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One-year clinical outcomes following non-surgical treatment of peri-implant mucositis with adjunctive diode laser application.

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Running Title: Diode laser in peri-implant mucositis

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ABSTRACT

Background: Limited information is available on the application of diode laser in the treatment of peri-implant diseases. The aim of this study was to investigate the clinical efficacy of the adjunctive application of diode laser in the non-surgical treatment of peri-implant mucositis during a 12-month follow-up period.

Methods: The sample was composed of 73 systemically healthy patients with one implant diagnosed with peri-implant mucositis (bleeding on probing [BoP] with no loss of supporting bone). Implants were randomly assigned to mechanical debridement with hand and powered instruments and 980-nm diode laser application (test group, N= 38) or mechanical debridement alone (control group, N= 35). At the completion of active treatment patients were included in a periodontal maintenance program. Recalls were provided every three months in both treatment groups for reinforcement in oral hygiene instructions and professional implant cleaning with rubber cups. Baseline parameters were repeated at 3 and 12 months postoperatively.

Results: Intragroup analysis showed that plaque index, BoP and probing depth presented statistically significant improvements when compared with baseline values (all P <0.001). No statistically significant difference in clinical outcomes was observed between treatment groups at each time point. At 12 months no significant difference in the percentage of sites showing BoP resolution was observed between test (60.9%) and control treatment (52.6%), as well.

Conclusion: Based on the present results, the adjunct use of diode laser showed little but not statistically significant additional benefits in the treatment of peri-implant mucositis after an observation period of one year.

Keywords: Dental implants; Inflammation; Lasers; Oral hygiene; Periodontal debridement.

INTRODUCTION

Dental implants have become an increasingly more common treatment modality to replace lost teeth. The prognosis of implant therapy in dentistry is relatively high with survival rates in the range of 95% after 10

years in function.[1] Nevertheless, peri-implant infections caused by biofilm accumulation may occur and may compromise the success of implant-supported rehabilitations.

Data from a recent systematic review reported a weighted mean prevalence for peri-implant mucositis of 43% (range 19% to 65%) and for peri-implantitis of 22% (range 1% to 47%).[2] Peri-implant mucositis is the reversible inflammation of the marginal soft tissue surrounding the implant without signs of bone loss, meanwhile peri-implantitis includes both soft tissue inflammation and progressive loss of supporting bone beyond biological bone remodeling.[3]

At the 2017 World Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions, it was emphasized that untreated peri-implant mucositis may progress into peri-implantitis, therefore it is important to treat early signs of peri-implant inflammation to prevent or limit marginal bone loss using appropriate strategies in plaque control and biofilm removal.[4] However, the complex geometry of the implant surface may limit the ability of the clinician to remove effectively soft and hard deposits below the mucosal margin by means of mechanical debridement alone.[5] Consequently, adjunctive treatments including the use of local antiseptics[6,7] air abrasive techniques[8,9] or probiotics[10], and more recently the application of laser or photodynamic therapy[11,12] have been proposed to improve treatment outcomes.

In-vitro studies have demonstrated that the CO2 laser, the diode laser (DL), and the erbium-doped yttrium aluminum garnet (Er:YAG) laser may be suitable for the irradiation of titanium surfaces, since the implant temperature did not increase significantly during their application.[13,14] The DL (810 – 980 nm) seems to be the only laser that offers surface preservation irrespective of the pattern and power setting when compared to CO2 or Er:YAG laser systems.[15,16] As the DL is not an ablative instrument, it can directly contact the implant surface without inducing melting, cracking, or crater formation.[17] Its use in implant therapy may be attractive due to its capacity of soft tissue penetration and complete removal of the pocket epithelium, its biostimulating effects and high antibacterial potential.[17,18] *In-vitro* and animal studies showed that biostimulation accelerates the mitotic processes within the irradiated tissues, modulates the connective tissue metabolism and enhances growth factors release promoting significant collagen production around the implant surface.[19]

