Clinical effects of photodynamic and low-level laser therapies as an adjunct to scaling and root planing of chronic periodontitis: A split-mouth randomized controlled clinical trial

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ABSTRACT

Background: There are limited clinical experiments addressing the effects of photodynamic therapy (PDT) and low-level laser therapy (LLLT) as an adjunct to conventional scaling and root planning (SRP) alone.

Aim: The aim of this clinical trial was to evaluate the clinical effects of adjunctive use of PDT, combination of PDT with LLLT as adjunct to conventional SRP alone in the treatment of chronic periodontitis.

Materials and Methods: In a single-centered randomized and controlled clinical trial, 24 patients (15 males and 9 females) with untreated chronic periodontitis were randomly assigned in a split-mouth design into three treatment groups which included Group I: SRP only, Group II: SRP and PDT (1% methylene blue [MB] solution), and Group III: SRP, PDT, and LLLT. Clinical parameters such as plaque index, gingival index, modified sulcular bleeding index, probing depth (PD), and clinical attachment level (CAL) were measured at baseline, 1, 3, and 6 months after therapy.

Results: Within each group, significant improvements ($P < 0.001$) were found for all variables in 6-month follow-up compared with baseline. The improvement in clinical parameters was significantly greater in Group III compared to Group I and Group II. The mean PD (mm) reduction from baseline to 6 months in Group I was $2.50 \pm 0.54$, Group II was $2.57 \pm 0.53$, and Group III was $3.14 \pm 0.50$. The mean CAL (mm) gain from baseline to 6 months in Group I was $2.63 \pm 0.47$, Group II was $2.55 \pm 0.44$, and Group III was $3.07 \pm 0.55$.

Conclusion: In patients with chronic periodontitis, a combination of a single application of PDT (using a 980 nm laser and MB) and LLLT provide additional benefit to SRP in terms of clinical parameters 6 months following the intervention.

Key words: Dental scaling, low-level laser therapy, photodynamic therapy, root planing

Periodontitis is a multifactorial disease that is associated with loss of the supporting tissues (i.e., periodontal ligament and alveolar bone) around the tooth. A major objective of periodontal therapy is to remove soft and hard, supra- and sub-gingival deposits from the root surface to stop disease progression. Mechanical scaling and root debridement have shown to be an effective treatment approach for periodontal disease. However, the limitations of scaling and root debriding have

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also been shown in the management of initially deep periodontal pockets and furcation involved lesions.[5]

In the last decade, applying lasers as an adjunctive or alternative to current mechanical treatment had a great run in the treatment of gingival inflammation.[4] Among laser applications, low-level laser therapy (LLL) is recommended for its pain reducing, wound healing promoter, and anti-inflammatory effects.[5]

Photodynamic therapy (PDT) has emerged in recent years as a new noninvasive therapeutic modality for the treatment of various infections by bacteria, fungi, and viruses.[6] This therapy is defined as an oxygen-dependent photochemical reaction that occurs on light-mediated activation of a photosensitizing compound that leads to the generation of cytotoxic reactive oxygen species, predominantly singlet oxygen.[7] This therapy can be applied topically to a periodontal pocket, hence avoiding overdoses. Other advantages of PDT include reducing the probability of side effects associated with the systemic administration of antimicrobial agents and minimizing bacterial resistance. The activities of virulence factors of Gram-negative bacteria are also reduced with PDT.[8] Among the many photosensitizers, cationic phenothiazinium, as toluidine blue O (TBO) and methylene blue (MB), was shown to be phototoxic to Gram-negative bacilli with red light irradiation.[9]

Taken together, it is conceivable that PDT in combination with LLLT might have biologically synergistic effects on control of microbial infections and the resultant inflammatory response as well as on the promotion of tissue healing. At present, to our knowledge till date, there are no long-term studies which combine PDT and LLLT as an adjunct to conventional scaling and root planing (SRP) alone of chronic periodontitis.

**MATERIALS AND METHODS**

The present split-mouth triple blinded randomized controlled clinical trial was carried out at a single center, comparing the clinical effects of the adjunctive use of a single episode of PDT, combination of PDT with LLLT as an adjunct to conventional SRP alone in the treatment of chronic periodontitis. The patients for this study were selected from outpatient section. The Ethical Committee of the Institution approved the study.

