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# Assessment of the Effect of Photodynamic Therapy on Treatment of Moderate-to-Severe Periodontitis; a Randomized Clinical Trial Study

Babak Amoian[1], Aida Mirzaee[2] & Seyed Mostafa Hosseini[3]

[1] Periodontology Department and Oral Health Research Center, School of Dentistry, Babol University of Medical Sciences, Babol, Iran

[2] Department of Periodontology, Babol Dental School, Babol University of Medical Sciences, Babol, Iran

[3] Department of Microbiology, Faculty of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran

Correspondence: Aida Mirzaee, Post Graduate Student, Department of Periodontology, Babol Dental School, Babol University of Medical Sciences, Babol, Iran. E-mail: ida.mirzaee65@gmail.com

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**Abstract**

**Background and Aim:** Photodynamic therapy is a localized non-invasive treatment modality for the periodontal disease. Some evidences have shown that this technique is effective in improving the treatment outcome. This study compared the effects of photodynamic therapy with and without scaling and root planing and scaling and root planing alone on the clinical parameters of the chronic periodontitis.

**Materials and Methods:** In this single-blind, randomized clinical trial, 30 chronic periodontitis patients (10 for each modality) were selected and three different methods; photodynamic therapy alone (Group1) by FotoSan 630 system, scaling and root planning (SRP) alone (Group2), scaling and root planing combined with photodynamic therapy (Group3) were done for them randomly. Clinical parameters of probing pocket depth (PPD), bleeding on probing (BOP), and clinical attachment level (CAL) were measured at the baseline and 3, 6 and 12 weeks later. One-sided analysis of variance test was used to analyze PPD and CAL among the treatment groups in each time interval while the paired comparisons were carried out by employment of Dunnett's test. The treatment groups were statically analyzed by the chi-square test regarding BOP.

**Results:** Before the treatment; no significant differences observed among treatment modalities regarding clinical parameters; while the differences were significant at three weeks ($p<0.0001$ for PPD and CAL; $p<0.001$ for BOP); six weeks ($p<0.0001$ for PPD and CAL, $p<0.002$ for BOP); and 12 weeks after the treatment (all: $p<0.0001$). The least PPD and CAL values and the most frequency of non-bleeding on probing status were measured for PDT+SRP modality at three, six, and twelve weeks after the treatment.

**Conclusion:** Photodynamic therapy supported the clinical parameters of periodontitis similar to SRP; however, PDT combined with SRP demonstrated a better result than that of SRP alone. Therefore, PDT combined with SRP can be used to improve outcomes of clinical parameters of periodontitis as compared to SRP alone in the short-term.

**Keywords:** photodynamic therapy, periodontitis, dental scaling, root planing

## 1. Introduction

Periodontitis is a multifactorial disease which is initiated and developed by destruction of the supporting tissues such as periodontal ligament and alveolar bone around the teeth. Poor oral hygiene, smoking, alcohol consumption, stress, and diabetes are some risk factors influencing this disease (Lindhe, Westfelt, Nyman, Socransky, & Haffajee, 1984). The objective of periodontal treatment is to remove the biofilm from the root surfaces and to stop the inflammation process through reducing the amount of pathogenic microorganisms on these areas. The success of such treatments is reliant on the effectiveness of removing biofilms and smear layer containing bacteria, endotoxins, and infected root cementum (Lindhe et al., 1984; Ramfjord et al., 1987).

There are evidences suggesting that non-surgical treatments such as scaling and root planing can improve the value of some clinical and microbial parameters (Lindhe et al., 1984; Ramfjord et al., 1987). However, sub and supragingival scaling and root planing cannot completely eliminate periodontal pathogens located in the deep

area around the teeth and do not prevent bacteria from spreading into the periodontal soft tissues. Besides, use of such treatment techniques may help bacteremia and endotoxaemia to develop (Giannelli, Formigli, Lorenzini, & Bani, 2015). As a supplementary treatment, several laser systems with various wavelengths, such as Er, diode, Cr: YSGG, Nd: YAG, and Er: YAG, have been recommended in order for treating periodontal diseases. Moreover, low level laser with a photosensitizing agent has been regarded as a useful technique for battling against bacterial contamination in periodontal pockets. The technique is known as antimicrobial Photodynamic therapy (a-PDT) (Chan & Lai, 2003; O'Neill, Hope, & Wilson, 2002).

