

Literature Review

The Effectiveness of Photodynamic Therapy as An Adjunct to Mechanical Debridement in Peri-Implantitis Treatment

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ABSTRACT

Background: Peri-implantitis is one of many factors that can cause implant failure, with common cases ranging from 1%-47% and the highest incidence ranging from 10.7%- 47.2%. Mechanical debridement (MD) is currently the standard for peri-implantitis treatment. However, MD has limitations in the removal of infected tissue. Moreover, the rough texture of the implant's surface and bacteria adhesion and colonization increases the difficulty in performing MD. To overcome these limitations, adjunct therapy is needed to increase peri-implantitis treatment effectiveness. One of those adjunct therapies, photodynamic therapy (PDT), is used to destroy bacterial cells and significantly reduce inflammatory cell infiltration around the implant. **Purpose:** To describe the effectiveness of PDT as an adjunct therapy to MD in peri-implantitis treatment through narrative review **Review:** PDT is effective in reducing the number of bacteria, plaque index (PI), bleeding on probing (BOP), probing depth (PD), crestal bone loss (CBL), and excessive proinflammatory cytokines (IL-6, IL-1 β , TNF- α) in patients. However, the effectiveness of PDT can be influenced by several factors, including patients' conditions, such as diabetes and smoking habits, types of photosensitizers used, and exposure time. **Conclusion:** PDT is an effective adjunctive therapy to MD in peri-implantitis treatment since it can improve clinical parameter values, significantly reduce *P. gingivalis*, and decrease proinflammatory cytokines.

Keywords: photodynamic therapy; medicine; peri-implantitis; dentistry; communicable disease

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INTRODUCTION

Implants are generally the treatment of choice for replacing missing teeth.¹ The use of dental implants within ten years has a high success rate with a percentage of 92.8%-97.1%, which shows that dental implants are an effective treatment for rehabilitating patients with partial or complete tooth loss. Despite its high success rate, dental implants are susceptible to biological complications, such as peri-implantitis.²

The prevalence of peri-implantitis ranges from 1%-47%, with the highest incidence of peri-implantitis occurring after ten years of use ranging from 10.7%-47.2%.² This condition begins with gingival or mucosal inflammation.³ Persistent inflammation will cause an increase in proinflammatory cytokines, such as IL-6 and TNF- α , activating osteoclastogenesis and causing damage in the supporting bone tissue around the implant. In this condition, peri-implantitis occurs.^{4,5} If the inflammation is

not treated promptly, bone damage could spread throughout the implant, leading to failure.²

Peri-implantitis can be exacerbated by systemic factors such as diabetes and smoking habits. Diabetes can increase advanced glycation end products (AGEs) in the periodontal tissue and serum, encouraging tissue damage through increased oxidative stress. Increased AGEs also promote the production of pro-inflammatory cytokines, including IL-6 and TNF- α , which play an important role in damage to peri-implant tissue.³ Meanwhile, smoking can increase pro-inflammatory cytokines, inhibit wound healing, and exacerbate infection around implants.⁶⁻⁸

Mechanical debridement (MD) is the standard for the treatment of peri-implantitis.³ This treatment aims to reduce local inflammation, reduce probing depth (PD), and reduce infection of the alveolar bone around dental implants.⁹ However, MD has some limitations in removing infected tissue. MD cannot reach deep periodontal pockets,

especially if the PD around the implant exceeds 5 mm, causing the periodontal ligament damage continues.^{4,9} The high intensity of MD treatment can also damage the root surface. In addition, the surface roughness of the implant and bacterial adhesion and colonization make MD difficult and less effective for treating peri-implantitis.⁴ In overcoming the limitations of MD, adjunct treatments are needed to increase the effectiveness of peri-implantitis treatment. Adjunct therapy can be done between the administration of other antibiotics. This treatment can reduce PD and bleeding on probing (BOP) but does not cure peri-implantitis. In addition, the increasing resistance of several types of bacteria makes this treatment challenging to achieve the desired results.³

To overcome the two limitations of antibiotics, photodynamic therapy (PDT) has been developed as an adjunct treatment to MD for curing peri-implantitis.¹⁰ PDT is an antimicrobial treatment method that uses a certain light length to activate photosensitizer molecules in the periodontal pocket. Activated molecules react with oxygen and form reactive oxygen species (ROS), which can destroy bacterial cells without damaging body tissues. PDT as adjunctive therapy for MD can also significantly reduce the infiltration of inflammatory cells, especially plasma cells and lymphocytes.^{3,4} This narrative review aims to describe the effectiveness of PDT as an adjunct therapy to MD in peri-implantitis treatment.

