J Clin Periodontol 2013; 40: 65–72 doi: 10.1111/jcpe.12024

Journal of Clinical Periodontology

Photoactivated disinfection using light-emitting diode as an adjunct in the management of chronic periodontitis: a pilot double-blind split-mouth randomized clinical trial

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Bassir SH, Moslemi N, Jamali R, Mashmouly S, Fekrazad R, Chiniforush N, Shamshiri AR, Nowzari H. Photoactivated disinfection using light-emitting diode as an adjunct in the management of chronic periodontitis: a pilot double-blind split-mouth randomized clinical trial. J Clin Periodontol 2013; 40: 65–72. doi: 10.1111/jcpe.12024.

Abstract

Aim: This split-mouth double-masked randomized controlled clinical study evaluated the effectiveness of photoactivated disinfection (PAD) using light-emitting diode (LED) as an adjunct in the management of patients affected by moderate to severe chronic periodontitis.

Materials and Methods: Sixteen patients affected by moderate to severe chronic periodontitis were enrolled. After scaling and root planing (SRP), each quadrant was assigned to one of the following groups: LED group (625–635 nm, maximum power density: 2000 mW/cm^2), photosensitizer group (tolouidine blue O, 0.1 mg/ml), PAD group (photosensitizer and LED) and control group (no adjunctive treatment). The adjunctive treatments were repeated after 7 and 14 days. The clinical parameters of bleeding on probing, probing pocket depth and clinical attachment level were measured at baseline and 1 and 3 months after SRP.

Results: At 1 and 3 months, all groups showed significant improvements with regard to all clinical parameters compared to baseline (all p: <0.001). There were no significant differences among groups in terms of changes of clinical parameters in any time interval (all $p > 0.05$).

Conclusion: The application of PAD using LED with the current setting did not have additional effects on clinical parameters in patients diagnosed with moderate to severe chronic periodontitis compared with SRP alone.

Key words: periodontal disease; periodontal pocket; periodontitis; photochemotherapy; randomized controlled trial

Accepted for publication 21 September 2012

Conflict of interest and source of funding statement

This study was supported by Laser Research Center in Dentistry (LRCD) of Tehran University of Medical Sciences (No. 89-01-97-10245). The authors declare that they have no conflict of interest.

Bacterial biofilm plays a key role in the aetiology of periodontitis (Socransky & Haffajee 2002). Hence, the main purpose of periodontal therapy is to eliminate the microbial causative factors (Teles et al. 2006). Conventional therapies often consist of mechanical debridement and adjunctive systemic or locally delivered antibiotics (Cobb 1996, Slots 2002). Although the adjunctive use of antibiotics may be effective in the elimination of periodontal pathogens (Lindhe et al. 1982a), the frequent use of antibiotics could lead to the development of bacterial resistance (Slots & Rams 1990) or patient related adverse effects (Haffajee & Socransky 1994). The difficulty to maintain a stable therapeutic concentration of antimicrobial agents in the periodontal pocket for a sufficient length of time is another problem related to the use of antimicrobial agents (Darveau et al. 1997, Feres et al. 2002). To overcome these problems, alternative antimicrobial approaches for periodontal treatment have been proposed.

Photodynamic therapy (PDT) is a non-invasive treatment procedure that involves the use of a dye as a photosensitizer, which binds to the target cells and is activated by photon of suitable physical parameters (Wilson 2004). During the activation process, the photosensitizer undergoes a transition from a low-energy ground state to a higher energy state. Subsequently, singlet oxygen, reactive oxygen species and other highly reactive free-radicals are formed, which are extremely toxic to certain cells and microorganisms (Konopka & Goslinski 2007, Maisch 2007). Photoactivated disinfection (PAD) is a term used to emphasize the disinfection action of PDT. A number of clinical studies have investigated the effect of adjunctive PAD using laser in the treatment of chronic periodontitis (Andersen et al. 2007, Braun et al. 2008, Christodoulides et al. 2008, Chondros et al. 2009, Lulic et al. 2009, Polansky et al. 2009, Ruhling et al. 2010, Theodoro et al. 2011). Some studies have shown promising results with regard to the efficacy of laser based PAD in treatment of periodontitis (Andersen et al. 2007, Braun et al. 2008, Lulic et al. 2009, Garcia et al. 2011, Giannelli et al. 2012). The results of two recent systematic reviews and meta-analyses are controversial with regard to clinical benefits of adjunctive PAD in the treatment of periodontitis (Atieh 2010, Azarpazhooh et al. 2010). Both studies indicated that there is further need for well designed, double-blind, randomized clinical trials.

