

Photodynamic therapy as an adjunctive to scaling and root planing in treatment of chronic periodontitis in smokers

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ABSTRACT

الأهداف: دراسة تأثير أحد الطرق العلاجية الحديثة (العلاج الفوتوديناميكي) في علاج أمراض اللثة والأنسجة الداعمة للأسنان لدى المدخنين.

الطريقة: شملت هذه الدراسة عينة من 54 سناً مصابة بجيوب لثوية عميقة (أكبر من أو يساوي 5 ملم) في 20 مريض من المرضى المدخنين والمصابين بأمراض الأنسجة الداعمة للأسنان، ومن ثم تم تقسيم الأسنان عشوائياً بحيث يتم علاج أحد الأسنان باستخدام العلاج التقليدي بينما يتم علاج السن المقابل في نفس المريض باستخدام العلاج الفوتوديناميكي بالإضافة للعلاج التقليدي. وتم فحص حالة الأنسجة الداعمة للأسنان قبل العلاج وبعد 3 أشهر من انتهاء العلاج، ومن ثم تم تحليل النتائج بعد إدخالها في برنامج إحصائي خاص.

النتائج: أظهرت النتائج تحسن ملحوظ في حالة اللثة بعد العلاج حيث قلت علامات المرض في كلا المجموعتين، وظهر التحسن بشكل أكبر في المجموعة التي تم استخدام العلاج الفوتوديناميكي فيها حيث قل متوسط عمق الجيوب اللثوية في هذه المجموعة بمقدار أكبر مقارنة بمجموعة العلاج التقليدي.

خاتمة: دلت نتائج البحث إلى وجود فائدة للعلاج الفوتوديناميكي في علاج أمراض الأنسجة الداعمة للأسنان لدى المدخنين.

Objectives: To compare photodynamic therapy (PDT) as an adjunctive treatment of chronic periodontitis with scaling and root planing (Sc/Rp) in smokers.

Methods: This is a split-mouth, single-masked randomized controlled clinical trial conducted at the Faculty of Dentistry, King Abdulaziz University, Jeddah, Saudi Arabia between May 2010 and March 2011. Fifty-four teeth with probing depth of ≥ 5 mm at one or more periodontal sites in 20 smokers diagnosed with moderate to severe chronic periodontitis were selected. In each patient, at least one tooth was randomly assigned to Sc/Rp plus PDT (test group) and the contra-lateral tooth was assigned to Sc/Rp

only (control). Plaque index (PI), bleeding on probing (BOP), probing depth (PD), recession and clinical attachment level (CAL) were recorded at baseline and 3 months after the periodontal treatment. Descriptive statistics and Wilcoxon signed ranked test were used for data analysis.

Results: There was a statistically significant improvement in PD, CAL, BOP, and PI after periodontal treatment in both groups. No statistically significant differences between the 2 groups in any of the periodontal parameters were found at baseline ($p>0.05$), but a statistically significant greater reduction in PD ($p=0.028$) and CAL ($p=0.044$) in the test compared to the control group was found at the 3-month follow up.

Conclusion: Photodynamic therapy might have an additional benefit to scaling and root planing when treating smokers affected with periodontitis.

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Periodontitis is a chronic infectious disease resulting from a complex interaction between pathogenic bacterial plaque biofilm and the host immunoinflammatory responses.¹ It affects approximately 72% of the Saudi population² and if left untreated, periodontitis may lead to tooth loss and may also increase an individual's risk of developing some systemic diseases such as cardiovascular diseases.³ Certain factors such as smoking, diabetes and genetics are known to increase individual's susceptibility to generalized periodontitis.⁴ Smoking is a strong risk factor for periodontitis having a destructive force that exceeds other known periodontitis risk factors.⁵ It has been suggested to negatively influence the host immune response toward periodontal pathogens through impairment of the immunological function of neutrophils and macrophage.^{6,7} Smokers also have a higher level of pro-inflammatory molecules such as tumor necrosis factor-alpha (TNF- α), prostaglandin E2 (PGE2), elastase, and matrix metalloproteinase-8 in gingival crevicular fluids (GCF) compared to non-smokers.^{6,7} Furthermore, GCF of smokers showed a decreased level of tissue breakdown regulators such as protease inhibitor (namely, α -1 antitrypsin and α -macroglobulin).⁸ As a result, smokers are more likely to have multiple deep pockets, clinical attachment loss, bone loss, and increased number of pathogenic bacteria.⁵ Smokers also have an inferior outcome to both surgical and nonsurgical periodontal treatment compared to non-smokers.^{9,10} Hence, smoking contribute to the vast majority of therapeutic failures or refractory cases suggesting that the long-term prognosis for the smoker patients is compromised for all modalities of periodontal therapy.^{5,11} Thus, periodontal treatment of smokers is more challenging and therefore, periodontal researchers are attempting to discover and utilize adjunctive treatments to scaling and root planing to overcome the difficulties associated with the conventional periodontal treatment in such patients. Systemic and local antimicrobial therapies have been used as an adjunct to periodontal treatment in management of periodontitis in smokers.^{12,13} The use of these methods, however has some limitations. The application of local antibiotic agents in treatment of patients diagnosed with generalized periodontitis and multiple sites of deep pockets are technically difficult.¹⁴ In addition, the concentration of local antimicrobial agents in the periodontal pockets are difficult to control.¹⁵ In regard to the systemic route of administration, the availability of insufficient concentration of the drug in the GCF and the worldwide increased concern of development of antibiotic resistance are major disadvantages.¹⁶ Thus, systemic antibiotics as an adjunctive to conventional periodontal treatment should be restricted to specific group of periodontal patients, such as those with