A distinction was made between chronic and aggressive periodontitis by clinical and radiographic findings as per the diagnostic features established from the literature. The basic differences used for diagnosis were age of onset, local factors in relation to site and amount of destruction, familial history, and radiographic findings. Chronic periodontitis was diagnosed by macroscopic, radiography, and probing pocket depth ≥5 mm. The dentition of the patients displayed at least one site in each quadrant of the mouth having probing depth (PD) ≥ 5mm and radiographic signs of alveolar bone loss. About 1% MB was used as a photosensitizer and 980 nm Diode Laser (DenLase, the Diode Laser Therapy System, from China Daheng Group, Inc.) was used in the present study.

**Inclusion criteria**
- Age: 18–60 years
- At least twenty teeth present
- At least one site in each quadrant of the mouth having probing depth ≥5 mm
- Signed informed consent.

**Exclusion criteria**
- Pregnant or lactating females
- Deleterious habits such as smoking and/or alcohol consumption
- Use of antibiotics within 6 months prior to the study
- Active periodontal treatment within last 6 months
- Systemic disease.

**Screening and examinations**
A total of 45 patients were screened out of which 24 patients in the age group of 24–55 years (15 males and nine females) were enrolled in the clinical trial. The following clinical parameters Plaque index (PI),[10] Gingival index (GI),[11] modified sulcular bleeding index (mSB1),[12] PDs, and clinical attachment level (CAL) were recorded at baseline, 1, 3, and 6 months. The probing pocket depth and CALs were measured using UNC-15 graduated periodontal probe. Measurements were done at selected sites. All measurements were performed by one experienced periodontal examiner, allowing an intra-experimental comparison of the values. Percentage agreement with another examiner within 1 mm was >96%. The probing angulation was standardized using an acrylic stent, on which a groove was marked representing the site chosen for the treatment based on the chart measurements earlier made on the patient. The reading was recorded to the nearest millimeter.

**Randomization**
After baseline examination, a simple randomization approach[13] using computer-generated random numbers was employed to assign patients in a split-mouth design (the sequence was concealed until interventions were assigned) to one of the following treatment modalities:
- Group I: SRP only
- Group II: SRP and single episode of PDT using 1% MB solution as a photosensitizer
- Group III: SRP, single episode of PDT using 1% MB solution and LLLT using a diode laser.

**Periodontal and adjunctive laser treatments**
On the first appointment, all patients received routine oral hygiene instructions and one-stage full-mouth conventional SRP employing both hand instruments (Hu-Friedy,
USA) and a piezoelectric ultrasonic handpiece (EMS) under local anesthesia of 2% lidocaine with 1:80000 adrenaline (Lignox 2% A; Indoco Remedies Ltd., L-32, Goa).

After SRP, the test teeth in Group III received additional LLLT using a biostimulation probe [Figure 1] provided by the manufacturer (DenLase; China Daheng Group, Inc., Beijing China). The laser was fired at the orifice of the gingival margin at a distance of approximate 1–2 mm, using a setting of 1.5W as a continuous wave. Each tooth received 3 min of exposure. The patients returned after 2 days for the final LLLT on the same test teeth.

On the second appointment, i.e., after 24 h the test teeth in Group II and Group III underwent a single episode of PDT. The periodontal pockets were filled with a 1% MB solution as photosensitizer employing a blunt cannula [Figure 2] starting from the bottom of the pocket to achieve both a complete filling of the pocket and coating of the root surface, which was left for 3 min before any excess was gently rinsed away. The remaining photosensitizer was activated for 30 s to 45 s per site [Figure 3]. The diode laser (DenLase; China Daheng Group, Inc. Beijing CHINA) was operated at a peak power of 5.0 W, with a pulse length of 200 µs and pulse interval of 200 µs (average power 1.0 W), using a 400 µm fiber-optic tip and a wavelength of 980 nm. The tip was initiated and introduced into the pocket with a smooth stroking action, starting coronally, and working toward the bottom of the pocket. Oral hygiene instructions were reinforced at 1, 3, and 6 months after the treatment.

Statistical analysis
The data were analyzed using the SPSS-software 19.00 program (SPSS Inc., Chicago, IL, USA). The intra-group comparison of PI scores and GI scores were compared between Group I, Group II, and Group III at various study intervals using Kruskal–Wallis one-way ANOVA test and inter-group comparison were done by using Mann–Whitney U-test. The intra-group comparison of clinical parameters such as mSBI, PD, and CAL was compared between Group I, Group II, and Group III at various study intervals using one-way ANOVA test and inter-group comparison was done by using Tukey’s multiple post hoc test. Differences were considered as statistically significant at $P < 0.001^*$. 

RESULTS
All 24 patients completed the 6 months study, with no patients reporting any postoperative pain, discomfort, or complications at any of the follow-up appointments. The approach of patients appeared to be positive toward the laser. Mean and standard deviation age in all the groups for males was 36.73 ± 8.46 and for females was 34.33 ± 6.80.

