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CLINICAL OUTCOMES AND MMP-8 LEVELS OF ADJUNCTIVE ER,CR:YSGG LASER THERAPY IN PERI-IMPLANTITIS TREATMENT

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Background: Peri-implantitis, a common inflammatory condition surrounding dental implants, results in implant failure without management. The classical mechanical debridement described previously is unlikely to respond to microbial recolonization or tissue inflammation. Various treatment modalities are also available including a 2780 nm Er,Cr:YSGG laser which seems to work on disease management and clinical outcome, with their specific targeting of biofilms and modification of the inflammatory response. To evaluate the combined effect of Er,Cr:YSGG laser and mechanical debridement on the clinical outcome and MMP-8 levels associated with treatment of peri-implantitis.

Methods: Forty subjects with peri-implantitis were randomly allocated to one of two groups: control (mechanical debridement alone) and the test (mechanical debridement and laser therapy). Clinical markers were assessed at baseline and within 3 months for plaque index (PI), gingival index (GI), pocket depth in peri-implant (PPD), and crestal bone loss (CBL), along with MMP-8. Statistical investigations included paired and independent t-tests up to $p < 0.05$ in significance.

Results: Both groups demonstrated significant improvements in PI, GI, and PPD ($p = 0.000$) after three months. However, the test group exhibited superior reductions in PI (0.34 ± 0.10 vs. 1.31 ± 0.19), GI (0.31 ± 0.07 vs. 1.43 ± 0.18), and PPD (1.84 ± 0.46 vs. 2.89 ± 0.14). MMP-8 levels also decreased significantly in the test group (1.31 ± 0.36 vs. 2.20 ± 0.18, $p = 0.000$). Crestal bone loss remained stable across groups ($p > 0.05$).

Conclusion: The adjunctive use of the Er,Cr:YSGG laser significantly enhanced clinical outcomes and reduced inflammatory markers in peri-implantitis treatment. This approach holds promise as an effective adjunctive therapy in clinical practice.

Keywords: Dental implants, Mechanical debridement, Non-surgical therapy, Peri-implant diseases, Peri-implantitis

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КЛІНІЧНІ РЕЗУЛЬТАТИ ТА ПОКАЗНИКИ MMP-8 ПРИ ЗАСТОСУВАННІ ER,CR:YSGG ЛАЗЕРА ЯК ДОДАТКОВОЇ ТЕРАПІЇ У ЛІКУВАННІ ПЕРІІМ-ПЛАНТИТУ

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Оцінено вплив Er,Cr:YSGG лазера (2780 нм) у поєднанні з механічним дебридментом на клінічні результати та рівні MMP-8 під час лікування періімплантиту. Сорок пацієнтів із періімплантитом були розділені на дві групи: контрольну (лише механічний

дебридмент) та тестову (механічний дебридмент плюс лазерна терапія). Клінічні параметри (індекс нальоту, ясневий індекс, глибина періімплантної кишені, втрата кісткової тканини) та рівні MMP-8 вимірювали на початку та через три місяці. Обидві групи продемонстрували значне покращення клінічних показників (p = 0,000). Проте тестова група показала кращі результати: зменшення індексу нальоту (0,34 ± 0,10 проти 1,31 ± 0,19), ясневого індексу (0,31 ± 0,07 проти 1,43 ± 0,18) та глибини кишені (1,84 ± 0,46 проти 2,89 ± 0,14). Рівні MMP-8 також значно знизилися (1,31 ± 0,36 проти 2,20 ± 0,18, p = 0,000). Додаткове застосування Er,Cr:YSGG лазера значно покращує клінічні результати та знижує запальні маркери при лікуванні періімплантиту.

Ключові слова: дентальні імплантати, механічний дебридмент, нехірургічна терапія, періімплантні захворювання, періімплантит.

