ORIGINAL RESEARCH

Antimicrobial Photodynamic Therapy and Er,Cr:YSGG Laser-assisted Periodontal Pocket Therapy for Treatment of Aggressive Periodontitis: A Randomized Controlled Clinical Trial

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Abstract

Aim: The aim of this study is to evaluate and compare the clinical effects of Er,Cr:YSGG laser-assisted pocket therapy (ELAPT) and antimicrobial photodynamic therapy (aPDT) as an adjunct to scaling and root planing (SRP) on clinical outcomes of the treatment of aggressive periodontitis.

Materials and methods: Twenty patients with age between 18 and 35 years who were clinically diagnosed with aggressive periodontitis were selected from the outpatient department of periodontics. On the basis of inclusion and exclusion criteria three different sites were selected in each patient and then assigned randomly to three groups of treatment modalities: aPDT (Group I), ELAPT (Group II), or SRP (Group III-control). PD reduction and CAL gain were compared to the baseline values—baseline, 3, 6, and 9 months.

Results: Both the treatment modalities assessed, produced significant improvements in terms of the two outcome variables: PD reduction and CAL gain compared to the baseline values ($p < 0 < 0.05$) after 9 months, although no significant difference was seen between the two groups for PD reduction and CAL gain.

Conclusion: Within the constraints, this study has shown promising results for the treatment of aggressive periodontitis using both the latest modalities photodynamic therapy (aPDT) and ELAPT. Future research with larger sample size shall be done to evaluate the effects of these modalities.

Clinical significance: The treatment of aggressive periodontitis has always posed a challenge for clinicians, but there have been no established protocols and guidelines for the efficient control of the disease. Conventional adjunctive anti-infectious therapies like systemic antibiotics and local drug delivery are available as an adjunct to SRP but they have not proven to be effective. Antimicrobial photodynamic therapy or laser-assisted pocket therapy could be explored as new possibilities of antibacterial treatment and used as adjunct to SRP for the treatment of aggressive periodontitis.

Keywords: Aggressive periodontitis, Er, Cr:YSGG laser, Lasers, Photodynamic therapy.

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Introduction

Aggressive periodontitis is a rapidly progressing disease which affects the otherwise systemically healthy individuals. It is characterized by a marked episodic and rapid destruction of periodontal tissues that results in early tooth loss.[1,2] It has been a challenge for the periodontists to treat this disease as the protocols and guidelines for the effective control of the disease have not been established.[3] Patients suffering from aggressive periodontitis display an inadequate host response to periodontopathogenic bacteria due to an increased expression of a wide variety of immunological and genetic risk factors.[4,5] The prevention of disease is based on suppression or elimination of periodontopathogenic bacteria[6-8] such as *Aggregatibacter actinomycetemcomitans* (*Aa*), *Porphyromonas gingivalis* (*Pg*), *Treponema denticola*, and *Tannerella forsythia*.[9] Traditional methods of treatment have focused on SRP alone.[10] But the effectiveness of SRP alone is limited[11,12] due to the tissue invading capacity of Aa and Pg.[13-15] The use of systemically administered antibiotics like amoxicillin and metronidazole as an adjunct to SRP has been shown to be effective in reducing or eliminating Aa and Pg and to improve the clinical outcomes.[11,12,16] But the use of systemic antibiotics have undesirable side effects and patients may develop bacterial resistance.[17,18]

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Advances in technology has led to the introduction of newer antimicrobial therapies like photodynamic therapy and ELAPT. Antimicrobial photodynamic therapy works on the concept of elimination of cells by using a photosensitizing

agent (optical absorption dye) and a light source (low intensity laser with appropriate wavelength). So, it promotes removal of micro-organisms causing periodontal disease. Antimicrobial photodynamic therapy targets the bacterial cells present in the biofilms.[19–21] In recent years, laser therapy has been used as an adjunct to mechanical periodontal therapy because of various advantages of lasers like sterilization effects, inhibition of inflammatory process, acceleration of wound healing, and bactericidal effects against periodontal pathogens.[22–24]

Er,Cr:YSGG is a hard and soft tissue laser which works on the hydrokinetic principle with a wavelength nearly similar to the peak of coefficient of water which is absorbed by the lipopolysachharides leading to bactericidal effects. It has shown to have notable bactericidal effects on both Pg and Aa, which are the main periodontopathogenic bacteria.[25]

Therefore, the aim of this study is to evaluate and compare the clinical effects of Er,Cr:YSGG laser and aPDT as an adjunct to SRP on clinical outcomes of the treatment of aggressive periodontitis.