Table 1. Data extraction from included articles

Author, year	Study design	Sample	Photo-sensitizer	Wave-length	Exposure time	Parameter	Result
Ahmed et al., 2020 ³	RCT	Peri-implantitis patients with type 2 diabetes mellitus (T2DM)		660 nm	10 s	PD, BOP, plaque score (PS), crestal bone loss (CBL), levels of IL-6 and TNF- α	PDT significantly reduced levels of PS ($p < 0.05$), BOP ($p < 0.05$), and PD ($p < 0.05$) at 3- and 6-months follow-up when compared with the baseline. PDT group has a comparable difference observed in BOP, PD, and CBL when compared to antibiotic gel therapy (AGT) PDT significantly reduced IL-6 and TNF- α levels at 3- and 6-months follow-up compared to baseline.
Alqahtani et al., 2019 ⁷	RCT	Peri-implantitis patients T2DM	Methylene blue	660 nm	60s	BOP, plaque index (PI), PD, and CBL	There was no significant difference in PI, BOP, PD, and CBL ($p > 0.05$) among cigarette smokers, waterpipe users, and never-smokers that underwent MD with or without adjunct PDT.
Labban et al., 2020 ¹¹	RCT	Peri-implantitis patients included cigarette-smokers, water-pipe users, or never-smokers	Indocyanine green (ICG)	810 nm	10 S	PD, BOP, PI, CBL, microbial count of <i>P. gingivalis</i> and <i>Treponema denticola</i> , levels of IL-1 β and IL-6	PDT significantly reduced levels of BOP ($p < 0.0001$), PD ($p = 0.001$), and CBL ($p = 0.04$), better than MD only. PDT non-significantly reduced PI level ($p > 0.05$) compared to MD only. PDT significantly reduced <i>P. gingivalis</i> and <i>T. denticola</i> ($p < 0.05$) on 3- and 6-months follow-up compared to baseline, while MD only on 3 months follow-up. PDT only showed a significant reduction in IL-1 β and IL-6 ($p < 0.05$) on 3-months' follow-up with no significant difference compared to MD only.
Almohareb et al., 2020 ¹²	RCT	Peri-implantitis patients	Methylene blue	670 nm	10 s	PS, PD, BOP, and microbial count of <i>P. gingivalis</i> , <i>T. denticola</i> , and <i>Tannerella forsythia</i>	PDT significantly reduced the level of BOP ($p < 0.05$) compared to amoxicillin and metronidazole treatment with adjunctive MD at 12-months' follow up. PDT significantly reduced <i>P. gingivalis</i> ($p < 0.05$) compared to amoxicillin and metronidazole treatment with adjunctive MD at 6-months' follow up.
Ohba et al., 2020 ¹³	RCT	Peri-implantitis patients	Toluidine blue	630 nm	30 s	PI	PDT non-significantly reduced the level of PI ($p > 0.05$) compared to the irrigation group.

REVIEW

In this review, a final of five articles were included. Table 1 shows the data extracted from 5 articles included in this review.

DISCUSSION

PDT procedure begins with the application of photosensitizer to deep periodontal pockets that cannot be easily reached by MD. The photosensitizer will accumulate on the infected tissue, then it will be activated by exposure of light within a certain wavelength.¹¹ The light activation causes the photosensitizer molecules to change from ground singlet state to excited singlet state. These molecules can return to the ground single state by emitting fluorescence or altering to excited triplet state via intersystem crossing.^{14,15}

