Review Article

Antimicrobial Photodynamic Therapy as an Adjunctive Modality in the Treatment of Chronic Periodontitis

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Abstract

Introduction: Due to penetration of pathogenic bacteria into the periodontal tissues in moderate to severe periodontitis, the mechanical methods are not sufficient in these cases. Therefore, administration of local/systemic antibiotic is recommended following mechanical root debridement. However, side effects of antibiotics such as microbial resistance and patient allergy led to development of alternative methods. One of the suggested methods is the antimicrobial photodynamic therapy (aPDT). aPDT is a local non invasive treatment modality without the side effects caused by antibiotics. The aim of this study was to collect the clinical articles related to the application of aPDT in the treatment of chronic periodontitis.
Method: In order to find related clinical articles, a search of PubMed, Google Scholar and Science Direct until 2012 was performed.
Results: A total of 11 articles were found. In 7 of the 11 articles, the assessment of aPDT led to a significant improvement in the clinical attachment and probing depth. In 4 studies, there was no difference between the scaling & root planing (SRP) and adjunctive application of aPDT. aPDT in most cases resulted in less gingival bleeding compare to SRP alone. Furthermore, its application in multiple doses was more effective in comparison to a single dose treatment.
Conclusion: It appears that aPDT is effective as an adjunctive therapy compared to conventional non_surgical treatment alone, and is recommended in multiple doses in order to achieve more appropriate results.
Keywords: Photodynamic therapy; periodontal disease; chronic periodontitis; clinical trial

Please cite this article as follows:
Moslemi N, Heidari M, Bouraima SA. Antimicrobial Photodynamic Therapy as an Adjunctive Modality in the Treatment of Chronic Periodontitis. J Lasers Med Sci 2012; 3(4):141-6

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Introduction

Periodontitis is an inflammatory disease which characteristics include gingival inflammation, loss of attachment apparatus, pocket formation and alveolar bone loss (1). Various pathogens including Aggregatibacter actinomycetemcomitans (A.a.) and Porphyromonas gingivalis (P.g.) are responsible for the host epithelial cells invasion and the resulting invasion of deeper tissues (2,3). The main purpose of periodontal treatment comprises removal of biofilm from root surface. Failure in the success of the mechanical debridement leads to tooth mobility and involvement of the furcation (4-6). The complexity of the anatomy of the root and furcation regions renders the access to the germs under the gingiva difficult. As a result, complete removal of bacterial germs with the mechanical method alone is impossible, and adjunctive treatments have been recommended to facilitate bacterial germs and plaque removal (7-9).

One of the adjunctive treatments is the administration of antibiotics. It has been demonstrated that antibiotics either systemic or local are effective in the reduction of periodontal pathogens (10,11). The use of antibiotics has two basic problems; the first one is maintenance of the drug therapeutic concentration in periodontal pockets for enough time to be certain of microorganism's elimination, since a collection of gram positive and gram negative bacteria in a polymeric matrix on the dental surface is an obstacle for the antimicrobial drug activity (12). Consequently, inappropriate drug concentration in sulcus and biofilms results in an insufficient antimicrobial effect. The second problem is the appearance of drug resistant strains of bacteria and changes in bacterial normal flora as a consequence of wide use of antibiotics (13, 14). In upcoming years, problems rising from treatments with antibiotics will increase for the following reasons:

1- Increased resistance to antibiotics
2- Increase of immunosuppressed patients (15)
3- Periodontal infections with various bacteria different from local pathogens, and the consequent need for different and multiple antibiotics (16)

Due to these factors, the efforts toward adjunctive treatment modalities continue. In 2003 the head of the American academy of Periodontology Michael P Rethman said "Taking into account the bacterial drug resistant strains due to the widespread use of antibiotics, antimicrobial photodynamic therapy(aPDT) can be an effective replacement therapy".

Antimicrobial Photodynamic Therapy

aPDT or Photoradiation therapy, or phototherapy, or photochemical therapy was first introduced by Raab in 1990 (17). Allison et al, named aPDT as a treatment composed of light and drug (18).

aPDT has three component:

1- Light
2- A substance sensitive to light (Photosensitizer)
3- Free radical and singlet oxygen (19)

When the photosensitizer is stimulated by its appropriate wavelength, it moves from its low energy state to a highly energized triple state. The long half life of the triple state results in reactions of the photosensitizer with the molecules of the medium and the oxygen in the tissues (20). The singlet oxygen and free radicals are produced which lead to tissue damage (19).

