



Review Article

Effect of Ozonated Extra Virgin Olive Oil Gel in The Treatment of Peri-Implant Mucositis: A Retrospective Analysis of 20 Cases

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Abstract

Peri-Implant Mucositis (PM) is inflammation that affects the soft tissues surrounding the implant with a prevalence between 19% and 65% and if left untreated, it precedes to periimplantitis. Over time several clinical protocols for the management of PM have been proposed. They include mechanical debridement alone or with additional chemical decontamination. A retrospective analysis was conducted to evaluate the effects of an extra virgin olive oil-based gel in the treatment of PM in support of mechanical decontamination procedures in 20 subjects. Statistically significant improvements in clinical outcomes (bleeding on probing -BoP, plaque index -PI and probing depth -PD) were observed by comparing the values at baseline to three observation periods ($p < 0.001$). Beyond the limits, this retrospective clinical study demonstrates that ozonated extra virgin olive oil gel allowed to effectively treat inflammation of peri-implant tissues and, due to its organoleptic characteristics and the absence of side effects, can represent a valuable therapy for the chemical management of peri-implant mucositis and for daily use in the context of supportive therapy.

Introduction

Tooth decay, periodontal disease, dental trauma are the main causes of tooth loss in the adult population. The treatment plan proposed to partial or total edentulous patients is implant-prosthetic rehabilitation. Dental implants allow to replace missing teeth and restore chewing function and acceptable aesthetics. Although implant placement is a validated gold standard therapy for the replacement of missing teeth, it is not free from

risks and complications that may result in implant failure [1-3]. Approximately 5 implants out of 100 over a 10-year period experience implant failure [4] Risk factors for peri-implant health are smoking and non-adequate oral hygiene maintenance that causes the selection of harmful bacterial strains that colonize and proliferate at the soft tissue-abutment interface [5-7]. These bacteria create a dysbiosis condition and, therefore, are responsible for triggering the inflammatory response in the peri-implant tissues, known as Peri-Implant Mucositis (PM).

PM, as defined during the 1st European Workshop on Periodontology (EWOP) in 1994, is a reversible disease that afflicts the mucosa around the implants, and which differs from peri-implantitis in the absence of bone resorption [8,9]. Clinically PM is characterized by the signs of inflammation (swelling, redness, pain) and, if not treated, may transition from a reversible to an irreversible condition. Peri-implantitis is the main cause of implant failure in the long term and it ranges between 19 and 65% [10]. In such clinical scenario, treatment of PM is crucial to achieve implant survival through decontamination procedures of implant components and customized at-home and in-office oral hygiene protocols to prevent inflammation of the peri-implant soft tissues [11,12] and to mechanically remove the bacterial biofilm [13-16]. Evidence-based recommendation support the association a chemical plaque control with the mechanical decontamination of peri-implant sites [17-19].

Chlorhexidine (CHX), due to its bactericidal and bacteriostatic action, is the most widely used antiseptic for the chemical control of peri-implant inflammation. [20-22] and the CHX products are the most frequently used to chemically treat PM [23,24]. On the other hand, due to the side effects such as mucosal irritation, fibroblast necrosis, dysgeusia and pigmentation of clinical crowns, CHX cannot be used on the daily basis over long time periods [25-27] Clinical and scientific evidence has identified innovative technologies aiming to maintain the balance of the oral ecosystem with a minimally invasive approach. Ozone therapy in Dentistry has shown broad-spectrum antimicrobial effects and anti-inflammatory properties and it improves the wound healing and tissue regeneration [28-30]. The formulations used are ozonated water and oil. A 2010 study compared the effectiveness of subgingival irrigation with chlorhexidine and that with ozonated water in periodontal treatment. The use of ozone compared to CHX has further reduced the plaque index, gingival index and bleeding index. [31] Meckenna et al. demonstrated a significant reduction in the clinical indexes of bleeding and plaque following ozone therapy in the treatment of PA [32].

