REVIEW ARTICLE

Role of Photodynamic Therapy in Non-Surgical Periodontal Treatment

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Abstract

Background and Aim: This study aimed to provide an overview about the efficacy of photodynamic therapy (PDT) as an adjunct to scaling and root planing (SRP) versus SRP alone in non-surgical periodontal therapy.

Materials and Methods: Randomized clinical trials (RCTs) with a minimum duration of 3 months, evaluating PDT+SRP versus SRP alone in non-surgical periodontal treatment of patients diagnosed with aggressive or chronic periodontitis who had at least 2 teeth with probing depth (PD) ≥4 mm, and in vitro studies evaluating the effect of adjunctive PDT on proliferation or viability of human gingival fibroblasts (HGFs) were included. An electronic search of the literature was carried out mainly through PubMed, Cochrane Library, and Google scholar for relevant English articles published from January 2011 to January 2021 using the following keywords: "photodynamic therapy" and "periodontitis" or "periodontal diseases".

Results: Twelve articles were reviewed in this study. Analysis of the clinical attachment level (CAL), PD, gingival index (GI), plaque index (PI), bleeding on probing (BOP) and microbiological counts of Aggregatibacter actinomycetemcomitans (A. actinomycetemcomitans) and Porphyromonas gingivalis (P. gingivalis) demonstrated variable outcomes. Five articles revealed significant improvement of clinical parameters in the PDT groups compared with the control group ($P<0.05$); five studies reported significant improvement of CAL ($P<0.05$). However, three studies found no significant difference between PDT and control groups in terms of CAL ($P>0.05$).

Conclusion: PDT+SRP could help improve the periodontal parameters, compared with SRP alone. Further studies are required to reach a stronger conclusion regarding the superiority of one over the other.

Key Words: Photochemotherapy; Root Planing; Periodontitis

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Introduction

Elimination of subgingival bacteria and regeneration of periodontal tissue on cementum are challenging tasks in treatment of periodontal diseases. In periodontal diseases, the bacteria may invade the cementum and radicular dentinal tubules up to 300 µm depth;[1] thus, the smear layer and residual bacteria inhibit the proliferation of fibroblasts and normal periodontal tissue regeneration on the cementum. The standard method of treatment is scaling and root planing (SRP), which cannot completely remove the smear layer and bacteria; therefore, adjuvant methods have been proposed to minimize this problem.[2,3]

Some of the available modalities include low level laser therapy (LLLT), high energy lasers, and antimicrobial photodynamic therapy (PDT). The aim of this review was to evaluate the efficacy of PDT as an adjunct to SRP in non-surgical periodontal treatment.

LLLT refers to the use of lasers in wavelength range of 600-1000 nm, low power range (mW) and low energy dosage (0.01 to 100 J/cm^2). [4, 5] LLLT is mainly used for soft tissue and does not cause hazardous thermal alterations in tissues. [5] Due to increased production of adenosine triphosphate, LLLT increases the fibroblast proliferation [5-7] and reduces the production of some pro-inflammatory cytokines; therefore, it has an anti-inflammatory effect. [8-10] LLLT also increases angiogenesis.[11] The most popular and commonly used low level lasers are He-Ne laser and diode lasers such as InGaAlP laser and GaAlAs laser.[5]

High-power lasers have bactericidal effects[8, 12] and by efficiently removing the calculus, they result in a rough surface.[3,13] Root surfaces treated by high power lasers enable better clot formation and gingival fibroblast attachment.[13,14] However, high-power lasers can cause a significant temperature rise. [15]

PDT is a method for inactivation of microorganisms and biological molecules.[16] This method has three main components:

[I] A safe visible light: a source of low-power visible light activates the photosensitizer. Human tissues transmit red light efficiently, and longer wavelengths result in deeper light penetration.[17]

[II] A photosensitizer

[III] Reactive oxygen species, which are capable of destroying the microorganisms.[18] Photosensitizers that are activated by light release oxygen reactive species which will lead to lethal photosensitization of bacteria.[19]

Photosensitizer is a chemical agent that is activated by a specific wavelength of light and has a lethal effect on cells. Photosensitizer accumulates selectively in tissues and makes a cytotoxic substance which produces the desired biological effects.[20] The most common photosensitizers that are utilized in dentistry are toluidine blue O (TBO), methylene blue (MB), indocyanine green (ICG), and curcumin. An ideal photosensitizer should display local toxicity only after activation by illumination and should be non-toxic to adjacent tissues.

