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Evaluation of the adjunctive use of Er:YAG laser or erythritol powder air-polishing in the treatment of peri-implant mucositis: A randomized clinical trial

Marco Clementini[1,2] | Simone Fabrizi[1] | Nicola Discepoli[3] | Margherita Minoli[1] | Massimo De Sanctis[1]

[1]Department of Periodontology, Vita-Salute San Raffaele University, Milan, Italy

[2]UniCamillus-Saint Camillus International University of Health Sciences, Rome, Italy

[3]Department of Medical Biotechnologies, Unit of Periodontics, University of Siena, Siena, Italy

Correspondence
Marco Clementini, CSO Academy, Rome, Italy.
Email: mclementini@me.com

Abstract

Aim: To assess the efficacy of Er:YAG laser (ERL) and erythritol powder air-polishing (AP) in addition to the submarginal instrumentation in the non-surgical treatment of peri-implant mucositis (PM).

Materials and Methods: Patients with at least one implant diagnosed with PM were included in the present 6-month randomized clinical trial (RCT). Implants were randomly assigned to one of the three treatment groups after submarginal instrumentation: AP (test 1 group), ERL (test 2 group) or no adjunctive methods (control group). The primary and secondary outcomes were, respectively, bleeding on probing (BoP) reduction and, complete disease resolution (total absence of BoP) and probing pocket depth (PPD) changes. The patient and the implant were considered the statistical unit. A multivariate logistic regression analysis was performed.

Results: A total of 75 patients were enrolled in the study. At each time point, significant BoP and PPD reductions were observed within each group. Intergroup analysis did not show statistically significant differences. Complete disease resolution ranged between 29% and 31%. The logistic regression showed that supramucosal restoration margin, PPD < 4 mm and vestibular keratinized mucosa (KM) significantly influenced the probability to obtain treatment success.

Conclusion: The adjunctive use of AP and ERL in PM non-surgical therapy does not seem to provide any significant or clinically relevant benefit in terms of BoP and PPD reductions and complete disease resolution, over the use of submarginal instrumentation alone. Baseline PPD < 4 mm, presence of buccal KM and supramucosal restoration margin may play a role in the complete resolution of PM.

KEYWORDS
Er:YAG laser, erythritol powder air-polishing, non-surgical treatment, peri-implant mucositis, submarginal instrumentation

1 | INTRODUCTION

Peri-implant mucositis (PM), as defined at the 2017 World Workshop (Heitz-Mayfield & Salvi, 2018), is an inflammatory lesion of the mucosa surrounding an endosseous dental implant in the absence of peri-implant marginal bone loss, beyond the physiological bone remodelling. It has been widely demonstrated the cause-effect relationship between biofilm accumulation and the development of experimental peri-implant mucositis in humans (Pontoriero et al., 1994; Zitzmann et al., 2001), thereby pointing out that oral microbiota represents the primary aetiological factor in the conversion from peri-implant health to PM. In this regard, Salvi et al. (2012) described the occurrence of PM after an experimental 3-week period of undisturbed plaque accumulation and the reversibility of the disease at the biomarker level after a 3-week period in which optimal plaque control was reinstituted.

PM is a frequent condition, with a prevalence between 43% (Derks & Tomasi, 2015) at the patient level and 37.7% (Vignoletti et al., 2019) at the implant level. As reported by Costa et al. (2012), implants affected by PM without regular adherence to supportive therapy present a higher incidence of developing peri-implantitis (PI) after 5 years. Thus, since PM is considered the precursor of PI, non-surgical treatment and supportive peri-implant therapy represent crucial preventive strategies to avoid the progression of PM to PI (Costa et al., 2012; Jepsen et al., 2015).

Measures to treat PM have been a focus of attention in recent years. The effectiveness of mechanical non-surgical treatment has been studied in several randomized controlled clinical trials (RCTs) that reported a significant reduction of clinical signs of inflammation, however, a complete disease resolution was not achieved in the majority of cases (Iorio-Siciliano et al., 2019; Menezes et al., 2016; Pulcini et al., 2019; Riben-Grundstrom et al., 2015). Therefore, adjunctive treatments by means of chemical delivery (Heitz-Mayfield et al., 2011; Iorio-Siciliano et al., 2019; Menezes et al., 2016; Pulcini et al., 2019), air-polishing with glycine powder (Ji et al., 2014; Riben-Grundstrom et al., 2015) and diode laser applications (Aimetti et al., 2019; Sanchez-Martos et al., 2020), have been evaluated. Nevertheless, currently, there is not enough evidence to support the use of any treatment protocol over others or whether combinations of procedures may provide added benefits (Jepsen et al., 2015; Verket et al., 2023). To date, no RCTs have tested the adjunctive use of erythritol-based air-polishing (AP) or Er:YAG laser (ERL) to the mechanical instrumentation in the management of non-surgical treatment of PM. Both treatment procedures seem to be able to improve bacterial plaque biofilm removal from the implant surface (Discepoli et al., 2022; Eick et al., 2017), however, their adjunctive clinical application also needs further investigation. Therefore, the aim of the present study was to assess the added benefit of the two aforementioned adjunctive methods (ERL and AP) over the submarginal instrumentation alone in the non-surgical treatment of PM.