generalized and high active disease.^{16,17} As a consequence, development of alternative antimicrobial approaches to manage smoker patients affected with periodontitis is warranted. Antimicrobial photodynamic therapy (PDT) could be a promising adjunctive to the conventional periodontal therapeutic methods especially in smokers. The principle behind a PDT is based on the binding of a photoactivatable compound (the photosensitizer) to the target cells and then activated by light of a suitable wavelength. During the activation process, free radicals are formed, which produce lethal cytotoxic effects on the target cells.^{18,19} Recently, studies have been published demonstrating a beneficial effect of adjunctive use of PDT in periodontal therapy.²⁰⁻²³ The objective of the present study was to assess the effect of photodynamic therapy as an adjunctive treatment of chronic periodontitis in smokers.

Methods. A single-blind, randomized, split mouth controlled trial was conducted between May 2010 and March 2011 in accordance with the principles laid down in Helsinki Declaration. Fifty-four teeth in 20 consecutive smokers were included. As a result of the very low prevalence of smoking among females, only male patients were included. Patients were selected from patients presenting for treatment at the Faculty of Dentistry's Clinics, King Abdulaziz University, Jeddah, Saudi Arabia. Patients 30 years of age or older who smoke ≥ 10 cigarettes per day for ≥ 5 years and suffer from generalized moderate to severe chronic periodontitis and have at least a pair of teeth with probing pocket depths of ≥ 5 mm at one or more periodontal site were included. Periodontitis was defined as marginal radiographic alveolar bone loss of $>20\%$ and/or CAL of 3 mm or more at 30% or more of the present teeth. Those with any of the following were excluded: 1) known systemic diseases, 2) systemic antibiotic treatment in the preceding 6 months, and 3) those who require antibiotics prophylaxis before periodontal examination. Informed consent was obtained from each participant prior to their enrollment and the study was reviewed and approved by the King Abdulaziz City for Science and Technology, and the Research Ethics Committee of King Abdulaziz University, Faculty of Dentistry.

At baseline, full medical and dental histories as well as periodontal examination (consisting of plaque [PI] and bleeding [BOP] scores, probing depth [PD], recession [RC] and clinical attachment level [CAL]) were recorded by a calibrated examiner who was blind to the treatment assignments. All periodontal measurements were performed on 6 sites per each tooth using a manual calibrated periodontal probe (Model UNC-15, Hu-Friedy Manufacturing Co., Inc., Chicago, IL, USA).

After baseline periodontal examination of each participant, at least one pair of teeth with probing depth ≥ 5 mm was selected, and then one tooth of each pair was randomly assigned to the test group and the contra-lateral tooth was assigned to the control group. Computer-generated random number table was used for randomization. All participants received oral hygiene instruction (OHI) and full mouth scaling and root planing (Sc/Rp). In addition, pockets ≥ 5 mm in the test group were treated with a single episode of PDT. The PDT was performed by a qualified dentist using a 670 nm non-thermal diode laser and a formulation comprising 0.01% methylene blue as the active ingredient (Ondine's Periowave, Ondine Biopharma Corp., Vancouver, BC). The Sc/Rp was performed by the same dentist using hand instruments (Gracey curettes, Hu-Friedy, Chicago, IL). Periodontal examination was repeated 3 months after the periodontal treatment by the same masked examiner who conducted the baseline examination.

