78 (1-beta). This suggests a high likelihood of detecting significant effects if they truly exist, maintaining a commonly accepted balance between Type I and Type II errors in our analysis.

Concerning power analysis, with a sample size of 60 participants, we obtained a significance level (alpha) of 0.05; the effect size, representing the magnitude of the observed difference, was estimated to be 0.5. Additionally, our analysis was powered at 0.78 (1-beta). That ensured a sufficient probability of detecting significant effects if they exist and a commonly accepted balance between Type I and Type II errors.

RESULTS

Sixty patients were included in the study. Sample features were as follows (Table II). Incidence of systemic diseases in the sample surveyed was as follows (Fig.2). A single surgery was performed for each patient. The surgical procedures were summarised as follows (Table III).

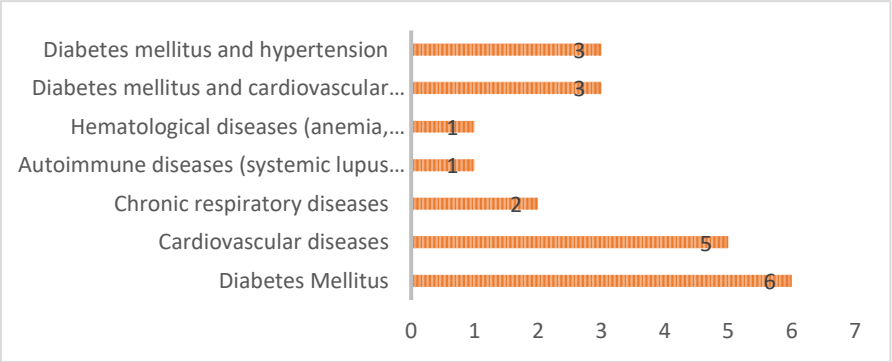

Fig. 2. *Incidence of systemic diseases in the sample surveyed.*

Table II. *Sample features according to gender, age, systemic diseases and smoking.*

	Sample features	
Gender	Female	31
	Males	29
Age	Average	46.5 years
	Range	21-72 years
Systemic diseases	Yes	24
	No	36
Smoking	Yes	16
	No	44

Table III. *Surgical procedures.*

Surgery	**Number of procedures**
Extraction of single extruded tooth	12
Extraction of third molar in partial bone impaction	10
Extraction of third molar in total bone impaction	12
Placement of single immediate load dental implant	10
Placement of axial dental implants supporting immediate load bridges	10
Placement of axial dental implants supporting full-arch immediate load prostheses.	9

Twenty-eight patients were prescribed chlorhexidine 0.20%, 32 with Ialunvance Complex. The results of the statistical analyses revealed notable findings regarding the factors influencing periodontal health outcomes.

BoP

The t-test analysis showed that bleeding on probing (BoP) after third molar extractions was significantly higher compared to other surgical procedures. The mean and standard deviation of BoP for third molar extractions were 3.5 ± 0.4, whereas for other surgical procedures they were 1.8 ± 0.2 ($p < 0.01$).

Gender differences were observed, with females exhibiting higher levels of BoP than males. The mean and standard deviation of BoP for females were 2.9 ± 0.3, while for males they were 2.1 ± 0.2 ($p < 0.05$). Smokers were found to have significantly higher BoP compared to non-smokers. The mean and standard deviation of BoP for smokers were 4.0 ± 0.5, while for non-smokers they were 2.2 ± 0.3 ($p < 0.01$).

The presence of systemic diseases did not yield significant differences in BoP. The mean and standard deviation of BoP for patients with systemic diseases were 2.7 ± 0.4, while for patients without systemic diseases they were 2.6 ± 0.3 ($p = 0.8$).

Statistically significant differences were found in BoP concerning the use of Ialunvance Complex versus Chlorhexidine mouthwash. The mean and standard deviation of BoP for Ialunvance Complex were 2.2 ± 0.2, whereas for Chlorhexidine they were 2.6 ± 0.4, demonstrating a significant improvement with the use of Ialunvance Complex ($p < 0.05$).

The results of Bleeding on Probing according to each category and related to each variable were summarized as follows (Fig.3).

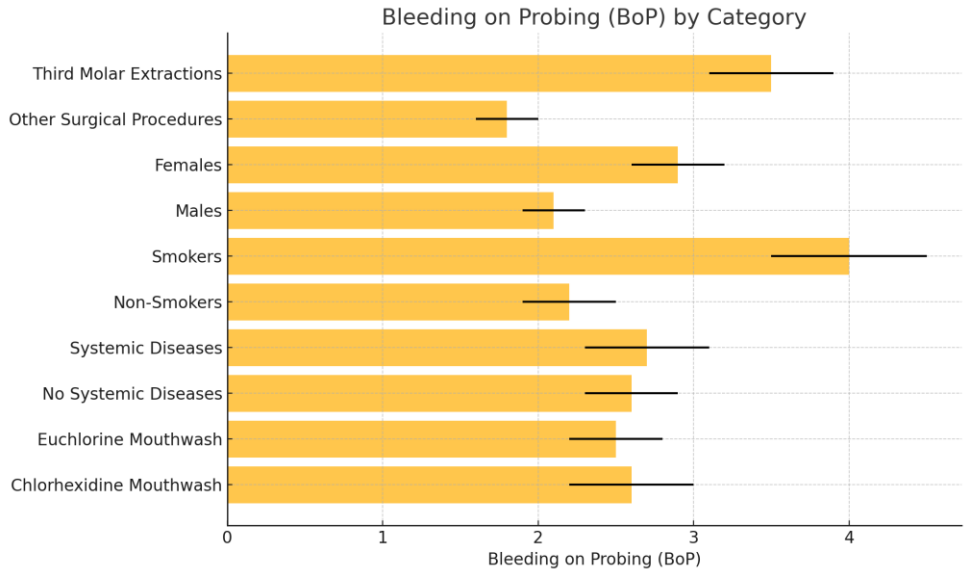

Fig. 3. *Mean BoP values and their standard deviations (represented by the error bars) for each category.*

The t-test analysis indicated that the Plaque Index (PI) following full-arch implant-prosthetic rehabilitations was significantly higher compared to other surgical procedures. The mean and standard deviation of PI for full-arch implant-prosthetic rehabilitations were 2.8 ± 0.5, whereas for other surgical procedures they were 1.6 ± 0.3 ($p < 0.01$).

No significant differences were noted in PI between genders. The mean and standard deviation of PI for females were 2.5 ± 0.4, while for males they were 2.4 ± 0.3 ($p = 0.5$). Smoking did not yield significant differences in PI. The mean and standard deviation of PI for smokers were 2.7 ± 0.4, while for non-smokers they were 2.6 ± 0.3 ($p = 0.6$).

The presence of systemic diseases did not yield significant differences in PI. The mean and standard deviation of PI for patients with systemic diseases were 2.7 ± 0.5, while for patients without systemic diseases they were 2.6 ± 0.3 ($p = 0.7$).

Furthermore, no statistically significant differences were found in PI concerning the use of Ialuvance Complex versus Chlorhexidine mouthwash. The mean and standard deviation of PI for Euchlorine were 2.6 ± 0.4, while for Chlorhexidine they were 2.7 ± 0.3 ($p = 0.8$).