2 | MATERIALS AND METHODS

2.1 | Ethical issues and study design

The study was performed in accordance with principles outlined in the revised Helsinki Declaration and was approved by the Ethical Committee of Vita-Salute San Raffaele University (on 07/06/2018 with the number of protocol "RCT Peri-Implantitis-1"—EC Reg. N. 95/INT/2018). The trial protocol was registered at ClinicalTrials.gov under number NCT03951636. Signed informed consent was obtained from all participants.

The present study was a single-masked (blinded examiner), single-centre, parallel design, three-arm, randomized controlled interventional trial with a 6-month follow-up. Randomization of patients was performed using a computer-generated list in a 1:1 proportion with a numerically balanced group. Allocation concealment was ensured by a clinician not involved in the recruitment and treatment of participants (MM), using sealed opaque envelopes that assigned patients to their respective treatment groups and that were opened once the submarginal instrumentation was completed. Both the operator who performed the treatments and the patients were not blinded to group assignment. The statistical analyses were performed with patients' coded group identification. Before participation, oral and written information about the study was provided and all patients signed a written informed consent prior to enrollment. The Consolidated Standards of Reporting Trials (CONSORT) guidelines were followed.

2.2 | Study population and eligibility criteria

Patients attending the Department of Periodontology of Vita-Salute San Raffaele University were recruited consecutively between July 2019 and January 2022. One calibrated examiner (SF) screened participants according to inclusion and exclusion criteria.

Adult (>18 years old) patients with at least one screw-type titanium implant exhibiting bleeding and/or suppuration on probing without a progressive radiographic bone loss (<2 mm) or bone level <3 mm were enrolled (Heitz-Mayfield & Salvi, 2018). Radiographic parameters were assessed at the baseline evaluation by means of a periapical X-ray taken using the long-cone parallel technique. Marginal bone levels (MBL) were assessed with a dedicated software program (ImageJ, National Institutes of Health) as the distance between the most coronal part of radiographic bone-to-implant contact and the most coronal osseointegrable surface of the implant on the mesial and distal aspect. Due to the unknown diameter of several implants, the dimension of the intra-oral radiographic sensors was used to set a scale for the measurement's calibration. All radiographic assessments were carried out by one investigator (MM). The intra-examiner calibration performed for marginal bone levels was 0.96 (95% confidence interval—CI [0.95; 0.99]). Further inclusion criteria were periodontally healthy patients or successfully treated stable periodontitis patients (Papapanou et al., 2018), smokers <10

cigarettes per day, no evidence of occlusal overload (evaluated by means of a check occlusion paper, the occlusal contacts showed appropriate adjustment), implant function time >1 year, full-mouth bleeding (FMBS) and plaque (FMPS) score <30%. In the case a patient exhibited more than one implant meeting the inclusion criteria, all implants were included and treated. Implants affected by peri-implantitis were not included in the present study and treated separately.

Pregnant or lactating women, patients with uncontrolled diabetes or systemic diseases that could influence the outcomes of the therapy, osteoporosis or under bisphosphonate medication, history of head and neck radiotherapy and incapability to perform oral hygiene measures due to physical or mental disorders were excluded. Hollow implants, implants with mobility, implants that previously undergone surgical treatment of peri-implantitis lesions and implants at which proper probing measurements could not be performed were also excluded.

2.3 | Clinical evaluations

At baseline, 1, 3 and 6 months after treatment one blinded and calibrated examiner (SF) assessed the following clinical parameters using a UNC periodontal probe (Hu-Friedy), with light probing forces, at six aspects (mesio-buccal, mid-buccal, disto-buccal, mesio-oral, mid-oral and disto-oral) per each included implant:

- Plaque index (PI): assessed dichotomously as the presence or absence of plaque along the mucosal margin and expressed in percentage.
- BoP: assessed dichotomously as the presence or absence of bleeding within 30 seconds after probing and expressed as a proportion of positive sites.
- PPD: measured in millimetres from the mucosal margin to the bottom of the probable pocket.

For each included implant the following parameters were also assessed:

- Keratinized mucosa width (KMW): measured in millimetres at the buccal and lingual aspect from the mucosal margin to the mucogingival junction.
- Level of the margin of the implant-supported prosthesis (submucosal or supramucosal): the level of the prosthesis margin was measured clinically in relation to the mucosal margin at the baseline evaluation and classified accordingly as submucosal or supramucosal.