Photosensitizer in excited triplet state can return to ground singlet state or generate ROS through two different mechanisms. In the first mechanism, an excited photosensitizer molecule produces ROS through an electron transfer process. While in the second mechanism, the photosensitizer molecule reacts directly with oxygen through energy transfer, producing another form of ROS, namely singlet oxygen.^{12,16} ROS generated by these two mechanisms are highly oxidative and cytotoxic. However, the cytotoxic effect of ROS is limited to the area where the photosensitizer is applied, thus allowing selective destruction. Furthermore, ROS can cause cell death of pathogenic bacteria in subgingival periodontal plaque, including *P. gingivalis*, by destroying the bacteria cell wall and through necrosis and apoptosis processes, without causing damage to surrounding host tissues.^{11,17}

The effectiveness of PDT as an adjunct therapy for MD was proven through several studies. Ahmed et al.³ compared the effectiveness of PDT and AGT as an adjunct treatment to MD in peri-implantitis patients with T2DM. The result of this study showed the PDT group had the lowest PS and BOP at the third month of observation compared to the control and AGT group. The significant decrease in PS was probably due to the effect of PDT given to the first group. Furthermore, PDT can cause marked decrease of inflammatory cells (namely plasma cells and lymphocytes) in the lamina propria of the subgingival connective tissue, thereby reducing BOP. Decrease in BOP was also due to the photosensitizer applied to the peri-implant pockets that could eliminate peri-implant pathogens.³

At 3 and 6 months of observation, marked reduction in TNF- α and IL-6 were also found. However, the decrease in the sixth month was not as big as the decrease in the third month. This could be due to the hyperglycemic effect of T2DM which triggers an increase in proinflammatory cytokines that could influence the effectiveness of PDT.^{3,11}

In addition to T2DM conditions that could influence the effectiveness of PDT, the frequency of PDT exposure

and the type of photosensitizer used can also influence its effectiveness. Study by Labban et al.¹¹ proved that repeated PDT could treat peri-implantitis better than a single session of PDT. In this study, PDT was applied 4 times, namely on day 1, 7, 17, and 27. In the subgingival environment with low oxygen levels, conventional photosensitizers cannot provide maximum antimicrobial effect. Therefore, this study utilized indocyanine-green due to its ability to work in low and even no oxygen environments.

Both Ahmed et al.³ and Labban et al.¹¹ studies excluded smokers in their sample choices. In the study by Alqahtani et al.⁷, smokers were included in the inclusion criteria of the sample choices. In non-smokers group, PDT as an adjunct therapy was effective to reduce PI, BOP, PD, and CBL at 3- and 6-months' follow-up. However, in the smokers group, PDT was only effective in reducing PI, BOP, and PD at 3 months observation time and there was no change in CBL. The decrease of PDT effectiveness in smokers group was due to the proliferation and development of pathogenic microbes, such as *P. gingivalis*, *Prevotella intermedia*, and *Aggregatibacter actinomycetemcomitans*. Therefore, lifestyle changes such as smoking cessation and improving oral hygiene are important in addition to MD and PDT therapy to increase the effectiveness of peri-implantitis treatment.⁷

Several literatures also compared the effectiveness between PDT and antibiotic as an adjunct therapy to MD in peri-implantitis treatment.^{10,12} Almohareb et al.,¹² stated that PDT was more effective in reducing *P. gingivalis* compared to amoxicillin and metronidazole. Furthermore, PDT has the potential to replace antibiotics as a safer adjunctive therapy for peri-implantitis since there were no side effects found in using PDT.^{10,12}

This review had several limitations. First, the PDT parameters used in the studies were inconsistent. There was no standardized benchmark for the type of photosensitizer, wavelength of light, exposure time, and frequency of PDT application used in the studies. These differences could potentially affect the antibacterial properties of PDT. Single sessions of PDT and short exposure times may reduce the ability to decrease bacteria and its anti-inflammatory effects.¹⁰ Furthermore, other heterogeneities in clinical trials from the literatures used, including inconsistent patient health status, influence of smoking activity on disease progression, and differences in observation time can also influence the PDT effectiveness in peri-implantitis treatment.

Within the limitations of this study, we concluded that PDT is an effective adjunctive therapy to MD in peri-implantitis treatment. PDT improved clinical parameter values, significantly reduced *P. gingivalis*, and decreased proinflammatory cytokines. In future studies, the effectiveness of PDT should be investigated using certain standards regarding the type of photosensitizer, wavelength of light, and frequency of PDT application used, thereby eliminating possible confounding variables.

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