Recent systematic reviews reported no definitive consensus about the effects of laser therapy in the

management of peri-implant mucositis due to methodological etherogeneity of the included studies, incomplete information on laser parameters and short follow-up period ranging form 4 to 12 weeks.[20,21] In a specialized panorama such as the one we have today, it is important also to consider whether it is single element or total arch rehabilitation; whether it is a case of healthy or problematic patients since success implant rates are high even in patients with HIV.[22]

Successful outcome in the treatment of peri-implantitis with the combined use of DL and mechanical debridement has been recently reported in the short term.[23-25] In view of these considerations, the aim of this 12-month follow-up clinical study was to analyze the adjunctive efficacy of DL irradiation in a non-surgical protocol for peri-implant mucositis.

MATERIALS AND METHODS

Experimental design and study population

This prospective study is a follow-up analysis of a recently published short-term randomized and controlled clinical study conducted at the Section of Periodontology, Department of Surgical Science, University of Turin (Italy) between September 2016 and November 2017.[26] It was approved by the Institutional Ethics Committee of the "AOU Città della Salute e della Scienza", Turin, Italy (protocol no 1001) and was conducted according to the Helsinki Declaration of 1975 (revised in 2000). Each patient provided a written informed consent before participation. Follow-ups were performed between January 2018 and September 2018. The CONSORT guidelines for reporting clinical trials were followed.

The baseline entry criteria included the following: 1) presence of one or more peri-implant mucositis sites with probing depth (PD) ≥ 4 mm combined with bleeding on probing (BoP) under light forces (0.25 N) with or without suppuration and without loss of supporting bone[27]; 3) implant loaded with a single-unit crown not interfering with the assessing of clinical parameters and with the oral hygiene procedures; 4) no evidence of occlusal overload (*i.e.* occlusal contacts revealed appropriate adjustment); 5) presence of keratinized tissue ≥ 2 mm around implants; 6) full-mouth plaque score (FMPS) and full-mouth bleeding score (FMBS) ≤ 20 % at the screening visit. Individuals were also required to be non-smokers, and to have healthy or treated periodontal conditions without residual pocket sites more than 5 mm deep following

active periodontal treatment. Exclusion criteria were as follows: 1) intake of antibiotics in the previous 3 months; 2) use of any medications affecting periodontal tissue conditions for a long time (phenytoin, cyclosporine, calcium channel blockers, biphosphonates); 3) systemic diseases or conditions that could interfere with the study outcomes (immune deficiencies, uncontrolled diabetes, radiotherapy in the head and neck area, hematological diseases, infectious diseases such as AIDS, hepatitis); 4) implants with a history of peri-implantitis; 5) any treatment intervention for peri-implant diseases within 3 months prior to study initiation.

Clinical protocol

Patients of both groups received individualized instructions in self-performed plaque control measures with the rolling brushing technique and interdental brush or floss, depending on the proximal space viability. Assignment to the test group (mechanical debridement and application of DL) and control group (mechanical debridement alone) was made using a computer-generated table by an independent operator who did not take part in the study. Using this list, cards with group identification were placed in numbered opaque envelopes. The responsible of the research (M.A.) broke the seal of the envelope just before treatment delivery and informed the clinician which treatment had to perform according to test or control protocol. The examiner and the patients were blinded to the group assignment.

The non-surgical protocol was described in details in a previous article.[26] Sites in the test group were treated first by 980-nm DL application using a 300-μm optical fiber, parallel to the implant surface, with a power of 2.5 W (average 0.7 W, time t_{on} = 30 μs, time t_{off} =70 μs, 30% dc, 10 kHz, fluence 120 J/cm^2) in a pulsed mode for 30 s. The tip was introduced by 1 mm less than the value obtained through the probing procedure and moved in both horizontal and vertical directions. Care was taken to prevent any coagulation and subsequent temperature increase by regular cleaning of the application tip via saline-dampened sterile gauze every 7-8 s. Hydrogen peroxide 10 vol irrigation was also performed for 10 s prior to and following laser application.[28] The implant surface was mechanically debrided with both power-driven devices (piezoelectric or magnetostrictive with implant dedicated tips) and manual instruments (titanium curettes) after DL. This procedure was replicated three times for each inflamed site.[29,30] Afterwards, biostimulation

therapy of the site was carried out using a specific handpiece with an output lens of about 1 cm in diameter, for 60 s at a power of 0.7 W, in continuous mode.[29,30] The handpiece was kept perpendicular to the peri-implant mucosa and was moved in a contact mode drawing small circles. The procedure was repeated the following day.[30]