The statistical analysis was performed using commercially available statistical software (SPSS 16.0 for Windows, SPSS, Chicago, IL). To compare the test and control groups, subject-level data on sites with pockets ≥ 5 mm at baseline were utilized. The changes in periodontal parameters after periodontal treatment at these sites was compared between the 2 groups

using Wilcoxon signed ranked test. The differences within each group before and after treatment were also compared using Wilcoxon signed ranked test. In an additional analysis, Chi square test was used to compare the 2 groups in regard to the distribution of sites with different probing depths post treatment and number of sites that showed a reduction of 2 mm or more after therapy. All the statistical tests were 2 tailed, and the level of significance was set at an alpha < 0.05 .

Results. Fifty-four teeth in 20 smoker male patients were included. Of these, 6 teeth in 3 patients (who were lost to follow up) were not included. Thus, the final analysis was conducted on 48 teeth in 17 patients with complete data. Of these, 7 patients contributed 4 teeth (2 pairs) each whereas the other 10 patients contributed 2 teeth (one pair) each. The total number of periodontal sites with probing depth ≥ 5 mm on these teeth was 121. The mean age of the study participants was 41.6 (± 9.6) years and the range was 30-56 years. Table 1 shows the clinical periodontal parameters of 17 smokers diagnosed with moderate to severe chronic periodontitis at baseline and 3-month post-treatment.

Table 2 shows the median of the clinical periodontal parameters at baseline and 3-month post-treatment. No statistically significant differences between groups were found at baseline examination in any of the

Table 1 - Clinical periodontal parameters of 17 smokers diagnosed with moderate to severe chronic periodontitis at baseline and 3-months post-treatment.

Variables	Photodynamic therapy (n=24 teeth)		Scaling and root planing only (n=24 teeth)	
	Baseline	3-months	Baseline	3-months
Probing depth (mm)	5.60 \pm 0.83	3.84 \pm 0.85	5.35 \pm 0.46	3.90 \pm 0.75
Gingival recession (mm)	0.73 \pm 1.05	0.82 \pm 1.01	0.83 \pm 1.20	0.90 \pm 1.10
Clinical attachment level (mm)	6.30 \pm 1.44	4.70 \pm 1.27	6.18 \pm 1.40	4.80 \pm 1.45
Bleeding on probing (%)	74.50 \pm 21.50	41.90 \pm 22.30	68.00 \pm 23.00	45.60 \pm 19.50
Plaque score (%)	78.50 \pm 16.10	41.90 \pm 17.90	75.90 \pm 15.80	43.60 \pm 16.60

Data are expressed as mean \pm SD

Table 2 - Median of clinical periodontal parameters of 17 smokers diagnosed with moderate to severe chronic periodontitis at baseline and 3-months post-treatment.

Variables	Photodynamic therapy (n=24 teeth)			Scaling and root planing only (n=24 teeth)			Between group [†] <i>p</i> -value
	Baseline	3-months	<i>P</i> -value*	Baseline	3-months	<i>P</i> -value*	
Probing depth (mm)	5.40	3.60	0.000	5.13	3.75	0.000	0.028
Gingival recession (mm)	0.60	0.50	0.181	1.00	1.00	0.590	0.990
Clinical attachment level (mm)	5.80	4.20	0.000	6.13	4.87	0.000	0.044
Bleeding on probing (%)	75.00	33.00	0.001	67.00	42.00	0.007	0.172
Plaque score (%)	83.00	33.00	0.000	75.00	42.00	0.001	0.186

**p*-value for the intra-group differences at baseline, [†]Between group *p*-value for the change in each periodontal parameter after treatment. At baseline, no statistically significant differences between groups were found (*p* $>$ 0.05)

clinical periodontal parameters. After periodontal treatment, both groups showed a statistically significant improvement in all clinical periodontal parameters. Between group comparisons, the change in PD was significantly higher in the test group compared to the control group ($p=0.028$). The decrease in clinical attachment level was also higher in the test group than in the control group, and was statistically significant ($p=0.044$). Other periodontal parameters showed no significant differences between the 2 groups.

Table 3 shows the percentage of periodontal sites with different probing depth at baseline and 3-month post-treatment. At baseline, 69% of pockets in the test group and 77% in the control group were 5 mm; whereas 31% of pockets were ≥ 6 mm in the test group and 23% in the control group. After treatment, no pocket was measured ≥ 6 mm in the test group whereas 5% of pockets were ≥ 6 in the control group. The percentage of periodontal sites that showed a reduction of ≥ 2 mm was 50% in the test and 47% in the control group. The differences between groups however, were not statistically significant ($p>0.05$).