The ozonation of vegetable oils (sunflower oil, olive oil, extra virgin olive oil, etc.) has further emphasized the properties of ozone. Patel demonstrated that the application of ozonated olive oil gel in addition to mechanical debridement in the treatment of chronic periodontitis resulted in a significant improvement in clinical and microbiological parameters over time and compared to the control groups [33]. Furthermore, a reduction in MMP-8 was observed following the use of ozonated extra virgin olive oil-based mouthwash in addition to scaling and root planing compared to SRP alone [34]. The objective of this retrospective clinical study was to evaluate the effectiveness of the professional topical application of a gel based on ozonated extra virgin olive oil in the treatment of peri-implant mucositis.

Materials and Method

Study Design

A retrospective clinical trial was conducted to evaluate clinical effects of the ozonated extra virgin olive oil gel in the treatment of PM. Topical gel applications on the inflamed site were repeated 4 times over a period of 3 weeks. The clinical parameters were assessed at baseline and at 6-, 12- and 24-week follow-up.

Study Population

Between 1st September and 15 November 2021, at the Department of Dental and Maxillofacial Sciences, Sapienza University of Rome, Italy, healthy patients with an implant affected by PM were enrolled in the study according to specific inclusion/exclusion criteria summarized in Table 1. This clinical study was performed in accordance with the Good Clinical Practice (GCPs) guidelines (1996) and Declaration of Helsinki of 1975, as revised in 2013. The diagnosis of PM was carried out with a millimeter periodontal probe (PCP-UNC 15, Hu-Friedy, Chicago, Illinois, USA) and an periapical x-rays was performed using using the Rinn XCP film holders. All patients recruited, after signing the Informed Consent form, underwent treatment protocol for mucositis and were followed up at regular intervals for a period of 6 months.

EXCLUSION CRITERIA:
• SEVERE SMOKERS (>10 CIG/DIE)
• PERIODONTAL DISEASE
• HISTORY OF PERIODONTAL DISEASE
• DIABETIS
• PHARMACOLOGICAL THERAPY WITH DRUGS THAT CAUSE HYPERPLASIA

Table 1: Exclusion criteria used for the sample selection.

Baseline visit (T0)

Collection of clinical parameters During the first visit, the patients underwent intra and extraoral clinical examination. As usual, periodontal probing was performed using the PCP 15 UNC probe and Pocket Depth (PD), Bleeding on Probing (BoP) and Plaque Index (PI) were noted in a periodontal chart before and subsequently in an electronic database. Full Mouth Bleeding Score (FMBS) and Full Mouth Plaque Score (FMPS) were calculated and recorded.

Mechanical decontamination procedure. Confirmed the diagnosis of perimplant mucositis, through clinical and radiographic indices, all patients underwent a session of deplaqueing

and debridement of the whole mouth. The D-BioTECH protocol [35] was applied for a mechanical decontamination that was both ergonomic and minimally invasive.

The glycine powder was delivered with the selective air polishing procedure having as a guide the topography of the dental plaque highlighted by the tritonal plaque detector.

Oral biofilm topography was used to instruct and motivate the patient to correct home oral hygiene lifestyles. The most appropriate devices were identified according to the customized clinical approach of the Tailored Brush Method [12] for home cleaning of oral and buccal surfaces. the use of Rubber interdental picks (GUM Soft-Picks Advanced, Sunstar Europe, Etoy, Switzerland) with different sizes depending on the shape and morphology of the interdental space was recommended.

After deplaquing, the tartar deposits were removed with a piezoelectric scaler (Mectron Combi Touch, Mectron Spa, Carasco, Italy) with steel tips (S1, Mectron Spa, Carasco, Italy) for dental surfaces and peek tips (implant cleaning SET S, Mectron Spa, Carasco, Italy) for implant surfaces.