At the patient level, age, gender, FMPS, FMBS, the number of implants and the history of periodontitis, were also reported. Diagnosis of history of periodontitis was made according to the threshold, clinical attachment loss (CAL) at >2 non-adjacent teeth, set by Papapanou et al. (2018). Furthermore, the number of cigarettes per day was recorded at each follow-up visit.

At the implant level, the level of disease resolution was defined as complete when BoP was = 0 out of six sites per implant (treatment success) and partial when BoP was <1, <2 and <3.

2.4 | Intra-examiner reproducibility

Five patients, each showing at least one implant diagnosed with PM, were used to calibrate the examiner (SF). The examiner assessed the patients on two different days, 7 days apart, just after standardizing a probing force of 0.20 N. Calibration was accepted if measurements at baseline and 1 week were within a millimetre for PPD and the same proportion of BoP-positive sites at >90 of the time. The correlation coefficient for the intra-examiner reproducibility was 0.98 (95% CI [0.96; 0.98]) and 0.91 (95% CI [0.87; 0.94]), respectively.

2.5 | Treatment protocol

All patients received individualized oral hygiene instructions: to brush under, around and in the peri-implant crevice and to use brushes in the interproximal area. Crowns or bridgeworks were not removed during submarginal instrumentation, and local anaesthesia was used as needed. Mechanical instrumentation of implant surfaces was performed using titanium curettes (Hu-Friedy) in all treatment groups (Appendix S1). After that, subjects were randomly assigned to one of three treatment groups: no adjunctive methods (control group); adjunctive use of AP (test group 1) or adjunctive application of ERL (test group 2) (Appendix S1).

In the test group 1, the Perio-Flow nozzle (AIR-FLOW Master Piezon; EMS) was placed in each site of the peri-implant pocket (mesial, oral, distal and buccal), allowing the erythritol powder (AIR-FLOW Powder PERIO; EMS) to exit for 5 s at an angle of 60–90° (Riben-Grundstrom et al., 2015), as recommended by the manufacturer. The handpiece was used in a circular motion from coronal to apical parallel to the implant surface in a non-contact mode. In the test group 2, each pocket was exposed to the Er:YAG laser light (AdvErL EVO, J. Morita USA Inc.) in a parallel and non-contact mode, emitting a pulsed infrared radiation at a wavelength of 2.940 nm, at an energy level of 100 mJ/pulse and frequency of 10 Hz (Fluence 12.7 J/cm^2) using a cone-shaped sapphire tip under water irrigation (Renvert et al., 2011).

In all implants, all treatments were performed by the same experienced operator (MC).

No antibiotics, anti-inflammatory drugs or antiseptic mouthrinses were prescribed, and all patients were enrolled in a supportive periodontal and peri-implant therapy, receiving supragingival professional implant/tooth debridement and reinstruction of oral hygiene measures every 3 months for the entire study period.

2.6 | Statistical analysis

Both the patient and the implant were considered the statistical unit. Mean values, standard error and 95% confidence intervals (CI) were calculated for each continuous variable, while proportion values, standard error and 95% confidence intervals were estimated for each categorical variable.

Radiographic peri-implant bone level mean (mm) was assessed performing the average between the mesial and distal measurement of each implant.

The changes in clinical parameters were compared intragroup and intergroup between baseline and the 1, 3 and 6-month follow-up.

The primary outcome was BoP (%) reductions at 6 months and the secondary endpoints were the complete disease resolution (%) and PPD (mm) changes at 6 months. The Shapiro–Wilk W test was conducted to evaluate the normal distribution of data. A Chi2 test and ANOVA with Bonferroni correction were respectively used for categorical and continuous variables for the intergroup and intragroup statistical analyses. All the analyses were based on the "per protocol" principle and the level of significance was set at p-value <.05.

A uni-level multivariate logistic regression analysis was performed to evaluate the impact of all variables at baseline (independent variables) on the treatment effectiveness at 6 months (evaluated as the total absence of BoP, dependent variable) and investigate which model predicts better in terms of specificity and sensibility the probability of obtaining complete disease resolution The best-fitting model was identified also considering the lowest Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) values. All statistical tests were conducted using a statistical tools package (STATA).

2.7 | Sample size

According to Philip et al., 2020, the sample size calculation was made for the primary outcome measure (BoP reductions) at the patient level, considering as clinically relevant a difference of 12% (+14%) in terms of BoP reduction between control and treatments groups at 6-months The sample size calculation suggests to include 25 patients per group with a power of 80% and an alfa error of .05, considering a potential drop out of 5% of individuals.

3 | RESULTS

The flow chart of the study is presented in Figure 1. A total of 75 patients (179 implants) affected by PM were enrolled and randomized, 25 per each group (58, 62 and 59 implants, for control, test 1 and test 2 groups, respectively). At baseline, patient characteristics (number of implants, age, gender, history of periodontitis, smoking status) and implant characteristics (submucosal restorative margin and mean bone level) were not significantly different between groups, thus indicating the homogeneity of data among the 3 groups (Table 1). All participants received the allocated procedure, and no drops out were observed. Peri-implant tissue healing was uneventful in all the patients.