More recently, non-laser light sources, such as light-emitting diodes (LED), have been suggested as novel light sources in PAD. These devices are more compact and portable and considerably less expensive compared to lasers (Takasaki et al. 2009). Another advantage of LED is that its irradiation is less harmful to the eyes than laser irradiation (Ishikawa et al. 2011). Previous *in vitro* study showed that LED-based PAD could effectively reduce the inflammatory response of macrophages to *Porphyromonas gingivalis* lipopolysaccharide adherent to titanium surface (Giannelli et al. 2011). An animal study demonstrated that application of LED-based PAD in ligature-induced periodontitis resulted in decreased bone resorption compared to application of photosensitizer alone (Carvalho et al. 2011). To the authors' knowledge, there is no randomized controlled clinical study evaluating the effect of adjunctive PAD using LED in the treatment of chronic periodontitis.

The aim of the present double-blind, randomized, controlled clinical trial was to evaluate the clinical effect of adjunctive PAD using LED in the management of chronic periodontitis. The hypothesis was that application of LED-based PAD as an adjunctive therapy could improve the clinical parameters in patients with moderate to severe periodontitis.

Material and Methods

Study population

The study was performed in full accordance with the principles outlined in the Helsinki Declaration of 1975, revised in 2008 in Seoul, Korea. The study protocol was reviewed and approved by the Clinical Research Ethics Board of Tehran University of Medical Sciences (No: 89-01-97-10245). Patients with clinical diagnosis of moderate to severe chronic periodontitis (Armitage 1999) were included in this study (ClinicalTrials.gov ID: NCT01330082). These patients were included in the study on the basis of following criteria: good general health, presence of at least two teeth with a probing depth of 4–6 mm in each quadrant, lack of furcation involvement and the presence of at least 16 remaining teeth with a minimum of four teeth in each quadrant (Braun et al. 2008). Patients with the following criteria were excluded: any systemic condition which could affect the outcome of periodontal therapy, periodontal treatment within the past 12 months, the use of systemic antibiotics within the last 6 months, smoking more than 10 cigarettes/day and pregnant or lactating female. All participants signed informed consent form after being informed about the treatment protocol.

Study design

This split-mouth double-masked randomized controlled clinical trial was conducted from April 2010 to May 2011. The patients were consecutively recruited from the department of periodontology of Tehran University of Medical Sciences. All patients were subjected to a full-mouth periodontal examination at six sites per tooth (excluding third molar). After oral hygiene instructions, all patients received full-mouth scaling and root planing (SRP) under local anaesthesia using both hand instruments and ultrasonic device. An experienced investigator who was not informed about the treatment allocation performed SRP.

According to a predefined computer-generated balanced block randomization table with a 1:1 allocation, each of the four quadrants in patients was assigned to one of the following treatment group: (1) Light-emitting diode irradiation (LED group); (2) toluidine blue O (TBO) photosensitizer (PS group); (3) PAD (TBO+ LED irradiation)(PAD group); and (4) SRP alone (control group). The random allocation sequence was generated by a clinical epidemiologist who was not aware of the treatment modalities using a computer software program (Microsoft Office Excel 2007, Microsoft Corp, Redmond, WA, USA). An investigator, who was not involved in data collection and treatment, performed the enrolment of patients and their assignments into interventions. A single trained operator who was masked about the clinical examinations and data collection undertook adjunctive treatment. Allocation concealment was obtained by sealed non-transparent envelopes. The sealed containers were opened just before the interventions. Patients did not receive information about the type of adjunctive treatment that was used in each quadrant.