In this technique, at first, a photosensitizing agent is injected into the desired area, next, the area is irradiated by a specific light beam, and under influence of LED light the photosensitizer will excite and acquire toxic properties against target pathogens and lastly inactivate or kill them. The photosensitizer should satisfy several criteria to be used in this technique; binding to pathogens selectively, capability of producing huge amount of free radicals, having a non-toxic effect on mucosal surfaces and tissues located surrounding the target area, and producing no hazard for people who use it are some of these criteria. Methylene blue meets these criteria and is one of the compounds used extensively in this regard. Another factor that should be taken into account in using such a technique is the wavelength of the light used for exciting the photosensitizer. Each compound can only be excited by a specific wavelength, otherwise it is unable to deliver free radicals and there will not be any treatment. Accordingly, the wavelength of the light source should be selected based on the chemical properties of the photosensitizer (Andersen, Loebel, Hammond, & Wilson, 2007).

The technique has several advantages: it is able to eliminate bacteria in a short time; it causes no harm to other surrounding tissues; it enables us to access and disinfect areas with a complex anatomical structure; it reduces the likelihood of bacteremia in patients with deficient immune; it reduces the dentine sensitivity after root planing; as a non-surgical method, there is no pain or swelling after such a treatment; and the cost of the treatment is acceptably low (Garcez et al., 2007; Hope & Wilson, 2006).

According to mentioned advantages, it can be hypothesized that if PDT be able to positively affect the treatment of periodontal diseases, it can be used, alongside other techniques such as scaling and root planing, as an adjuvant treatment for improving the quality of overall treatment of periodontal diseases. However, although there have been some reports suggesting the usefulness of a-PDT in treating such diseases, the results of studies conducted in this area have been contradictory in some cases. These inconsistencies can be due to several variables influencing the outcome of treatment, such as different laser systems with different light intensity, various exposure times, and different photosensitizing agents. Likewise, the type and severity of diseases, the number of treatment sessions, and diversity in individual skills of specialist performing such a treatment are other factors which can influence the successfulness of the treatment (Fontana et al., 2009).

So it seems necessary to perform more researches in this area in order to evaluate and compare the effects of such variables. Accordingly, the present study was conducted to compare the effects of three methods; photodynamic therapy alone, scaling and root planing alone, photodynamic therapy combined with scaling and root planning in treating moderate-to-severe periodontitis.

## 2. Method

### *2.1 The Participants and Requirements*

In a single-blind controlled, randomized clinical trial, a total of 30 patients diagnosed with a moderate-to-severe chronic periodontitis, confirmed by a periodontist, were selected to be evaluated. The sample size was determined based on several similar studies(Alwaeli, Al-Khateeb, & Al-Sadi, 2015; Andersen et al., 2007). Clinical Attachment Level (CAL) was the main parameter used by the periodontist for diagnosing periodontal disease. The parameter was measured using a periodontal probe, and cases with a CAL more than 4 mm were regarded as a moderate-to-severe periodontitis.

It should be noted that all patients who referred to the dentistry faculty of Babol University of Medical Science, Babol, Iran, were examined and included in the study if they satisfied the inclusion criteria of the study (Rasolabadi et al., 2015). Inclusion criteria were as follows; age above 18 years, having more than 20 healthy teeth, having at least an area with the pocket depth of 4 mm or more in at least two quadrants of the mouth with bleeding on gentle probing, and the patient who had a plaque index value less than 30 percent (before measuring the desired variables, the patients were unified in terms of the bacterial plaque index). Moreover, the exclusion criteria of the study were as follows; pregnancy, receiving scaling and root planing, or antibiotic therapy during the last six months before the beginning of the study, a history of extensive subgingival restorations, crowns, partial dentures and dental implants, smoking, and suffering from systemic diseases which affect the periodontal status of patients.