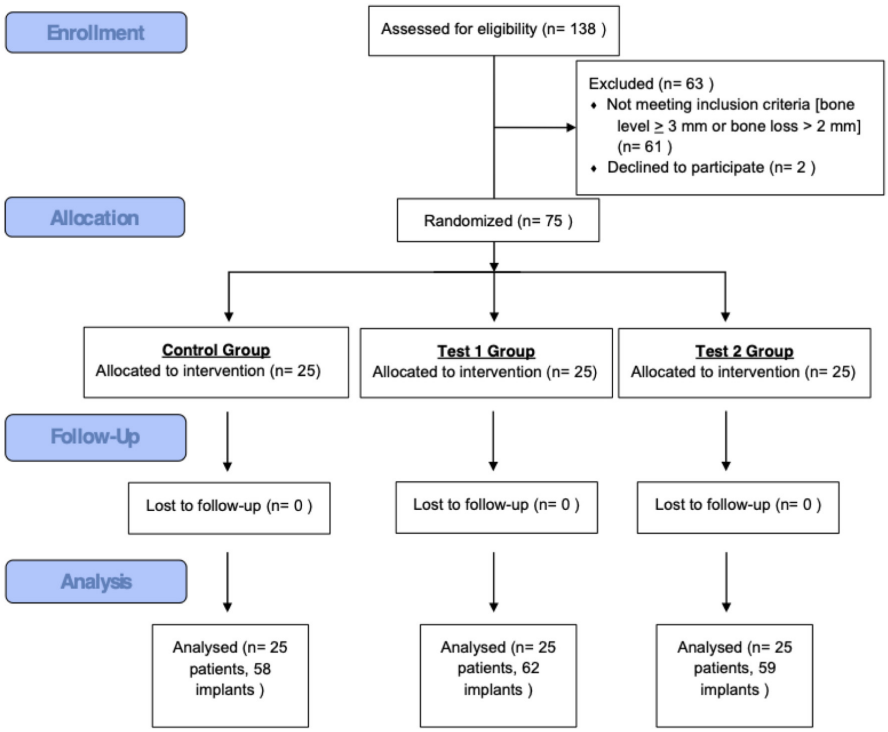

FIGURE 1 CONSORT flow diagram of the study.

TABLE 1 Baseline patient and implant characteristics.

Variables	Total ($n=75$)	Control group ($n=25$)	Test 1 group ($n=25$)	Test 2 group ($n=25$)	p-value
n° implants	179	58	62	59	.382
mean n° implants per patient	2.39	2.32	2.48	2.57	.642
Age (mean ± SD)	57.1 ± 9.8	55.7 ± 10.1	58.2 ± 9.6	57.5 ± 9.8	.637
Males/females	39/36	12/13	14/11	13/12	.514
History of Periodontitis, n (%)	41 (55)	13 (52)	16 (64)	12 (48)	.497
Light smokers, n (%)	11 (15)	4 (16)	4 (16)	3 (12)	.623
Submucosal Restorative Margin (n/tot implants [%])	102/179 (57)	32/58 (55)	31/62 (50)	39/59 (66)	.191
Implant mesial mean bone level (mm), mean [95% CI]	0.47 [0.27; 0.63]	0.53 [0.34; 0.71]	0.43 [0.26; 0.60]	0.46 [0.28; 0.64]	.740
Implant distal mean bone level (mm), mean [95% CI]	0.50 [0.30; 0.68]	0.58 [0.37; 0.79]	0.41 [0.24; 0.59]	0.52 [0.33; 0.71]	.449

Note: Light smokers: <10 cigarettes per die. Control group received a mechanical instrumentation (MI), while test 1 and 2 groups received MI combined with AP and ERL, respectively.

Abbreviations: CI, confidence interval; SD, standard deviation.

3.1 | Clinical outcomes

3.1.1 | Primary outcome

At the patient-level analysis, intragroup statistically significant BoP reductions were observed for all three groups between baseline and each time point (Table 2; Appendices S2 and S4). BoP changes were noted 1 month after non-surgical therapy and residual BoP scores did not reveal additional significant changes after 3 and 6 months. The adjunctive use of AP and ERL did not provide added statistically significant clinical benefits when compared to mechanical instrumentation alone in reducing BoP over the entire study period ($p=.936$). The three treatment modalities yielded similar clinical improvements with comparable reductions (Table 2).

3.1.2 | Secondary outcomes

At the subject-level analysis, means and 95% CI values of the secondary outcomes evaluated at baseline, 1, 3 and 6 months after treatment are represented in Table 2. FMPS and FMBS remained below the inclusion criteria (30%) during the entire experimental period. Intragroup statistically significant reductions were detected for FMPS, FMBS, PPD and PI at 1, 3 and 6 months after non-surgical therapy. However, there were no statistically significant differences observed among the three treatment groups for any of the variables.