Significant reductions of PI scores were observed in all the groups from baseline to 1-month interval, highest reduction of PI score was observed in Group III [Table 1]. The inter-group comparison revealed the reduction of PI scores was
statistically significant between Groups I–III at 3 months, and between Groups II–III at 3 months and 6 months. Reduction in GI scores were highest at 1 month, 3 months, and at 6 months in Group III, which were found to be statistically significant (\( P < 0.001 \)) [Table 2]. Reduction in mSBI scores was highest at 3 months and at 6 months in Group III, which were found to be statistically significant (\( P < 0.001 \)) [Table 3].

Reduction in PD scores was highest 1 month, 3 months, and at 6 months in Group III, which were found to be statistically significant (\( P < 0.001 \)) [Table 4]. The inter-group comparison of reduction in PD scores at all the study intervals as shown in Table 4 between Groups I and II was not statistically significant. Inter-group comparison of PD scores between Groups II and III was statistically significant at 3 months and 6 months. Significant reductions of CAL scores were observed in all the groups at various intervals; however, reduction in CAL scores was highest 1 month, 3 months, and at 6 months in Group III, which were found to be statistically significant (\( P < 0.001 \)) [Table 5].

PDT can achieve excellent tissue ablation with strong bactericidal and detoxification effects, one of the most promising new technical modalities for nonsurgical periodontal treatment by avoiding antimicrobial treatment. The adjunctive or alternative use of LLLT with PDT may facilitate treatment and has the potential to improve healing.

### DISCUSSION

In the initial phase of periodontal therapy, debridement of the diseased root surface is nonsurgically treated by mechanical SRP, primarily by using manual or power-driven instruments. However, complete removal of bacterial deposits and their toxins from the root surface within the periodontal pockets is not always achieved with only the use of conventional mechanical therapy.\(^{[14]}\) Recently, the benefits of lasers, such as ablation, bactericidal, and detoxification effects, as well as photo-biomodification, have been reported to be useful for the periodontal pocket.

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**Table 1: Inter-group comparison of Groups I, II, and III with plaque index scores at different time points by Mann-Whitney U-test**

| Groups              | Means±SD                  | Reduction from baseline to study interval time                  |
|---------------------|---------------------------|------------------------------------------------------------------|
|                      | Baseline 1\(^{st}\) month | 3\(^{rd}\) month | 6\(^{th}\) month | Baseline - 1\(^{st}\) month | Baseline - 3\(^{rd}\) month | Baseline - 6\(^{th}\) month |
| Group I             | 2.49±1.73                 | 1.21±0.89          | 0.76±1.28          | 1.60±0.52              | 0.84±0.32             | 1.49±0.53             | 1.69±0.47             |
| Group II            | 2.54±1.70                 | 1.21±0.82          | 0.84±1.33          | 1.73±0.49              | 0.89±0.39             | 1.73±0.34             | 2.01±0.41             |
| Group III           | 2.53±1.56                 | 0.75±0.26          | 0.97±1.78          | 2.27±0.81              | 1.30±0.49             | 1.70±0.48             | 1.95±0.44             |
| Groups I versus II (P) | 0.2420               | 0.8920             | 0.901              | 0.7320               | 0.4010               | 0.6420               | 0.6420               |
| Groups I versus III (P) | 0.4930             | 0.2040             | 0.001*             | 0.000*             | 0.0580               | 0.0010*             | 0.0000*             |
| Groups II versus III (P) | 0.8350             | 0.2940             | 0.004*             | 0.000*             | 0.2160               | 0.0060*             | 0.0010*             |

*\( P < 0.001 \), statistically significant. SD=Standard deviation

**Table 2: Inter-group comparison of Groups I, II, and III with gingival index scores at different time points by Mann-Whitney U-test**

| Groups              | Means±SD                  | Reduction from baseline to study interval time                  |
|---------------------|---------------------------|------------------------------------------------------------------|
|                      | Baseline 1\(^{st}\) month | 3\(^{rd}\) month | 6\(^{th}\) month | Baseline - 1\(^{st}\) month | Baseline - 3\(^{rd}\) month | Baseline - 6\(^{th}\) month |
| Group I             | 2.42±0.31                 | 1.57±0.39          | 0.91±0.36          | 0.63±0.34              | 0.84±0.37             | 1.50±0.34             | 1.78±0.37             |
| Group II            | 2.33±0.42                 | 1.51±0.44          | 0.94±0.38          | 0.54±0.25              | 0.82±0.43             | 1.39±0.44             | 1.79±0.49             |
| Group III           | 2.36±0.38                 | 1.52±0.35          | 0.77±0.31          | 0.19±0.18              | 0.84±0.28             | 1.59±0.36             | 2.17±0.45             |
| Group I versus Group II (P) | 0.6600             | 0.7630             | 0.8510             | 0.3110               | 0.8350               | 0.3500               | 0.7010               |
| Group I versus Group III (P) | 0.7940             | 0.6850             | 0.1750             | 0.0000*             | 0.6790               | 0.2570               | 0.0010*             |
| Group II versus Group III (P) | 0.8740             | 0.9500             | 0.1720             | 0.0000*             | 0.5210               | 0.1010               | 0.0040*             |

