Treatment of Periodontal Disease by Photodisinfection Compared to Scaling and Root Planing

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Abstract

• **Objective:** The aim of the present study was to compare the effectiveness of a photodisinfection process to that of scaling and root planing (SRP) for non-surgical periodontal treatment.

• **Methodology:** Thirty-three subjects with moderate to advanced periodontal disease were randomly treated in one of three study arms with either photodisinfection (PD) alone (Group 1) using a diode laser and photosensitizer combination, with SRP alone (Group 2), or with SRP and PD combined (Group 3). Clinical assessments of bleeding on probing (BOP), probing pocket depth (PPD), and clinical attachment level (CAL) were made at baseline, three weeks, six weeks, and 12 weeks following therapy.

• **Results:** No difference in any of the investigated parameters was observed at baseline between the three groups. The mean value of BOP decreased in the PD group (Group 1) from baseline by 71% at six weeks and 73% at 12 weeks, and in the SRP alone group (Group 2) from baseline by 43% at six weeks and 56% at 12 weeks. The BOP in the combined SRP + PD group (Group 3) decreased from baseline by 65% at six and 59% at 12 weeks. The sites treated with PD alone demonstrated mean CAL gains of 0.09 ± 0.38 mm and 0.14 ± 0.65 mm at six and 12 weeks, respectively. Those sites treated with SRP alone demonstrated mean CAL gains of 0.37 ± 0.34 mm and of 0.36 ± 0.35 mm at six and 12 weeks, respectively. The final group of SRP + PD demonstrated mean CAL gains of 0.92 ± 0.62 mm and 0.86 ± 0.61 mm at six and 12 weeks, respectively (p < 0.01 for six weeks and p < 0.02 for 12 weeks when compared to SRP alone). The sites treated with SRP alone demonstrated mean PPD reductions of 0.78 ± 0.47 mm and 0.74 ± 0.43 mm at six and 12 weeks, respectively. Those sites treated with SRP alone demonstrated mean PPD reductions of 0.78 ± 0.47 mm and 0.74 ± 0.43 mm at six and 12 weeks, respectively. The final group of SRP + PD demonstrated mean PPD reductions of 1.16 ± 0.39 mm and 1.11 ± 0.53 at six and 12 weeks, respectively (p < 0.06 for six weeks and p < 0.05 for 12 weeks when compared to SRP alone).

• **Conclusion:** Within the limits of the present study, it can be concluded that SRP combined with photodisinfection leads to significant improvements of the investigated parameters over the use of SRP alone.

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Introduction

Periodontitis is an inflammatory reaction of the tissues surrounding a tooth, usually resulting from the extension of gingival inflammation induced by the bacteria residing in the plaque biofilms on the subgingival tooth surface. This inflammation can cause long junctional epithelium loss in the normally healthy sulcus, thereby developing periodontal pockets. Further connective tissue attachment loss, formation of intrabony defects, and, ultimately, the possible loss of the tooth can result. This multifactorial disease affects up to 30-50% of the adult population, and is associated with local as well as systemic symptoms. The chronic nature, as well as the complexity and variety of the associated subgingival bacterial biofilms, are responsible for the numerous virulence factors and inflammatory markers characteristic of chronic periodontitis. Mechanical removal of the biofilms has been the conventional approach to periodontitis therapy. Various local and systemic antibiotic regimens have been utilized in the treatment of periodontitis, but in most cases only slight improvements over mechanical debridement have been noted, along with concern about the development of increasing antibiotic resistance. Numerous other therapies have been advocated for the treatment of periodontal disease with similar results. This work examines the effect of a new subgingival chemotherapeutic regimen, called photodynamic disinfection, in the treatment of periodontal disease.