At the implant-level analysis, changes in clinical parameters between baseline and each time point (1, 3, 6 months) are summarized in Table 3. Intragroup statistically significant reductions were observed for BoP, PPD and PI at each time point, while no intergroup differences were noted (Appendices S3 and S5). Buccal KMW remained stable over the study period for all three treatment protocols and did not show any significant intergroup difference at all evaluated time points with respect to baseline.

At the implant level, the frequency distribution of disease resolution after 6 months is presented in Table 4. The distribution is stratified according to the number of BoP-positive sites (0, <1, <2, <3). A total of 17 out of 58 implants (29%) in the control group, 19 out of 62 implants (31%) in the test 1 group and 17 out of 59 implants (29%) in the test 2 group exhibited a complete disease resolution (total absence of BoP). There was no statistically significant difference observed between groups ($p=.974$).

3.2 | Regression analysis

The significant predictor variables of the model that influenced the probability to obtain treatment success at 6 months were identified as follows: supramucosal restoration margin ($p<.001$), baseline mean PPD < 4 mm ($p=.015$) and presence of vestibular KM ($p=.002$) (Table 5). The supramucosal margin of the restoration presented a 9.17 times greater probability of disease resolution compared to the submucosal restoration margin. Additionally, a baseline mean PPD < 4 mm had an odds ratio (OR) of 2.63 and for every mm increase of KMW there was a 2 times higher chance of achieving BoP = 0 at 6 months.

4 | DISCUSSION

The results of the present RCT show that the use of AP or ERL as an adjunct to submarginal instrumentation of the implant surface affected by PM did not result in either significant additional improvements in clinical parameters (BoP and PPD scores) or complete disease resolution (BoP = 0 out of six sites per implant). Intragroup

TABLE 2 Changes in clinical parameters at the patient level over the 6-month experimental period for the three groups.

Parameters	Group	Baseline	1 month	Δ 0–1 month	3 months	Δ 0–3 months	6 months	Δ 0–6 months
FMPS (%)	Control	29.24 [24.49; 33.99]	22.44 [19.20;25.67]	6.8*	24.89 [21.60; 28.18]	4.35*	24.05 [21.01; 27.09]	5.19*
	Test 1	32.16 [26.23; 38.09]	24.6 [19.09; 30.11]	7.56*	27.2 [22.42; 31.98]	4.96*	26.48 [22.74; 30.22]	5.68*
	Test 2	32.8 [24.81; 40.78]	23.32 [16.92; 29.72]	9.48*	24.64 [19.24; 30.04]	8.16*	25.96 [22.14; 29.78]	6.84*
FMBS (%)	Control	19.46 [14.35; 24.57]	11.64 [9.38; 13.90]	7.82*	13.8 [11.68; 15.91]	5.66*	13.68 [11.52; 15.84]	5.78*
	Test 1	20.8 [16.00;25.60]	11.96 [10.07; 13.84]	8.84*	14.2 [12.70; 15.70]	6.6*	13.88 [12.57; 15.19]	6.92*
	Test 2	24.68 [17.57; 31.79]	12.68 [9.99; 15.37]	12.00*	13.44 [11.14; 15.74]	11.24*	13.56 [11.44; 15.67]	11.12*
BoP (%)	Control	87.21 [81.26; 93.17]	34.90 [24.07; 45.73]	52.31*	36.56 [25.56; 47.55]	50.65*	37.89 [26.98; 48.80]	49.32*
	Test 1	84.08 [77.15; 91.01]	35.01 [23.03; 46.99]	49.07*	36.81 [24.79; 48.84]	47.27*	36.61 [24.81; 48.42]	47.47*
	Test 2	87.62 [81.41; 93.84]	32.37 [18.40; 46.35]	55.25*	35.71 [21.99; 49.42]	51.91*	34.82 [20.74; 48.90]	52.8*
PI (%)	Control	89.15 [83.16; 95.14]	32.37 [23.78; 40.95]	56.78*	35.09 [26.08; 44.10]	54.06*	41.90 [31.33; 52.46]	47.25*
	Test 1	84.19 [76.16; 92.22]	24.44 [14.21; 34.68]	59.75*	27.11 [17.23; 36.99]	57.08*	32.78 [21.90; 43.66]	51.41*
	Test 2	89.95 [84.06; 95.84]	24.43 [13.76; 35.10]	65.52*	28.72 [17.15; 40.30]	61.23*	31.21 [19.53; 42.89]	58.74*
PPD (mm)	Control	4.15 [3.85; 4.44]	3.19 [2.99; 3.40]	0.96*	3.21 [2.99; 3.42]	0.94*	3.24 [3.02; 3.45]	0.91*
	Test 1	3.91 [3.47; 4.34]	3.11 [2.78; 3.44]	0.8*	3.13 [2.80; 3.46]	0.78*	3.15 [2.82; 3.49]	0.76*
	Test 2	3.99 [3.72; 4.25]	3.14 [2.95; 3.34]	0.85*	3.18 [2.98, 3.38]	0.81*	3.16 [2.95; 3.36]	0.83*

Note: Control group received a mechanical instrumentation (MI), while test 1 and 2 groups received MI combined with AP and ERL, respectively. Δ shows the intra-group difference of every clinical parameter between baseline and each time point.