*\( P < 0.001 \), statistically significant. SD=Standard deviation

**Table 3: Inter-group comparison of Groups I, II, and III with modified sulcular bleeding index scores different time points by Tukey’s multiple post hoc test**

| Groups              | Means±SD                  | Reduction from baseline to study interval time                  |
|---------------------|---------------------------|------------------------------------------------------------------|
|                      | Baseline 1\(^{st}\) month | 3\(^{rd}\) month | 6\(^{th}\) month | Baseline - 1\(^{st}\) month | Baseline - 3\(^{rd}\) month | Baseline - 6\(^{th}\) month |
| Group I             | 2.22±0.27                 | 1.54±0.32          | 0.82±0.37          | 0.46±0.24              | 0.69±0.28             | 1.41±0.44             | 1.77±0.34             |
| Group II            | 2.24±0.22                 | 1.46±0.34          | 0.80±0.29          | 0.42±0.22              | 0.78±0.30             | 1.43±0.32             | 1.81±0.31             |
| Group III           | 2.19±0.34                 | 1.45±0.34          | 0.61±0.21          | 0.19±0.13              | 0.75±0.40             | 1.58±0.41             | 2.00±0.39             |
| Groups I versus II (P) | 0.9880             | 0.6830             | 0.9890             | 0.0700*             | 0.6060               | 0.9750               | 0.8960               |
| Groups I versus III (P) | 0.9110             | 0.6160             | 0.0500*             | 0.8420             | 0.8240               | 0.2990               | 0.8500*             |
| Groups II versus III (P) | 0.8420             | 0.9940             | 0.0700              | 0.8420             | 0.9300               | 0.4100               | 0.1510               |

*\( P < 0.001 \), statistically significant. SD=Standard deviation
Table 4: Inter-group comparison of Groups I, II, and III with probing depth scores different time points by Tukey's multiple post hoc test

| Groups          | Baseline Mean±SD | 1st month Mean±SD | 3rd month Mean±SD | 6th month Mean±SD | Reduction from baseline to study interval time Mean±SD |
|-----------------|------------------|-------------------|-------------------|------------------|------------------------------------------------------|
|                 |                  |                   |                   |                  | Baseline - 1st month Baseline - 3rd month Baseline - 6th month |
| Group I         | 6.16±0.40        | 5.22±0.51         | 4.43±0.47         | 3.65±0.49        | 0.94±0.42 1.72±0.47 2.50±0.54 |
| Group II        | 6.13±0.38        | 5.09±0.42         | 4.28±0.39         | 3.57±0.41        | 1.04±0.28 1.85±0.41 2.57±0.53 |
| Group III       | 6.36±0.40        | 5.24±0.48         | 4.12±0.47         | 3.23±0.29        | 1.12±0.53 2.25±0.62 3.14±0.50 |
| Groups I versus II (P) | 0.9720 | 0.6130 | 0.4660 | 0.0440* | 0.6800 0.6610 0.9140 |
| Groups I versus III (P) | 0.1660 | 0.9830 | 0.0470* | 0.7390 | 0.2900 0.0020* 0.0000* |
| Groups II versus III (P) | 0.1050 | 0.5050 | 0.4340 | 0.7390 | 0.7780 0.0240* 0.0010* |

*P<0.001, statistically significant. SD=Standard deviation

Table 5: Inter-group comparison of Groups I, II, and III with clinical attachment level scores at different time points by Tukey's multiple post hoc test

