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Review

Is mechanical curettage with adjunct photodynamic therapy more effective in the treatment of peri-implantitis than mechanical curettage alone?

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ABSTRACT

Background: The aim of the present study was to review the pertinent literature on the effects of mechanical curettage (MC) with and without adjunct photodynamic therapy (PDT) for the management of peri-implantitis.
Methods: The addressed focused question was "Is PDT effective in the treatment of peri-implantitis?" A search without language or time restrictions up to March 2016 was conducted using various key words. The exclusion criteria included; review papers, in vitro Studies, case reports, commentaries, interviews, and letters to the editors.
Results: In total 9 studies were included. Among them 5 studies were clinical and 4 were experimental. All the studies used PDT as an adjunctive to MC in their test groups. The laser wavelengths used ranged from 660 nm to 830 nm. One study showed significant reduction of the bleeding scores, inflammatory exudates and *Aggregatibacter actinomycetemcomitans* count in group with PDT as an adjunctive when compared to MC and 0.2% chlorhexidine. However, in four clinical studies comparable periodontal parameters were reported when PDT is used as an adjunct to MC was compared to MC in treatment of peri-implantitis. In three experimental studies, outcomes were significantly better in group with PDT as an adjunct to MC when compared to MC alone at follow-up.
Conclusion: The role of PDT as an adjunct to MC in the treatment of peri-implantitis is debatable. Further longterm randomised control trails are needed to justify the role PDT as an adjunct to MC in treatment of peri-implantitis.

Contents

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1. Introduction

The use of dental implants over past decades has increased exponentially and is considered as a viable treatment alternative for partially and completely edentulous patients given its high predictability and success rate [1,2]. With an increasing number of implants placed, complications associated with implants such as peri-implant diseases have also increased, occuring with a frequency ranging from 1% to 47% [3]. Peri-implant mucositis is the reversible inflamation of soft tissue without any signs of loss of supporting bone around the dental implant in function [4–7]. Peri-implant mucositis if left untreated can eventually lead to peri-implantitis. Peri-implantitis is an inflamation of tissues around an osseointegrated implant in function, resulting in soft tissue inflamation with loss of supporting bone beyond the biological remodelling of bone and eventually leading to loss of implant [4–7].

The presence of persistant bacterial biofilm on the implant surface is the most common etiological factor for peri-implantitis [5]. The traditional treatment for peri-implant diseases was surgical flap elevation and mechanical curettage (MC). It has been reported that sufficient decontamination through mechanical curettage is not possible because bacteria are protected in micro-irregularities of the implant surfaces [8]. Adjunct therapies have been developed to improve the prognosis of peri-implantitis. Adjunctive use of local and systemic antibiotics have shown better clinical and microbiological outcomes in treatment of peri-implantitis [9]. However increased bacterial resistance to antibiotics had made this option challenging. Attempts have been made to enhance MC using laser therapy. Studies [10–13] have shown that photodynamic therapy (PDT) with diode lasers can significantly reduce bacteria and decontaminate implant surface with letal photosensitization. PDT includes the use of low level lasers for decontamination of implant surfaces and reduction of bacterial count in periodontitis [14,15]. Mechanism of action of PDT involves three elements: light from laser, a photosensitizer and oxygen [16]. The photosensitizer, when light activated, forms reactive oxygen species and radicles in the membranes of microorganisms, which thereby kills the microorganisms [17].

The use of PDT as an adjunctive to MC has shown significant improvements in clinical outcomes [15,18,19]. In a clinical trial by Bombeccaei et al. [18], peri-implantitis patients treated with PDT as an adjunctive to MC showed significant difference in clinical periodontal parameters as compared to group with MC and 0.2% chlorhexidine as an adjunctive. However, studies by Basseti et al. [20] and Schar et al. [21] showed no difference in clinical periodontal parameters in patients treated with PDT as an adjunctive to MC. Therefore, there appears to be a disagreement with regard to the bactericidal efficacy of PDT as an adjunct to MC in treatment of peri-implantitis. Due to the controversy in efficacy of PDT as an adjunctive, the aim of the present study was to review the pertinent literature on the effects of PDT for the management of peri-implantitis.

2. Materials and methods

2.1. Focused question

Based on guidelines of systematic review and meta-analysis (PRISMA) [22], a specific question was constructed. The focused question was "Is PDT effective in the treatment of peri-implantitis?"