Materials and Methods

Patient Population

Twenty patients of either sex (7 males and 13 females, between the age of 18 and 35 years; mean age 25.15 ± 4.47 years) were selected from the patients referred to the Outpatient Department of Periodontics. Patients fulfilling the inclusion criteria were included in the study (registered at ClinicalTrials.gov as CTRI/2017/09/009753) after explaining the nature, potential risks, and benefits of their participation and obtaining a signed written informed consent. The study protocol was reviewed and approved by the Institutional Research Ethics Committee and was conducted in accordance with the Declaration of Helsinki of 1975, as revised in 2000.

Sample Size Calculation

Sample size calculation was done so that the power of the study was kept at 80% to recognize a significant difference of 1 mm between groups with a 95% confidence interval ($\alpha = 0.05$).

Inclusion and Exclusion Criteria

All patients were diagnosed with aggressive periodontitis. The selected patients had a minimum of 20 teeth, with at least one tooth in each posterior sextant and at least one posterior sextant with a minimum of three natural teeth and presence of ≥5 mm of attachment loss around at least seven teeth, excluding first molars and central incisors. Criteria for exclusion from the study were periodontal treatment within the last 6 months; systemic diseases that could influence the outcome of therapy; pregnancy; smoking; and ingestion of systemic antibiotics within the last 6 months.

Experimental Design

This split mouth, double blind; randomized controlled clinical trial was performed from February 2014 to December 2016.

Randomization and Allocation

Different quadrants were randomly allocated by lottery draw system to one of the three treatment groups [aPDT (Test I), ELAPT (Test II), or SRP (control group)].

Treatment Protocol

Patients were taken up for phase-I therapy which included thorough supragingival and subgingival SRP. The patients were placed on strict oral hygiene maintenance program. On re-evaluation after 4–6 weeks of initial therapy full mouth Plaque Index (PI), and Gingival Index (GI) were recorded, and treatment (aPDT or ELAPT) was planned only if the PI and GI scores were ≤1.

A total of 60 pairs of teeth were included from three different quadrants, each tooth of each quadrant exhibited a PD ≥5 mm on at least two aspects of the tooth. In each quadrant, one tooth was randomly treated, with aPDT (SRP+aPDTSRP+aPDT—Group I), ELAPT (SRP+ELAPT—Group II), or SRP alone (SRP—Group III). All patients were treated by the same experienced operator. Sites with deepest PD were selected for evaluation, and acrylic stents were fabricated for standardization of measurement of PD and CAL.

In the SRP+aPDTSRP+aPDT* (Helbo Photodynamic Systems, Walldorf, Germany) group, the photosensitizer was applied from the bottom of the periodontal pockets in a coronal direction. After 3 minutes, the pockets were rinsed with normal saline. The diode soft-laser light with a wavelength of 670 nm and a maximum power of 75 mW was used subgingivally. The irradiation was performed using an optical fiber probe of 0.6 mm in diameter. Light was applied in six sites of each tooth. Each site was irradiated for 10 seconds (power density, 0.25 W/cm^2; fluency per site, 2.49 J/cm^2; fluency per tooth, 14.94 J/cm^2).

For Er,Cr:YSGG laser assisted periodontal pocket therapy (Waterlase, Biolase, California, USA) (SRP+ELAPTSRP+ELAPT) no local anesthesia was given. The following settings were used for ELAPT: power—1 W, water—10%, air—12%, and frequency—20 Hz. A 600 µ sapphire laser tip (9 mm length) was used and inserted into the gingival sulcus till the base of the pocket. The laser tip was then retracted 1 mm from the base and activated. The tip was moved apico-coronally (vertically) and mesiodistally (horizontally) in brushing or sweeping motions in the pocket. The tip of the laser was pointed such that the energy would be directed parallel to the root and removing the inner epithelial lining of the sulcus. Each pocket was lased for 60 seconds.

Patients were given oral hygiene instructions, and recalled after 3, 6, and 9 months, for evaluation of clinical parameters.

Clinical Measurements

Clinical parameters GI, PD, and CAL were recorded at baseline, 3, 6, and 9 months after treatment. Plaque index was used to assess the oral hygiene of the participants.

Examiner Calibration

All clinical examinations were carried out by a non-blinded single examiner (KC). To assess the intra-examiner reliability, a calibration session was done using 10 non-study subjects. Full mouth PD scores were measured twice with 5 days interval. The intra-examiner correlation was calculated as 93.2% reproducibility.

Statistical Analysis

Statistical Package for Social Sciences (SPSS) Version 16 was used for the statistical analysis. The repeated measures ANOVA test was chosen for the multiple comparisons of the groups in mean PD and CAL. The *post hoc* Tukey's test was used for pairwise comparison among these groups. The significance level was set at 5% (confidence—95%). Data are presented as mean ± SD.