The control group received the same treatment procedures, but the laser was applied into the peri-implant sulcus without activation. The duration of the procedure lasted between 6 and 9 min in both test and control sites. Patients in both groups were included in a periodontal maintenance program by two experienced dental hygienists (Lo.Bo., N.G.) two after completion of active treatment of peri-implant disease. Recalls were scheduled at 3, 6 and 12 months for reinforcement in oral hygiene instructions and professional implant cleaning with rubber cups and polishing paste.

Clinical measurements

Clinical peri-implant parameters were assessed at baseline and after 3 and 12 months by the same experienced and blinded examiner (E.E) using the same plastic probe with a force not exceeding 0.25 N. Five patients with at least one implant with peri-implant mucositis were used for the examiner calibration. Patient evaluation was performed separately twice with a 24-hour interval. Calibration was accepted if reproducibility deviation of the measurements was within 1 mm from baseline to 24 hours in > 90% of measurements.

The following parameters were assessed on six sites per implant: plaque index (PI) and BoP, which were recorded assigning a binary score (0 =absence, 1=presence); and probing depth (PD) measured as distance between from the peri-implant mucosal margin to the bottom of the sulcus. Mucosal recession (REC) was measured from the implant shoulder to the peri-implant mucosal margin at mid-buccal and mid-lingual aspects. Periapical radiographs were taken before collection of data to confirm bone loss <2 mm from the implant shoulder as a consequence of the bone healing remodelling process. The FMPS and FMBS were also assessed at baseline, at 3 and 12 months postoperatively.

Statistical analysis

Data were recorded in a Microsoft Excel file and analysed with statistical software (SPSS for Mac, SPSS version 24.0, IBM Corporation, Armonk, NY, USA). Each patient contributed with one implant to the

study, therefore the patient was regarded as the statistical unit.

Data were first examined for normality by the Kolmogorov-Smirnov test, and if the data did not achieve normality, analyses were performed using non-parametric methods. The unpaired t test (FMPS, PD) and the Mann-Whitney U test (PI, BoP, FMBS) were used to evaluate the difference in each parameter between two treatment protocols at each observation interval. Differences between groups were tested using the Chi-square test for qualitative variables. The Bonferroni correction was applied for multiple comparisons. Repeated-measures ANOVA and the Friedman test were applied to evaluate the influence of time on each parameter within each treatment group, followed by *post-hoc* tests (Newman-Keuls test and Dunn test). The level of statistical significance was fixed at 5%.

RESULTS

As reported in Figure 1, 98 patients of the original study who were willing to attend the periodontal maintenance therapy at the University of Turin were considered for enrollment. Twenty-five patients dropped out following four to six months due to personal reasons or because they moved away or they discontinued the supportive therapy. Finally, a total of 73 highly motivated and compliant patients were followed during the first year postoperatively and included in the analysis: 38 were treated with DL application and mechanical debridement (test group, mean age: 59.2 ± 9.3 years) and 35 with mechanical debridement alone (control group, mean age: 62.1 ± 6.8 years). The baseline characteristics of the subject sample are summarized in Table I. All patients had cement-retained implant restorations. The restoration-abutment interface was 0.5 to 1 mm below the mucosal level. No extracoronal residual cement was detected at radiographic and clinical examination.

The comparative analysis between test and control groups over the experimental period in relation to periodontal clinical parameters is shown in Table II. Between-group analyses did not indicate statistically significant differences in any of the baseline clinical parameters. FMPS and FMBS remained below 20% during the experimental phase in both treatment groups. No adverse effects were observed in any of the experimental groups.