The results of Plaque Index according to each category and related to each variable were summarized as follows (Fig.4).

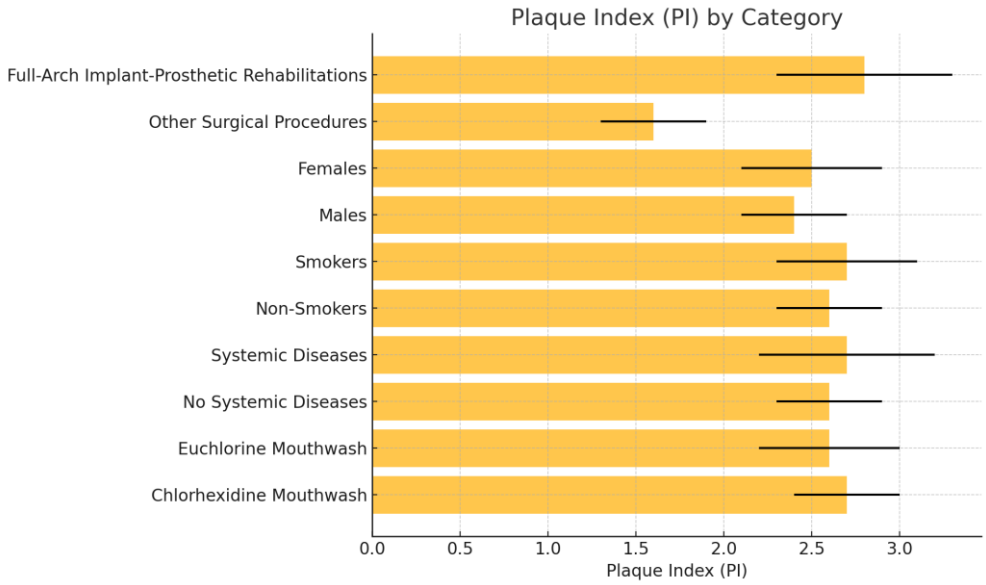

Fig. 4. *Mean PI values and their standard deviations (represented by the error bars) for each category.*

DISCUSSION

The aim of study was to compare Chlorhexidine 0.20% and Ialunvance Complex in the post-operative management of patients undergoing oral and implant surgery, and to evaluate Placque Index (PI) and Bleeding on Probing (BoP) values according to type of mouthwash used, patient age, systemic diseases, smoking and surgical procedure.

Concerning BoP the obtained results suggest that, after third molar extractions, it was significantly higher compared to other surgical procedures. Similar results were reported by Stella et al. (27) who, in their clinical study of 23 patients, evaluated the periodontal parameters of second molars following third molar avulsion and reported a significantly higher BoP. Contrasting results were reported by Pham et al. (28) who reported that, following avulsion of impacted third molars, the periodontal parameters of second molars, including BoP, were significantly lower and continuously improving.

With respect to gender, females exhibited higher levels of BoP than males. In this regard, the multicentre study by Zimmermann et al. (29) evaluated the possible impact of dental, socioeconomic, blood and biochemical factors on periodontal parameters and reported that there were no statistically significant differences between the sexes in terms of BoP. As stated by several studies (30-33), BoP values were also reported to be significantly higher in smoking than in non-smoking patients.

About the role of systemic diseases on BoP, the results obtained in the present study show no association. Contrasting results were reported by Herrera et al. (34) who reported a correlation between periodontal diseases and certain systemic diseases such as cardiovascular diseases, diabetes and respiratory diseases. These findings were confirmed by Ko et al. (35-36) and Schwarz et al. (37). In contrast, in accordance with our results, other authors have reported that systemic diseases, provided they are compensating, do not affect periodontal and peri-implant parameters (38).

The comparison of BoP indices between the use of Ialunvance Complex and Chlorhexidine mouthwashes revealed statistically significant differences favoring Ialuvance Complex. These findings align with recent research suggesting that different antiseptic agents can have varying degrees of effectiveness in reducing gingival inflammation and bleeding. Studies have demonstrated that Chlorhexidine, despite its well-documented efficacy in controlling plaque and gingivitis, can cause adverse effects such as tooth staining and taste alteration, which might influence patient compliance and ultimately its effectiveness in clinical practice. A systematic review highlighted that Chlorhexidine's side effects necessitate the exploration of alternative agents that could provide similar or enhanced benefits without the associated drawbacks (39).

On the other hand, Ialuvance Complex, which is less commonly discussed in the literature, appears to offer a comparable or even superior alternative to Chlorhexidine. The lower BoP indices associated with Ialunvance Complex suggest that it could be more effective in promoting periodontal health, potentially due to its different mode of action or patient tolerability. Recent studies have shown that herbal-based and alternative mouthwashes, like those containing Euchlorine, can be effective against common oral bacteria and reduce gingival inflammation, supporting the potential benefits observed in this study (40).

Concerning PI, following full-arch implant-prosthetic rehabilitations was significantly higher compared to other surgical procedures. Similar results were obtained in a six-year retrospective clinical study evaluating full-arch implant prosthetic rehabilitations. The study indicated that posterior sites exhibited greater plaque accumulation compared to anterior sites, likely due to the difficulty in maintaining hygiene in these areas (41).

No significant differences were noted in PI between genders, suggesting that gender does not play a substantial role in influencing plaque accumulation around dental implants. One possible explanation for this finding is that both males and females in these studies were subjected to similar oral hygiene protocols and follow-up care, which likely minimized any gender-based disparities in plaque control. Consistent and thorough oral hygiene practices are essential for all patients regardless of gender to maintain low PI levels and prevent peri-implant complications (41).

In contrast to what has been reported by other authors (42,43), in our study, smoking and systemic diseases did not yield significant differences in PI.

In addition, no statistically significant differences were found in the PI about the use of Ialunvance Complex mouthwashes compared to chlorhexidine-based ones.

Studies have shown that Ialunvance Complex, with its oxidizing action, effectively reduces bacterial load without the common side effects associated with chlorhexidine, such as tooth staining and taste alteration. This makes it an available alternative for patients who might experience adverse reactions to chlorhexidine (14). Furthermore, research has confirmed that both mouthwashes maintain similar efficacy in controlling plaque accumulation, ensuring that patients receive adequate protection against peri-implant diseases regardless of the mouthwash used (44).

CONCLUSIONS

Within the limitations of this study, Ialuvance Complex mouthwash could be considered more effective than Chlorhexidine 0.20% in reducing Bleeding on Probing. Although the Plaque Index was significantly higher in full-arch implant-prosthetic rehabilitations, it was not influenced by gender, smoking status, or the type of mouthwash used. Systemic diseases did not significantly impact either Bleeding on Probing or Plaque Index, suggesting that the choice of mouthwash and surgical procedure are more critical factors in post-operative management. Further clinical studies may be necessary to confirm the obtained results.

Author Contributions

Conceptualization, E.P. and R.V.; methodology, R.V.; software, A.B.; validation, E.P., R.V; formal analysis, S.S.; investigation, R.V.; resources, A.B.; data curation, B.D.; writing—original draft preparation, G.T.; writing—review and editing, X.X.; visualization, E.P.; supervision, E.P. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Ethics Committee of Vita-Salute San Raffaele University n.180/INT/2021, Dental School Department of Dentistry IRCCS San Raffaele Hospital, Milan, 20132, Italy.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Conflict of interest

The authors declare that they have no conflict of interest.