The cytotoxic products have a short half life (0.04μs) and a limited effect radius (0.02μm). Because of the limited O_2 migration from the production site, the primary cell damage location depends on the localization and local aggregation site of the photosensitizer. As a result aPDT is perfect for local application without damage to cells further away (21,22).

Advantages of the use of aPDT in periodontal treatments

1- Bacterial resistance to aPDT is less probable, since the singlet oxygen and the free radicals interact with different cells structures and in different metabolic ways.
2- aPDT is a local non invasive modality and does not damage the tissues surrounding the target location and even the micro flora around.
3- aPDT eliminates the non accessible pathogens in the periodontal pockets in a short time, it is then beneficial to the clinician and the patient.
4- The risk of bacteremia after periodontal treatment with aPDT is the least.
5- There is no need for antibiotic prescription.
6- There is no need for local application of anesthetics, and damage to the bacteria occurs in a shorter time (less than 60s) (19).

The aim of this study was to review of the effects of aPDT in the treatment of chronic periodontitis. For this purpose all clinical studies performed in this field were reviewed.

Methods

In order to find related clinical articles, a search of PubMed, Google Scholar and Science Direct till 2012 was performed. We collected a total of 11 articles. The keywords were comprised of photodynamic therapy, clinical studies, chronic periodontitis and periodontal disease. All the articles collected were in the full text format and in English.

Review of literature

In table1 a summary of the clinical studies performed in the domain of aPDT effects in treatment of chronic periodontitis is listed (Table1).

Table 1. Summary of clinical studies performed in relation to the effects of photodynamic therapy in chronic periodontitis treatment

Author / Year	Study type	Test Group	Control Group	Laser and photosensitizer characteristics	Number of doses	Clinical findings
Andersen R et al (23) 2007	Randomized Clinical Trial (33 patients)	aPDT and SRP+ aPDT	SRP	Diode 670nm 150mW Phenothiazine Chloride (Methylene Blue)	Single dose	Statistical significant improvement in CAL and PPD for test group
Braun A et al (24) 2008	Split Mouth Randomized Clinical Trial (20 patients)	SRP+ aPDT	SRP	Diode 660nm 100mW Phenothiazine Chloride	Single dose	More reduction of CAL, SFFR, BOP and PPD for test group, equal increase in GR in two groups
Christodoulides N et al (25) 2008	Randomized Clinical Trial (24 patients)	SRP+ aPDT	SRP	Diode 670nm 75mW Phenothiazine Chloride	Single dose	No difference for CAL and PPD; remarkable improvement for FMBS in test group
Chondros P et al (26) 2009	Randomized Clinical Trial (24 patients)	SRP+ aPDT	SRP	Diode 670nm 75mW Phenothiazine Chloride	Single dose	No difference for CAL and PPD; remarkable improvement for FMBS in test group
Polansky R et al (27) 2009	Clinical Trial (58 patients)	SRP+ aPDT	SRP	Diode 680nm 75mW Phenothiazine Chloride	Single dose	aPDT wasn't effective in improving PPD and BOP
Ruhling A et al (28) 2010	Clinical Trial (54 patients)	aPDT	SRP	Diode 635nm 100mW Tolonium Chloride	Single dose	No difference in CAL and PPD
Pejcic A et al (29) 2010	Randomized Clinical Trial (34 patients)	SRP+ aPDT	SRP	Low level laser 670nm 150mW	Multiple doses	Improvement in CAL, GCF and PPD in aPDT group
Lui J et al (30) 2011	Randomized Clinical Trial (24 patients)	SRP+ aPDT	SRP	Diode 940nm	Multiple doses	Improvement in BOP and GCF in short time in aPDT group
Aykol G et al (31) 2011	Randomized Clinical Trial (24 patients)	SRP+ aPDT	SRP	Diode 808nm 0.25W	Multiple doses	Improvement in CAL, BOP and PPD in test group
Cappuyns et al (32) 2011	Randomized Clinical Trial (24 patients)	aPDT SDL	SRP	Diode 660nm Phenothiazine Chloride	Multiple doses	Improvement in PPD, BOP and GR in all 3 groups
Noro Filho et al (33) 2012	Randomized Clinical Trial (12 patients HIV+)	SRP+ aPDT	SRP	Diode 660nm Methylene Blue	Single dose	Better results in CAL and PPD in aPDT group

SRP: Scaling and Root planning; aPDT: antimicrobial photodynamic therapy; PPD: Periodontal Pocket Depth; CAL: Clinical Attachment Level; BOP: Bleeding on Probing; GR: Gingival Recession; GCF: Gingival Crevicular Fluid; SFFR: Sulcus Fluid Flow Rate; SDL: Soft Diode Laser; nm: nanometer; mW: milli watt

In a randomized clinical trial performed in 2007 by Andersen et al, 33 patients suffering from chronic periodontitis were randomly placed in three groups. In group1 aPDT, in group2 scaling & root planing (SRP+) aPDT (Diode laser) and in the control group SRP alone was applied. The results of this study showed that the addition of aPDT to SRP from a statistical point of view significantly improved the clinical attachment level (CAL) and the probing pocket depth (PPD) (23).