Abbreviations: BoP, bleeding on probing; FMBS, full-mouth bleeding score; FMPS, full-mouth plaque score; PI, plaque index; PPD, probing pocket depth.

*Means a statistically significant intra-group difference (*p*-values <.05).

TABLE 3 Changes in clinical parameters at the implant level over the 6-month experimental period for the three groups.

Parameters	Group	Baseline	1 month	Δ 0–1 month	3 months	Δ 0–3 months	6 months	Δ 0–6 months
BoP (%)	Control	88.22 [83.80; 92.64]	37.64 [29.09; 46.20]	50.56*	39.66 [31.17; 48.14]	48.56*	40.23 [31.78; 48.68]	47.99*
	Test 1	85.48 [80.79; 90.18]	35.22 [26.85; 43.58]	50.26*	37.63 [29.35; 45.92]	47.85*	37.63 [29.45; 45.81]	47.85*
	Test 2	85.31 [80.74; 89.88]	36.72 [27.68; 45.77]	48.59*	40.40 [31.23; 49.56]	44.91*	41.81 [32.63; 50.98]	43.5*
PI (%)	Control	87.93 [82.32; 93.55]	38.51 [30.54; 46.47]	49.42*	41.67 [34.04; 49.29]	46.26*	48.28 [40.63; 55.92]	39.65*
	Test 1	84.95 [79.49; 90.40]	26.61 [18.78; 34.45]	58.34*	30.11 [22.30; 37.92]	54.84*	37.10 [29.61; 44.58]	47.85*
	Test 2	85.59 [80.86; 90.33]	27.97 [20.38; 35.55]	57.62*	32.30 [24.43; 39.98]	53.29*	36.44 [28.81; 44.07]	49.15*
PPD (mm)	Control	4.23 [3.96; 4.50]	3.27 [3.07; 3.46]	0.96*	3.29 [3.09; 3.49]	0.94*	3.31 [3.12; 3.51]	0.92*
	Test 1	3.96 [3.67; 4.24]	3.12 [2.91; 3.33]	0.84*	3.15 [2.94; 3.35]	0.81*	3.17 [2.96; 3.38]	0.79*
	Test 2	4.02 [3.76; 4.28]	3.25 [3.05; 3.45]	0.77*	3.27 [3.07; 3.47]	0.75*	3.26 [3.06; 3.46]	0.76*
KMW (mm)	Control	2.6 [2.25; 2.95]	2.59 [2.23; 2.94]	0.01	2.52 [2.16; 2.88]	0.08	2.59 [2.23; 2.94]	0.01
	Test 1	2.55 [2.22; 2.87]	2.50 [2.19; 2.81]	0.05	2.50 [2.19; 2.81]	0.05	2.50 [2.19; 2.81]	0.05
	Test 2	2.61 [2.18; 3.03]	2.46 [2.06; 2.85]	0.15	2.46 [2.06; 2.85]	0.15	2.46 [2.06; 2.85]	0.15

Note: Control group received a mechanical instrumentation (MI), while test 1 and 2 groups received MI combined with AP and ERL, respectively.

Abbreviations: BoP, bleeding on probing; KMW, Keratinezed Mucosa Width (referred to the vestibular aspect); PI, plaque index; PPD, probing pocket depth. Δ shows the intra-group difference of every clinical parameter between baseline and each time point.

*Means a statistically significant intra-group difference (*p*-values <.05).

TABLE 4 Frequency distribution of complete (BoP = 0) and partial (BoP ≤1, ≤ 2, ≤ 3) disease resolution at 6 months in the three treatment groups at the implant level.

	Control group 58 implants	Test 1 group 62 implants	Test 2 group 59 implants	Intergroup *p*-value
BoP = 0	17/58 (29.31)	19/62 (30.65)	17/59 (28.81)	.974
BoP ≤1	21/58 (36.21)	22/62 (35.48)	22/59 (37.29)	.979
BoP ≤2	27/58 (46.55)	35/62 (56.45)	30/59 (50.85)	.553
BoP ≤3	38/58 (65.52)	45/62 (72.58)	39/59 (66.10)	.650

Note: Control group received a mechanical instrumentation (MI), while test 1 and 2 groups received MI combined with AP and ERL, respectively.