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Review

SYSTEMIC EVALUATION AND GOOD PRACTICE OF THE SURGICAL PATIENT IN TREATMENT WITH ANTICOAGULANTS OR ANTIAGGREGANTS: NARRATIVE REVIEW

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ABSTRACT

Objective: The aim of the following scientific research is to evaluate the management of patients in anticoagulant and antiaggregant therapy during dental surgical procedures, and at the same time assess and analyze the risk of thrombosis or bleeding depending on whether the drug is discontinued or not. *Methods:* It is carried out a research and analysis of systemic reviews in the English language that were about the application of artificial intelligence in dental fields, using databases such as Web of Science, Scopus, PubMed, using keywords "oral surgery" ,"anticoagulants and oral surgery". *Results:* Patients on anticoagulant or antiaggregant therapy can undergo dental surgery without stopping the medication, provided local measures are taken to control bleeding. Discontinuation of therapy is not recommended due to the risk of thromboembolic events, especially with warfarin and antiaggregants. The new oral anticoagulants (NAO) require only a possible dose adjustment in high-risk cases. Risk assessment through the ASA classification and type of procedure is crucial for safe management. *Conclusions:* The dental management of patients on anticoagulant or antiaggregant therapy requires a balance between hemorrhagic risk and thromboembolic risk. Discontinuation of therapy is not recommended; local measures to control bleeding are better and specialists should be consulted if necessary.

KEYWORDS: *Oral health, anticoagulant, blood, oral surgery, dental management*

INTRODUCTION

The objective of the following scientific research is to evaluate the management of patients in anticoagulant and antiaggregant therapy during dental surgical procedures, and at the same time assess and analyse the risk of thrombosis or bleeding depending on whether the drug is discontinued or not (1). Thrombosis is a pathological process characterized by the formation of a clot within a blood vessel, which can occlude an artery and prevent normal blood flow to tissues, causing hypoxia and potentially ischemic damage such as heart attack (2). The severity of the damage depends on the

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type of vessel involved. Causes may include factors such as smoking, obesity, physical inactivity, coagulation disorders, use of oral contraceptives and changes in prothrombin time (3).

It is estimated that in our country, the patients treated with oral anticoagulants (OA) are more than one million, equivalent to 1.5-2% of the general population, although it is known that these drugs are underused compared to the conditions for which they are indicated. Their use has been growing over the last 20 years mainly due to the evidence that has demonstrated the great effectiveness of these treatments in preventing stroke in atrial fibrillation. The recent market introduction of DOAC's has given a major boost to the use of AOs in relation to the simplification of treatment that these drugs have allowed. It is therefore expected that a much larger proportion of people will be subjected to such treatments in the near future (4).

Treatment involves the administration of oral anticoagulants (e.g. warfarin) to prevent complications such as atrial fibrillation, ischemic stroke or deep vein thrombosis, with regular monitoring of coagulation parameters, especially PT and INR, which must remain between 2 and 3. Patients with a history of thrombotic events are often given antiplatelet or anticoagulant therapy to prevent the formation of new clots (5). Oral anticoagulants, especially dicumarols such as warfarin (Coumadin) and acenocoumarol (Sintrom), act by interfering with the activation of certain coagulation factors that depend on vitamin K to be functional (5,6). By inhibiting the action of this vitamin, drugs make blood less coagulable. There is thus a direct antagonism between dicumarols and vitamin K, which is why the latter can be administered as an antidote in case of overdose of the drug.

Vitamin K comes both from the diet (in foods such as green leafy vegetables) and from endogenous production by the intestinal bacterial flora, thus ensuring a constant supply. Anticoagulant and antiaggregating drugs are a crucial factor to consider when planning dental surgery or implants, as they significantly influence the intra- and post-operative hemorrhagic risk. Among the anticoagulants, warfarin is an indirect drug that acts at the hepatic level by inhibiting vitamin K, essential for the synthesis of certain coagulation factors (7). This mode of action results in a delayed effect both at the beginning and at the end of treatment, as the anticoagulant effect depends on the half-life of the coagulating factors already present in the blood, which can be up to 60 hours. In addition, individual variability related to absorption, drug elimination, liver health and concomitant intake of other drugs or substances makes the control of warfarin complex. Despite these limitations, an important advantage of warfarin is the ability to monitor its effect through the INR, a reliable laboratory index that allows you to accurately assess the degree of anticoagulation of the patient and, therefore, the risk of bleeding and thromboembolism during a surgery. However, the risk of thromboembolism resulting from even a temporary discontinuation of therapy may last for 6-7 days, and the management of this discontinuance requires careful medical supervision. In order to reduce this risk, the so-called "bridging" with heparin was introduced in the past, but today it is considered in most cases ineffective and expensive. New oral anticoagulants (NOA), such as dabigatran, apixaban and rivaroxaban, offer easier and safer management.

Dabigatran, which acts directly on thrombin, has a half-life of 12-14 hours and reaches the peak in 2-3 hours; apixaban and rivaroxaban, direct inhibitors of factor Xa, reach the peak in 3-4 hours (8). Compared to warfarin, these drugs have less individual variability, are less prone to food and other drug interactions, and do not require periodic laboratory testing. Their discontinuation prior to dental surgery may occur with 24-hour notice, significantly reducing the window of thromboembolic risk compared to the 6-7 days required for warfarin (9). However, NOA does not have a specific laboratory indicator to directly monitor the anticoagulant effect, which requires more clinical attention. The main indications for anticoagulant therapy include the presence of heart valve prostheses, episodes of deep vein thrombosis, atrial fibrillation, pulmonary embolism and cerebrovascular disease (10).

The most common antiaggregant drugs include acetylsalicylic acid, thienopyridines (ticlopidine, clopidogrel, prasugrel), indobufen, picotamide and dipyridamole. These act by preventing platelet aggregation and are mainly used in the secondary prevention of ischemic events, such as myocardial infarction, stroke and coronary stent occlusion. The use of anticoagulants or antiaggregants inevitably leads to an increased risk of hemorrhage, since they interfere with the coagulative cascade and the formation of a stable clot.

The ASA classification is a useful tool for assessing a patient's general physical condition before surgery, allowing doctors to estimate the risk of post-operative complications. This classification, consisting of six grades plus an "E" extension for emergencies, takes into account the patient's systemic condition and severity. The anesthetic assessment is based on a thorough clinical and instrumental analysis to identify any comorbidities that could affect the patient's response to anesthesia and surgery. In patients with coagulation disorders, tests such as platelet count, PT/INR and APTT are essential to assess the risk of bleeding. In the dental context, the management of patients on anticoagulant or antiaggregant therapy requires a personalized evaluation of hemorrhagic risk, which varies according to the intended procedure, the medications taken and the patient's general clinical condition (6). The simplest procedures generally do not involve a high risk of haemorrhage and can be performed without changing current therapy. On the contrary, more invasive

procedures require greater caution, possibly specialist consultation and local hemostasis measures. Clinical experience and scientific evidence show that severe haemorrahagic complications are rare in patients who continue anticoagulant therapy during dental procedures. However, conditions such as liver failure, kidney failure, myelopathies or cancer treatments can significantly increase the risk of bleeding and require careful pre-operative evaluation, even in collaboration with the specialist (11). Other factors that influence risk include taking drugs such as NSAIDs, SSRIs or carbamazepine, which may interfere with coagulation (10). For this reason, a complete pharmacological history and careful evaluation of the patient's haemorrhagic history is essential (12). The presence of coronary stents or mechanical heart valves requires particularly careful management, with the involvement of the cardiologist before any therapeutic variation. In summary, the correct management of patients under anticoagulant or antiaggregant therapy in dentistry is based on a multidimensional evaluation of the hemorrhagic risk, balanced with the thromboembolic risk, Always taking a personalised approach based on the best available evidence (7).