In another randomized clinical trial done by Braun et al in 2008, with the aim of comparison of the clinical results of root debridement with or without aPDT in the treatment of chronic periodontitis, 20 patients were randomly divided in two groups (Split mouth design). All the patients underwent SRP, and in two quadrants aPDT (Diode laser with 660nm and 100mW, photosensitizer: Phenothiazine chloride) was applied. At the beginning of the study, at one week and three months after treatment the sulcus fluid flow rate (SFFR), bleeding on probing (BOP), PPD and gingival recession (GR) were assessed. In all criteria investigated, except for gingival recession better results were obtained in the aPDT group, but there was no difference between the two groups for gingival recession (24).

Christodoulides et al performed a randomized clinical trial in 2008. They randomly allocated 24 patients with chronic periodontitis in two groups, SRP+ aPDT (Diode laser with 670nm and 75mW) and SRP. Between these two groups no statistical significant difference in CAL and PPD was found, but the full mouth bleeding score (FMBS) was significantly lower in the SRP+ aPDT group (25).

In 2009, in another randomized clinical trial, Chondros et al randomly put Twenty-four patients of chronic periodontitis in maintenance phase in two groups of SRP and SRP+ aPDT (Diode laser with 670nm and 75mW/cm^2, 60s every tooth, photosensitizer: Phenothiazine chloride). The two groups were assessed for two periods of times, at 3 and 6 months. Between the two groups no statistical significant difference was recorded for PPD, CAL and plaque index (Plaque score), but FMBS was significantly reduced in the SRP+ aPDT group (26).

Polansky et al in a randomized clinical trial in 2009 assessed the bactericidal effect of aPDT. In that study, they randomly placed 58 patients suffering from chronic periodontitis in two groups of SRP and SRP+ aPDT (Diode laser with 680nm and 75mW). No statistical significant difference was found for PPD, CAL and BOP between the two groups. Based on those results, the use of aPDT in a single treatment session didn't show remarkable clinical effects compared to the conventional treatment method (SRP) (27).

Ruhling et al in their randomized clinical trial evaluated the effects of aPDT on persistent pockets. they randomly placed 25 patients in a aPDT group (Diode laser with 635nm and photosensitizer: Tolonium chloride) and 29 patients in an ultrasonic debridement group. There was no statistical significant difference between the two groups in Plaque index, BOP and PPD, and they rejected their hypothesis stating that aPDT is preferable compared to periodontal mechanical treatment (28).

In a clinical study Pejcic et al evaluated the anti inflammatory effect of SRP and aPDT on gingiva. Seventeen patients were placed in the SRP +aPDT group (Low level laser with 670nm in 10 successive days after performing SRP) and 17 patients in the ultrasonic debridement group. The Plaque index, BOP, PPD, CAL and Gingival Crevicular Fluid (GCF) were assessed. They stated that the use of aPDT combine to the periodontal conservative treatment (SRP) was significantly effective in the reduction of inflammation (29).

The combined SRP and aPDT treatment was compared to the periodontal non surgical treatment on chronic periodontitis in a randomized clinical trial by Lui et al in 2011. Twenty-four patients suffering from this condition were investigated. In this split mouth study, the patients were randomly divided in two groups SRP and SRP +aPDT (Diode laser with 940nm for 3 days). BOP and GCF decreased more in the control group one month after treatment, but at 3 months after no difference was seen. Also, interleukin1β decreased more in the SRP +aPDT group than in the control group after one week after. They concluded that the use of aPDT in addition to periodontal non surgical treatment (SRP) was effective in the improvement of periodontal disease in the short term (30).

In a randomized clinical trial performed in 2011 by Aykol et al, 24 patients with chronic periodontitis were randomly placed in two groups of SRP and SRP +aPDT (Diode laser with 808nm and 0.25W at day 1, 2 and 7). Then all the patients were divided in two cigarette smoking and non cigarette smoking groups. In the SRP +aPDT group, either smoking or non smoking, BOP, CAL and PPD showed improvements, they reached the conclusion that aPDT can be effective as an adjunctive periodontal treatment (31).