Over the past decade, extensive investigation has been carried out into the antimicrobial action of photosensitizing agents and light. When certain molecules absorb light, they may undergo an electronic transition to the singlet excited state (electron spins paired). The excited state can decay back to the ground state through a triplet (electron spins unpaired), and this triplet state can transfer energy directly to molecular oxygen (one of the few biological molecules naturally found in a triplet ground state). The triplet energy exchange can cause oxygen to undergo an electronic transition to its singlet state, and this highly reactive moiety can cause microbial cell death by several mechanisms, including lipid peroxidation, enzyme system inhibition, protein agglutination, and by reaction with other biological systems. Wilson first proposed the use of lethal photosensitization as a tool for the treatment of periodontal disease. This was initially shown
to be effective in rats with the killing of Porphyromonas gingivalis and the associated decreased bone loss.\(^5\)

There are numerous compounds exhibiting photosensitizing properties, and it therefore becomes essential to choose a compound meeting certain criteria, such as selective binding properties to bacteria, minimal staining of mucosal surfaces, high quantum yield of free radicals, long history of safe use, and demonstrated efficacy against the targeted pathogens.\(^6\) Methylene blue (a tricyclic phenothiazine) fulfills these criteria well, and has been chosen as a highly suitable antimicrobial photosensitizer by several authors.\(^7,8\) Methylene blue has demonstrated a 100-year history of safe use in humans and a very low toxicity profile.\(^9\)

The use of lethal photosensitization for the killing of periodontopathogenic organisms may provide specific benefits in the treatment of periodontitis, including the lack of development of antibiotic resistance, the ability to treat the full depth of the pocket, the inactivation of virulence factors associated with Gram-negative bacteria,\(^10\) the ease of use, and the ability to kill tissue-associated microorganisms.

While it has been shown over many studies that standard mechanical debridement can achieve about a one millimeter mean reduction in pocket depth,\(^11\) clinicians also need to consider other factors when treating patients with nonsurgical therapy, including the efficacy of plaque removal.\(^12\) Studies have shown that there is a decreasing efficacy in plaque removal with increasing pocket depth,\(^13,14\) and this is associated with a corresponding decrease in treatment efficacy. Nonsurgical therapy is also not efficacious in the suppression of Actinobacillus actinomycetemcomitans because this organism is tissue-invasive, and indeed this may be one reason for failure of mechanical therapy in some pockets. Use of local drug delivery devices as a monotherapy remains controversial since root planing alone often achieves a similar result. In general, use of local drug delivery devices should be reserved for sites in patients who fail to respond to mechanical instrumentation. Use of antibiotic therapies must be balanced with the risk of increasing antibiotic resistance now occurring.\(^1\)

This study is the first reported clinical trial using photodisinfection for the treatment of chronic periodontitis. This trial was designed to achieve several goals, including the evaluation of the photosensitizer and light application techniques, evaluation of the adverse event profile, comparison of the adjunctive technique to SRP alone, and finally to evaluate the possible utility of using photodisinfection alone in a small, non-statistically significant group of subjects. The information obtained from this study will be used to design larger clinical studies to evaluate the treatment of periodontitis in different subject groups.

Materials and Methods

This study was approved by Western Institutional Review Board, Olympia, WA, USA, and was conducted according to ICH guidelines for Good Clinical Practice and the ethical principles of the Declaration of Helsinki. This was a randomized controlled trial of thirty-three adult subjects with chronic adult periodontitis from the Everett, Washington, USA area based on the following criteria:

i. Subjects had to be over the age of 18, in generally good health, with no allergies to methylene blue or with G6PD deficiency.

ii. Subjects had to have more than 20 teeth.

iii. Subjects had to have at least four or more sites with pocket depth of 6 mm or greater in at least two quadrants of the mouth, with bleeding on gentle probing.

iv. Subjects needed to have calcifications on less than 80% of teeth surfaces by the investigator’s estimate in order to verify a moderate degree of professional or personal oral hygiene.

v. Subjects needed to be available for the duration of the study, and to sign an Informed Consent Form.

vi. Pregnant or lactating women were excluded.

vii. Subjects were excluded if they had any periodontal instrumentation or antibiotic therapy in the previous four months.

viii. Subjects were excluded if they had any systemic condition which might influence the course of periodontal disease or treatment (i.e., HIV/AIDS, uncontrolled diabetes).

ix. Subjects were excluded if they had any systemic condition which required antibiotic coverage for routine periodontal procedures.

x. Subjects were excluded if they had any active malignancy of any sort.

At the baseline visit, all subjects reviewed and signed the informed consent form. The subject’s demographic information, medical and dental history were collected and the inclusion/exclusion criteria were reviewed. The first five subjects were placed into the photodisinfection only group (Group 1). The subsequent 28 subjects were provided SRP by the same clinician, after which a randomization envelope was opened and the subjects were randomized to one of two treatment groups: Group 2 of scaling and root planing (SRP) only, and Group 3, a combination of PD and SRP. In order to bring all subjects to the same SRP and measurement standard, only one treating clinician was used.