Treatment procedure

The light source used in this study was a LED in the red spectrum (wavelength: 625–635 nm, power peak at 628 nm; maximum output power density: 2000 mW/cm^2; FotoSan; CMS Dental, Copenhagen, Denmark). A dedicated tolouidine blue O (TBO) with a concentration of 0.1 mg/ml (FotoSan agent medium viscosity, FotoSan; CMS Dental, Copenhagen, Denmark) was used as the photosensitizer. All procedures were carried out according to the protocol recommended by the manufacturer. Adjunctive therapies were performed at six sites around all teeth (mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual, distolingual). Special safety glasses were provided to the patients, operator and dental assistant to prevent possible eye damage by the LED irradiation. In the LED group, each site was exposed to LED light by employing a long tip inside the sulcus for 10 s continued by using the blunt tip on the outside of the sulcus for another 10 s. In the PS group, TBO was meticulously applied using a blunt needle at the bottom of the sulcus in a coronal direction. Sites assigned to PAD group received the both mentioned treatments. Three minutes after application of photosensitizer, excess of the photosensitizer was rinsed and LED was irradiated. The control group did not receive any adjunctive treatment.

Adjunctive treatment was repeated in the same manner after 7 and 14 days. Just before application of adjunctive therapies, mechanical plaque removal was performed. All patients were recalled for oral hygiene re-instruction and oral prophylaxis procedure biweekly for one month and then monthly until three months. The prophylaxis protocol included oral hygiene re-instruction and polishing (as needed).

Examiner calibration

All clinical parameters were measured by a calibrated examiner who was not aware of the treatment allocation. At two separate sessions 48 h apart, duplicate measurements of pocket probing depth, clinical attachment level and bleeding on probing were obtained from five patients who were not related to the study. Calibration was accepted if percentage agreement between measurements at baseline and after 48 h was more than 90 %.

Clinical measurements

Sites with clinical attachment loss of ≥ 3 mm and concomitantly periodontal pocket depth of 4–6 mm were set for defining an experimental site. Experimental tooth referred to a tooth with at least one experimental site. Clinical parameters were recorded at baseline, 1 and 3 months after intervention. Plaque index (PI) (Loe & Silness 1963) was employed to assess the oral hygiene status of the patients throughout the study period. Bleeding on probing (BOP) was recorded based on the presence or absence of bleeding up to 30 s after probing at the experimental sites. Pocket probing depth (PPD) was measured from the free gingival margin to the bottom of periodontal pocket. Clinical attachment level (CAL) was measured as the distance from the cementoenamel junction to the base of periodontal pocket. The measurements were rounded to the nearest 0.5 mm. For all probing measurements, the Williams-style periodontal probe (Hu-Friedy, Chicago, IL, USA) was used.

Change in PPD was defined as the primary outcome variable. Changes in CAL and BOP were considered the secondary outcome variables.

Calculation of sample size

A power calculation was performed to determine the sample size. The patient was considered the study unit. The sample size was determined to provide 80% power to recognize a significant difference of 1 mm between groups and the standard deviation of 0.8 (Chondros et al. 2009) with a 95% confidence interval ($\alpha = 0.05$), considering the change in PPD as the primary outcome variable. Therefore, a sample size of 16 patients would be required.

Statistical analysis

A patient-level statistical analysis was performed for each of the clinical parameters. Normal distribution of data was tested with the Kolmogorov–Smirnov test. As mean values were used for the analysis, PPD and CAL values were normally distributed (Z scores: 0.67 and 1.34, p-values: 0.75 and 0.053 respectively) (Fig. 1). Analysis of variance test (ANOVA) was used to compare the mean values of continuous parameters. Repeated measure analysis was used to compare baseline, 1-month and 3-month for continuous parameters. Chi-square test was used for the comparison of BOP at site level in different treatment groups.

Multilevel logistic regression analysis (based on site level and patient level) was used to obtain odds ratios for describing the association of the values of PPD at 3 months with PAD group. A significance level of 0.05 was used for all comparisons.

Results

This study was started in April 2010 and ended in May 2011. Sixteen patients (eight women and eight men) completed the three-month study period. The mean age of patients was 50.3 ± 8.7 years (range: 40–63 years). Three patients were smokers. Demographic characteristics and the frequency of experimental teeth and sites in different treatment groups are shown in Table 1. The post-operative healing was uneventful in all cases and no adverse events or complications were observed throughout the study.