Introduction

The field of implant dentistry, which began almost 40 years prior, radically changed the way patients viewed tooth replacement. This development, pioneered by Branemark, brought us precision-machined titanium screws to restore edentulous people. Although extremely effective, dental implants are not immune to complications since their failures primarily occur due to peri-implant diseases such as peri-implant mucositis and peri-implantitis. Peri-implant mucositis is the redness and swelling of the gum tissue and unless addressed, it may progress to more serious problems. Peri-implantitis, a more severe variant of infection, leads to bone loss around the implant and thereby may disrupt the implant stability and cause implant failure [1]. It follows that although oral implants are effective as a whole, these peri-implant diseases continue to have an important impact on the long-term outcome in their longevity.

Peri-implant diseases are mostly caused by bacteria, and some well-known pathogens have destructive virulence factors; however, the development of peri-implantitis is primarily influenced by the host immune response. When a dysbiotic microbial challenge causes an imbalance in the production of inflammatory mediators, host cells produce toxic substances. Excess production of these toxic products results in tissue degradation of oral implants. The triggering of the pathology is accompanied by immune-cell activation that affects the modulation of inflammatory mediators such as cytokines, chemokines, prostaglandins, and proteolytic enzymes. This dysregulation then impairs the integrity of connective tissue and bone metabolism [2].

Since the last ten years, researchers have increasingly invested more attention in investigating cytokines for inflammation including interleukin-1 beta (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) and enzymes such as matrix metalloproteinase-8 (MMP-8) and MMP-9 in the peri-implant crevicular fluid (PICF) to improve the estimation and detection of peri-implant diseases [3]. Neutrophil collagenase (MMP-8) is a main enzyme in the matrix metalloproteinase family, which consists of zinc–dependent proteases that play a critical role in the degradation of ECM. Several cell types produce MMP-8 including neutrophils, fibroblasts, and osteoclasts mediating its roles in physiological and pathological pathways including inflammation and tissue remodeling. MMP-8 specifically degrades type I collagen, the principal protein in connective tissue and bone. This breaking down of collagen can result in a reduction in the structural integrity of tissues and bones, which could result in alveolar bone loss – a critical attribute of peri-implantitis [4].

The main aim of the peri-implantitis treatment is to combat infection. The primary focus of extant clinical method for peri-implantitis management has largely focused on controlling the subgingival dysbiotic biofilm in the process of its therapeutic strategy in order to restore the balance between the microbial flora and host. This will involve some recommendations regarding good oral hygiene, or nonsurgical mechanical debridement of the peri-implant pockets. However, in spite of the paucity of studies evaluating the efficacy of peri-implantitis therapies, recent clinical trials, and systematic reviews suggest nonsurgical mechanical methods alone are not a conclusive treatment strategy to achieve disease control. This limitation is likely because of inadequate disinfection; these may enable the peri-implant pocket to recolonize itself by pathogenic microbes and aid in the disease progression. This recolonization often comes from pathogens previously embedded in peri-implant tissues. And local factors, including deep pockets, difficult root anatomy or rough implant surface may prevent proper and successful mechanical debridement [5].

The role of lasers in decontaminating infected implant surfaces and management of peri-implant inflammation has increased in recent years owing to the selective calculus removal process and their bactericidal and hemostatic properties. Erbium lasers have been shown to kill bacterial biofilms, effectively removing them from titanium disks, in vitro studies. Moreover, microscopic studies have confirmed that these lasers provide a safe operation and do not compromise the integrity of titanium implant fixtures [6]. In the light of this context, the present study aims to evaluate the effect of the 2780 nm erbium-chromium-yttrium-scandium-gallium-garnet (Er,Cr:YSGG) laser and mechanical therapy on clinical outcomes and MMP-8 in peri-implant crevicular fluid following non-surgical management of peri-implantitis.

Materials and Methods

1. Ethical Standards Compliance:

This prospective clinical trial was performed per the Helsinki Declaration and approved by Saveetha University Ethical Committee (IHEC/SDC/FACULTY/24/PERIO/263). Forty patients, aged 25-60 years, all with peri-implantitis (2017), as defined by European Federation of Periodontology and American Academy of Periodontology [7].