Both treatments were associated with comparable and statistically significant reduction in mean PI and PD

values after 3 and 12 months of healing (all $P < 0.001$). Mucosal recessions of 1 to 3 mm were observed in 9 subjects (four test and five controls).

Regarding BoP scores, pair-wise comparisons showed that there were significant reductions in the percentage of sites with BoP from baseline to 3-month follow-up for both test and control groups ($P < 0.001$), with little apparent change between 3 and 12 months ($P > 0.05$). There was no statistically significant difference in the changes in BoP between the test and control groups at any assessment time ($P > 0.05$).

As reported in Table III, disease resolution at 12 months was obtained in 92 out of 151 (60.9%) sites diagnosed for peri-implant mucositis and in 12 of 38 (31.6%) implants in the test group. In the control group disease resolution was obtained in 61 out of 116 (52.6%) sites diagnosed for peri-implant mucositis and in 9 of 35 (25.7%) implants. The differences between the treatment groups were not statistically significant ($P =0.172$ and $P =0.692$). Patients with previous history of periodontitis experienced less improvement in BoP scores regardless of the treatment applied only at 3-month follow-up ($P = 0.001$). At 12 months the differences were not longer statistically different. Comparable PI values were detected at both 3- and 12-month examinations ($P > 0.05$).

DISCUSSION

The results from the present study, despite significant clinical improvements in both the experimental groups, indicate no statistically significant differences between the test and control procedures in controlling the peri-implant inflammation over a 12-month period. Based on the Sanz & Chapple definition, disease resolution was obtained in 60.9% of sites and in 31.6% of implants diagnosed for peri-implant mucositis in the test group at 12 months.[31] At this time point a complete resolution of BoP was achieved in 52.6% of sites and 25.7% of the implants in the control group treated with mechanical debridement alone.

Comparable reduction in the percentage of BoP-positive sites was obtained in other clinical studies in which mechanical debridement alone or in combination with topical application of chlorhexidine or glycine powder was performed to remove bacterial biofilm around implants.[6-8,11,32] Other clinical studies have also

demonstrated similar results when evaluating efficacy of chlorhexidine in mouthrinse formulation, but its application has been associated with unwanted local side effects.[33-35]

A recent systematic review reported residual BoP scores between 14.7% and 47.5%, indicating that complete resolution of inflammation could not be expected at all implant sites regardless of the non-surgical protocol tested.[36] Conflicting data on BoP reduction after laser application are reported in literature.[20] A potential benefit of DL therapy in combination with mechanical debridement was identified in some clinical studies in which significant reductions in BoP were achieved.[12,37] This favorable effect was attributed to the coagulation or vaporization of the inflammatory tissue after laser irradiation, but it could support the role of maintenance protocol in addition to active treatment in guaranteeing the control of clinical inflammation.[17] However, as the presence of mucositis or peri-implantitis was not clearly demarcated in the analysis of the treatment outcomes, therefore, controversy still exists.[12] As reported in previous systematic reviews these inconclusive findings may be due to incomplete information about laser therapy.[20,21] The laser setting, the number of laser applications as well as the optic fiber diameter could influence the photo-thermal action, likely affecting the anti-bacterial and detoxifying effect and consequently the anti-inflammatory action. No additional benefit had been found when laser treatment was used secondary to mechanical debridement.[38] Although a previous study indicated the impact of frequency of laser application on the overall effect of laser treatment[39], the majority of studies in the literature provided only one laser session.[12,40] It might be hypothesized that a single laser irradiation is effective in temporarily reducing the inflammatory response.