2.2. Selection criteria

The eligibility criteria were as follows: (a) clinical trials; (b) interventions evaluating efficacy of PDT in treating peri-implantitis; (c) studies reporting one or more clinical periodontal parameters as outcome including clinical attachment loss, plaque index, gingival index or bleeding on probing; (d) studies reporting immunological and bacterial profile in vivo after PDT application. The exclusion criteria included; review papers, in vitro studies, case reports, commentaries, interviews, and letters to the editors.

2.3. Search strategy

A search without language or time restrictions up to March 2016 was conducted in MEDLINE/PubMed, EMBASE, Scopus, ISI Web of knowledge, and Google-Scholar databases to address our focused question. A systematic approach to literature searching was used to identify the appropriate papers that report the efficacy of PDT as an adjunctive in the treatment of peri-implantitis. Electronic database searches were performed using different combinations of Medical Subject Headings (MeSH) terms and free text words: 1. Photodynamic therapy; 2. photosensitizing agents; 3. Peri-implantitis; 4. Clinical studies; 5. Randomized controlled trials; 6. Experimental studies; and the combinations. Original studies were hand searched to find any articles that could have been missed during the initial search. Two authors (AG and FV) performed hand search on following journals: Journal of Clinical Periodontology, Journal of Periodontology, Clinical Oral Investigation, Journal of Dental Research, Lasers in Medical Science, Journal of Photochemistry and Photobiology, Photo-diagnosis and Photodynamic Therapy, JOMI and Journal of Research and Science. Any disagreements regarding study selection were resolved via discussion.

2.4. Screening methods and data abstraction

Three authors (AG, SVK and SP) performed the screening independently after reviewing the title and the abstracts of articles that fulfilled the selection protocol. The data from the selected studies was tabulated according to the (a) study design, (b) demographic characteristics of the participants, (c) their follow-ups, (d) study outcome, (e) laser characteristics, (f) type of photosensitizer, (g) outcome of the studies.

2.5. Study selection

Initially, 42 studies were identified. After screening of the titles and abstracts, 27 studies were excluded and a total of 15 studies were selected for thorough full-text screening. In the final stage of screening 6 studies were further excluded leaving 5

Table 1
General characteristics of included studies.

Study		Age range (yrs)	Mean age (yrs)	Gender F/M	Study design	Number of implants
Bombeccari et al. [18]	Human	33–64	46	24/16	RCT	40
Angelis et al. [23]	Humans	25–80	59	42/38	RCT	80
Bassetti et al. [20]	Humans	27–78	58	20/20	RCT	40
Esposito et al. [16]	Humans	25–80	59	42/38	RCT	80
Schar et al. [21]	Humans	27–78	58	20/20	RCT	40
Shibli et al. [15]	Dogs	NA	2	NA	Experimental Study	40
Hayek et al. [10]	Dogs	NA	4	NA	Experimental Study	18
Htet et al. [24]	Dogs	1.5- 2	NA	NA	Experimental Study	30
Sousa et al. [19]	Rabbits	7 months	NA	NA	Experimental Study	8

randomized controlled trials [16,18,20,21,23] and 4 experimental studies [10,15,19,24] (Table 1).

2.6. Methodological study quality assessment

Methodological quality of the included studies was independently assessed by two authors (AG, SP) according to a scoring system developed by the CASP quality scale for reporting randomized controlled trials. This scale is used to score randomized controlled trials on the basis of three items which are randomization, blinding of examiner or patients, and an account of all the patients i.e. loss to follow-up. The scores range from 0 to 12 points with higher score indicating higher study quality.

Quality Assessment of included studies was performed using the Critical Appraisal Skills Program Cohort Study Checklist [25]. A systematic approach based on 12 specific criteria was used, which were as follows: (a) Study issue is clearly focused, (b) Cohort is recruited in an acceptable way, (c) Exposure is accurately measured, (d) Outcome is accurately measured, (e) Confounding factors are addressed, (f) Follow-up is long and complete, (g) Results are clear, (h) Results are precise, (i) Results are credible, (j) Results can be applied to the local population, (k) Results fit with available evidence, and (l) There are important clinical implications. Each criterion was given a response of either "Yes," "No," or "Cannot tell." Each study could have a maximum score of 12. Critical Appraisal Skills Program scores were used to grade the methodological quality of each study assessed in the present systematic review (Table 4).