The 30 participants were randomly distributed in three groups. In this regard, first each patient was labeled with a number from one to thirty based on the time sequence in which they referred for treatment, next, using the RANDBETWEEN function of Microsoft excel (Office 2013; Microsoft Corporation, Seattle, Washington) a series of random numbers within this range were generated. Lastly, the first ten numbers were located in the group 1 and treated with the photodynamic therapy alone, the second ten numbers were located in the group 2 and treated with the method of scaling and root planing, and the final ten numbers were located in group 3 and treated with all two methods of photodynamic therapy alongside scaling and root planing.

*2.2 Variables of the Study*

The variables used for assessing the effectiveness of three different treatment procedures were as follows;

Probing pocket depth (PPD); the length between gingival margins to the base of the gingival sulcus in millimeter (Carranza & Newman, 1996).

Bleeding on probing (BOP); Presence or absence of bleeding on probing after 30 seconds in the buccal and lingual area (Carranza & Newman, 1996).

Clinical Attachment Level (CAL); the length between CEJ and the base of gingival sulcus in millimeter.

It is worth mentioning that all three groups were unified based on these variables (Carranza & Newman, 1996).

*2.3 Procedures*

As mentioned previously, the photodynamic therapy was the only method employed for treating Group 1 patients. The photosensitizer used in this regard was methylene blue (MERCK, Germany) with a concentration of 10 mg/ml. The solution was injected into the periodontal pockets using an insulin syringe for at least 60 seconds (Figure 1). In the next step, according to the guidelines published by the manufacturer, periodontal pockets were washed with distilled water. Then, using FotoSan 630 (CMS dental, wavelength: nm630, power: 2000-4000 mw/cm2) and 15 mm Perio tip all periodontal pockets were irradiated for at least 30 seconds on each side of the; buccal and lingual (Figure 2). Because of a uniform beam provided by FotoSan (CMS dental, Denmark) system, it was possible to irradiate all periodontal pockets uniformly. Figure 1 and Figure 2 show this procedure.

For treating Group 2 and 3 patients the scaling and root planing were performed in two sessions by a skilled clinician. At first, scaling was performed using an ultrasonic device (LED DTE D5, WoodPecker, China) and an ultrasonic dental handpiece (DTE HD-7L, Zhengzhou Smile Dental Equipment Co., Ltd.). Next, in order for root planing and elimination of remaining calculi, a specific gracey curette was utilized. Moreover, in Group 3, the photodynamic therapy was performed immediately after scaling and root planing processes.

Figure 1. Injection of photosensitizer into the periodontal pockets

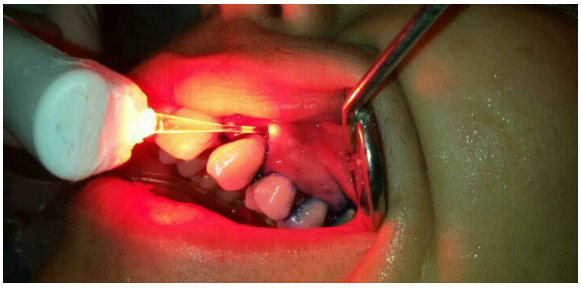

Figure 2. Irradiation of the periodontal pockets by the light-emitting Perio tip

All variables described in the previous section were measured before applying the treatments. After treating participants with the three different procedures, these variables were measured again in three time intervals; at three weeks, six weeks, and twelve weeks after the treatment. These time intervals were selected according to the previous studies (Alwaeli et al., 2015; Andersen et al., 2007). These series of examinations, for measuring the desired variables, were carried out by a clinician who was not aware which type of treatment had been employed for each patient.