At baseline, clinical measurements were obtained from all teeth (6 sites per tooth) and all future treatment sites ≥ 6 mm were identified. The clinical measurements were pocket probing depth (PPD) in mm made at six sites per tooth, bleeding on probing (BOP), and clinical attachment level (CAL). Once subjects were enrolled, they were assigned to the respective groups. Subjects who were randomized to the PD + SRP group (3) and the SRP alone group (2) all received SRP in two to four sessions by the same clinician. For those subjects in the combined arm, the PD procedure was performed immediately following SRP. In the PD alone group, the qualifying sites were all treated without SRP. All measurements were repeated at three, six, and 12 weeks following therapy along with a clinical examination in all groups.

Photosensitizer and Laser

The photosensitizer used consisted of 3,7-Bis(dimethylamino)phenazathionium chloride trihydrate (methylene blue) 0.005% (w/v), suspended in a balanced solution of phosphate buffered saline with hydroxymethylcellulose as a mucoadhesive viscosity agent (Periowave® Treatment Kit, Ondine Biopharma Corporation, Vancouver, BC, Canada). The photosensitizing
solution was applied directly into each affected pocket with a Dentsply (York, PA, USA) 23 gauge blunt ended side-port irrigating needle to allow complete irrigation to the apex of the pocket (Figure 1). A diode laser (Periowave™), with a wavelength of 670 nm and a maximum power of 150 mW was employed. A flexible fiber optic cable attached to a custom-designed stainless steel autoclavable handpiece was used. The handpiece accommodated a disposable light-diffusing tip that was configured similar to a periodontal probe to allow access to the periodontal pocket. A uniform light distribution was emitted from the distal 7 mm of the tip. This allowed for complete light distribution throughout the periodontal pocket (Figure 2). All treatments were performed at a continuous power setting of 150 mW. An irradiation time of 60 seconds was used per site constituting an average energy density of 10-20 J/cm² per site depending on the size of the periodontal pocket. The light diffusing tip was gently moved around the pocket during the illumination cycle.

For the statistical analysis, per-subject average comparisons were carried out using student’s t-test; per-subject average comparisons weighted by the number of qualifying pockets per subject was carried out using weighted least-square regression analysis, and pocket depth data was additionally analyzed for p-value via the Generalized Estimating Equations (GEE) method.15

Results

The thirty-three treated subjects had a mean age of 53 years, ranging from 18-75 years; there were 22 women and 11 men in the study. There were a total of 622 individual sites treated. No treatment-related adverse events were reported during the study.

A significant increase in clinical attachment level was observed after both six and 12 weeks when the PD + SRP subjects (3) were compared to SRP alone (2) controls (Figure 3). The sites treated with PD alone (1) demonstrated mean CAL gains of 0.09 ± 0.38 mm and 0.14 ± 0.65 mm at six and 12 weeks, respectively. Those sites treated with SRP alone (2) demonstrated mean CAL gains of 0.37 ± 0.34 mm and 0.36 ± 0.35 mm at six and 12 weeks, respectively. Group 3 (SRP + PD) demonstrated mean CAL gains of 0.92 ± 0.62 mm and 0.86 ± 0.61 mm at six and 12 weeks, respectively (p < 0.01 for six weeks, and p < 0.02 for 12 weeks when compared to SRP alone [2]) The addition of photodisinfection to SRP (3) gave an approximately three-fold improvement in CAL.

The bleeding on probing (BOP) results revealed significant improvement in all groups, as can be seen in Figure 4. The mean value of BOP decreased in the PD group (1) from baseline by 71% at six weeks and 73% at 12 weeks, and in the SRP alone group (2) from baseline by 43% at six weeks and 56% at 12 weeks. The BOP in the combined SRP + PD group (3) decreased from baseline by 65% at six weeks and 59% at 12 weeks.
The probing pocket depth (PPD) reductions in the three groups are represented in Figure 5. The sites treated with PD alone (1) demonstrated mean PPD reductions of 0.69 ± 0.33 mm and 0.67 ± 0.44 mm at six and 12 weeks, respectively. Those sites treated with SRP alone (2) demonstrated mean PPD reductions of 0.78 ± 0.47 mm and 0.74 ± 0.43 mm at six and 12 weeks, respectively. The SRP + PD group (3) demonstrated mean PPD reductions of 1.16 ± 0.39 mm and 1.11 ± 0.53 mm at six and 12 weeks, respectively (p < 0.06 for six weeks and p < 0.05 for 12 weeks when compared to SRP alone [2]).