Results

All participants completed the study and reported 100% compliance. The postoperative healing was uneventful in all the cases.

No complications such as abscesses or infections were observed throughout the study.

The plaque scores and GI were significantly reduced compared to baseline. All treated pockets demonstrated a significant reduction in PDs and gain in clinical attachment in all the three groups. Table 1 shows mean PI before and after phase I therapy. The mean PI was below 1 after phase I therapy (0.77 ± 0.159).

Gingival index was measured for all the three groups at baseline, 3, 6, and 9 months. The mean GI was found to be 1.91 ± 0.177, 0.28 ± 0.29, 0.28 ± 0.245, and 0.16 ± 0.245 at baseline, 3, 6, and 9 months among the ELAPT group. Among the aPDT group, the mean GI was found to be 1.89 ± 0.314, 0.29 ± 0.235, 0.27 ± 0.221. and 0.28 ± 0.202 at baseline, 3, 6, and 9 months, respectively. The mean GI was found to be 1.97 ± 0.251, 0.27 ± 0.240, 0.27 ± 0.243, and 0.30 ± 0.234 at baseline, 3, 6, and 9 months among the SRP group. There was a statistically significant difference between the mean GI at baseline and at 3, 6, and 9 months among all the three groups (Table 2).

Probing Depth

The mean PD at baseline was 8.05 ± 1.928, 7.89 ± 0.994, and 7.89 ± 1.370 for aPDT, ELAPT, and SRP groups, respectively and there was no statistically significant difference between the groups at baseline. There was a significant reduction of mean PD at 3, 6, and 9 months in all the three groups. For aPDT group, the mean PD was 4.79 ± 1.183, 4.53 ± 1.645, and 4.21 ± 1.81 at 3, 6, and 9 months, respectively. For ELAPT group, the mean PD was 4.63 ± 1.739, 3.95 ± 1.470, and 4.11 ± 1.696 at 3, 6, and 9 months, respectively. For SRP group, the mean PD was 5.63 ± 1.382, 5.10 ± 1.286, and 4.84 ± 1.119 at 3, 6, and 9 months, respectively. When mean PD at baseline was compared with that at 3 months for the aPDT, ELAPT, and SRP groups, it was found to be statistically significant ($p < 0 < 0.05$). There was reduction in mean PD from 3 to 6 months in all the three groups but it was not statistically significant. The mean PD increased slightly in ELAPT group from 6 to 9 months but it was statistically insignificant (Table 3).

The mean PD reduction at 3 months was found to be 4.70 ± 1.809 among the aPDT group, 4.55 ± 1.731 among the ELAPT group, and 5.55 ± 1.394 among the SRP group. The mean PD reduction at 6 months was reported as 4.53 ± 1.645 among the aPDT group, 3.95 ± 1.470 among the ELAPT group, and 5.10 ± 1.286 among the SRP group. The mean PD reduction at 9 months was found to be 4.21 ± 1.813 among the aPDT group, 4.10 ± 1.696 among the ELAPT group, and 4.84 ± 1.119 among the SRP group. The mean PD reduction at 3, 6, and 9 months between the three groups was not found to be statistically significant ($p > 0 > 0.05$) when a comparison was done (Table 4).

This implies that although the PD decreased significantly in all the three treatment groups compared to baseline, but there was no statistically significant difference between the three treatment modalities (aPDT, ELAPT, and SRP).

Table 1: Comparison of full mouth plaque index before and after phase I therapy

Plaque index	*Mean ± SD*	*p value*
Before phase I therapy	1.41 ± 0.299	0.000*
After phase I therapy	0.77 ± 0.159	

*$p<0.05$

Clinical Attachment Level

The mean CAL was 8.00 ± 1.054, 4.68 ± 1.635, 4.26 ± 1.195, and 4.26 ± 1.628 at baseline, 3, 6, and 9 months, respectively among the ELAPT group. The mean CAL at baseline, 3, 6, and 9 months was 8.21 ± 1.902, 4.89 ± 1.969, 4.53 ± 1.645, and 4.37 ± 1.832, respectively among the aPDT group. The mean CAL was 8.21 ± 1.134, 5.94 ± 1.311, 5.37 ± 1.211, and 4.94 ± 1.129 at baseline, 3, 6, and 9 months, respectively among the SRP group. The comparison of mean CAL at baseline and at 3 months for aPDT, ELAPT, and SRP groups was found to be statistically significant ($p < 0 < 0.05$) whereas the comparison of mean CAL at 3–6 months and 6–9 months was not statistically significant for all the three groups (Table 5).