*2.4 Statistical Analysis*

IBM SPSS software package version 21 was used for implementing statistical tests. The descriptive statistics used for representing mean and standard deviation of variables before and after the treatments. The normality of the data was investigated using the Kolmogorov-Smirnov test. Moreover, the values of PPD and CAL in different time intervals before and after the treatments were compared with each other using analysis of variance (ANOVA) and post hoc Dunnett's test. The Chi-square test was applied for analyzing the data associated with BOP. In order to assess the trend of changes in various time intervals ANOVA, repeated measures, and McNemar test was used. All statistical tests were performed at the 0.05 level of significance.

*2.5 Ethical Issues*

The study has been approved by the ethical committee of the university. The study also has been registered in the Iranian registry of clinical trial with the code of "IRCT201512251760N44". Moreover, all patients signed the agreement consent to participate in the present study.

## 3. Results

The present study was carried out on 30 patients who suffered from moderate-to-severe chronic periodontitis. The patients were randomly categorized in three groups. The demographic characteristics of these groups are summarized in Table 1.

Table 1. Demographic characteristics of each group

| Group | Number of patients in the group | | | Age average (SD) | Range (year) | |
|---|---|---|---|---|---|---|
| | Male | Female | Total | | From | To |
| Group 1 | 4 | 6 | 10 | 39.0 (6.54) | 28 | 50 |
| Group 2 | 5 | 5 | 10 | 36.4 (7.12) | 26 | 45 |
| Group 3 | 3 | 7 | 10 | 30.6 (5.73) | 24 | 43 |

After screening and categorizing the patients, fortunately, there was no loss and all patients completed the study.

Moreover, in the present study, 192 dental sites were assessed before and after implementing three different treatment processes. Table 2 represents the data obtained for PPD. The mean and standard deviation values are presented in this table at various time intervals both before and after the implementation of the treatment methods. The results of ANOVA test at each time point are demonstrated in the rightmost column of this table. Accordingly, it can be inferred that the three groups had a similar status in terms of PPD before the treatments, however, after implementing the three methods of treatments, the value of PPD for all the treatment methods was improved consistently. The results of the repeated measures ANOVA test are also presented in the last row of this table, which emphasize on the significant changes of variables over time (P-value=0.001).

From this table, moreover, we can infer that the use of the scaling and root planing (SRP) were resulted in a better outcome in comparison with that of photodynamic therapy (PDT) and the use of both PDT and SRP had a better outcome than those obtained by PDT or SRP separately.

Table 2. The results of the study for probing pocket depth (PPD) variable

| Treatment type / Time intervals | PDT (mm) | SRP (mm) | PDT+SRP (mm) | P-value |
|---|---|---|---|---|
| Before the treatments | 4.64±1.79 | 4.48±1.84 | 4.81±2.11 | 0.258 |
| Three weeks after the treatment | 3.24±1.47 | 2.64±1.33 | 2.31±1.37 | <0.001 |
| Six weeks after the treatment | 2.9±1.41 | 2.19±1.23 | 1.56±1.09 | <0.001 |
| Twelve weeks after the treatment | 2.9±1.44 | 1.93±1.07 | 1.48±0.96 | <0.001 |
| P-value | <0.001 | <0.001 | <0.001 | |

Table 3 also represents the data related to CAL obtained from the present study. The results of ANOVA test at each time point are presented and in the rightmost column of this table. Similar to PPD, it is observed that three groups had a similar condition in terms of this variable before the implementation of treatments (P-value=0.311). However, applying the combination of the two treatments (PDT and SRP) on patients improved the values of these variables significantly (P-value<0.05). According to the repeated measures ANOVA test (P-values are presented in the last row of this table), all the treatment methods improved the CAL overtime consistently (P-value<0.05). Furthermore, it can be inferred from the table that using the both techniques of PDT and SRP alongside each other had a better outcome than what we achieved when we used each of them lonely.

