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Review Article

Applications of Photodynamic Therapy in Management of Periodontal Disease - A Review

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Abstract :

A novel noninvasive photochemical approach for infection control, namely photodynamic therapy, has received much attention in the treatment of oral diseases which requires three nontoxic ingredients namely visible harmless light, a photosensitizer and oxygen are involved in this therapy. It is based on the principle that a photosensitizer binds to the target cells which when activated by light of a suitable wavelength results in the production of singlet oxygen and other very reactive agents that are extremely toxic to certain cells and bacteria. This article highlights the application of photo-dynamic therapy in management of periodontal disease and its current status.

Introduction

The biggest objective of periodontal therapy is to eliminate the bacterial deposits and niches by removing supra and subgingival plaque.

Currently this is being performed by mechanical methods such as tooth brushing and non-surgical therapy which results in significant clinical improvement. However, conventional mechanical therapy cannot completely remove all periodontal pathogens due to the presence of inaccessible areas and bacterial invasion into host tissues.

Since the 1990's PHOTOTHERAPY or the application of light energy with lasers has been used as an effective means of decontaminating periodontal pockets. Lasers have demonstrated effective killing of periodontal pathogens associated with periodontal and peri-implant diseases. These high level lasers bring about their bactericidal effects by thermal denaturation or direct ablation.

In spite of their substantial bactericidal action, there is limited clinical evidence that these lasers can produce a greater reduction in subgingival flora than traditional mechanical therapy. These lasers may also result in excessive ablation, thermal coagulation, carbonization or necrosis of root, connective tissue, bone or underlying pulp.[6]

The use of contemporary photodynamic therapy was first reported by the Danish physician, Niels Finsen (1901). He successfully demonstrated photodynamic therapy by employing heat– filtered light from a carbon – arc lamp (The FinsenLamp) in the treatment of a tubercular condition of the skin known as Lupus Vulgaris. Niels Finsen won a nobel prize for his work on phototherapy in 1903.[1,2]

The concept of cell death induced by the interaction of light and chemicals was first reported by OsarRaa[15] medical

student working with Professor Herman Von Tappeiner in Munich. Subsequent work in the laboratory of Von Tappeiner (1907) coined the term "Photodynamic action" and showed that oxygen was essential. Much later, Thomas Dougherty and co-worker[16] at Roswell Park cancer institute, Buffalo, New York, clinically tested Photodynamic therapy. In 1978, they published striking results in which they treated 113 cutaneous or subcutaneous malignant tumors and observed a total or partial resolution of 111 tumors. The active photosensitizer used in this clinical trial was called Hematoporphyrin Derivative. It was John Toth, who renamed it as Photodynamic therapy.

The basic phenomenon requires that the photosensitizer within periodontal pockets be light activated or excited from its so-called ground or singlet state (which is a single peak if analyzed spectrophotometrically) into either a doublet or triplet state. This leads to the transfer of energy (electrons) that precipitates the formation of singlet oxygen species, which are cytotoxic, thereby mediating bacterial kill.[3,4] Typically, the light must be of a specific wavelength as described by authors,but even broad-spectrum light can also activate photosensitizers such as toluidine blue.[5]Photo sensitizers are activated by red light between 630 and 700 nm corresponding to a light penetration depth from 0.5 cm (at 630 nm) to 1.5 cm at (700 nm) which is sufficient for periodontal treatment [7].

Antimicrobial photo sensitizers such as porphyrins, phthalocyanines and phenothiazines (e.g. methylene blue and toluidine blue O) have been reported to penetrate into gram-positive and gram-negative bacteria. The positive charge seems to promote the binding of the photosensitizer to the gram-negative bacterial membrane and leads to its localized damage, resulting in an increase in its permeability. Hence, toluidine blue O and methylene blue are commonly used in a PDT.

Other photosensitizers can also be used for clinical use, such asmesotetra-hydroxyphenyl-chlorin (mTHPC, temoporfin, Foscan), benzoporphyrin derivative monoacid A (BPD-MA,Visudyne), 5- or daminolevulinic acid (ALA, Levulan) and the methyl ester of ALA (Metvix). The latter two agents are not photosensitizers but are prodrugs converted by the body to protoporphyrin IX (or the methyl derivative for Metvix) via the heme biosynthetic pathway when applied topically.

Lasers used in the past included argon and Nd:YAG lasers. Currently, helium neon and gallium-aluminium-arsenide diode lasers are being used. Their wavelength ranges from 488-514nm for argon and 630-690nm for the diode lasers. High level energy ;lasers are not used to activate the photoactive dye as a relatively low exposure produces a high bactericidal effect.Recently, non-laser light sources such as light emitting diodes have been suggested as new light activators. These LED devices are more compact, portable and their cost is much less as compared with traditional lasers.

Recently, in Canada, a product called Periowave was used for the treatment of periodontitis. The Periowave product consists of a laser system with a custom-designed hand piece and patient treatment kits of methylene blue. A kit that includes phenothiazine chloride for clinical photodynamic therapy is now available Helbo; Photodynamic Systems .Similar kits that include toluidine blue O are also available.