Patients showed a mean full-mouth plaque index of 2.15 ± 0.35 at baseline that was reduced to 0.75 ± 0.26 and 0.82 ± 0.39 after 1 and 3 months respectively. Mean values for PI, BOP, PPD and CAL on patient level in different treatment groups at baseline, 1 and 3 months post-treatment are shown in Table 2. At baseline, no significant differences were noted among the treatment groups with regard to PI, BOP, PPD and CAL. One and 3 months after treatment, all treatment groups showed significant improvement in all clinical parameters (Table 2).

Frequency of BOP and mean values for PI, PPD and CAL on site level in different treatment groups at baseline,

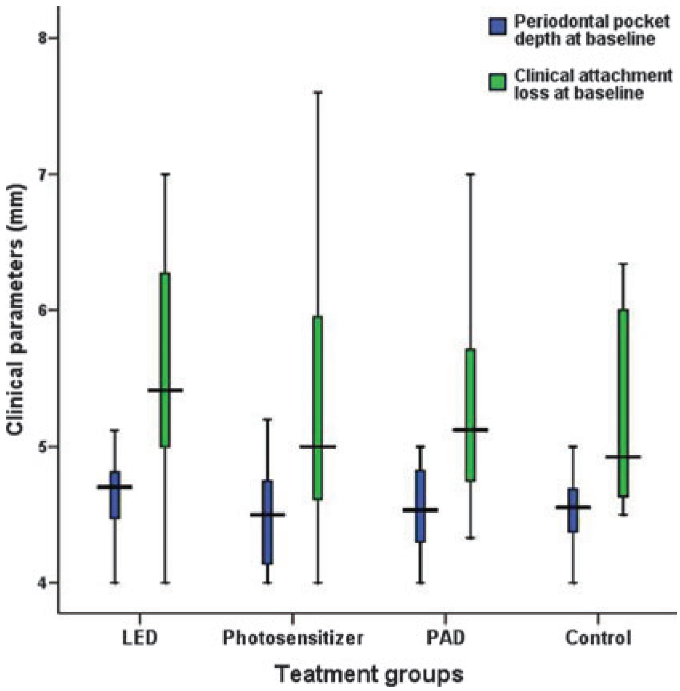

Fig. 1. Distribution of the values of periodontal pocket depth and clinical attachment loss in different treatment groups at baseline. LED, Light-emitting diode; PAD, photoactivated disinfection.

Table 1. Demographic characteristics of the patient population at baseline

	All	Groups			
		LED	PS	PAD	Control
Mean age± SD (range)	50.3 ± 8.7 (40–63)	–	–	–	–
Gender (F/M)	8/8	–	–	–	–
Smoking (Yes/No)	3/16	–	–	–	
Total number of experimental teeth*	199	50	47	52	50
Total number of experimental sites*	396	96	90	119	91
Mean frequency of experimental teeth* per patient (±SD)	12.5 ± 2.5	3.2 ± 1.0	2.9 ± 0.8	3.2 ± 0.9	3.1 ± 0.9
Mean frequency of experimental sites* per patient (±SD)	24.7 ± 7.7	6.0 ± 2.8	5.6 ± 2.8	7.4 ± 4.2	5.7 ± 3.1

*Experimental teeth/sites refer to teeth/sites with PPD: 4–6 mm.
F, Female; M, Male; PPD, pocket probing depth; LED, Light-Emitting Diode; PS, photosensitizer; PAD, Photoactivated Disinfection; mm: millimetre.

1 and 3 months post-treatment are shown in Table 3.

There were no statistically significant differences between the treatment groups with regard to changes in clinical parameters at any time point (all $p > 0.05$) (Table 4).

To allow more comprehensive comparisons between the groups, the sites were subset into baseline PPD categories of "4 mm $\leq$ PPD < 5 mm" and "(PPD $\geq$ 5 mm". According to the categories of the initial PPDs, no statistical significant differences were found between the treatment groups (Table 5).