Therefore, in the present study, according to the available evidence, the implant surface was mechanically debrided with both power-driven devices and manual instruments after the DL irradiation three times for each site requiring treatment.[22]

The selection of irradiation parameters was based on previous investigations.[29,30] DL decontamination is based on its photo-thermal effect and tissue penetration.[17,18] According to Kreisler et al. the successful outcomes of non-surgical periodontitis treatment with DL irradiation can be mainly attributed to the complete removal of the epithelial lining of periodontal pockets.[38] The bactericidal effect is due to a localized increase in temperature, which exerts a bactericidal effect and inactivates bacterial endotoxins.[41]

When used according to appropriate parameters, DL does not cause visible changes on implant surface, and does not generate a temperature increase of more than 47°C.[15] It also enhances the mitotic process within the irradiated tissues and modulates connective and bone tissue metabolism, leading to significant collagen production during periodontal tissue healing.[19,42]

DL irradiation might be influenced by the presence of several body fluids that are commonly associated with inflamed periodontal and peri-implant pockets, due to its affinity for hemoglobin and other pigments.[17] In the present study the laser tip was inserted parallel to the implant shoulder in non-contact mode and treatments were performed at the sulcus along the abutment surface. In order to prevent any coagulation and temperature increase, regular check and cleaning of the application tip were carried out every 7-8 s.[14] No visible thermal damage was detected on the mucosal surface. Moreover, anesthesia was not performed, thus patients could complain of any intraoperative pain.

It is important to consider that peri-implant mucositis is a multifactorial disease affected by numerous local and systemic factors. In the current study a lower decrease in BoP scores, without reaching statistical significance, was observed at three months after treatment in patients with a previous history of periodontitis. One explanation of this finding may be the changes in proportion of bacterial species between patients affected or not by periodontal disease and the individual responsiveness to plaque bacteria. In literature very few studies have taken into account this aspect, however they failed to observe any additional benefit in favor of additional laser therapy compared to conventional debridement alone on the peri-implant microbiota.[23,43] In the present study no microbiologic analysis was performed. It should be noted that all periodontally compromised patients had a history of successful treated periodontitis: no residual pocket sites were present, oral hygiene standards were satisfactory (FMPS <20%) and inflammation was under control (FMBS <20%). This may explain the lack of statistically significant differences between healthy non-susceptible and periodontitis-susceptible participants.

An interesting finding by Heitz-Mayfield et al. was the negative effect of a submucosal restorative margin on the treatment outcome.[6] Implants with supramucosal restoration margins showed greater improvement following the treatment of peri-implant mucositis compared with those with submucosal restoration margins. In the present study all test and control implants had an epimucosal positioning of the crown

margin. This ensured that no residual cement was left after cementation as confirmed by radiographic examination and through clinical assessment at the time of enrollment. Remaining cement excess can result in a local inflammatory response, which has been documented as a cause of peri-implant diseases.[44,45] This is a relevant topic even if most of the studies dealing with the treatment of peri-implant mucositis did not take into account for this aspect. Furthermore, prosthetic design allowed adequate access for biofilm control. When considering the present findings, it is important to have in mind the differences in the histology as well as in the immune response to bacterial plaque accumulation around implant sites and natural teeth as demonstrated in experimental gingivitis studies.[46]

CONCLUSION

Both treatment modalities resulted in a statistically significant reduction in inflammation and PD at peri-implant mucositis sites over a 12-month observation period. A complete disease resolution could not be achieved at all implant sites regardless of the instrumentation method applied. The adjunct use of DL showed little but not statistically significant additional benefits in the treatment of peri-implant mucositis.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported. The study was supported by the authors' own institutions.

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Table I. Baseline characteristics of patients (mean ± standard deviation or N [%])

Parameters	Test Group	Control Group	*p* value test vs control
	38	35	
Age (years)	59.2 ± 9.3	62.1 ± 6.8	0.129 [a]
Females [n, (%)]	24 (63)	23 (66)	0.307[b]
History of treated periodontitis [n, (%)]	12 (32)	13 (37)	0.617[b]
Duration of implants (years)	6.3 ± 3.2	5.7 ± 2.8	0.334 [a]

[a]Unpaired *t* test
[b]Chi-square test

Table II. Changes in clinical parameters (mean ± standard deviation, and median) over the 12-month experimental period in both treatment groups