The mean CAL gain at 3 months was found to be 4.60 ± 1.635 among the aPDT group, 4.80 ± 1.962 among the ELAPT group, and 5.85 ± 1.348 among the SRP group. The mean CAL gain at 3 months between the three groups was found to be statistically significant ($p < 0 < 0.05$) upon comparison implying that aPDT and ELAPT are more effective in CAL gain at 3 months when used as an adjunct to SRP. At 6 months, the mean CAL gain was reported to be 4.53 ± 1.645 among the aPDT group, 4.26 ± 1.195 among the ELAPT group, and 5.27 ± 1.211 among the SRP group. There was a statistically significant difference ($p < 0 < 0.05$) in the mean CAL gain values among the three groups at 6 months. The mean CAL gain at 9 months was found to be 4.36 ± 1.832 among the aPDT group, 4.26 ± 1.628 among the ELAPT group, and 4.94 ± 1.129 among the SRP group. The mean CAL gain when compared at 9 months between the three groups, it was not found to be statistically significant ($p > 0 > 0.05$) (Table 4).

This implies that there was significant gain in CAL in all the three treatment groups compared to baseline. The difference in mean CAL gain was statistically significant at 3 and 6 months but was not statistically significant at 9 months showing that both aPDT and ELAPT are more effective in gaining clinical attachment loss when used as an adjunct to SRP at 3 and 6 months compared to SRP alone.

Discussion

In the present study, the clinical application of aPDT and ELAPT was tested as an adjunct to SRP for the treatment of aggressive periodontitis. Antimicrobial photodynamic therapy has many advantages like there is very low risk of developing photo-resistant species even after multiple treatments or inducing any mutagenic effects. Also, it has broad-spectrum activity against gram-positive and gram-negative bacteria, yeasts, fungi, and parasitic protozoa as well as inactivate viruses. It has been reported that aPDT can kill microbial cells rapidly (in minutes) specifically biofilm infections that are resistant to antimicrobials, compared to antibiotics and antifungals which can take days to work while allowing for selectivity against microorganisms vs host tissues.[26] Its main limitations are weak antimicrobial activity against gram-negative bacteria, solubility, specificity, and cost.[27]

When using Er,Cr:YSGG lasers for periodontal pocket therapy, they have shown very shallow penetration in tissue with a wavelength of 2.78 µm posing minimal thermal risk to the deeper tissues compared with other lasers and provide a better surface for the attachment of blood derived components on roots.[28,29] It is also reported that Er,Cr:YSGG laser increases cell attachment and migration on the root surfaces.[30]

In addition to the bacterial reduction, Er,Cr:YSGG lasers also help in coagulation of open blood vessels and de-epithelialization of

Table 2: Comparison of mean values of gingival index at baseline, 3, 6, and 9 months

GI	*ELAPT*	*aPDT*	*SRP*
Baseline	1.91 ± 0.177	1.89 ± 0.314	1.97 ± 0.251
3 months	0.28 ± 0.291	0.29 ± 0.235	0.27 ± 0.240
6 months	0.28 ± 0.245	0.27 ± 0.221	0.27 ± 0.243
9 months	0.16 ± 0.245	0.28 ± 0.202	0.30 ± 0.234
p value	0.000*	0.000*	0.000*

*$p<0.05$

Table 3: Comparison of mean values of probing depth at baseline, 3, 6, and 9 months

Probing depth	*ELAPT*	*aPDT*	*SRP*
Baseline	7.89 ± 0.994	8.05 ± 1.928	7.89 ± 1.370
3 months	4.63 ± 1.739	4.79 ± 1.183	5.63 ± 1.382
6 months	3.95 ± 1.470	4.53 ± 1.645	5.10 ± 1.286
9 months	4.11 ± 1.696	4.21 ± 1.81	4.84 ± 1.119
p value	0.000*	0.000*	0.000*

*$p<0.05$

Table 4: Comparison of mean values of probing depth reduction and CAL gain at baseline, 3, 6, and 9 months

		ELAPT	*aPDT*	*SRP*	*p value*
PD reduction	3 months	4.55 ± 1.731	4.70 ± 1.809	5.55 ± 1.394	0.129
	6 months	3.95 ± 1.470	4.53 ± 1.645	5.10 ± 1.286	0.062
	9 months	4.10 ± 1.696	4.21 ± 1.813	4.84 ± 1.119	0.303
CAL gain	3 months	4.60 ± 1.635	4.80 ± 1.962	5.85 ± 1.348	0.046*
	6 months	4.26 ± 1.195	4.53 ± 1.645	5.27 ± 1.211	0.041*
	9 months	4.26 ± 1.628	4.36 ± 1.832	4.94 ± 1.129	0.353