Abbreviation: BoP, bleeding on probing.

TABLE 5 Multivariate logistic regression analysis (dependent variable: complete disease resolution; independent variables: restoration margin, baseline PPD ≤ 4 mm, baseline vestibular KM, tobacco, constant).

Variables	OR	95% CI	*p*-value
Restoration margin	9.17	4.06–20.73	.000*
Baseline PPD ≤ 4 mm	2.63	1.20–5.75	.015*
Baseline Vestibular KM	1.64	1.19–2.25	.002*
Tobacco	0.91	0.83–1.00	.059
Constant	0.02	0.01–0.09	.000*

Note: Pseudo R2: 0.2507; AIC: 166.1; BIC: 182.0; AUC: 0.845; Sensibility: 60.4; Specificity: 87.3.

Abbreviations: CI, confidence interval; KM, keratinized mucosa; OR, odds ratio; PPD, probing pocket depth.

*Indicates the parameters that showed a statistically significant correlation with treatment success at 6 months (*p*-values <.05).

statistically significant differences were observed at all evaluated time points with respect to baseline, and complete disease resolution was achieved in 29%–31% of implants, in the three groups.

Intergroup statistical analysis, at both subject and implant level, displayed no differences between the three treatment groups (Tables 2 and 3).

After 6 months, BoP decreased, ranging between 48% and 53% at the patient level and between 44% and 48% at the implant level, which seems to be a greater reduction compared to what was observed in previously published RCTs (Aimetti et al., 2019; Menezes et al., 2016; Pulcini et al., 2019; Riben-Grundstrom et al., 2015) and a systematic review (Barootchi et al., 2020). An explanation for this greater reduction could be the lower baseline mean values of BoP in the aforementioned studies compared to our findings, where the mean scores at baseline ranged from 84% to 88% and from 85% to 88% at the patient and implant level, respectively.

At 6 months, PPD reduction obtained by all treatment modalities ranged between 0.8 and 0.9 mm both at the patient and implant level. This is a greater reduction when compared to previous studies published in the literature (Aimetti et al., 2019; Barootchi et al., 2020; Ji et al., 2014; Menezes et al., 2016). Again, it may be speculated that in the present study, it has been achieved a greater PPD reduction since the mean PPD at baseline was higher (baseline PPD values from 3.9 to 4.15 mm and from 3.96 to 4.23 mm at the patient and implant level, respectively). Furthermore, all treatments were performed by a single experienced periodontist and mechanical instrumentation of the implant surface was performed with titanium hand instruments, which could have been more traumatic compared to ultrasonic devices. Although the orientation of the curettes was always adapted to the implant surface, an unintentional curettage with the removal of the crevicular/junctional epithelium could have been performed.

Therefore it may have led to a greater recession of the peri-implant mucosa, especially in implant sites presenting a thin phenotype (subgroup with KM <2 mm).

In our study the 29%, 31% and 29% of implants respectively in the control, test 1 and test 2 groups met the success criteria of complete disease resolution at 6 months (Table 4). The frequency distribution of the parameter "disease resolution" was similar to that reported recently with mechanical instrumentation alone (Aimetti et al., 2019), or in combination with chlorhexidine (Heitz-Mayfield et al., 2011), sodium hypochlorite gel (Iorio-Siciliano et al., 2019), glycine powder air-polishing (Ji et al., 2014; Riben-Grundstrom et al., 2015) and diode laser (Aimetti et al., 2019).

Despite the current scientific evidence available showing the efficacy of the non-surgical PM treatment in improving clinical parameters, a complete disease resolution is seldom reported, regardless of the treatment protocol adopted (Barootchi et al., 2020; Chuachamsai et al., 2022; Salvi & Ramseier, 2015; Schwarz, Becker, & Renvert, 2015; Schwarz, Becker, & Sager, 2015).

In order to collect data also of a partial disease resolution, different thresholds of residual bleeding around implants after treatment were evaluated. As a result, a higher proportion of implants achieved the success criteria of a partial disease resolution (BoP at <1, <2 and <3 sites out of six sites per implant) compared to implants showing a complete disease resolution (total absence of BoP). (Table 4). According to Karlsson et al. (2019) and Berglundh et al. (2021) the presence of BoP at <50% of the sites (1–2 aspects) demonstrated a weaker association with the progression of the disease (future bone loss) than the presence of BoP at >50% of the sites (3–4 aspects). Moreover, probing on implants with an inadequate prosthesis design and contour could determine a trauma of the peri-implant mucosa, and hence potentially bleeding due to an inappropriate probe inclination rather than the presence of a residual inflammation. In agreement with a very recent systematic review on the outcome measures used in clinical studies on peri-implant mucositis and peri-implantitis (Derks et al., 2022) the BoP and PI dichotomous indexes

have been assessed since they are the most used outcome measures in the last 10 years. However, data from the present study may suggest to distinguish between different types of bleeding on probing around implants (Mombelli et al., 1987) and indicate the real need for additional therapy when a minimal spot of bleeding still remains after therapy.