Majority of the studies which was conducted has proved that photodynamic therapy can also be used as an adjunct to scaling and root planing.

In the studies by Fontana et al, the reduced susceptibility of biofilms was caused by reduced penetration of methylene blue into a biofilm and its retention in the outer layers of biofilm clusters as revealed by confocal scanning laser microscopy [8]. Similar findings were obtained by O'Neill et

al. [9], who studied toluidine blue-mediated a PDT. It has been suggested that water channels can carry solutes into or out of the depths of a biofilm, but they do not guarantee access to the interior of the cell clusters [10], the diameter of which may range from 20 to 600 μm[11].

A recent RCT study evaluated the treatment of patients with aggressive periodontitis by means of nonsurgical periodontal therapy in conjunction with either systemic administration of amoxicillin and metronidazole or 2 times topical application of PDT.[12]The results found that both treatment protocols resulted in statistically significant improvements in PD reduction, gain of CAL, compared with baseline.

The systemic use of amoxicillin and metronidazole yielded, however, at both 3 and 6 months, statistically significantly higher reductions in mean PD compared with the treatment using PDT.[13]

In vitro studies

Dobson and Wilson 1992 showed that low level helium neon laser irradiation with toluidine blue was effective against Porphyromonas gingivalis, Fusobacterium nucleatum, Aacomitansans Streptococcus sanguis.

Sarkar and Wilson 1993 reported that toluidine blue with helium neon laser killed oral bacteria within samples of subgingival plaque of chronic periodontitis patients. This demonstrated the efficacy of photodynamic therapy on bacteria within biofilms as well.

Henry, Sarkos et al demonstrated that argon laser irradiation could kill black pigmented bacteria – Prevotella and Porphyromonas species even in the absence of PS dye as the endogenous porphyrins of these species act as PS.

Numerous studies have also demonstrated that this therapy is effective in the detoxification of bacterial endotoxins as well.

In vivo studies

Animal studies have been performed to clarify the clinical response to photodynamic therapy. Komerik et al 2003 demonstrated a significant reduction in P gingivalis after treatment of experimentally induced periodontitis in rats using toluidine blue and diode laser.

Qin et al reported a significant reduction in total bacterial flora and inflammatory cell infiltrate after PDT. Also, a number of studies by Komerik et al have shown a decrease in alveolar bone resorption after photodynamic therapy.

Thus, general evidence suggests that PDT can suppress periodontal pathogens and reduce clinical signs of inflammation. However, there is a lack of evidence to prove that this effect can occur in a single course or dose and further studies need to be performed in this regard.

Few studies conducted clinically are as follows:

- Yilmaz et al in 2002 compared scaling and root planning with photodynamic therapy compared to SRP alone and PDT alone. After one month, clinical and microbiologic improvements were observed in only in SRP + PDT group and SRP group. They concluded that photodynamic therapy did not provide any additional benefit over conventional mechanical debridement.
- Two randomized control trials were performed by Anderson et al in 2007 – studied the combination of SRP and PDT and found significant improvement in all clinical parameters. Braun et al in 2008 concluded that clinical outcomes of SRP can be improved by adjunctive PDT in chronic periodontitis patients.
- de Oliveria et al in 2007 reported on the outcome of PDT for the treatment of aggressive periodontitis and concluded that the beneficial effects of PDT were more pronounced in moderate and shallow pockets.

From above mentioned studies which was conducted clinically,few advantages are listed below:

Adjunctive use of PDT to SRP results in higher reduction in bleeding on probing compared to SRP alone. Also, higher pocket depth reduction and clinical attachment gain is seen.

Based on its successful application on the treatment of periodontal disease, photodynamic therapy has been proposed as an adjunct for bacterial elimination in the treatment of periimplantitis.

Thus these studies conclude that PDT can effectively reduce the prevalence of pathogens on implant surfaces without causing any side effects to the bone or implant surfaces.

Current status

Even after reviewing all the currently available data, it is still not clear which photosensitizer and light source are the most suitable combination to obtain the desired bactericidal effect. Currently, toluidene blue and methylene blue are most commonly used. It is also not known which component is more important.

Manufacturers recommend that PDT should be performed repeatedly during the first week of healing. However, in most clinical situations it is only being performed in a single episode. Multiple courses may improve healing outcomes.

No study comparing the antimicrobial effects of PDT compared with that of local/systemic antibiotics, therefore it is still unclear whether PDT monotherapy could be used as an alternative to systemic or local antibiotics in patients with aggressive periodontitis or severe chronic periodontitis.

In future periodontal therapy, PDT could be used adjunctively to conventional mechanical treatment to treat moderate-severe periodontitis during non-surgical/ surgical/supportive therapy. Regarding periimplantitis, PDT may be regarded as an adjunct following debridement in surgical therapy.

PDT may be used as an aid to mechanical plaque control to attain high levels of bacterial eradication. A “photobrush” system can be created by combining a brush that emits a harmless diode or LED and a toothpaste that includes the appropriate photosensitizer.

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