| Groups          | Baseline Mean±SD | 1st month Mean±SD | 3rd month Mean±SD | 6th month Mean±SD | Reduction from baseline to study interval time Mean±SD |
|-----------------|------------------|-------------------|-------------------|------------------|------------------------------------------------------|
|                 |                  |                   |                   |                  | Baseline - 1st month Baseline - 3rd month Baseline - 6th month |
| Group I         | 6.63±0.53        | 5.84±0.64         | 4.83±0.49         | 4.00±0.39        | 0.79±0.38 1.80±0.38 2.63±0.47 |
| Group II        | 6.59±0.50        | 5.71±0.41         | 4.84±0.38         | 4.04±0.37        | 0.88±0.27 1.75±0.36 2.55±0.44 |
| Group III       | 6.76±0.59        | 5.67±0.60         | 4.57±0.69         | 3.69±0.52        | 1.09±0.34 2.19±0.48 3.07±0.55 |
| Groups I versus II (P) | 0.9680 | 0.7080 | 0.9990 | 0.1940 | 0.6240 0.0230 0.8370 |
| Groups I versus III (P) | 0.6800 | 0.5470 | 0.2110 | 0.9400 | 0.0080* 0.0040* 0.0070* |
| Groups II versus III (P) | 0.5290 | 0.9640 | 0.1940 | 0.9400 | 0.0080* 0.0010* 0.0010* |

*P<0.001, statistically significant. SD=Standard deviation

treatment, and the application of lasers has been suggested as an adjunctive or alternative tool to conventional periodontal mechanical therapy.\cite{15}

Recently, PDT has been used to treat localized microbial infections because the free radicals that are formed during PDT might be toxic to the bacteria. Biostimulation has been reported in the literature with doses between 0.001 and 10 J/cm² as a therapeutic window.\cite{16} LLLT also decreases the amount of inflammation and accelerates wound healing by changing the expression of genes responsible for the production of inflammatory cytokines in vivo.\cite{17}

This study is a first of its kind to investigate the long-term clinical effects of PDT and combined course of a single episode of PDT with LLLT as an adjunct to nonsurgical mechanical therapy in the treatment of chronic periodontitis. In a recent study by Lui et al.,\cite{18} PDT was combined with LLLT as a synergistic treatment modality, and no attempt was made to distinguish their respective therapeutic effects. To our knowledge, there are no studies which investigated all the three treatment modalities (SRP, PDT, and LLLT) clinically on a long-term basis, and thus prompted us to explore further to find their efficacy in the treatment of chronic periodontitis.

Qadri et al.\cite{19} reported a significant decrease in PI values, on the laser-treated side, in accordance with this study for Group II. Yilmaz et al.\cite{20} compared SRP + PDT versus SRP alone, but there were no statistically significant differences.

In the present study, by inter-group comparison, the mean GI difference from baseline to 6 months, there was statistical significance between Group I versus Group III and Group II versus Group III however no significance between Group I versus Group II. This indicates that adjunctive use of PDT and LLLT is better than PDT and SRP alone in the reduction of PI scores. Even though the methodology of studies were not the same, Qadri et al.\cite{19} found in their study that additional treatment with low-level lasers reduced periodontal gingival inflammation and PD; the results of our study are parallel to their study. Contrary to our findings, Lai et al.\cite{21} suggested that low-power laser did not result in any additional clinical benefit. This might be a result of their application power density being low (2.83 mW/cm²) and having limited application sites. The use of different kinds of lasers, doses, and duration preclude a comparison of these studies with our study.

In the present study, by inter-group comparison, the mean mSBI difference from baseline to the 6th month observation period in all the three groups. By inter-group comparison, the mean mSBI difference from baseline to the 6th month, there was a statistical significance between Group I versus Group III at the end of the 3rd month and Group I versus Group II at the end of the 6th month; however, no significance between Group II versus Group III was
observed. This indicates that the adjunctive use of combined PDT and LLLT is better than PDT and SRP alone in the reduction of mSBI scores. Lui et al.\textsuperscript{[18]} (SRP + PDT + LLLT) reported a significant reduction in the percentage of sites with bleeding on probing from 84% at baseline to 8% at 3 months ($P < 0.001$) compared to SRP alone which is in accordance with our study for Group III.

In a recent study by Lui et al.\textsuperscript{[18]} the test teeth (SRP + PDT + LLLT) exhibited a greater reduction in mean PD at 1 month when compared to control teeth (SRP alone). In our study, a greater reduction in mean PD at the end of 3 months was seen in Group III as compared to Group I. There was a statistical significant increase in CAL gain in Group I and Group II however inter-group comparison was found to be statistically insignificant.

**CONCLUSION**

Dentistry is varying with induction of modern science to practice dentistry.\textsuperscript{[23]} The present clinical trial suggests that all the three treatment strategies seem to benefit the patients with chronic periodontitis, combination of a single application of PDT (using 980 nm Diode laser and MB) and LLLT provide additional benefit to SRP in terms of clinical parameters 6 months following the intervention compared to the other two groups.

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**Conflicts of interest**

There are no conflicts of interest.

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