Results from multilevel logistic regression models showed that there was no association between the values of PPD (based on site level and patient level) at 3 months after therapy with PAD group (Table 6).

Discussion

The present double-blind split-mouth randomized clinical study was designed to evaluate the clinical effectiveness of adjunctive photodynamic therapy using LED in the treatment of moderate to severe chronic periodontitis. The results showed that all treatment modalities led to significant improvements in PPD, CAL and BOP. Considering 1 mm as the minimum detectable difference in the primary outcome variable, there were no significant differences between the groups for any parameter throughout the study period.

The baseline values of PI and BOP were significantly high. The plaque index reduced significantly after 1 and 3 months. However, BOP was still observed in more than 50% of experimental sites. This observation suggests that complete resolution of inflammation was not achieved even in the presence of significant PPD reduction.

The results of this study are in accordance with those of other clinical studies that did not support the clinical advantage of adjunctive photodynamic therapy (using laser) in the treatment of patients diagnosed with chronic periodontitis (Christodoulides et al. 2008, Chondros et al. 2009, Polansky et al. 2009, Ruhling et al. 2010). A recent split-mouth clinical trial evaluated clinical and microbiological effects of adjunctive PAD (diode laser, 660 nm, TBO as photosensitizer) in the treatment of patients affected by chronic periodontitis. This study showed that single session of PAD or TBO did not improve clinical parameters compared with SRP alone, although it did result in reduction of potential periodontal pathogens (Theodoro et al. 2011).

The current results are not in line with some other clinical studies that reported improvement in clinical outcomes for the photodynamic therapy in combination with scaling and root debridement (Andersen et al. 2007, Braun et al. 2008, Lulic et al. 2009, Sigusch et al. 2010). Andersen et al. showed that a combination of SRP and PAD (diode laser 670 nm and methylene blue as photosensitizer) in patients affected by moderate to advance periodonti-

Table 2. Mean values (standard deviation) for plaque index, bleeding on probing, probing pocket depth and clinical attachment level on patient level in different treatment groups at baseline, 1 and 3 months post-treatment

	LED (Number of sites = 96)	PS (Number of sites = 90)	PAD (Number of sites = 119)	Control (Number of sites = 91)	*p*-value
PI					
Baseline	2.56 (0.28)	2.45 (0.30)	2.45 (0.28)	2.52 (0.26)	0.60
1 month	0.8 (0.18)	0.75 (0.21)	0.72 (0.22)	0.74 (0.23)	0.76
3 months	0.83 (0.21)	0.78 (0.22)	0.76 (0.23)	0.77 (0.19)	0.82
BOP					
Baseline	1.00 (0.0)	0.98 (0.05)	0.99 (0.02)	1.00 (0.0)	0.51
1 month	0.76 (0.19)	0.70 (0.27)	0.79 (0.21)	0.88 (0.12)	0.12
3 months	0.58 (0.29)	0.50 (0.32)	0.61 (0.19)	0.66 (0.24)	0.37
PPD (mm)					
Baseline	4.65 (0.29)	4.48 (0.38)	4.53 (0.33)	4.54 (0.27)	0.55
1 month	3.55 (0.56)	3.43 (0.53)	3.56 (0.57)	3.42 (0.33)	0.79
3 months	3.20 (0.43)	3.00 (0.42)	3.19 (0.55)	3.16 (0.39)	0.59
CAL (mm)					
Baseline	5.56 (0.86)	5.30 (0.93)	5.34 (0.80)	5.21 (0.68)	0.68
1 month	4.32 (0.86)	4.23 (0.84)	4.33 (0.90)	4.07 (0.61)	0.79
3 months	4.10 (0.87)	3.80 (0.81)	3.95 (0.99)	3.81 (0.73)	0.72

*<0.05.
** 0.01.
***<0.001.
PI, Plaque Index; BOP, Bleeding on Probing; PPD, pocket probing depth; CAL, clinical attachment level; PS, photosensitizer; LED, Light-Emitting Diode; PAD, Photoactivated Disinfection; mm, millimetre.