Oral surgery is traditionally considered a low-risk procedure, but there are specific situations and interventions that can increase the risk of bleeding. In these cases, it is crucial to assess the severity of the bleeding and whether it poses a risk to the patient's life. For the management of hemorrhagic events in subjects receiving direct oral anticoagulants (DOAC), several strategies have been proposed (13,14). These include the possibility of altering the pharmacokinetics of the drug by reducing its absorption through the administration of activated carbon, an option indicated for dabigatran and apixaban and also considered potentially useful for rivaroxaban and edoxaban, Although specific studies are lacking. In the case of dabigatran, due to its low binding to plasma proteins, the use of hemodialysis for its elimination may also be considered (13). Other measures include the use of antifibrinolytic agents, such as tranexamic acid and aminocaproic acid, which have demonstrated a good safety profile and effectiveness in improving perioperative haemostasis. In situations of potentially lethal bleeding, the administration of plasma factors such as concentrated prothrombin complexes, frozen fresh plasma or cryoprecipitates may be used, although the clinical efficacy of these options requires further confirmation. For dabigatran, there is a specific approved antidote, idarucizumab (Praxbind®), available in the European Union since 2015, making this drug the first among DOAC's to have a reversal agent; Other antidotes such as andexanet alfa and ciraparantag are still in the experimental phase (15).

Before oral surgery, it is important to take preventive measures to reduce the risk of bleeding, such as using local anesthetics and limiting osteotomy during extractions. Careful curettage is essential to prevent infection and use resorbable sutures, with the possible use of hemostatic agents such as oxycellulose soaked in tranexamic acid. In patients receiving warfarin or other anticoagulants, it is essential to monitor the INR, which must be less than 4 to proceed with the procedure without stopping therapy. If the INR is too high, surgery should be postponed and the attending physician should be informed. If the INR is acceptable, the procedure can be carried out with measures to control the risk of hemorrhage. For patients receiving new anticoagulants (NOA), the INR is not useful to monitor coagulation. Dabigatran uses aPTT, while rivaroxaban uses PT. These drugs have a rapid effect and short half-life, allowing for rapid anticoagulant adjustment. In patients with thrombosis or pulmonary embolism, it is recommended to delay dental procedures until the start of standard doses. For low-risk hemorrhage operations, it is not necessary to discontinue therapy, while for those at higher risk, it is recommended to suspend or delay the morning dose of the drug. The risk of thromboembolic or hemorrhagic complications is low, but depends on the procedure and the patient. All these assessments are valid to avoid accidents and complications during dental surgical therapies, thus avoiding the risk of bleeding (15).

METHODS

Research and analysis of systemic reviews in the English language were carried out regarding the application of artificial intelligence in dental fields, using databases such as Web of Science, Scopus, and PubMed. Inclusion and exclusion criteria were adopted for the selection of studies. Included and analysed are systematic reviews, excluding meta-analyses, case reports and case series. The filters used for the search were "systematic review", "review", "free full text", custom range publication date of seven years "2018-2024". The selected studies have been grouped according to the scope of AI in dentistry. This review utilized MeSH keywords "oral surgery" ,"anticoagulants and oral surgery".

RESULTS

From the results of the research conducted, it was found, in accordance with recent guidelines, that patients treated with anticoagulant or antiplatelet can face dental operations without discontinuing drugs, provided that local measures are taken to control bleeding. Discontinuation of therapy is not recommended for thromboembolic risk, especially with warfarin and antiaggregants. The new oral anticoagulants (NOA) require only a dose change in case of high-risk

interventions. Risk assessment by ASA classification and the type of procedure envisaged are essential for safe management.

CONCLUSIONS

According to the results of the following research conducted we can conclude that in patients treated with anticoagulants or platelet antiaggregants for cardiovascular conditions with high thromboembolic risk, perioperative management in dentistry requires attention. Although taking these drugs may increase the risk of hemorrhage complications, discontinuation can lead to an increased risk of thromboembolism. In summary, the management of patients on anticoagulant or antiaggregant therapy requires a balance between controlling hemorrhagic risk and preventing thromboembolic events, taking local hemostasis measures and consulting specialists when necessary.

Conflict of interest

The authors declare that they have no conflict of interest.

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Review

SYSTEMIC EVALUATION AND GOOD PRACTICE OF THE SURGICAL PATIENT IN TREATMENT WITH BISPHOSPHONATES: NARRATIVE REVIEW

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ABSTRACT

Objective: The purpose of this article is to analyse the use of bisphosphonates in the treatment of pathologies characterized by an increase in bone resorption, with particular attention to one of the most important adverse effects associated with this pharmacological class: Osteonecrosis of the maxillary organs (ONJ). Bisphosphonates, widely used in the treatment of pathologies with increased bone resorption, act by inhibiting osteoclastic activity and inducing cellular apoptosis. However, their use, especially in conjunction with oral surgery, is associated with the risk of osteonecrosis of the jaw (BRONJ/MRONJ), a rare but potentially serious complication. *Methods:* A search was performed on PubMed, not inserting "article type" filters. using the keywords "oral bisphosphonates AND tooth extraction", "oral surgery AND bisphosphonates AND osteonecrosis". The adverse effects of some drugs such as those of certain classes of antibiotics in the management of osteonecrosis of the jaws were also evaluated. *Results:* The results of the research, after the process of identification and selection of the articles to be analyzed were as follows: the main complication observed in patients treated with oral bisphosphonates was osteonecrosis of the maxillary, the incidence of which appears to be related to the duration of therapy. The data collected show a significant prevalence of lesions in the posterior region of the mandible and, in some cases, delayed healing of post-extraction wounds. Variables such as anatomical location, age, sex, comorbidity and systemic risk factors were also analyzed, confirming the multifactorial role in the onset of the disease. *Conclusions:* Current research is investigating the role of the oral microenvironment in alveolar bone homeostasis and in the pathogenesis of osteonecrosis associated with bisphosphonates or Denosumab (BRONJ/MRONJ). A response-focused approach from the oral environment could open up new preventive perspectives and contribute to a broader understanding of the biological mechanisms involved in this complication.

KEYWORDS: *Oral health, bone, bone loss, bisphosphonate, surgery, dental, dental surgery*

INTRODUCTION

Bisphosphonates are drugs derived from inorganic pyrophosphate, characterized by a P-C-P bond that makes them resistant to enzymatic hydrolysis. Their main action takes place at the bone level, where they bind with high affinity to

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calcium ions, accumulating in areas of bone remodeling. During the bone resorption process mediated by osteoclasts, the acidic pH of the resorption gaps promotes the release of bisphosphonates from the bone mineral component, allowing their entry into the osteoclasts via endocytosis (1).