PDT is beneficial in periodontal treatment, since it is non-invasive, does not damage the adjacent tissues, and is capable of eliminating inaccessible pathogens in periodontal pockets. [21] The aim of this review was to evaluate the efficacy of PDT as an adjunct to SRP in non-surgical periodontal treatment. The main focused question addressed in this review was “does adjunctive PDT provide superior outcomes compared with SRP alone?”

Materials and Methods

An electronic search of the articles was done mainly through PubMed, Google Scholar and Cochrane Library, using the following keywords: "photodynamic therapy" and “periodontitis" or “periodontal diseases”. This search aimed at collecting the relevant English articles published from January 2011 to January 2021. Finally, 12 articles were selected. The selection algorithm is explained in Figure 1.

Inclusion criteria

1. Randomized clinical trials (RCTs) with the

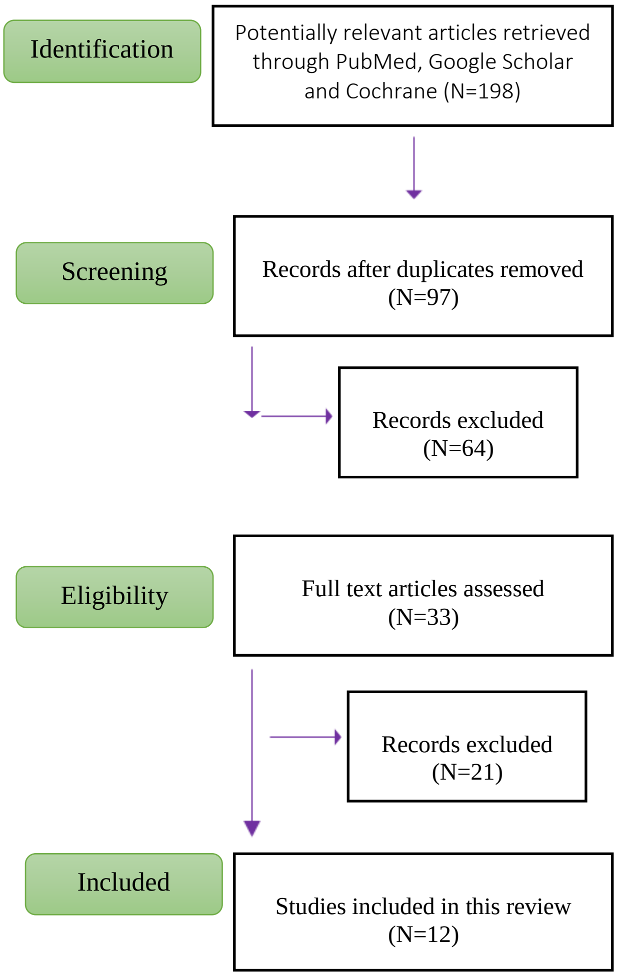

Figure 1. Flowchart of article selection

following characteristics were included in this review:

- Non-surgical treatment of patients suffering from chronic or aggressive periodontitis
- Participants should have at least 2 teeth with probing depth (PD) ≥4 mm
- RCTs that examined PDT as an adjunctive treatment to SRP (hand instrumentation or ultrasonic scaler)
- Studies with at least 3 months of duration

-RCTs evaluating clinical parameters and/or microbiological counts of perio-pathogenic bacteria such as Aggregatibacter actinomycetemcomitans (A. actinomycetem-comitans) and Porphyromonas gingivalis (P. gingivalis).

2.In vitro studies evaluating the adjunctive effects of PDT on proliferation, or viability of human gingival fibroblasts (HGFs).