2. Informed Consent:

Participants were randomly assigned either the Mechanical Debridement or Laser Therapy condition (control = 20/20, test = 20/20). All persons provided written informed consent and were advised about the risks and benefits of the treatment. We used G*Power Software, Version 3.0, and the mean and standard deviation of a previous study [8], and significance (e.g., 0.05 and 80% power) produced 40 patients.

3. Study Protocol:

3.1. Patient Selection: Participants in this study were 25–60 years of age, and had one working dental implant in the mandibular first molar region for at least six months diagnosed with peri-implantitis. All implants were produced by the same company (SLA®, Straumann, Basel, Switzerland) and were covered with sandblasted, large-grit, acid-etched surfaces. All of these implants were installed at bone level using a platform-switched connection and loaded after three months by cement-retained, porcelain-fused-to-metal restorations. Patients had good periodontal and systemic health. The study excluded smokers, women who were pregnant or breastfeeding, individuals who had received antibiotics or other medications within the past six months, patients with systemic diseases, as well as individuals with both a current and a past history of periodontitis.

3.2. Mechanical Debridement and Laser Treatment Protocol: All participants underwent mechanical debridement with a sterile titanium curette (ImplacareTM II 204S, Hu-Friedy®, Chicago, USA), and peri-implant pockets were irrigated with 0.12% chlorhexidine gluconate. The same mechanical procedures were performed in both the control and test groups. On the same day as mechanical debridement, laser treatment was performed in the test group with the use of 2780 nm Er,Cr:YSGG laser (Waterlase, USA) with a 500 μm diameter, 14 mm long optic fiber tip. We set laser parameters at 1.5 W power, 75 Hz frequency, 40% air, and 50% water. Each patient received a new tip, and the rays were irradiated in parallel, sweeping motions from coronal to apical sites at a 15–30° angle toward the implant surface, at a rate of 1 mm/s. Standard oral hygiene instructions were provided to all participants.

3.3. Clinical Measurements: Clinical parameters such as plaque index (PI), gingival index (GI), and peri-implant probing depth (PPD) were evaluated. PI was determined with the Silness and Loe index and a mean score from four implant site surfaces (distal, mesial, facial, and lingual). GI was also measured by averaging the Loe and Silness index from four surfaces. PPD was measured by measuring the distance from the marginal gingiva to the sulcus base at six sites (mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual, and distolingual) with a probe (Hu-Friedy Colorvue®, Chicago, USA), as well as the average depth.

3.4. Radiographic Measurements: Digital periapical radiographs were obtained using the paralleling angle method. Crestal bone loss (CBL) was assessed by measuring the distance from the implant platform to the highest coronal bone level at mesial and distal sites, with the average recorded.

3.5. MMP-8 Analysis: Sterile cotton was used to isolate the selected implant sites while supragingival plaque was removed with sterile curettes. PICF was collected using microcapillary pipettes. The samples were then stored at –20 °C in order to further investigate the amounts of MMP-8 using an enzyme-linked immunosorbent assay kit. The Human MMP-8 ELISA Kit (Elabscience®, US) was used according to the manufacturer's protocol. The absorbance of the substrate color reaction was determined spectrophotometrically at 450 nm ± 2 nm and the values were reported in ng/mL. The detection range of the kit was 0.16–10 ng/mL.

Clinical and radiographic assessments and PICF collection were performed at baseline and at a 3-month follow-up.

3.6. Statistical Analysis: Data were analyzed using Statistical Package for the Social Sciences (SPSS, Version 23.0; IBM Corp., Armonk, NY, USA). There was a parametric distribution as shown by Shapiro-Wilk and Kolmogorov-Smirnov tests. We also compared groups for several variables: age, PI, GI, PPD, CBL, and MMP-8 levels using independent t-tests, and gender distribution through Chi-square. Intragroup comparisons with paired t-tests were computed. Statistical significance was defined at $p < 0.05$.