While the results from all groups are shown above, it should be noted that Group 1 contained only five subjects, and due to this small sample size, it is not possible to make statistical conclusions from this group. A larger randomized controlled trial would be necessary to fully evaluate the use of photodisinfection alone for the treatment of periodontitis. The results from Groups 2 and 3 showed a statistically significant beneficial effect of photodisinfection in addition to scaling and root planing over scaling and root planing alone. This effect is represented in Table I.

![Figure 5. Probing pocket depth (PPD) reductions in mm. Group 1 (PD alone), Group 2 (SRP alone), Group 3 (SRP + PD)](image)

<table>
<thead>
<tr>
<th>Improvement Observed Comparing SRP + PD (3) vs. SRP Alone</th>
<th>At 6 Weeks</th>
<th>p-value</th>
<th>At 12 Weeks</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attachment Level</td>
<td>230%</td>
<td>0.02</td>
<td>239%</td>
<td>0.02</td>
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<tr>
<td>Probing Pocket Depth</td>
<td>152%</td>
<td>0.03</td>
<td>150%</td>
<td>0.07</td>
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</table>

**Discussion**

It has been shown by Wilson that photodynamic therapy using red light is effective against numerous bacteria involved in caries, periodontal diseases, and root canal infections in conjunction with several different photosensitizers. The use of photodisinfection in clinical trials was based on results obtained by Soukos, et al., which demonstrated that the light dosages required to kill *S. sanguis* were much lower than those necessary to reduce fibroblast and keratinocyte viability. In another study, it was shown that the optimal activation time was 60 seconds, corresponding to an energy density of about 20 J/cm².

Oral biofilms have been established as one of the primary agents responsible for chronic periodontitis. These complex biofilm communities are highly effective at protecting themselves from external assault, such as that experienced during the use of antibiotics. In addition, bacteria in biofilm form have demonstrated potent up- and down-regulating capabilities on local cytokine expression, in such a way as to evade the host’s inflammatory and immunological protective mechanisms. Wilson and others have shown that low molecular-weight cationic photosensitizers, such as methylene blue, can rapidly penetrate these biofilms and upon light activation, can lethally disrupt the bacteria as well as the biofilm ultrastructure, providing an innovative approach to disinfection of these remarkably resistant sessile communities.

There are weaknesses to this study, including the small number of subjects in Group 1 and the lack of full examiner blinding. Statistical analysis was not carried out on Group 1 due to the small sample size.

The purpose of this study was to evaluate the use of a photodisinfection treatment both alone and in conjunction with SRP in subjects with chronic periodontitis, compared to subjects who received SRP alone. Improvements were seen in all three groups but with statistically significant differences. Clinical attachment level (CAL) is viewed as the gold standard when looking at the effects of treatments designed to improve chronic periodontitis. In this study, it was shown that the addition of photodisinfection to SRP improved outcomes at 12 weeks nearly three-fold. This was a statistically, as well as a clinically significant result, and underscores the potential utility of this approach.

While bleeding on probing (BOP) results showed the best response in the photodisinfection-alone group, the sample size for this group was too small to allow statistically valid conclusions to be made.

The probing pocket depth (PPD) showed similar improvement in the photodisinfection-alone group, as well as the SRP-alone group. However, the addition of photodisinfection to SRP improved the results of SRP by approximately 50%. In this particular study, only one photodisinfection treatment was carried out, and it may be that subsequent additional treatments may be needed to affect an optimal outcome for some patients.

The final results of this study suggest that photodisinfection therapy is an effective non-invasive approach to treating chronic periodontitis. The results showed a significant reduction in bleeding on probing, improvement in clinical attachment level, and a decrease in pocket depth. This modality may be used in association with traditional methods of periodontal care such as scaling and root planing, or in some cases by itself, depending on the clinical situation. These encouraging results suggest that photodisinfection for chronic periodontitis warrants further investigations as a potential alternative to antibiotic therapy.

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**References**