*$p<0.05$

Table 5: Comparison of mean values of clinical attachment level at baseline, 3, 6, and 9 months

CAL	*ELAPT*	*aPDT*	*SRP*
Baseline	8.00 ± 1.054	8.21 ± 1.902	8.21 ± 1.134
3 months	4.68 ± 1.635	4.89 ± 1.969	5.94 ± 1.311
6 months	4.26 ± 1.195	4.53 ± 1.645	5.37 ± 1.211
9 months	4.26 ± 1.628	4.37 ± 1.832	4.94 ± 1.129
p value	0.000*	0.000*	0.000*

*$p<0.05$

the gingival pocket.[31,32] The only disadvantage of Er,Cr:YSGG laser is that it is expensive.

Cases were selected on the basis of clinical diagnosis of aggressive periodontitis, i.e., patient age <35 years and rapid progression of periodontal disease as elicited by history. No antibiotics were used in this protocol; therefore, their adjunctive effect would not interfere with the results of either group. Data from the present study indicated that non-surgical treatment of aggressive periodontitis with aPDT or ELAPT as an adjunct to SRP led to statistically significant improvements in investigated parameters at 3, 6, and 9 months after treatment within the groups. But there was no statistically significant difference in the intergroup comparison for PD reduction at 3, 6, or 9 months. Although a statistically significant difference was seen between the groups in CAL gain at 3 and 6 months. These results were very difficult to compare since there are no similar clinical studies dealing with aggressive periodontitis.

Antimicrobial photodynamic therapy and laser therapy have been proposed as an alternative or adjunct to conventional SRP as a result of excellent tissue ablation, the ability to reach sites that conventional SRP cannot, and bactericidal and detoxification effects against bacterial pathogens in deep pockets. Photodynamic therapy has been suggested as an alternative to chemical antimicrobial agents to eliminate subgingival species and treat periodontitis. *In vitro* studies evaluating the use of aPDT on oral bacteria showed that the combination of a photosensitizer with low-power laser irradiation was effective in killing Aa, Pg, and Fusobacterium nucleatum[33] Theodoro et al.[34] has shown an improvement in all clinical and microbiological periodontal parameter at 180 days compared to baseline with the use of aPDT with SRP. A study by de Oliveira et al.[19] has reported significant reduction in PD and gain in CAL in the treatment of aggressive periodontitis at 3 months which is in concordance with the present study.

Dyer and Sung[35] reported that the use of Er,Cr:YSGG laser to treat moderate to advanced periodontal pockets along with SRP led to significant PD reduction and gain in CAL for more than 2 years. These results are similar to the present study.

Conventional SRP does not completely eliminate periodontal pathogens located in areas which are inaccessible to periodontal instrumentation.[36,37] Therefore, the use of other antimicrobial therapies like photodynamic therapy and lasers may be used as an adjunct to SRP.[19,35]

It has been reported that multiple episodes of aPDT adjunctive to non-surgical treatment did not improve significantly the clinical, immunological, and microbiological parameters when compared with SRP alone for periodontal treatment in smokers[38] whereas it has shown significant improvements in clinical parameters for the treatment of severe chronic periodontitis.[39]

Franco et al.[40] in their systematic review reported that it was not possible to state that repeated applications of aPDT, in association with non-surgical treatment of residual pockets, have effective clinical effects in the periodontal maintenance therapy.

With respect to the measurement of clinical outcome, there are several studies reporting conflicting results for the efficacy of laser assisted pocket therapy or aPDT as an alternative or adjunct to conventional SRP.[19,41-45] In a study reported by Borekci et al.[45] the use of PDT as an adjunct to non-surgical periodontal treatment does not lead to any beneficial effects in the treatment of generalized aggressive periodontitis.

Further investigations with larger sample size are required to evaluate the effects of both the modalities.

Conclusion

This randomized controlled clinical trial gives promising results for the treatment of aggressive periodontitis using photodynamic therapy and Er,Cr:YSGG laser assisted pocket therapy as an adjunct to SRP compared to SRP alone in terms of clinical attachment gain for first 6 months.

Ethical Approval

The study protocol was reviewed and approved by the Institutional Research Ethics Committee and was conducted in accordance with the Declaration of Helsinki of 1975, as revised in 2000.

Informed Consent

A signed written informed consent was obtained from the study participants after explaining the nature, potential risks, and benefits of their participation in the study.

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