Research results and their discussion

Group 1 consisted of 11 males and 9 females with an average age of 45.2 ± 3.85 years and Group 2 consisted of 10 males and 10 females averaging 44.7 ± 3.89 years of age. Groups in the two groups showed no significant difference in gender and age (p-values of 0.72 and 0.75, respectively).

Table 1 shows comparisons at baseline and 3 months between control (Group 1) and test group (Group 2). Participants in both groups exhibited similar baseline indices of PI, GI, PPD, and MMP-8 levels ($p > 0.05$). At three months, however, the greater reductions for Group 2 in PI (0.34 ± 0.10 vs. 1.31 ± 0.19, $p = 0.000$), GI (0.31 ± 0.07 vs. 1.43 ± 0.18, $p = 0.000$), and PPD (1.84 ± 0.46 vs. 2.89 ± 0.14, $p = 0.000$) were remarkable. Group 2 also presented significantly lower MMP-8

Table 1

Intergroup comparison of clinical and biomarker outcomes at baseline and 3 months

Variable	Baseline Group 1 (Control)	Baseline Group 2 (Test)	p value (Baseline)	3-month Group 1 (Control)	3-month Group 2 (Test)	p value (3 months)
Plaque Index (PI)	2.03 ± 0.11	2.04 ± 0.12	0.736	1.31 ± 0.19	0.34 ± 0.10	0.000*
Gingival Index (GI)	2.04 ± 0.12	2.02 ± 0.16	0.674	1.43 ± 0.18	0.31 ± 0.07	0.000*
Peri-implant Pocket Depth (PPD)	4.87 ± 0.25	4.85 ± 0.25	0.855	2.89 ± 0.14	1.84 ± 0.46	0.000*
Crestal Bone Loss (CBL)	0.44 ± 0.03	0.43 ± 0.04	0.331	0.45 ± 0.04	0.44 ± 0.04	0.643
MMP-8 Levels (ng/mL)	4.30 ± 0.34	4.27 ± 0.37	0.819	2.20 ± 0.18	1.31 ± 0.36	0.000*

* – Statistically significant.

(1.31 ± 0.36 vs. 2.20 ± 0.18, p = 0.000). CBL remained stable in both groups (p > 0.05).

Table 2 shows intragroup improvements over 3 months. PI, GI, PPD and MMP-8 levels (p = 0.000; significantly lower in both groups) were also significantly lower in group 2 across groups, which demonstrated more favourable groupwise performance. These outcomes demonstrate the laser's higher effectiveness in improving clinical and inflammatory parameters.

Peri-implantitis due to the complex inflammatory conditions of the interstitial surrounding tissues of dental implants, makes it an important complication, which limits the success of these implants in a long-term period. Although mechanical therapy continues to play a decisive role in non-surgical treatment, its effectiveness may be improved by the addition of adjunctive technologies. Out of them; Er,Cr:YSGG laser in particular has been of interest for being able to improve clinically and molecularly. Here we aim to assess the synergistic effects of Er,Cr:YSGG laser treatment with the mechanical treatment in the treatment of peri-implantitis in terms of clinical parameters and biomarker dynamics.

We observed substantial improvements in three-month follow-up clinical outcomes for the key peri-implant parameters (plaque index [PI], gingival index [GI], probing pocket depth [PPD]). These results are consistent with previous studies showing the efficacy of laser therapy alongside mechanical debridement. Notably, the reduction in PPD is one of the most influential indicators of successful treatment for peri-implantitis management; it is more closely associated with reduced inflammation and tissue health. Yet, no significant changes in crestal bone loss (CBL) remained constant, indicating that long period of observation would be required to observe more clearly to consider the possible bone-level variations.