Exclusion criteria

RCTs with:

- less than 10 patients per group
- less than 2 teeth per patient with PD≥4 mm
- the ones that assessed PD<4 mm

-follow-up period less than 3 months

-studies examining PDT in surgical procedures or dental implants

Outcome measures

Clinical, biological and microbiological parameters were assessed in this review. The measures included: changes in (I) clinical attachment level (CAL) or relative attachment level, (II) PD, (III) gingival index (GI), (IV) bleeding on probing (BOP), (V) sulcus bleeding index (SBI), (VI) plaque index (PI), (VII) HGF proliferation or viability, (VIII) A. actinomycetemcomitans count, and (IX) P. gingivalis count.

Results

In total, 97 articles were initially identified in the electronic databases. Sixty-four trials were excluded, since they were irrelevant to the main subject or did not meet the inclusion criteria. Twelve articles including 10 RCTs and 2 in vitro studies were included and processed after the final stage of selection.

The wavelengths of lasers used in these studies ranged from 628 to 810 nm. Photosensitizers used in these studies were MB, TBO and ICG.

Main outcome of the studies:

1.Photosensitizers

ICG[22] is a photosynthetic anion that is activated at a wavelength of approximately 800 nm and leads to optical oxidation. At low concentrations, ICG has no toxic effects on the body and is excreted with no harm.[23,24] Laser-activated ICG is efficient against Gram-positive and Gram-negative bacteria.[23] Low power lasers used along with ICG could be effective on various oral biofilm bacteria as well as periodontal pockets.[25]

Four split-mouth RCTs used ICG as photosensitizer[26-29] with laser wavelength of 810 nm[26,28,29] or 808 nm.[27] All four studies had one single episode of antimicrobial PDT. Three trials found that adjunctive antimicrobial PDT, when compared with SRP alone, promoted statistically significant improvement in CAL and reduction of PD (P<0.05),[26,28,29] and one study showed statistically significant improvement of GI in the PDT group compared with SRP alone (P<0.05).[26] In a study conducted by Hill et al,[27] after a two-week interval, the sulcular fluid flow rate decreased significantly in the PDT group compared with SRP alone (P≤0.05). In the same study,[27] SRP+PDT had no significant superiority over SRP alone regarding BOP, relative attachment level, PD, gingival recession or reduction of periodontal pathogenic microorganisms (P>0.05). Three studies found that SRP+PDT and SRP alone resulted in similar significant reductions in PI (P<0.05).[26,28,29] Gandhi et al,[26] also showed reduction of A. actinomycetemcomitans in the PDT group which was significant compared with SRP alone (P<0.05); in contrast, P. gingivalis reduction was not significant compared with the control group (P>0.05).

Joshi et al.[28] reported similar significant reduction of modified sulcus bleeding index in PDT+SRP and SRP groups (P<0.05). Similarly, Shingnapurkar et al.[29] found similar significant reduction of GI in PDT+SRP and SRP groups (P<0.05).

TBO and MB are efficient photosensitizers, capable of inactivating bacteria, viruses and fungi. TBO was the photosensitizer of choice in different studies conducted on P. gingivalis.[30,31]

In 4 studies, TBO was the photosensitizer of choice;[1,32-34] two were in vitro studies in which the tooth fragments received single application of PDT with a laser wavelength of 660 nm.[1,32] Two other articles were split-mouth RCTs using single application of 630 nm[33] and 635 nm lasers.[34] Goh et al.[33] revealed significant improvement of PD and CAL in the PDT group compared with SRP alone after 3 months of follow-up (P≤0.05). However; after 6 months, the parameters had similar significant improvements in the test and control groups. The results of a RCT conducted by Mallenini et al.[34] revealed a significant difference in PI, PD, SBI, CAL, and P. gingivalis colony count between PDT+SRP and SRP groups at 1 and 3 months follow-ups.

In one in vitro study, adhesion and proliferation of osteoblasts in the PDT group increased significantly, compared with the control group; however, proliferation and adhesion of HGFs did not increase significantly, compared with the control group.[32] In an in vitro study by Karam et al,[1] PDT significantly increased the HGF's viability, compared with the control group.