Bisphosphonates are divided into two main categories: nitrogen-free ones, which are incorporated as toxic and non-hydrolysable ATP analogues, and those containing nitrogen (such as alendronate, risedronate, zolendronate), which inhibit the enzyme FPP synthase, stopping the production of isoprenoids in the mevalonate pathway (2,3). This block interferes with the prenylation of GTPases proteins, which are essential for osteoclastic function, inducing the accumulation of toxic metabolites and reducing bone resistance capacity (4). The therapeutic use of bisphosphonates is particularly indicated in bone pathologies characterized by excessive osteoclastic activity, such as osteoporosis, Paget's disease and tumoral osteolysis, including those caused by multiple myeloma. BPs can be administered orally or intravenously, with an oral bioavailability of less than 1%. Oral bisphosphonates, such as alendronate and risedronate, are frequently used in the treatment of osteoporosis, while intravenous bisphosphonates, such as zolendronate, are used in patients with bone metastases or malignant hypercalcemia, to improve survival and quality of life (5).

In recent decades, the use of bisphosphonates has seen a significant increase, with prescriptions amounting to around 30 million annual doses in the US and over 190 million worldwide. In Italy, in 2013, bisphosphonates accounted for 85% of the drugs prescribed for osteoporosis. Their spread has led to a growing interest in the dental community regarding possible interactions between treatment with dental implants and the use of bisphosphonates, especially among adult patients over 40 years old, who are the main users of these drugs. The second and third generation bisphosphonates, which contain nitrogen, bind more firmly to bone hydroxyapatite, increasing therapeutic efficacy but also potential interaction with other therapies (6,7).

The wide spread of these drugs and their relevance in the treatment of bone diseases have raised important questions in dentistry, especially regarding side effects such as osteonecrosis of the mandible, that may occur in patients treated with bisphosphonates, especially after dental surgery or the insertion of dental implants (8).

Osteonecrosis of the mandible (ONJ) is a rare condition first described in 2003 in cancer patients treated with bisphosphonates. It is manifested by the exposure of the mandibular or maxillary bone, or by the presence of a fistula that persists for more than eight weeks. The initial cases were mainly related to dental extractions or other conditions that accelerate bone turnover. ONJ is diagnosed when there is bone exposure in the maxillofacial region, which does not heal after eight weeks, in patients treated with anti-resorptive agents such as bisphosphonates or denosumab, and without a history of radiation therapy. The diagnosis is based on careful clinical evaluation and instrumental examinations, excluding other causes of dental pain. The disease may remain asymptomatic for long periods, from weeks to months (9).

The ONJ Task Force has identified significant risk factors, with intravenous use of bisphosphonates as the most important. Other risk factors include radiation therapy, dental extractions, chemotherapy, periodontal diseases, and the use of oral bisphosphonates. Although osteonecrosis of the jaw is a rare side effect (less than one case per thousand treated patients), it is important to consider the safety of using bisphosphonates, especially in patients with other concomitant diseases, such as rheumatoid arthritis, diabetes and treatment with glucocorticoids, which may increase the risk of ONJ (10).

The observation that both bisphosphonates and Denosumab (DMAb) can cause ONJ led to investigating the common mechanisms between the two treatments. Bisphosphonates promote the apoptosis of osteoclasts and accumulate in bone, where they persist for a long time. In contrast, DMAb inhibits osteoclast bone resorption without accumulating in the bone and causing apoptosis. The pathophysiology of ONJ is complex and multifactorial, but it manifests mainly in the maxillary bones, which have unique anatomical and microbiological characteristics that make them vulnerable to bacterial infections. The teeth erupt from the maxillary bones, bursting through the oral epithelium, allowing infectious agents in the oral cavity to invade the bone through the space between the epithelium and the teeth or root canal. In addition, the oral mucosa lining the maxillary bone is thin, so infections resulting from lesions of the mucosa can easily spread to the underlying bone. Dental plaque is home to numerous bacteria, which can act as a source of infection, and inflammation caused by caries, pulpitis or periodontal disease can spread to the jaw bone. Finally, the maxillary bone is frequently exposed to the oral cavity as a result of invasive dental treatments such as dental extractions, increasing the risk of infection and developing ONJ (10).

A promising option in bone surgery for ONJ is the use of solid-state lasers, whose active medium consists of yttrium-aluminium-garnet crystals (Er :YAG, 2940 nm) or yttrium-scandium-gadolinium Chromium and erbium garnet (Er,Cr :YSGG, 2790 nm). These devices have a high affinity for hydroxyapatite and water, making them particularly effective in interacting with mineralized tissues (11). The Er :YAG laser, in particular, allows "cold" ablation, that is without significant thermal effects: it does not cause coagulation or carbonization of tissues, and the induced thermal rise on the bone and in the environment is significantly lower than that generated by traditional rotating instruments. Thanks to an

extremely low penetration depth (approximately 0.1 mm), this type of laser guarantees high operational safety and allows highly precise and minimally invasive surgeries to be performed. The surgical action is based on photothermal reactions that result in vaporization of irradiated tissues, turning them into gas or plasma (12).

ONJ is a condition associated with poor oral health, oral surgery, and the use of powerful anti-resorption agents. In an attempt to prevent ONJ, the optimization of oral health prior to initiation of therapy with BPs and DMAB is emphasized, which has been shown to be effective in reducing risk (13). The recommendations include:

i. completion of the necessary oral surgery prior to the start of anti-resorption therapy;
ii. administration of antibiotics 2-4 days before and 7-10 days after the procedure;
iii. Antimicrobial mouth rinse;
iv. proper wound closure after tooth extraction;
v. maintaining good oral hygiene.

The vast majority of cases (> 90%) of ONJ occurred in cancer patients. Therefore, it is recommended by the Task Force that when these patients undergo invasive oral surgery, their anti-resorption therapy should be suspended until soft tissue healing has occurred, even if they do not there is no evidence to support this recommendation in terms of changing the outcome of the dental procedure. Since the pharmacological effects of DMAb are transient and reversible, this recommendation may still be useful (14,15). On the contrary, since bisphosphonates are characterized by long-term bone deposition, discontinuation of treatment is not expected to have a significant and immediate impact on bone remodeling. However, since the absorption of BPs is greatly increased at local bone injury sites, discontinuing therapy after oral surgery may reduce local deposition of the drug in the maxillary bones, as demonstrated by the histomorphometric analysis and immunohistochemistry (13,16).

Studies have shown that the risk of developing this disease can be substantially reduced if patients are assessed by a dentist and preventive measures are taken (11).

METHODS

A search was performed on PubMed search engine and Google Scholar not inserting filters "article type". The key words “oral bisphosphonates AND tooth extraction", "oral surgery AND bisphosphonates AND osteonecrosis" were used. The adverse effects of certain drugs such as those of some classes of antibiotics in the management of osteonecrosis of the maxillary bones have also been evaluated.