The adjunctive analysis of the multivariate regression model shed light on both patient and site-specific variables that can act as prognostic factors (Table 5). Baseline PPD < 4 mm, supramucosal restoration margin and presence of buccal KM seem to statistically influence the resolution of the disease. An important factor that influences the probing depth is the deep implant positioning. Findings reported by Chan et al. (2019) are in line with the outcomes of the present study: deeper mucosal tunnels (>3 mm) modified the resolution of experimental PM at transmucosal implants, resulting in a delayed and incomplete inflammation resolution compared with shallower mucosal tunnels (<1 mm). Moreover, results obtained in an in vitro study by Discepoli et al. (2022) confirm that from 4 mm on, the cleaning efficacy of debridement with ultrasonics, with or without the adjunctive use of AP, was statistically lower. Accordingly to the present findings, Heitz-Mayfield et al. (2011) reported that the presence of a submucosal restoration margin showed a lower therapeutic improvement compared with supramucosal restoration margins. This factor may have limited not only the insertion of the instruments, but also patients' accessibility to oral hygiene measures. Prevention and management of peri-implant disease are strongly correlated with the accessibility for professional and self-performed biofilm control and even in the case of shallow peri-implant sulci (PPD ≤4 mm) the removal of the prosthesis is indicated (Discepoli et al., 2022). In this regard, a recent study by de Tapia et al. (2019) demonstrated a higher complete disease resolution in a group of patients that received the non-surgical mechanical therapy in combination with the removal and the modification of the implant-supported prosthesis contour with respect to the control group's patients.

In this study, another important parameter for PM resolution is the presence of KM, with a 2 times higher chance of a complete disease resolution at 6 months for every mm increase of KM. This is in agreement with the most recent literature on the importance of having KM around an implant (Sanz et al., 2022). It has been observed that implants exhibiting <2 mm of KM were associated with more brushing discomfort and hence higher PI and BoP scores in comparison with implants showing a KM > 2 mm (Souza et al., 2016).

The identification of site/implant level characteristics related to treatment success, observed in the present study, needs to be further investigated in future studies and may contribute to the identification of thresholds indicative of disease resolution.

Limitations of the present RCT rely on the potential impact of the lack of blinding during treatment procedures. However, allocation concealment until the submarginal instrumentation was completed reduced this impact. Furthermore, the study may be underpowered to detect significant differences among treatment groups. Nonetheless, the sample size was determined in order to assure an adequate power to detect statistical significance, no patients were lost at the 6-month visit and a low variability of results was noted. Other aspects to be taken into account are that prosthesis contours were not modified and the majority of the rehabilitations were cemented-retained, therefore, it was not possible to remove the suprastructures. This may have hampered not only the biofilm removal (de Tapia et al., 2019) but also the accuracy of the probing measurements. According to a recent systematic review conducted on PM management in the last 10 years (Derks et al., 2022) only 6% of studies removed prostheses for the purpose of probing. Furthermore, the authors found that only 25% of studies focused on the site or implant level for the key outcome measures, while the majority did report patient-level data. Therefore, this may represent a strength of the present study since it has been conducted in both a patient- and implant-level analysis.

5 | CONCLUSION

The adjunctive use of AP and ERL in the non-surgical therapy of PM does not seem to provide any significant or clinically relevant benefit in terms of BoP and PPD reductions and complete disease resolution, over the use of submarginal instrumentation alone. The three treatment modalities yielded similar clinical improvements. At 6 months complete disease resolution was obtained in the 29% of implants in the control and ERL groups and 31% of implants in the AP group. Baseline PPD <4 mm, presence of buccal KM and supramucosal restoration margin may play a role in the complete resolution of PM.

AUTHOR CONTRIBUTIONS

Marco Clementini: Conceptualization; Data curation; Investigation; Methodology; Visualization; Project administration; Resources; Validation and writing – original draft and review & editing of the manuscript. **Simone Fabrizi:** Conceptualization; Data curation; Investigation; Methodology; Visualization; Resources; Formal analysis and writing – review & editing of the manuscript. **Nicola Discepoli:** Methodology, software; Formal analysis and writing – review & editing of the manuscript. **Margherita Minoli:** Data curation; Investigation; Visualization; Validation; Resources, and writing – original draft and review & editing of the manuscript. **Massimo de Sanctis:** Conceptualization; Validation; Supervision; Writing – review & editing of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors report no conflict of interests related to the study.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Marco Clementini https://orcid.org/0000-0002-1827-5200
Nicola Discepoli https://orcid.org/0000-0003-1805-2899
Margherita Minoli https://orcid.org/0000-0002-5299-1753
Massimo De Sanctis https://orcid.org/0000-0002-5915-566X

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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