Previous studies have identified the success of the addition of laser therapy as an adjunct to treatment with peri-implantitis. In a randomized controlled trial of Chen JH et al. [9] 23 patients with PI were compared in Er:YAG laser therapy with mechanical debridement. Patients were randomized to Er:YAG laser or ultrasonic scaling. The effects on PPD, GI post-6 months after the intervention by both groups were significant, although they showed a significantly larger response with laser treatment leading to better decontamination and anti-inflammatory effects. An experimental study looked at the combination of erbium laser therapy with mechanical debridement in another group of 20 patients, comprising 32 implants with moderate-to-severe peri-implantitis. A review of clinical parameters including PI, GI, PPD, GR, and CAL at baseline, three months, and 6 months of follow-up. The combined treatment received significant improvement over all measures, indicating that the laser can facilitate tissue healing and decontamination [10]. For example, when erbium lasers were compared with air-abrasive devices in treating peri-implantitis, both methods proved to be effective; however, the erbium laser resulted in greater precision and preservation of surrounding tissues, indicating its utility in peri-implantitis management [11].

Pommer B et al. [12] also reported the highest success rates in peri-implantitis treatment using erbium laser decontamination versus implantoplasty or their combination. Likewise, Wang CW et al. [13] investigated the adjunctive use of an erbium laser in the surgical management of peri-implantitis associated with bone defects. In the study, patients had infrabony defects who underwent implantoplasty and bone grafting, and the test group received additional erbium laser therapy to remove inflammatory tissue and decontaminate the implant surface. At the 6 month follow-up period, the test group showed more significant reductions in pocket depth compared to the controls, demonstrating clinical improvement of both groups. Similar results were described by Schwarz F et al. [14]. The most recent meta-analysis concluded that Er:YAG lasers offer significant advantage to patients with peri-implantitis, encompassing effective decreases in pocket depth and gingival recession [15]. Consistent with our findings, our study showed large reductions in both PI, GI, and PPD in the peri-implantitis-affected implants as a result of the combination of laser therapy and mechanical debridement occurring within a 3-month period.

In addition to clinical parameters, our study found significant reductions in MMP-8 levels in patients treated with the combined therapy. According to the review, MMP-8, which is a major biomarker associated with tissue degeneration and inflammation, is a key indicator of the quality of peri-implant tissue. The decrease in MMP-8 levels might be one consequence of the anti-inflammatory action of Er,Cr:YSGG lasers. Alpaslan Yayli NZ et al. [16] studied how mechanical therapy applying 940 nm diode and 2780 nm Er,Cr:YSGG lasers to non-surgical peri-implantitis treatment improves response. The 50 patients

Table 2

Intragroup comparison of clinical and biomarker outcomes from baseline to 3 months

Variable	Baseline Group 1 (Control)	3-month Group 1 (Control)	p value (Group 1)	Baseline Group 2 (Test)	3-month Group 2 (Test)	p value (Group 2)
Plaque Index (PI)	2.03 ± 0.11	1.31 ± 0.19	0.000*	2.04 ± 0.12	0.34 ± 0.10	0.000*
Gingival Index (GI)	2.04 ± 0.12	1.43 ± 0.18	0.000*	2.02 ± 0.16	0.31 ± 0.07	0.000*
Peri-implant Pocket Depth (PPD)	4.87 ± 0.25	2.89 ± 0.14	0.000*	4.85 ± 0.25	1.84 ± 0.46	0.000*
Crestal Bone Loss (CBL)	0.44 ± 0.03	0.45 ± 0.04	0.672	0.43 ± 0.04	0.44 ± 0.04	0.731
MMP-8 Levels (ng/mL)	4.30 ± 0.34	2.20 ± 0.18	0.000*	4.27 ± 0.37	1.31 ± 0.36	0.000*

* – Statistically significant.

were randomized into three groups, namely mechanical therapy by itself, diode laser and Er,Cr:YSGG laser combination with mechanical therapy. At baseline and 6 months, clinical parameters (GI, PI, PPD) and MMP-9 levels were measured. In all conditions the improvements in GI, PI and PPD were significant, but the greatest decrease in the severity of PPD was achieved and MMP-9 decreased by the Er,Cr:YSGG group. The Er,Cr:YSGG laser showed better clinical and molecular efficacy.