3. Results

3.1. General characteristics of included studies

In total, 9 studies [10,15,16,18–21,23,24] were included. Five studies [16,18,20,21,23] were clinical in design and 4 studies [10,15,19,24] were performed in animal models (Table 1).

3.2. Laser and photosensitizer related parameters

All the studies [10,15,16,18–21,23,24] used diode lasers with wavelengths ranging between 660 nm and 830 nm. Power output and duration of irradiation ranges between 11 mW–100 mW and 40–180 (seconds) respectively. Toluidine blue and Phenothiazine chloride were used as photosensitizers in five [15,16,18,23,24] and two studies [20,21], respectively. Methylene blue and Polycyclic aromatic hydrocarbon paste was used as photosensitizers in studies by Sousa et al. [19] Hayek et al. [10] respectively (Table 2). In all studies [10,15,18–21,24] photosensitizer was placed in the periodontal pockets ranging about 3–5 min, then the photosensitizer was thoroughly cleaned and irradiated using diode lasers. In the studies by Angelis et al. [23] and Esposito et al. [16] the information about the photosensitizers and Lasers used remained unclear.

3.3. Clinical studies

All the studies [16,18,20,21,23] were randomized control trials (RCT). The number of male and female participants ranged between 16–38 and 20–42, respectively [16,18,20,21,23]. The age of the participants ranged between 25 and 80 years and mean age was between 46 and 59 years. The number of implants placed in studies [16,18,20,21,23] ranged between 18–80 implants (Table 1). In 5 studies [16,18,20,21,23] PDT was used as an adjunctive with MC (MC) in treatment of peri-implantitis. Two studies [20,21] used Titanium curettes and glycine based powder air polishing and 1 study [18] used plastic scalers for MC. In the control groups of all the RCT [16,18,20,21,23], MC was done in the similar way as the test group. In the control groups, along with the MC 0.2% chlorhexidine was used by Bombeccariet al. [18] and minocycline was used by Bassetti et al. and Schar et al. [20,21] (Table 3).

3.4. Experimental studies

Among the 4 studies [10,15,19,24] in animal models, three [10,15,24] were done in dogs and one [19] was done in tibia of Rabbits. The number of implants placed in experimental studies [10,15,19,24] ranged between 16 and 40 implants. MC with PDT as an adjunct was done in the test groups of all experimental studies [10,15,19,24]. In addition to PDT, guided bone regeneration (GBR) was performed in test groups of 1 study [15]. In the control groups of all experimental studies [10,15,19,24] MC was done. Along with the MC 0.12% chlorhexidine, GBR and 1% NaOCl was used as an adjunctive in studies done by Hayek et al. [10], Shibli et al. [15] and

Table 2
Laser and photosensitizer parameters of included studies.

Study	Photosensitizers	Concentration	Type of laser	wavelength (nm)	Power (mW)	Time (s)
Bombeccari et al. [18]	TBO	100 mcg/mL	Diode	810	NA	100
Angelis et al. [23]	TBO	100 mcg/mL	NA	NA	NA	80
Bassetti et al. [20]	phenothiazine chloride	NA	Diode	660	100	40
Esposito et al. [16]	TBO	100 mcg/mL	NA	NA	NA	80
Schar et al. [21]	phenothiazine chloride	NA	Diode	660	100	40
Shibli et al. [15]	TBO	100 mcg/mL	Diode	830	50	80
Hayek et al. [10]	Ploycyclic aromatic hydrocarbon paste	NA	Diode	660	40	180
Htet et al. [24]	TBO	100 mcg/mL	Diode	830	50	60
Sousa et al. [19]	Methylene blue	NA	Diode	660–675	11	60

Table 3
Clinical and radiographic parameters of the included studies.

study	Test	Control	Follow-up (Weeks)	Assessed Parameters	Results
Bombeccari et al. [18]	MC + PDT	MC + 0.2% CHX	24	BI, MC, IE	Outcomes were significantly better for test group as compared to control at follow up.
Angelis et al. [23]	MC + PDT	MC	16	PI, BS, PPD	Outcomes in both groups at follow up were comparable.
Bassetti et al. [20]	MC + PDT	MC + AB	52	PPD, CAL, BS, MC, IL-1b	Outcomes in both groups at follow up were comparable.
Esposito et al. [16]	MC + PDT	MC	52	BI, PI, BG PPD	Outcomes in both groups at follow up were comparable.
Schar et al. [21]	MC + PDT	MC + AB	12	BI, PI, CAL, PPD	Outcomes in both groups at follow up were comparable.
Shibli et al. [15]	MC + PDT + GBR	MC + GBR	20	RO, BG	Outcomes were significantly better for test group as compared to control at follow up.
Hayek et al. [10]	MC + PDT	MC + 0.12%CHX	NA	MC	Outcomes in both groups at follow up were comparable.
Htet et al. [24]	MC + PDT	C 1: Er:YAG C 2: Bur alone	12	BG	Outcomes were significantly better for test group as compared to control at follow up.
Sousa et al. [19]	MC + PDT	MC + 1% NaOCl	4	MC, TS	Outcomes were significantly better for test group as compared to control at follow up.