In a split mouth randomized clinical trial by Cappuyns et al in 2011, 32 patients with antecedent of non surgical treatment for chronic periodontitis were divided in 3 groups SRP, Diode laser (810nm wavelength) and aPDT (660nm wavelength and photosensitizer: Phenothiazine chloride). All 3 groups showed improvement in parameters of PPD, BOP and GR and there was no significant difference between the 3 groups (32).

Noro Filho G et al in a split mouth randomized clinical trial in 2012, randomly placed 12 patients infected with HIV, and with antecedent of chronic periodontitis in 2 groups SRP and aPDT as an adjunctive treatment (660nm wavelength and photosensitizer: Methylene blue). In the evaluation performed, after 6 months improvements in CAL and PPD were observed and they concluded that the combination of SRP and aPDT can have more benefits in the treatment of these patients (33).

Results & Discussion

The results of the studies performed on the effects of aPDT in the reduction of pockets depth and clinical attachment are different. Although most of the studies used a Diode laser, none of them mentioned which laser, photosensitizer, wavelength, density, energy and duration is more effective. Results obtained from the study performed by Chan and Lai suggest that the wavelength and energy density are both important factors in the efficacy of lasers, and that wavelength and optimal dose with an appropriate photosensitizer are practical variables in the bactericidal process (34). It seems that the difference in these factors led to different results.

Application of multiple doses of laser is more effective than the use of single dose (35). But in 8 of the reviewed studies, laser was applied as a single dose, which also influences the results obtained. In the studies in which laser was used in multiple doses more convenient results were obtained. In the review article performed by Malik et al in 2010, it was stated that no benefits was seen in the additional treatment with aPDT (in addition to SRP) for patients suffering from chronic periodontitis. They justified it by the fact that aPDT has to be used multiple times during the first weeks of treatment in order to increase the antimicrobial effect and that the use of single dose is not effective (36). In a study performed by Soukos et al in 2011, it was mentioned that the short time of exposure to light can be one of the reason for the lack of effect of aPDT in studies and that the repetition of photodynamic therapy (5 times in 2 weeks) as an adjunctive treatment to mechanical debridement leads to improvement of results obtained (37).

Though the use of laser have led to similar results to SRP in most of the studies, it's not possible to ignore its benefits which include less skill, less treatment time, effect rapid onset, lack of need for anesthesia, absence of creation of resistant bacterial flora. It appears that the most usefulness of laser is during the maintenance phase, because in this phase the need for SRP is high, so it prevents the excessive removal of dental tissue and consequently it prevents dental hypersensitivity. It also improves dental hypersensitivity following surgery. And because of its bactericidal character it is possible to restrain the prescription of antibiotics after surgery. Since laser results in reduction of bacteremia, it is perhaps possible to use it in patients with high risks of infectious endocarditis .Takasaki et al expressed that due to its low economical cost, aPDT can be an appropriate modality in the treatment of periodontal diseases. Additionally, because of the possibility of local application it is possible to avoid the prescription of systemic antibiotics in the treatment of infections. Moreover, that the high concentration of the chemical substance of aPDT in the site of infection results in the effective elimination of bacteria without any side effects for the host tissues (38).

It should be noted that low-level laser therapy showed a in full mouth bleeding score (FMBS) compared to SRP. It appears that laser is effective in the initial stages of inflammation such as vessel permeability increase, endothelium thinning and vessel wall ulceration. Eduardo et al in 2010 in a systematic review stated that low level laser is effective in the improvement of inflammatory processes, wound healing and rapid epithelialization (35).

It's not hard to believe that low level laser can be used in home to control plaques (tooth brush having a low level laser and tooth paste or mouthwash containing photosensitizer) (39), which can be promising for many periodontal treatments in order to improve plaque control,However,further studies are needed to evaluate its efficacy.

Even though it seems that low level laser improves results of clinical findings in periodontology, it has to be used on a clean and free of germs surface, so it is effective as an adjunctive treatment not a primary one (35).

As a result, aPDT as an adjunctive treatment in addition to other periodontal treatments is more effective than conventional periodontal treatments alone. In addition, the multiple use of aPDT compared to its use as a single dose is more effective. Considering that the effective role of laser in the treatment of periodontal diseases has been proven, it is suggested that different types of photosensitizers, lasers, wavelengths and powers been compared in order to obtain the best and most effective clinical results. Number of sessions, durations and frequencies are other laser characteristics that have to be evaluated to determine the best possible configuration and periodicity.

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