Table 3. Frequency (%) of bleeding on probing and mean values (standard deviation) for plaque index, probing pocket depth and clinical attachment level on site level in different treatment groups at baseline, 1 and 3 months post-treatment

	LED (Number of sites = 96)	PS (Number of sites = 90)	PAD (Number of sites = 119)	Control (Number of sites = 91)	*p*-value
PI					
Baseline	2.56 (0.49)	2.45 (0.50)	2.48 (0.50)	2.49 (0.50)	0.51
1 month	0.79 (0.40)	0.73 (0.44)	0.73 (0.45)	0.71 (0.45)	0.63
3 months	0.82 (0.38)	0.75 (0.43)	0.77 (0.42)	0.74 (0.43)	0.60
BOP					
Baseline	96 (100%)	89 (98.9%)	118 (99.1%)	91 (100%)	0.60
1 month	75 (78.1%)	69 (76.7%)	93 (78.1%)	78 (85.7%)	0.41
3 months	60 (62.5%)	52 (57.8%)	75 (63.0%)	58 (63.8%)	0.83
PPD (mm)					
Baseline	4.67 (0.60)	4.50 (0.56)	4.60 (0.64)	4.53 (0.56)	0.19
1 month	3.59 (0.92)	3.42 (0.74)	3.60 (0.90)	3.42 (0.73)	0.60
3 months	3.28 (0.77)	3.00 (0.73)	3.21 (0.89)	3.17 (0.81)	0.63
CAL (mm)					
Baseline	5.64 (1.23)	5.36 (1.25)	5.18 (1.06)	5.21 (1.11)	0.53
1 month	4.50 (1.38)	4.28 (1.30)	4.15 (1.12)	4.08 (1.15)	0.65
3 months	4.23 (1.27)	3.85 (1.36)	3.75 (1.14)	3.83 (1.22)	0.72

*$p < 0.001$.
PI, Plaque Index; BOP, Bleeding on Probing; PPD, pocket probing depth; CAL, clinical attachment level; PS, photosensitizer; LED, Light-Emitting Diode; PAD, Photoactivated Disinfection; mm, millimetre.

tis resulted in significant improvements in clinical outcomes (Andersen et al. 2007). Similar results were obtained by two randomized clinical studies that reported statistically better results in sites treated with adjunctive PAD (diode laser 660 nm and phenothiazine chloride as photosensitizer) compared with SRP alone (Braun et al. 2008, Sigusch et al. 2010).

In 10 maintenance patients with residual pockets (PPD $\geq$ 5 mm), repeated applications of PAD (diode laser 670 nm, and phenothiazine chloride as photosensitizer) resulted in significant improvement of clinical outcomes after 6 months. The authors reported that the mean reduction of PPD in PAD treated patients were significantly higher than that of control group (0.67 mm *versus* 0.04 mm) (Lulic et al. 2009).

Different types of photosensitizer, light source and irradiation parameters could partially explain controversial results between previous studies.

Although these studies demonstrated statistically significant improvements in sites treated with adjunctive PAD, their additional improvement in probing pocket depth and clinical attachment level were minor (0.2–0.6 mm). As a reduction in PPD of 1–3 mm could routinely be accomplished with scaling and root debridement (Morrison et al. 1980, Badersten et al. 1981, Lindhe et al. 1982b, Cobb 2002), it is questionable whether these slight improvements in clinical parameters by adjunctive PAD are of any clinical relevance.

It should be noted that in this study, the range of mean values of baseline PPD in different groups was between 4.5 and 4.6 mm. At 3 months, all treatment groups showed improvements compared with baseline and the range of mean values of PPD reduced to 3–3.2 mm. As all treatment groups received SRP, the effectiveness of SRP may have masked the adjunctive benefit of PAD.

The results of this study revealed that application of adjunctive PS alone (PS group) had no additional effect compared with control group. This finding is in line with the results of a recent *in vitro* study that showed that application of photosensitizer without laser irradiation was not able to reduce bacteria within a layer of 10 μm in an artificial biofilm model. The authors suggested that laser was an essential part of antimicrobial photodynamic therapy (Schneider et al. 2012).

The results of recent clinical studies showed that application of erbium: yttrium–aluminium–garnet (Er:YAG) laser as a monotherapy for chronic periodontitis did not have any additional advantage over conventional SRP in terms of clinical outcomes (Krohn-Dale et al. 2012, Ratka-Kruger et al. 2012, Soo et al. 2012).