RESULTS

The results from the analysis of selected studies indicate that the main complication observed in patients undergoing oral therapy with bisphosphonates is ONJ, the incidence of which appears to be closely related to the duration of pharmacological treatment. In particular, there was a significant prevalence of osteonecrotic lesions in the posterior mandible region. In some cases, delayed healing of post-extraction surgical wounds has also been documented. The survey examined additional clinical and demographic variables, such as the anatomical location of lesions, the age and sex of patients, the presence of comorbidities and several systemic risk factors. The data confirms the multifactorial nature of the onset of osteonecrosis, highlighting the importance of a preventive and multidisciplinary approach in the management of patients treated with anti-resorptive drugs.

CONCLUSIONS

Considering the results of the following treatment, it can be concluded that osteonecrosis of the maxillary bones represents a serious complication associated with therapy with bisphosphonates and DMAb, in particular following invasive dental procedures. Pathogenesis is multifactorial and involves the oral environment, duration of treatment and presence of comorbidities. Prevention strategies focus on optimizing oral health before resorption therapy begins, including prophylactic dental procedures, antibiotic use, antimicrobial rinsings and proper closure of post-extraction wounds. In high-risk cancer patients, temporary discontinuation of therapy is recommended in case of oral surgery. Conservative management is preferred in most cases, whereas surgery may be required in patients with advanced ONJ. The risk increases in the presence of untreated dental infections, and extraction, if unavoidable, should be performed carefully to reduce bone trauma and promote healing.

Conflict of interest

The authors declare that they have no conflict of interest.

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Review

SYSTEMIC EVALUATION AND GOOD PRACTICE OF THE SURGICAL PATIENT WITH CARDIOVASCULAR DISEASE: NARRATIVE REVIEW

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ABSTRACT

Objective: The objective of the study was to evaluate the correct management of dental patients undergoing oral surgery, suffering from cardiovascular disease. *Methods:* Research and analysis was carried out of systemic reviews in the English language that were about the application of artificial intelligence in dental fields, using databases such as Web of Science, Scopus, and PubMed. *Results:* Based on the results of the study, we can conclude that the 980 nm diode laser is a useful tool in the treatment of periodontitis in post-myocardial infarction patients, as it is painless, eliminates the risk of bleeding, reduces the need for anaesthesia and causes accelerated tissue healing. It also proves to be a valid therapeutic alternative, as it prevents cardiac overload due to the adrenergic reaction induced by dental surgery, which can trigger acute ischemic events. *Conclusions:* The use of the 980 nm (1 W, continuous wave) diode laser in patients with post-myocardial infarction periodontitis helps to reduce the depth of the periodontal pockets (7 mm) and lowers the bacterial load, delaying recolonization during a 3-month observation period. It has no significant effect on bleeding at the probe (BOP), clinical attack level (CAL) or plaque control index (PCR), nor does it significantly reduce pathogens related to cardiovascular disease. However, as it is painless, reduces bleeding and accelerates healing without the need for anaesthesia, laser represents a valid and less invasive therapeutic alternative, reducing cardiac stress and the risk of ischemic events.

KEYWORDS: *Oral health, oral surgery, cardiovascular disease, laser, dental disease, heart disease*

INTRODUCTION

Cardiovascular diseases, which include ischemic heart disease (such as acute myocardial infarction and angina pectoris) and cerebrovascular disease (such as ischemic and hemorrhagic stroke), are the main causes of morbidity, disability and mortality in Italy (1). Although many of these conditions are preventable, non-modifiable risk factors such as age, sex and familiarity are associated with modifiable lifestyle and behavioral factors such as smoking, alcohol, poor diet and sedentary behavior, which in turn promote the development of diabetes, obesity, hypercholesterolemia and high blood pressure. Patients with cardiovascular disease who report to the dentist can be distinguished by primary pathology,

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which may include arrhythmias, heart failure, ischemic heart disease, high blood pressure and those who have undergone cardiac surgery (2). The dental management of these patients requires a personalized approach, considering the cardiovascular condition and related risks associated with dental operations (3).

Cardiovascular diseases in Italy affect a significant number of people, with a prevalence of about 2%, rising to 6-9% in the most advanced age groups (70-79 years and 80-89 years). In the last 15-20 years, prevalence has increased, leading to an increase in annual expenses for the National Health Service. Heart failure is a condition in which the heart cannot contract or relax properly, preventing proper blood circulation (4). This leads to reduced organ perfusion and fluid accumulation, causing edema and difficulty breathing. Diseases that develop into heart failure include ischemic cardiomyopathy, high blood pressure and valvular disease. The symptomatology varies depending on whether the failure concerns the right or left side of the heart, with signs such as edema in the lower limbs, turgor of the jugular and ascites, in the case of right cardiac insufficiency, and dyspnea and ortopnea for the left (4). When the disease progresses, congestive heart failure develops, characterized by venous stasis and reduced peripheral perfusion.

Ischemic heart disease, which affects about 2.5-4% of the Italian population, is caused by an insufficient supply of blood and oxygen to the heart muscle. The main causes are atherosclerosis and coronary spasms, which reduce blood flow in coronary arteries (5). Ischemic heart disease can manifest itself in the form of angina pectoris, which presents as a retrosternal chest pain radiating to the left arm, precipitating during stress or physical activity. Angina occurs when the heart does not receive enough oxygen due to a narrowing of the coronary arteries. This condition can be further worsened by stress situations, such as those induced by oral surgery, which increase cardiac demand and may trigger acute seizures.

Myocardial infarction is the necrosis of a part of the heart muscle caused by the obstruction of a coronary artery, with common symptoms such as chest pain, cold sweating, malaise, nausea and vomiting. The pain, which may radiate to the neck, jaw, arms and back, initially occurs for short periods and can develop into angina pectoris (4). The latter, a transient ischemia, is a sign of a potential future heart attack.

Arterial hypertension, which affects one third of the population, is characterized by blood pressure above 140/90 mmHg. The pathology can lead to serious complications such as hypertensive heart disease, nephropathy and chronic encephalopathy. Dental or surgical procedures can cause high blood pressure peaks, increasing the risk of hypertensive crisis or heart attack (5). Antihypertensive drugs can also cause side effects such as hypotension and syncope.

Arrhythmias, which affect between 10% and 17% of the population, are alterations in the heart rhythm that can be caused by problems of conduction of the heart. They can manifest as tachycardia, bradycardia or extrasystole and are an important risk factor during surgical dental procedures. Arrhythmias can be classified into hyperkinetic (tachycardia), hypokinetic (bradycardia) and ectopic (extrasystole).

Finally, patients undergoing cardiac surgery, such as heart valve replacement or coronary bypass, require careful dental management because these procedures affect their cardiovascular condition (6). Cardiac surgery also includes operations for aneurysms, aortic dissections and pacemaker implantation. The dental management of these patients must consider the risk of complications related to their cardiovascular condition and treatments received (7).

The formulation of an adequate diagnostic and therapeutic plan is based on a proper perioperative risk assessment, which includes both medical and surgical risks (7). The medical risk assessment takes into account factors such as the patient's age, systemic diseases and existing pharmacological or surgical therapies. The patient's disease can be classified into three stages of medical risk: low, medium and high. The surgical risk assessment, on the other hand, considers the operating environment, the anesthesia and the anatomical district involved in the operation. Non-surgical therapies are divided into non-invasive, simple or extended, with a surgical risk generally absent or reduced. Surgical therapies are classified as simple, complex and extensive, with a surgical risk that can be reduced, moderate or high. The American Society of Anesthesiologists has also created a classification to assess the patient's physical state in relation to anesthetic risk, which must be considered in close correlation with surgical risk (8,9).