BI: Bleeding Index, PI: Plaque Index, BS: Bleeding score, PPD: Probing pocket depth, CAL: Clinical attachment loss, BG: Bone height gain, RO: Re-osseointegration, IE: Inflammatory exudates, MC: Microbial counts, TS: Tensile strength.

Sousa et al. [19] respectively. Htet et al. [24] compared the efficacy of PDT against 2 different groups receiving Er: YAG laser, and bur alone. In the study by Sousa et al. [19] sterile discs, discs treated with a titanium brush (TiB), discs treated with the combination of TiB and PDT and discs treated with TiB and 1%NaOCl plus 0.2% CHX were implanted in rabbit tibia (Table 3).

3.5. Main outcome of the studies

All RCT [16,18,20,21,23] reporting clinical periodontal parameters, showed that PDT as an adjunctive was effective in the treatment of peri-implantitis along with MC. Bombeccari et al. [18] showed significant reduction of the bleeding scores, inflammatory exudates and *A. actinomycetemcomitans* count in group with PDT as an adjunctive when compared to MC and 0.2% CHX. In 4 studies [16,20,21,23] improvements in clinical parameters in groups with PDT as an adjunct to MC and MC alone were comparable. In two studies [20,21], Minocycline administration as an adjunct treatment to MC was equally effective in clinical periodontal outcomes when compared to application of PDT alone as an adjunctive.

Shibli et al. [15] showed significant increase in bone fill and reosseointegration in group with PDT and GBR as an adjunctive to MC when compared to group with MC and GBR. The study by Hetet et al. [24] showed increase in vertical bone height in the group with PDT when compared to group with Er:YAG laser and Titanium bur alone group. However, group with Titanium bur and citric acid as an adjunctive reported more increase in vertical bone height than group with PDT as an adjunctive. Results by Sousa et al. [19] reported increase in tensile strength of the implant in group with PDT as an adjunctive when compared to group with MC and 1% NaOCl. Significant reduction in Gram negative anaerobes after treatment with PDT as an adjunctive was reported in two studies by Shibli et al. [15] and Sousa et al. [19], however the results were comparable to their respective control groups (Table 3).

4. Discussion

In the present systematic review, we evaluated the influence of PDT in treatment of peri-implantitis. Results from approximately 44% of the studies [15,18,19,24] showed significant improvements in outcomes of group with PDT as an adjunct to MC compared to MC with other adjunctive treatments. However approximately 56% of studies [10,16,20,21,23] reported no differences in outcomes when PDT is used as an adjunct to MC compared to MC.

A number of factors may have influenced these results. For example, the type of photosensitizer used may have influenced the outcomes of the PDT. Photosensitizers derived from Perinaphthenone have shown pronounced bactericidal effects against bacteria like *Porphyromonas gingivalis* [26]. In present review a variety of photosensitizers such as polycyclic hydrocarbons [10,20,21], Toluidine blue [15,16,18,23,24], methylene blue [19] were used. All studies [15,16,18,23,24] that used toluidine blue was at a concentration of 100 mcg/ml. Majority of studies [15,16,18–21,23,24] used photosensitizer in liquid solution, however, Hayek et al. [10] used paste based photosensitizer: composed of 10% urea peroxide, 15% detergent, and 75% carbowax. Liquid photosensitizers has been known to stain implant surface and the adjacent tissues, leaving esthetic problems to patients and dentists [27]. However, paste based photosensitizer can be easily removed through saline irrigations, without any esthetic damage [10]. It is likely that the antimicrobial activity of these photosensitizers may have influenced the PDT outcomes in these studies.

Table 4
Assessing the quality of included studies using CASP scale.