Table 4. Changes of bleeding on probing [frequency (percentage)] and pocket probing depth and clinical attachment loss [mean(SD)] in different treatment groups from baseline to 1- and 3-month examination

	Treatment groups (Number of sites)	1 month	3 months
Changes in BOP	LED (96)	21(21.9%)	36(35.4%)
	PS (90)	20(22.2%)	37(41.1%)
	PAD (119)	25(21.0%)	43(36.1%)
	Control (91)	13(14.3%)	33(36.2%)
Changes in PPD (mm)	LED (96)	1.09 (0.42)	1.44 (0.41)
	PS (90)	1.10 (0.48)	1.49 (0.56)
	PAD (119)	0.98 (0.37)	1.30 (0.04)
	Control (91)	1.12 (0.19)	1.38 (0.28)
Changes in CAL (mm)	LED (96)	1.10 (0.40)	1.45 (0.40)
	PS (90)	1.07 (0.46)	1.50 (0.56)
	PAD (119)	1.01 (0.42)	1.39 (0.53)
	Control (91)	1.12 (0.21)	1.40 (0.28)

BOP, Bleeding on Probing; PPD, pocket probing depth; CAL, clinical attachment level; PS, photosensitizer; LED, Light-Emitting Diode; PAD, Photoactivated Disinfection; mm, millimetre.

Table 5. Changes of pocket probing depth [mean(SD)] considering the baseline pocket probing depth in different treatment groups from baseline to 1- and 3-month examination

	LED	PS	PAD	Control	*p*-value
Baseline PPD (4 $\leq$ PPD < 5mm)					
1 month	0.92 (0.53)	0.87 (0.56)	0.98 (0.35)	0.82 (0.53)	0.41
3 months	1.02 (0.54)	1.20 (0.61)	1.17 (0.38)	1.08 (0.63)	0.39
Baseline PPD (PPD $\geq$ 5mm)					
1 month	1.18 (0.84)	1.30 (0.74)	1.01 (0.81)	1.39 (0.74)	0.09
3 months	1.63 (0.80)	1.83 (0.85)	1.48 (1.09)	1.63 (0.82)	0.30

PPD, pocket probing depth; PS, photosensitizer; LED, Light-Emitting Diode; PAD, Photoactivated Disinfection; mm, millimetre.

Table 6. Results from multilevel logistic regression models for the association of probing pocket depth (based on site level and patient level) at three months after therapy with photoactivated disinfection group

PPD (mm)	Site level				Patient level			
	SE	OR	95% CI	*p*-value	SE	OR	95% CI	*p*-value
≤ 3		1				1		
$>3, \leq 4$	0.45	0.52	0.22–1.27	0.15	1.29	0.18	0.01–2.29	0.19
$>4, \leq 5$	0.38	0.63	0.30–1.32	0.22	1.30	0.12	0.01–1.55	0.11
>5	0.46	0.41	0.16–1.07	0.06	–			

PPD, Probing Pocket Depth; SE, Standard Error; OR, Odds Ratio; CI, Confidence Interval; mm, millimetre