The assessment of cardiac patients before, during and after non-cardiac surgery is crucial to avoid cardiovascular complications. Patients at risk include those with myocardial ischemia, valvopathies, heart failure, arrhythmias and other heart conditions. Surgery and postoperative pain can increase the heart's oxygen demand, causing ischemia and other complications (10). Risk assessment is based on the patient's condition and the planned intervention, using diagnostic tests such as echocardiograms, stress tests and biomarkers. Pre- and post-operative drugs, such as beta-blockers and ACE inhibitors, may reduce the risk. In addition, the use of NSAIDs in cardiac patients should be limited as it can cause serious side effects. Every year in Europe, about 5.9 million non-cardiac operations are performed on heart patients, with a perioperative mortality ranging from 0.8% to 1.5%. The risk of heart complications, such as heart attack or arrhythmia, increases depending on the type of surgery (10-12).

Antibiotic prophylaxis in oral surgery prevents endocardial infections caused by transient bacteriaemia during surgeries. Amoxicillin is administered one hour before surgery and, if necessary, six hours later. For penicillin allergies,

clindamycin, cephalexin or azithromycin are used. For patients with heart disease, nitroglycerin may be used to prevent ischemic events. In patients with Prinzmetal angina, therapy with calcium antagonists is maintained. Aspirin can be stopped before surgery only if hemostasis is difficult to control. The management of cardiovascular risk varies according to the patient: with reduced risk trinitrin is recommended, while for moderate and high risk, premedication with sedation, oxygen and trinitrin is necessary (8,13).

The laser was introduced to dentistry in the 1970s and has since been used for treatments of oral diseases, including dental and soft tissue interventions such as periodontitis, endodontics and aesthetic dentistry. The lasers used include solid-state (Nd :YAG, Er :YAG), gas (CO2) and semiconductor (diode) lasers. An important advantage of the laser in dentistry is the reduction of bleeding, especially useful for patients with heart or coagulopathies, reducing the need for pre- and post-operative pharmacological prophylaxis (9,14,15).

A clinical study conducted in 2019 evaluated the effectiveness of 980 nm diode laser in the treatment of periodontitis in patients after myocardial infarction. The study involved 36 patients with periodontitis, who were divided into two groups: one treated with scaling and root planing (SRP) and the other with SRP followed by laser therapy. The laser-treated group showed a significant reduction of deep periodontal pockets (PPD 7 mm) and a reduction in bacteria, without adverse effects. After 3 months of treatment, both groups showed a significant reduction in bleeding at the probe (BOP) and plaque control index (PCR), but there were no statistically significant differences between the groups. However, in the laser-treated group, a higher percentage of deep pockets was reduced to less deep pockets, indicating clinical improvement compared with the control group. In summary, laser treatment added to SRP has shown a potential benefit in the treatment of periodontitis in post-infarction patients by reducing deep pockets and improving the effectiveness of treatment (9,16).

DISCUSSION

The additional use of the 980 nm (1 W, continuous wave) diode laser has led to a significant reduction in the depth of periodontal pockets above 7 mm, allowing patients to avoid surgical treatments after a myocardial infarction. No effects were observed in the lower depth periodontal pockets. The laser treatment reduced the total number of bacteria and delayed recolonization during the 3-month observation period. However, the additional use of diode laser after radicular sanding (SRP) had no significant effects on BOP, clinical attack level (CAL) or PCR.

In addition, the use of diode laser has not further reduced levels of Porphyromonas gingivalis, Treponema denticola and Tannerella forsythia, key pathogens linking periodontitis and cardiovascular disease. In the control group, a significant increase in the number of Capnocytophaga gingivalis was observed.

Based on the results of the study, we can conclude that the 980nm diode laser is a useful tool in the treatment of periodontitis in post-myocardial infarction patients, as it is painless, eliminates the risk of bleeding, reduces the need for anaesthesia and causes accelerated tissue healing. It also proves to be a valid therapeutic alternative, as it prevents cardiac overload due to the adrenergic reaction induced by dental surgery, which can trigger acute ischemic events (17).

CONCLUSIONS

The additional use of 980 nm, 1 W, CW laser allows a significant reduction in pocket depth 7 mm, which allows the patient to avoid surgical treatment after myocardial infarction; no effect has been seen in lower pockets. The diode laser reduces the total number of bacteria and delays recolonization during a 3-month observation period. The additional use of a diode laser after SRP has no significant effect on BOP, CAL and PCR. Additional use of a diode laser in patients with periodontitis and after myocardial infarction does not further reduce the levels of Porfiromonas gingivalis, Treponema denticola and Tannerella forsythia, which are key pathogens that link periodontitis and cardiovascular disease. In the control group, a significant increase in the number of Capnocytophaga gingivalis bacteria was observed. Within the limits of our study, we can conclude that the 980nm diode laser may be a useful tool in the treatment of periodontitis in patients after myocardial infarction because: it is not painful , eliminates the risk of bleeding , often there is no need for anaesthesia , determines an accelerated healing of tissues and therefore proves to be a valid therapeutic alternative since it prevents the cardiac overload caused by adrenergic reaction following dental surgery (stress, anxiety and pain) may trigger acute ischemic heart disease.

In general, cardiovascular disease is an important cause of morbidity and mortality, and its proper management, even in dental settings, is essential to avoid acute complications.

Conflict of interest

The authors declare that they have no conflict of interest.

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Review

SYSTEMIC EVALUATION AND GOOD PRACTICE OF THE SURGICAL PATIENT IN PREGNANCY: NARRATIVE REVIEW

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ABSTRACT

Objective: The study aims to review the international scientific literature on dentistry and pregnancy, with the aim of assessing: the most common oral diseases during pregnancy, their causes and risk factors; the relationship between oral diseases and complications for mother and newborn; diagnostic procedures, safe dental and pharmacological treatments during pregnancy, including any contraindications; precautions to be taken by the dentist during oral procedures. *Methods:* The research was conducted using Medical Subject Headings (MeSH) and non-MeSH words, combined via Boolean operators ("AND", "OR"), to search for articles on pregnancy, pregnant patients, dentistry, dental care, oral hygiene, periodontitis and periodontal disease. *Results:* The research selected 146 relevant articles, with a focus on 46 with more scientific evidence, on topics such as dentists' knowledge of pregnancy and oral diseases, excluding less relevant articles or with less scientific evidence. *Conclusions:* Out of a total of 146 articles on pregnancy dentistry, only 46 were evaluated for their high scientific evidence. We can conclude that the review provides an updated and useful summary for clinical practice and research, covering professional preparation, oral health and perinatal complications, and clinical management of pregnant patients.

KEYWORDS: *Pregnancy, dental treatment, oral health, mother, newborn*

INTRODUCTION

This study aims to review the international scientific literature on dentistry and pregnancy in order to assess: the most common oral diseases during pregnancy, their causes and risk factors; the correlation of oral pathology to adverse events involving the pregnant woman and the newborn; diagnostic procedures, dental and pharmacological treatments that can be safely performed during pregnancy, including contraindications; precautions to be taken by the dentist during oral procedures (1).