Table 3. The results of the study for the clinical attachment level (CAL) variable

| Treatment type / Time intervals | PDT (mm) | SRP (mm) | PDT+SRP (mm) | P-value |
|---|---|---|---|---|
| Before the treatments | 4.63±1.52 | 4.81±1.76 | 4.55±1.82 | 0.311 |
| Three weeks after the treatment | 3.54±1.31 | 3.74±1.6 | 3.13±1.51 | <0.001 |
| Six weeks after the treatment | 3.1±1.34 | 3.23±1.56 | 2.43±1.38 | <0.001 |
| Twelve weeks after the treatment | 3.28±1.4 | 2.88±1.47 | 2.15±1.19 | <0.001 |
| p-value | <0.001 | <0.001 | <0.001 | |

The results associated with BOP also are presented in Table 4. Similar to the two previous variables, there was no significant difference between the three groups before the treatments (P-value=0.07). We also see that applying the combination of the two treatments (PDT and SRP) improved the values of this index over time consistently. Using SRP had a better outcome than that of PDT in all time intervals except the first three weeks. Moreover, using PDT and SRP both together was by far the most successful method in treating such a disease.

Table 4. The results of the study for BOP variable

| Treatment type / Time intervals | PDT (mm) | SRP (mm) | PDT+SRP (mm) | P-value |
|---|---|---|---|---|
| Before the treatments | 64 (100%) | 61 (100%) | 62 (96.9%) | 0.07 |
| Three weeks after the treatment | 21 (32.8%) | 29 (43.9 %) | 9 (14.3 %) | <0.001 |
| six weeks after the treatment | 20 (31.3 %) | 10 (15.2 %) | 5 (7.8 %) | <0.001 |
| twelve weeks after the treatment | 36 (56.3%) | 26 (39.4%) | 1 (1.6%) | <0.001 |
| p-value | <0.001 | <0.001 | <0.001 | |

## 4. Discussion

The present study was set to evaluate the effectiveness of three treatment methods, SRP, PDT, and the combination of SRP and PDT, in treating chronic periodontitis. Thirty patients were selected and categorized in three groups. The effectiveness of treatment methods was evaluated using three indices, including PPD, CAL, and BOP. The results of the study revealed that all the three groups of patients were statistically similar in terms of these three indices. However, after the implementation of treatment methods, significant differences were observed among them. All three treatment modalities had a significant effect on the indices evaluated in the present study.

The overall results of the present study confirmed that using SRP and PDT alongside each other is more effective than when we use each of them alone. (Sgolastra, Petrucci, Gatto, Marzo, & Monaco, 2013) carried out a study in this area and assessed the effectiveness of PDT as a supplement of SRP. The results of that study indicated that the combination of PDT and SRP was the preferred method in treating chronic periodontitis, which is in agreement of the results obtained from the present study. Moreover, the superiority of PDT combined with SRP over SRP alone also has been demonstrated by (Alwaeli et al., 2015). In the same vein, (Birang, Shahaboui, Kiani, Shadmehr, & Naghsh, 2015) described that using PDT in addition to SRP would improve the overall outcome of the treatment.

One of the main limitations of the present study was that the effect of treatment methods was assessed only in

the short term. The same problem has been observed in most of studies conducted in this area.

However, there have been studies which describe that using PDT following SRP does not improve the treatment outcome. For instance, (Pourabbas et al., 2014) employed PDT using a 638 nm laser system and toluidine blue as a photosensitizer agent in patients suffering from chronic periodontitis to improve the treatment of SRP but they did not observe any improvement over the next three months.

The positive effect of PDT on the treatment outcome probably is because of its capability in destroying pathogens by triggering type 1 reactions (initiated by super oxidase, anionic hydroxyl, and free radicals) and type 2 reactions (initiated by singlet oxygen). Reactive oxygen species are able to irreversibly inactivate bacteria by altering their protein's properties, damaging their respiratory chain, and changing their nucleic acid (Braun, Dehn, Krause, & Jepsen, 2008; Fontana et al., 2009; Wainwright, 1998). Periodontopathogenic bacteria have the capability to cause harm to periodontal tissue and it should be considered that they may remain active after applying SRP treatment and continue their destructive activity of these tissues, so it seems to be a necessity to use other treatment techniques after a primary one.