Chemical decontamination procedure. After careful mechanical decontamination of the site affected by mucositis, a gel based on ozonated extra virgin olive oil was applied (Perioral3, Gemavip, Italy).

When the anatomy of the site and the laxity of the soft tissue allowed it, the gel was applied directly into the peri-implant sulcus, letting the gel fall from the dispenser, otherwise a syringe fitted with a blunt needle was used for its application (Figure 1).



Figure 1: Topical application of gel based on ozonated extra virgin olive oil through single-use syringe with blunt needle.

The application of the gel to the peri-implant site was repeated every 7 days for 3 weeks (These three sessions were considered part of the baseline procedures)

Post-treatment indications

After each application of the Perioral3 gel, each patient received the following indications:

- do not rinse or drink for the next 30 minutes.
- do not eat solid food for the next 3 hours.

For the home chemical control of plaque, a mouthwash based on ozonated olive oil (Ialozon Blu, Gemavip, Italy) was prescribed twice a day for 3 weeks.

Follow-up visits

All patients underwent follow-up visits at 6 (T1), 12 (T2) and 24 (T3) weeks from the last topical application of Perioral3 and during which periodontal screening was performed and PD, BOP and PI were detected and noted in periodontal chart and in electronic database.

At the end of the observation period (T3), all patients were advised to use a toothpaste based on ozonated extra virgin olive oil (Ialozon Blu Toothpaste, Gemavip, Italy).

Statistical Analysis

The evaluation of the effects of the application of Perioral 3, in addition to mechanical debridement, on the clinical parameters of patients affected by peri-implant mucositis was carried out with specific statistical procedures for the parameter measurement scales. The binary parameters (presence / absence of plaque and bleeding at the site affected by PA) were evaluated by the Cochran Q test and, if significant for the 4 times, pairwise comparisons were evaluated with the McNemar test. Full Mouth Plaque Score (FMPS) and Full Mouth Bleeding Score (FMBS) are parameters expressed as a percentage and were evaluated by repeated measures ANOVA. Pocket depth, measured with a 5-level ordinal scale, was evaluated by Friedman's test and, if significant, pairwise comparisons were evaluated by Wilcoxon's test.

The significance threshold was set at 0.05 and Sidak's correction was applied for multiple comparisons (in pairs between the 4 times). SPSS 27.0 software was used to carry out the analyzes.

Results

Twelve male and eight female patients were recruited for the study. The twenty patients with an average age of 55.7 ± 9.3 and an average DMFT of 15.7 ± 3.9 were treated for peri-implant mucositis through the topical application of Perioral 3 in addition to mechanical debridement. The clinical parameters, PD, FMPS, FMBS, BoP and PI (of the site affected by mucositis), were collected at baseline and in the three observation periods (T1, T2 and T3). According to Cochran's Q Test the presence of plaque

and of BOP in the situs changes significantly across time ($p < 0.001$), however the changes occurred only with respect to the baseline evaluation when all patients showed the presence of plaque and of bleeding. (Table 2) Friedman test indicated significant changes in PD in each patient treated, both buccal and oral side. ($P < 0.001$). For oral (lingual/palatal) PD value, the reduction was significant at T1, T2 and T3 vs. T0 and at T3 vs T1, while for buccal PD value the reduction was significant at T1, T2 and T3 vs. T0 (Table 3 and 4).

BoP *

T0	T1	T2	T3
20	6	4	1

Table 2: Number of patients with bleeding on probing of the peri-implant mucosa in different timepoints.

Test Statistics^a

	PD_T1 - PD_T0	PD_T2 - PD_T0	PD_T3 - PD_T0	PD_T2 - PD_T1	PD_T3 - PD_T1	PD_T3 - PD_T2
Z	-3.207 ^b	-3.626 ^b	>-3.704 ^b	-2.449 ^b	-2.828 ^b	-1.414 ^b
Asymp. Sig. (2-tailed)	.001	.000	.000	.014	.005	0.157
				NS after Bonferroni correction	Significant after Bonferroni	NS

Table 3: Maximum PD value detected around the implant across the time for palatal/lingual side.