Pregnancy is a physiological state that involves numerous systemic and local changes in the female body to support the growth of the fetus. Among these are hormonal changes that lead to an increase in estrogen and progesterone useful to support the cerscitis of the fetus. It also induces changes in various organs, including the mouth where gingivitis, granulomas, and gynecoid may develop. Gingivitis in pregnancy, mainly caused by plaque and increased inflammatory

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response, affects 60-75% of women (2). Although the composition of the plaque does not change, the body's response is enhanced. Treatment focuses on oral hygiene education and plaque prevention, with more effective interventions throughout the pregnancy. Adverse events during pregnancy, such as preterm delivery and pre-eclampsia, pose significant risks to maternal and fetal health. Some studies have suggested that periodontal treatment may reduce the risk of preterm delivery and other adverse effects. Preeclampsia, which involves maternal and fetal syndromes, has been linked to periodontal disease in some studies, but the results are mixed (2). The 2013 meta-analysis by Sgolastra et al. showed a correlation between periodontal disease and preeclampsia, but also required further studies (3).

Numerous studies have shown that routine preventive, diagnostic and restorative dental treatments-including periodontal therapy-do not increase the risk of adverse outcomes in pregnancy (1,2,4). Despite this, many women do not access or receive dental care during the perinatal period. Possible factors include lack of insurance coverage or limited access to services. Women who receive fillings, extractions or treatment during the second trimester of pregnancy do not have higher rates of adverse outcomes at birth than those who do not undergo such care. Dental practitioners should recommend early intervention when necessary and work with the patient to define the most appropriate restorative treatments and materials, considering the potential risks of untreated caries during pregnancy (4).

Periodontal treatment aims to reduce inflammation and plaque to preserve teeth and prevent tissue damage. Although some reviews have suggested a possible benefit, the 2017 COCHRANE report found no significant evidence that periodontal treatment reduces the risk of preterm delivery. However, there is evidence of low quality that suggests a reduced risk of low birth weight. In addition, a recent study showed that periodontal treatment reduces inflammatory biomarkers but had no significant impact on adverse events. In conclusion, it is not clear whether periodontal treatment prevents preterm delivery, but it could reduce the risk of low birth weight. There is insufficient evidence to determine the best periodontal treatment to prevent adverse outcomes in pregnancy. Another pregnancy-related disease is Epulide can be treated surgically if it causes significant problems, with options such as electrocoagulation, cryotherapy or laser, preferably in the second trimester. Prevention is based on good dental hygiene and regular visits to the dentist (5).

In pregnancy it is preferable to avoid medications, but some are considered safe. The drug therapy most commonly prescribed for conservative and endodontic therapies, does not include side effects. However, some medications such as antibiotics or local anesthetics may need to be prescribed with caution. Nevertheless, the drugs used exclusively in dentistry do not cause anatomical and physiological alterations during fetal development, with possible craniofacial malformations, including craniosynostosis, cleft palate and dental defects (6,7). The recommended antibiotics are penicillins and, in case of allergy, macrolides. Tetracyclines, chloramphenicol and metronidazole are contraindicated. Paracetamol is the first-choice analgesic-antipyretic drug. The use of local anesthetics is safe, but prilocaine should be avoided because of the risk of methemoglobinemia (3). Vasoconstrictors are not contraindicated, but should be used with caution and in limited doses, avoiding the use in case of threat of miscarriage or premature birth. During pregnancy, simple dental procedures such as non-complex extractions and conservative treatments can be performed, but major surgical procedures are avoided. Several studies have identified the mechanisms by which these drugs can affect craniofacial progenitor stem cells, highlighting the absolutely harmless role of specific transcription factors in the signal mediation of protein synthesis. Finally, we stress the importance of non-pharmacological therapies in women of childbearing age and pregnancy, proposing an individual analysis of the risk-benefit balance of dental visits during this period (7-10). Regular check-ups and oral hygiene sessions are recommended to prevent disorders related to hormonal effects on the oral mucosa (8). Common problems include gingivitis, pregnancy cleanses and caries, also favored by nausea, reflux and diet changes. Treating these conditions early helps to avoid complications and reduces the need for drugs that are potentially hazardous to the fetus, in fact, the use of certain drugs during pregnancy, especially during the first weeks of the formation of the fetus can be teratogenic factors, such as causing alterations in some genes with the formation of genetic diseases such as dysplasia cleido cranio, or stem cell mutations that will lead to the formation of defense cells such as mast cells (11,12).

MATERIALS AND METHODS

The research was carried out by identifying the specific Medical Subject Headings (MeSH) in the thesaurus dictionary of the National Library of Medicine (NLM), and non-MeSH words, using them to search for the job, individually or in association with each other - through the use of Boolean operators "AND", "OR": Pregnancy; Pregnant patient; Pregnant women; Dentistry; Dental care; Dental treatment; Oral hygiene; Oral hygiene; Periodontitis; Periodontal disease.

The articles were selected according to the following criteria: publication dates from 1 January 2000 to 2021; languages including English and Italian; and article types including guidelines, meta-analysis, systematic reviews, and revisions. The articles must report on the relationship between pregnancy and oral health, the knowledge of dentists about pregnancy and its effects on oral health, the possible biological correlation between oral diseases and the incidence of

perinatal adverse events and, Finally, the additional precautions that the dentist must take in diagnosing and treating the pregnant woman. The results of the research were read through the titles and abstracts. All articles that did not were related to the purpose of this review were excluded. Studies that did not include human subjects were excluded.

RESULTS

The research yielded 373 results. Abstracts and titles of each article were examined. Articles that were not related to the topic were excluded. We have therefore obtained the full texts of all potentially eligible articles. After full reading, 146 articles were selected, and the remaining ones were discarded as unsuitable because they were not relevant to the purpose of the study. Repeated titles in the various searches have also been excluded. Selected articles published after 1 January 2000 were on the following topics: knowledge of the dentist about pregnancy and its effects, the possible correlation between oral diseases (especially periodontal), the incidence of perinatal adverse events and, finally, the additional precautions that the doctor must implement in the diagnosis and treatment of pregnant women. A further selection was made on the basis of the level of scientific evidence, with greater consideration given to 46 publications including systematic guidelines, meta-analyses and reviews, extending research to non-systematic reviews if the results are unsatisfactory. The remaining 100 articles were not completely excluded from this work but were considered less related to the subject of the review and correspond to a lower level of scientific evidence.

CONCLUSIONS

In conclusion, the analysis of the literature has made it possible to select 146 relevant articles published after 1 January 2000, which deal with fundamental aspects related to dentistry during pregnancy, including the preparation of the professional, the correlation between oral health and perinatal complications, and clinical precautions to be taken during treatment of pregnant patients. A subsequent assessment of methodological quality identified 46 studies with high scientific evidence, used as the main basis for this review. The remaining 100 articles, although considered in the review process, were considered secondary support due to their lower scientific relevance or quality. This rigorous selection has ensured an up-to-date and reliable synthesis of current knowledge, providing a useful reference for clinical practice and future research in the field of dentistry and pregnancy.

Conflict of interest

The authors declare that they have no conflict of interest.

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