Variables	Group	Baseline		3 months		$\Delta_{0\text{-}3\ months}$	12 months		$\Delta_{0\text{-}12months}$
FMPS (%)	**Test**	16.6 ± 3.5	18.0	17.1 ± 2.9	18.0	-0.5 ± 4.3	17.3 ± 2.7	18.0	-0.7 ± 4.1
	Control	18.0 ± 3.6	19.0	17.6 ± 3.8	18.1	0.4 ± 4.9	16.9 ± 3.4	18.3	1.1 ± 4.8
Difference between groups		NS[c]		NS[d]			NS[d]		
FMBS (%)	**Test**	14.1 ± 4.1	15.0	15.6 ± 3.8	15.2	-1.5 ± 3.4	14.4 ± 4.0	14.0	-0.3 ± 5.2
	Control	14.9 ± 3.9	15.6	16.3 ± 2.9	17.0	-1.4 ± 4.5	15.5 ± 3.6	15.0	-0.6 ± 5.7
Difference between groups		NS[c]		NS[d]			NS[d]		
PI Implant (%)	**Test**	49.6± 20.7[a]	41.7	10.5± 15.7[b]	0	39.1 ± 26.7	15.8 ± 14.9	16.7	33.8 ± 26.1
	Control	44.8± 28.5[a]	33.3	12.9± 17.2[b]	0	31.9 ± 31.4	18.6 ± 16.1[b]	16.7	26.2 ± 30.1
Difference between groups		NS[c]		NS[d]			NS[d]		
BoP Implant (%)	**Test**	63.6± 24.2[a]	58.3	23.3± 17.4[b]	16.7	40.3 ± 32.1	25.8 ± 24.1[b]	33.0	37.8 ± 30.2
	Control	59.5± 25.0[a]	50.0	26.7± 23.9	16.7	32.8 ± 29.6	27.6 ± 25.5[b]	16.7	31.9 ± 26.6
Difference between groups		NS[c]		NS[d]			NS[d]		
PD Implant (mm)	**Test**	3.6 ± 0.7[a]	3.5	3.0 ± 0.6[b]	2.8	0.6 ± 0.7	3.1 ± 0.7[b]	3.0	0.5 ± 0.9
	Control	3.8 ± 0.6[a]	3.4	3.1 ± 0.4[b]	3.2	0.7 ± 0.5	3.3 ± 0.6[b]	3.2	0.5 ± 0.7
Difference between groups		NS[c]		NS[d]			NS[d]		

FMPS, Full-Mouth Plaque Score; FMBS, Full-Mouth Bleeding Score; PI, Presence of plaque; BoP, Presence of bleeding on probing; PD, Probing depth; NS, difference between groups not statistically significant ($P > 0.05$)

[a] $P < 0.001$, p values represent changes among the three time points (ANOVA or Friedman test).

[b] $P \leq 0.001$, *p* values represent longitudinal changes from baseline (Newman-Keuls test or Dunn test).

[c] Mann-Withney *U* test or Unpaired *t* test

[d] Bonferroni-corrected Mann-Whitney *U* test or Bonferroni-corrected *t* test

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Table III. Number and percentage of implants with corresponding numbers of BoP-positive sites over the study period.

	N (%) of implants Baseline		N (%) of implants 3 months		N (%) of implants 12 months	
	Test	**Control**	**Test**	**Control**	**Test**	**Control**
0	0 (0)	0 (0)	11 (29)	9 (26)	12 (31)	9 (26)
1	1 (3)	2 (6)	14 (37)	8 (23)	6 (16)	7 (20)
2	6 (16)	9(26)	6 (15)	11 (31)	13 (34)	12 (34)
3	10 (26)	9 (26)	4 (10)	5 (14)	4 (10)	5 (14)
4	6 (16)	8 (22)	1 (3)	2 (6)	0 (0)	1 (3)
5	6 (16)	5 (14)	1 (3)	0 (0)	3 (9)	1 (3)
6	9 (23)	2 (6)	1 (3)	0 (0)	0 (0)	0 (0)

BoP, bleeding on probing.

Figure 1. Flow chart of the study.