Test Statistics^a

	PD_T1 - PD_T0	PD_T2 - PD_T0	PD_T3 - PD_T0	PPD_T2 - PPD_T1	PPD_T3 - PPD_T1	PPD_T3 - PPD_T2
Z	-2.887 ^b	-3.217 ^b	-3.176 ^b	-2.236 ^b	-2.449 ^b	-.577 ^b
Asymp. Sig. (2-tailed)	.004	.001	.001	.025	.014	.564
				NS after Bonferroni correction	NS after Bonferroni correction	NS

Table 4: Maximum PD Value detected around the implant across the time for buccal side.

A statistically significant reduction was observed, using the ANOVA test, in FMPS and FMBS following treatment ($p < 0.001$).

Discussion

Implant-prosthetic rehabilitation represents a highly predictable treatment becoming the gold standard for the replacement of missing teeth. The increasing number of implants corresponds to an increasing number of complications. Among these, mucositis and peri-implantitis are the most relevant. [9] Intercepting and treating PM before it evolves into peri-implantitis constitutes a fundamental preventive measure to preserve the osseointegration of the fixture. Over time several clinical protocols for the treatment of PM have been proposed. They include mechanical debridement alone or with additional chemical decontamination. The present retrospective clinical study was conducted with the aim of evaluating the clinical effects of the ozonated extra virgin olive oil gel in the treatment of peri-implant mucositis. [14-17] Specifically, the restitutio ad integrum of the epithelial-connective tissue junction, undermined by bacteria and the inflammation sustained by them, was investigated. This study represents further evidence of the effectiveness of ozonated oil in addition to mechanical decontamination maneuvers. The clinical protocol described in this trial effectively made it possible to treat mucositis, reducing plaque and bleeding indices. These results are comparable with those obtained by McKenna and Colleagues [32].

The organoleptic characteristics of the product increased the patients' compliance and satisfaction for the treatment. In fact, no drop-out was recorded. The sensory properties of the products that are indicated to patients, as part of the TBM approach [12], must be carefully considered because they have a significant impact on the subjects' adherence and on the efficiency of the correct at-home oral hygiene procedures. The promising results of this clinical protocol underlined that the treatment of PM must consider mechanical and chemical decontamination of the inflamed site together, and also that motivation and patients' education with customized protocols are essential to achieve peri-implant soft tissue stability in the long follow-up.

The absence of side effects or complications in the six months of observation showed that products based on extra virgin olive oil can be safely and effectively administered even for a prolonged time, unlike chlorhexidine-based products [25]. Moreover, the lack of side effects of ozonated extra virgin olive oil is a non-negligible factor also because it makes the product suitable for daily use in the context of supportive therapy. Its biocompatibility with soft tissue cells and the absence of alcohol in its composition make it valid for administration in patients concomitantly suffering from other inflammatory diseases of the oral mucosa, such as lichen planus [36]. The presence of an oily vector constitutes a further advantage for ozone therapy with topical application, as the drug, due to its increased viscoelasticity, adapts well to the surface to be

treated, penetrating the depth of the site. This observation could justify the absence of statistically significant differences reported following the use of ozonated water in the treatment of mucositis, compared to the negative control group by Butera and colleagues. [37] A small sample size, a lack of a control group, a short follow-up period, are the main limitations for the present study. Further clinical studies will be needed to investigate with more details the effects of applying ozonated extra virgin olive oil gel on the peri-implant tissues. Also, considerations of patients with a gender-based approach is needed, as inflammatory conditions may vary between genders and different age groups.

Conclusion

Despite the limitations, the present study showed that ozonated extra virgin olive oil gel, due to its biocompatibility, organoleptic properties and the absence of toxicity and side effects, can represent an effective therapy for the chemical treatment of peri-implant mucositis.

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