In addition, Yamamoto A et al. [17] showed that surgical reconstructive therapy impacted different protein biomarkers as well as bacterial profiles in peri-implantitis and comparing the outcome with and without adding adjunctive Er:YAG laser application. Guided bone regeneration after mechanical debridement and characterization of bacteria and PICF samples were performed in patients over 6 months. Immune/microbial load was decreased because inflammatory markers – IL-1β and MMP-9 – were reduced substantially following treatment. Importantly, the group receiving Er:YAG laser therapy exhibited more pronounced reductions in inflammation and bacterial levels, indicating the high contribution of this laser to improve clinical and microbial outcomes during peri-implantitis healing. In line with these findings, a follow-up study also showed that non-surgical Er:YAG laser treatment mitigates peri-implant tissue destruction by decreasing MMP-9 levels in PICF.

Furthermore, based on a recent systematic review of 42 host-derived biomarkers, such as MMP-1, MMP-3, MMP-8, and MMP-9, reductions were recorded following adjunctive laser therapy in peri-implant disease management [18]. In addition to these observations, the combination treatment with mechanical debridement had a significant decrease in MMP-8 at each site of peri-implantitis at 3 months, a conclusion that emphasizes the dual therapeutic approach that is well documented in previous studies. Several possible mechanisms, in line with previous work, are proposed to clarify this phenomenon. Laser treatment with Er,Cr:YSGG laser is also effective in decreasing pro-inflammatory cytokines including IL-1β and TNF-α that are essential in the activation of MMPs including MMP-8. Laser therapy dampens the stimulation of the inflammatory reaction, reducing the induction of MMP-8 production [19]. Moreover, fibroblast proliferation and collagen synthesis by laser therapy facilitate tissue repair, lowering inflammation of tissue, and also suppressing levels of MMP-8 related to tissue degradation [20]. The Er,Cr:YSGG laser also effectively cuts through bacterial biofilms on implant surfaces, reducing bacterial load and subsequently the inflammatory response that drives MMP-8 and provides a significant boost to clinical effectiveness.

Hence the study emphasises the potential benefit for adding Er,Cr:YSGG laser therapy as an adjunct to non-surgical peri-implantitis treatment, indicating positive clinical and biomarker effects. The reliability is enhanced by the use of consistent peri-implantitis definitions, standardized implant characteristics (implant-abutment connections, platform switching, cement-retained porcelain-fused-to-metal crowns, etc.), and a single-team approach to surgical technique. Strict inclusion and exclusion criteria were followed to minimize host-related variability. However, there are several limitations; the periapical radiographs used in evaluation of crestal bone loss may not be sensitive enough for subtle changes and biomarker evaluation was limited to MMP-8. Long-term efficacy and molecular mechanisms underlying this novel treatment modality will be elucidated in research extending follow-ups and expanding biomarker analyses.

Conclusions

This study shows that Er,Cr:YSGG laser therapy with mechanical debridement for the non-surgical treatment of peri-implantitis can be effective. Clinical results were remarkably improved with reductions in the plaque index, gingival index, probing depth, and the MMP-8 levels. More studies with longer follow-up times are needed to definitively demonstrate the lasting benefits of this procedure. This novel combo therapy has much potential to advance the management of peri-implantitis.

Author Contributions

Conceptualization and study design: AR, SP, GM.

Methodology and clinical protocol: AR.

Data curation and investigation (patient recruitment/ clinical measurements/sample collection): AR.

Formal analysis: AR.

Writing–original draft: SP, HU.

Writing–review & editing: MMM, SP, HU, GM.

Supervision: MMM, HU, GM.

All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate. The study protocol was approved by the Ethics Committee (IHEC/SDC/FACULTY/24/PERIO/263). The study was conducted in accordance with the Declaration of Helsinki. Written informed consent for participation in the study and for the processing of personal data was obtained from all patients.

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Conflict of Interest. The authors declare no conflict of interest.

Availability of Data and Materials. The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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