The light source used in the previous clinical studies was laser. This study is the first clinical trial evaluating the effect of PAD using LED in the treatment of chronic periodontitis. The characteristics of the light produced by LEDs are different from those of lasers. Lasers produce intense coherent, collimated and monochromatic beams of light while LEDs are neither coherent nor collimated and generate fairly wideband of wavelengths. On the other hand, the wideband emission of LED (625–635 nm) causes the light emission in almost the entire absorption spectrum of TBO (632 ± 8 nm). This may promote optimization of the photodynamic process (Zanin et al. 2006). Note worthily, toluidine blue O is regarded as the photosensitizer of choice in eradication of important pathogens involved in periodontitis (Usacheva et al. 2003). A recent *in vitro* study showed that LED photodynamic therapy was highly efficient in deactivation of *Porphyromonas gingivalis* lipopolysacharide adherent to titanium surface (Giannelli et al. 2011). An experimental study in rats revealed that the application of LED photodynamic therapy was more effective than that of photosensitizer alone in the suppression of bone resorption and the expression of inflammatory cytokines in ligature-induced periodontitis. The results were reported 7 days after treatments. Different from this study, the LED wavelength range was 440–480 nm and the photosensitizer was eosin (Carvalho et al. 2011). Unlike these promising results from the *in vitro* and animal studies, the adjunctive photodynamic therapy using LED did not improve the clinical outcome in this human study. There may be different reasons for these diverse results. It was shown that the effect of PAD on the viability of microorganisms is decreased up to 50% in biofilm bacteria in comparison with planktonic culture (Fontana et al. 2009). Moreover, the presence of serum-derived gingival crevicular fluid and blood in the periodontal pocket could dramatically reduce the efficacy of PAD in clinical situations (Matevski et al. 2003). In addition, several factors including photosensitizer type and concentration, period of maintenance of drug within the tissue, time for biological response, the PH of the target site, the presence of exudates, the mode and frequency of photosensitizer application, the availability of oxygen and the irradiation parameters could also influence the biological response to PAD (Wilson 2004, Soukos & Goodson 2011).

The limitations of this study should be considered before interpreting the findings. In this randomized double-masked clinical trial, just clinical parameters were evaluated. As PAD is based on eradication of microorganisms, microbiological analysis could assess changes in periodontal pathogens. In addition, the follow-up period of this study was relatively short. This limitation could be justified, since the results of a recent meta-analysis showed that PAD provides short-term (until 3 months) benefits in terms of clinical parameters (Sgolastra et al. 2011). Another limitation of this clinical trial was the use of a periodontal probe that was not pressure-calibrated to standardize probing forces. This study was designed as a split-mouth trial. One of the disadvantages of split-mouth studies is that treatment may have effects on experimental sites other than those, which they were assigned to (Hujoel & DeRouen 1992). In other words, there is a significant possibility of "spillover effect" (Lesaffre et al. 2009). In addition, intra-oral translocation of periodontopathogens during the healing period may explain the similar results obtained from different treatment modalities in the same patient (Quirynen et al. 2001). This notion can explain the relatively high percentages of experimental sites with positive BOP despite of low of plaque scores at 1 and 3 months.

The power calculation and the results indicate that this study probably did not have adequate power to detect the 1-mm difference between treatment modalities.

Currently, there is no established protocol for adjunctive photodynamic therapy following the conventional non-surgical periodontal treatment. Therefore, further studies with other combination of photosensitizers and light sources are needed to determine the most desirable effects in clinical situations and to establish the optimal parameters of irradiation and drug concentration for maximum clinical benefit.

Conclusion

Within the limitations of this study, it is concluded that the adjunctive PAD using LED as the light source did not result in significant clinical improvement in patients diagnosed with moderate to advance chronic periodontitis. Further clinical studies with longer follow-up, taking into account the microbiological outcomes and with different light sources and photosensitizers are required before any definitive conclusion can be made about the clinical relevance of PAD in the treatment of periodontal disease.

Acknowledgement

The authors thank all patients who participated in this study. We acknowledge Dorsun Teb Pars Co. for providing LED device. We also thank Dr. Alipasha Meysamie, Associate professor of Department of Community Medicine, Tehran University of Medical Sciences for his special helps.

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Clinical Relevance

Scientific rationale for the study: Problems associated with the use of antibiotics have led to shift to new antimicrobial concepts with fewer complications, such as photoactivated disinfection (PAD). Previous studies using PAD with laser as a light source have shown promising results. More recently, light-emitting diode (LED) devices have been suggested as novel light sources in PAD. These devices are more compact and portable and considerably less expensive and less harmful to the eyes compared with lasers. The aim of this randomized controlled clinical study was to evaluate the effect of PAD using LED as the light source in the treatment of moderate to severe chronic periodontitis.

Principal findings: Scaling and root planing resulted in significant improvement of clinical parameters of patients with chronic periodontitis. Application of PAD did not provide additional effects.

Practical implications: Use of LED-based PAD with the current setting cannot be suggested to achieve an improvement of clinical parameters in patients with moderate to severe chronic periodontitis.