Discussion. Smoking exerts a negative influence on the outcome of non-surgical as well as surgical periodontal therapy resulting in a smaller pocket depth reduction and less attachment gain. Thus, there is a need for adjunctive methods to augment the effect and enhance the outcome of non-surgical periodontal treatment in smokers. Recently, there was a growing interest in the use of PDT to combat anaerobic bacteria that grow in the periodontal pocket and lead to periodontal disease and subsequently tooth loss.²⁴ The present study investigated the efficacy of scaling and root planing (Sc/Rp) plus PDT compared to Sc/Rp alone in treatment of chronic periodontitis in smokers. Three months after periodontal therapy, both

groups showed a statistically significant reduction in the investigated clinical periodontal parameters (PD, CAL, BOP, and plaque scores). There was a decrease of >1 mm in PD in both groups which are in line with findings of studies reporting on the outcome of non-surgical periodontal therapy.^{25,26} The PDT group, however showed a higher and statistically significant reduction in PD and CAL than the control group. Although, physical plaque biofilms removal by Sc/Rp is an essential part of periodontal therapy, complete removal of plaque, and calculus is not always possible especially in inaccessible sites such as deeper pockets and furcation areas. Thus, the better clinical outcome in the PDT group compared to the control group in the present study might be attributed partly to the effect of photosensitization on viability of periodontal pathogens. The PDT kills target cells by the cytotoxic action of singlet oxygen produced by means of a non-toxic dyes in combination with harmless visible light of an appropriate wavelength.^{18,19} This method has been shown to be effective at killing different pathogenic microorganisms in vivo and in vitro.^{18,19,27-29} Komerik et al²⁷ successfully demonstrated killing of *Porphyromonas gingivalis* in the gingival crevices of rats without damaging the adjacent periodontal tissues. In a more recent study, Pinherio et al²⁸ showed a significantly greater reduction in the percentage of viable bacteria in periodontal pockets treated with PDT (96%) compared to those treated with Sc/Rp only (81%). Furthermore, other studies have shown that PDT is equally effective in killing antibiotic resistant bacteria.^{18,29} Another possible explanation for the superior outcome in the PDT group might be attributed to the effect of PDT on angiogenesis and thus bringing more oxygenation to the treated areas. Laser phototherapy has recently been shown to increase angiogenesis in animal studies,^{30,31} which might be important in smokers where periodontal angiogenesis in response to inflammatory stimuli is inhibited.³²

The results of the present study support findings of previous human studies in which Sc/Rp combined with PDT has led to a statistically significant improvement in probing depth over the Sc/Rp alone during initial and supportive periodontal maintenance therapy.^{17,21,23} The results are also in line with findings of animal studies in which, the effect of PDT in treatment of experimentally-induced periodontitis was examined in normal and immunosuppressed rat models and their results showed less bone loss in the PDT group than the Sc/Rp only group.^{33,34} In contrast, our results differ from findings of other human studies in which Sc/Rp combined with PDT was not found to have an additional effect to Sc/Rp alone in treatment of chronic

Table 3 - Periodontal sites with different probing depth (PD) of 17 smokers diagnosed with moderate to severe chronic periodontitis at baseline and 3-months post-treatment and sites that showed a reduction of ≥ 2 mm in depth after treatment.

Variables	Scaling and root planing only (n=64 sites)		Photodynamic therapy (n=57 sites)	
	Baseline	3-months	Baseline	3-months
<i>Probing depth (mm)</i>				
≤ 3	-	24 (37.5)	-	26 (45.6)
4	-	23 (35.9)	-	12 (21.1)
5	44 (68.8)	17 (26.6)	44 (77.2)	16 (28.1)
≥ 6	20 (31.3)	0 (0.00)	13 (22.8)	3 (5.3)
Sites reduced ≥ 2 mm in PD	-	32 (50.0)	-	27 (47.4)

Differences between groups were not statistically significant ($p>0.05$).
Data are expressed as number and percentage (%)

periodontitis in systemically healthy individuals,³⁵ and in those affected with diabetes.³⁶

One of the limitations of this study is that a single application of PDT was used; thus, it is unclear if multiple PDT application will further improve the outcome of non-surgical periodontal therapy. Another limitation is that only male patients were included thus, the effect of photodynamic therapy in treatment of chronic periodontitis in female smokers is not clear.

In conclusion, data from the present study showed that the adjunctive use of PDT to Sc/Rp improved the PD and CAL reduction compared to Sc/Rp only. Further studies to confirm or refute the present findings and to examine the effect of multiple PDT application during maintenance periodontal therapy in smokers are warranted.

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Illustrations, Figures, Photographs

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