Study	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Total
Bombeccari et al. [18]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	12
Angelis et al. [23]	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	10
Bassetti et al. [20]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	12
Esposito et al. [16]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11
Schar et al. [21]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	11
Shibli et al. [15]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	10
Hayek et al. [10]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Htet et al. [24]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	10
Sousa et al. [19]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9

Laser parameters could have an overall effect on the bactericidal efficacy of PDT. Diode laser application as an adjunctive to scaling and root planning has been shown to improve the clinical results for periodontal disease [28]. Studies have shown that fiber diameter of the laser has an influence on overall energy output and power density [29,30]. It is noteworthy that none of the studies [10,15,16,18–21,23,24] in the present review reported the fiber diameter they used, which makes it difficult to determine actual amount of energy released during the process of PDT. Studies [10,15,16,18–21,23,24] in the present review used wide range of PDT parameters wavelengths range from 660 nm to 830 nm, duration 40 to180 s and power 1 mW to 100 mW. Hayek et al. [10] used wavelength of 660 nm for about 180 s. Whereas, Shibli et al. [15] used wavelength of 830 nm for 80 s. It would be necessary to define the threshold laser parameters at which beneficial effect of laser application could be expected. Two studies [16,23] have not reported any laser parameters, which makes it difficult to govern the actual amount light energy delivered during the use of PDT. Hence, the efficacy of use of PDT as an adjunctive in treatment of peri-implantitis remains doubtful.

Local and systemic antibiotics delivery has been used as an adjunctive therapy in treatment of peri-implantitis. Two studies [20,21] compared the use of PDT with antibiotic treatment; both as an adjunct to MC in treatment of peri-implantitis. Outcomes of both the studies [20,21] showed comparable results among test and control groups. One explanation from a clinical standpoint PDT has an advantage when compared to antibiotic treatment because there is a possibility of developing bacterial resistance on multiple antibiotic applications. However, this effect has not been reported with use of PDT. Similar studies [31,32] which compared the efficacy of PDT with systemic antibiotics in management of aggressive periodontitis, showed comparable outcomes at follow up. Therefore, further clinical studies are required to compare the efficacy of PDT with localized antibiotic treatment; as an adjunctive to MC in treatment of peri-implantitis.

Chlorhexidine (CHX) has been known to be used in implant surface decontamination in the treatment of peri-implantitis. Two studies [10,18] PDT compared to the adjunctive use of Chlorhexidine gel and PDT in the treatment of peri-implantitis. Bombeccari et al. [18] reported a significant reduction in the bleeding scores and *A. actinomycetemcomitans* count in the group treated with PDT when compared to group treated with 0.2% chlorhexidine. It is speculated that substantivity and bacterial growth inhibitory effects of CHX may have influenced the results. Interestingly, in the study by Hayek et al. [10] no difference was found between CHX and PDT groups. It is noteworthy that the follow-up period in the study by Bombeccari et al. [18] was 24 weeks while Hayek et al. [10] evaluated the bacterial counts immediately after treatment. It is likely that this variation in the follow-up period may have influenced the results.

Most of the clinical studies [16,20,21,23] reported comparable results in groups with receiving PDT as an adjunctive. It is possible that in a clinical setting patient's oral hygiene status, habits such as tobacco smoking and chewing, and the systemic disorders like poorly controlled diabetes may affect the tissue response to PDT. Habitual tobacco use has been shown to have deleterious effects on periodontium and also compromise the outcomes of the periodontal therapy. Smokers were included in two studies [16,23], both the studies reported a comparable outcomes in groups with and without PDT. It is possible that habitual smoking would have influenced the overall efficacy of the PDT. Moreover, all the clinical studies in the present review had excluded patients with systemic diseases and presumably choose healthy individuals as study participants. It is speculated that PDT as an adjunctive to MC is an effective treatment approach in treating peri-implantitis in patients with type 2 diabetes. One possible explanation to this is, study by Al Amri et al. [33] reported dramatic decrease in the mean HbA1c levels at 6 months follow-up among patients that received MC and PDT compared with those that received MC alone. Hence, additional randomized control trails are needed to evaluate the efficacy of PDT as an adjunct in treatment of peri-implantitis in patients with systematic diseases.

5. Conclusion

The role of PDT as an adjunct to MC in the treatment of peri-implanttis is debatable. Further longterm randomised control trails are needed to justify the role PDT as an adjunct to MC in treatment of peri-implantitis.

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