The efficiency of PDT depends on several factors; the output power of the laser system and the concentration of a photosensitizer agent are some of the factors that should be taken into account in inferring the results of studies carried out in this area. Most researches have used diode laser systems in their studies, however, they have not made it clear that which type of photosensitizer agent has a better result, which power output is more effective, and how long the optimum time of irradiation is. Logically, these variables play a role in the final outcome of treatment. Moreover, applying PDT several times successively would result in a more favorable outcome than does applying it once. In this regard, (Soukos & Goodson, 2011) demonstrated that applying PDT five times per two weeks may improve the outcome of treatment.

Diode laser systems utilized in PDT may produce wavelengths which are absorbable by hemoglobin and would produce oxygenated hemoglobin and melanin; this phenomena happens when the wavelengths produced by laser systems belong to the infrared region (Moritz et al., 1998). Mechanism of action of low level laser therapy includes optical receivers' involvement in the electron transport chain on the mitochondrial membrane. Light absorption leads to a short-term activation of the respiratory chain and triggers the synthesis of nucleic acid compounds (Yu, Naim, & Lanzafame, 1997). Irradiation of low level lasers has additional effects on fibroblast proliferation, increase the number of cells by inducing secretion of growth factors, and enhance the differentiation of fibroblasts to myofibroblasts (Kreisler, Christoffers, Al−Haj, Willershausen, & d'Hoedt, 2002), all these processes can be effective in treating the periodontal disease.

Although PDT is shown to be an effective technique in treating periodontal diseases, it can be harmful to surrounding tissues because of its thermal effects. Using low power diode laser systems has been indicated to cause the least of these adverse side effects (Schoop et al., 2004), for example, (Nagayoshi et al., 2011) reported that the irradiation of such laser systems at the power of five watts for as long as 60 seconds led to an increase in the temperature of surrounding tissue equal to five Celsius degrees (Nagayoshi et al., 2011).

In the present study, light emitted from an LED with the wavelength of 630 nm and at the power of 2000-4000 $mw/cm^2$ was supplied by PhotoSan 630 device. In the studies carried out by (Chondros et al., 2009) and (Christodoulides et al., 2008), the diode laser with the wavelength of 630 nm and output power of 75 mwatts was used. However, the wavelength of 660 nm was applied by (Alwaeli et al., 2015). The main disadvantage of diode-based laser systems is their adverse side effects on surrounding tissues. These systems should only be applied by an experienced dentist. In contrast, in the present study LED light was used which has no side effect and, more importantly, it can be applied even by an assistant without so much experience.

The photosensitizer agent used in the present study was methylene blue with the concentration of 10 mg/ml. The agent is able to absorb a wide wavelength range and after activation is very effective in inactivating bacteria, virus, and fungus (Zanin, Goncalves, Junior, Hope, & Pratten, 2005). The agent, moreover, has been used by several studies such as a study carried out by (Giannelli, Formigli, Lorenzini, & Bani, 2012).

## 5. Conclusion

It can be concluded from the present study that PDT and SRP, when used separately, has the same outcome in terms of their capability in treating chronic periodontitis. However, when they are applied alongside each other, the outcome of the treatment improves and a better result is accomplished. Accordingly, it is recommended that PDT, as a non-aggressive treatment, should be employed after the implementation of other treatments such as scaling and root planing.

**Recommendation for Future Studies**

It is recommended for future studies to investigate the effect of other photosensitizers rather than methylene blue. Moreover, the laser output power and various wavelengths can be the subject of future studies. In addition, the long term effect of PDT is another factor which should be evaluated in future researches.

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**Competing Interests Statement**

The authors declare that there is no conflict of interests regarding the publication of this paper.

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