Four RCTs used MB as photosensitizer.[35-38] In a split-mouth RCT by Corrêa et al,[35] single application of PDT with 660 nm laser resulted in increased gain of CAL and increased reduction of PD compared with SRP alone (P<0.05). The same study showed significant reduction of A. actinomycetem-comitans in the PDT group 3 and 7 days after treatment (P<0.05) while the SRP group did not show any significant reduction of A. actinomycetemcomitans (P>0.05). The study revealed no significant intra- or inter-group reduction in P. gingivalis.

In a split-mouth RCT by Katsikanis et al,[36] single session PDT with 670 nm laser did not cause any significant improvent in BOP and PD, compared with the control group (P>0.05). Pulikkotil et al.[37] used single session PDT with 628 nm laser in a split-mouth RCT and found no significant differences between PDT+SRP and SRP alone in case of PD, CAL, plaque score and A. actinomycetocomitans count. BOP was the only clinical parameter that decreased significantly in the PDT group, compared with the SRP group (P<0.05).

Segarra-Vidal et al. [38] investigated the effect of three sessions of PDT with 670 nm laser on improving clinical parameters (PI, PD, clinical recession, CAL, BOP, gingival crevicular fluid volume) and reduction of periopathogenic bacteria in a parallel design RCT. A. actinomycetocomitans was the only parameter that decreased significantly in the PDT+SRP group compared with the SRP group (P<0.05). Other parameters did not show significant intergroup differences.

2.Clinical and biological parameters

All 10 clinical trials reported that PDT as an adjunct to SRP was effective in treatment of periodontitis.[26-29,33-38] Five articles revealed significant improvements in clinical parameters after PDT compared with the SRP group.[26,28,29,33,34] Five studies reported significant gain of CAL, compared with SRP alone.[26,28,29,33,34] However, in three studies, no significant difference was reported between PDT and control groups in terms of CAL.[27,35,38]

In five studies, PDT had significant effects on reduction of PD, compared with the control group.[26,28,29,33,34] However, in five studies, no significant difference was found between PDT and control groups in terms of PD.[27,35,36,38] One study showed significant improvement of GI in the PDT group, compared with SRP alone.[26] Intergroup comparison in one study reported a significant reduction of SBI in the PDT group.[34]

In four studies, PDT and control groups did not differ significantly in PI.[26,27,35,38] Also, in three studies that examined BOP, no significant difference was found between the PDT group and the SRP group;[27,36,38] however, in one study, BOP decreased significantly in the PDT group compared with the SRP group (P<0.05).[37] In an in vitro study by Karam et al,[1] PDT significantly increased the HGF's viability, when compared with the control group. In an in vitro study by Rafael Ferreira et al,[32] when compared with the control group, adhesion and proliferation of osteoblasts in the PDT group increased significantly; however, adhesion and proliferation of HGFs did not increase significantly.

3. Microbiological parameters

Regarding the microbiological parameters, three articles showed reduction of A. actinomycetemcomitans [26,35,38] and two studies showed a decrease in P. gingivalis in the PDT group, which were significant compared with the control group.[33,34] Hill et al.[27] reported none-significant reduction in the number of A. actinomycetemcomitans and P. gingivalis in the PDT group compared with the control group (P>0.05). In a study by Pulikkotil et al,[37] there was no significant reduction of A. actinomycetemcomitans in the test group, compared with the control group. In a study by Segarra-vidal et al,[38] PDT did not significantly decrease P. gingivalis in the PDT group compared with the control group.

In total, all included studies demonstrated that PDT was significantly effective in improving the clinical[26-29,33-38] or biological parameters. [1,32]

Conclusion

The present review suggests that PDT could help improve the outcomes of periodontal parameters, compared with SRP alone in treatment of periodontitis. However, due to the limited evidence and heterogeneity in materials, methods and parameters of the included studies, superiority of adjunctive PDT over SRP alone is not certain. Further studies are required to reach a stronger conclusion.

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