Review Article

Comprehensive Review on Antimicrobial Photodynamic Therapy in Periodontology

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Abstract

Mechanical biofilm removal using scaling and root planing is the mainstay of both surgical and non-surgical periodontal therapies, however, its effectiveness is restricted in areas of anatomical complexity of tooth roots and soft-tissue penetrating periodontopathogens. Adjunct systemic and local antibiotics have been used in the literature with some amount of success to enhance the outcome of conventional mechanical debridement but frequent practice of systemic antimicrobials may cause the emergence of resistant microorganisms and shift in the microflora. Local drug delivery evolved as a substitute to systemic antibiotics, but its usage is based on number of sites, cost/benefit ratio, and patient compliance. To overcome the above limitations, photodynamic therapy (PDT) is being increasingly used as an adjunct to periodontal therapy. Although discovered more than 100 years ago and principally used for cancer and age-related macular degeneration, its antibacterial property has been recently considered in wake of growing antibacterial resistance. PDT's major advantages are its specificity to the targeted cells, with no collateral damage and lack of resistance development among bacterial species. In periodontal literature, though evidence is still developing in the favor of PDT, there is already a definitive interest and keenness for its usage in patients not responding to conventional treatment and patients with risk factors such as smoking and diabetes.

Keywords: Periodontitis, Antibiotic resistance, Bactericidal, Inflammatory mediator.

Introduction

Chronic periodontitis is described as an infective disease which results in inflammation of the supportive tissues around the teeth causing attachment loss progressively along with progressive destruction of bone.[1] It manifests clinically in the form of periodontal pocket and gingival recession. A key role is played by bacterial biofilm and inflammatory mediators such as cytokines in the etiology of periodontitis.[1,2]

Both non-surgical and surgical periodontal therapies aim at the reduction of bacterial load by eliminating the dental plaque and calculus. Conventional non-surgical therapy includes mechanical debridement using hand instrumentation and ultrasonic instrumentation. These conventional treatment methods, that is, scaling and root planning (SRP), however, do not wholly exterminate the periodontal pathogens completely. Incomplete removal is due to anatomical complexity of the tooth roots and the ability of the bacteria to invade the soft tissues.

Some therapeutic adjunctive, such as systemic and local antibiotics, have been used in the literature with some amount of success to augment the effect of conventional mechanical debridement by suppressing the periodontal pathogens in cases not responding to conventional treatment.[3]

Systemic antimicrobial therapy has few limitations as the microorganisms receive safe niche from the biofilm environment and also requisite drug concentration fail to reach the gingival crevicular fluid (GCF).[4] Furthermore, repeated and extended usage of systemic antimicrobials brings undesirable side effects such as the emergence of resistant microorganisms and shift in the microflora. The above disadvantages have limited the use of antimicrobials.[5] Although local drug delivery (LDD) evolved as an alternative to systemic antibiotics, the use

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Received: 22 Sep, 2021; **Accepted:** 05 Dec, 2021; **Published:** 18 Dec, 2021

How to cite this article: Sharma D, Prasanth T, Satisha TS, Kosala M, Mudgal I. Comprehensive Review on Antimicrobial Photodynamic Therapy in Periodontology. J Res Adv Dent 2022;13(1):41-49.

Access this article online

Website: www.jrad.co.in

DOI: https://doi.org/10.53064/jrad.2022.13.1.114

of the same depends on number of sites, cost, and patient compliance.[6]

To overcome most of the problems and complications related to the local and/or systemic use of antibiotics, a relatively novel application of therapy, photodynamic therapy (PDT) has been advocated. Although discovered more than 100 years ago by its killing effect on microorganisms, PDT has found most success as a treatment for cancer and age-related macular degeneration.[7] In PDT, a photochemical reaction ensues on light-mediated stimulation of a photosensitizing compound in the presence of oxygen conditional environment which generates cytolethal reactive oxygen species (ROS), with singlet oxygen in predominance, having selective toxic effects on the microorganisms. PDT's major advantages are its specificity to the targeted cells, with no collateral damage, initiation of activity only on specific light exposure, and the lack of resistance development among bacterial species, which is frequent in case of indiscriminate use of antibiotics.[8]

History of PDT

The principle of PDT, as shown in Figure 1, was accidentally discovered in 1900 by the medical student, Oscar Raab in Munich, who was involved in a study on the toxicity of the dye acridine red on *Paramecium* spp. as part of his doctoral thesis (Raab, 1900). In following years, Von Tappeiner coined the term "photodynamic action" and attested that the presence of oxygen is essential in photodynamic action. Later on, von Tappeiner applied this approach with Albert Jesionek clinically for the treatment of skin carcinomas (Jesionek and Tappeiner, 1905) and coined the term "photodynamic phenomenon" (Tappeiner, 1909).[9] Over the years, as shown in Figure 1, more advances have been made in anticancer PDT and different photosensitizers (PSs) have been discovered. In 1999, the Food and Drug Administration approved the PDT to treat precancerous skin lesions of the face or scalp.

While anti-cancer PDT is clinical reality now for 25 years at least, for example, in the treatment of actinic keratosis or basal cell carcinoma, antimicrobial applications of the photodynamic process have only been rediscovered in response to the emergence of the first drug-resistant infections in the health-care sector during the early 1990s.[10]

Antibacterial PDT (aPDT) was first introduced in 1960. Macmillan used toluidine blue (TBO) against microorganisms such as bacteria, algae, and yeast. Other dyes including methylene blue (MB), rose Bengal, Eosin Y, neutral red, acridine orange, crystal violet, and rhodamine 6G were presented as a PS and it was established that cationic dyes are more effective against bacteria than anionic PS.[8]

However, the discovery of penicillin (1928 – Alexander Fleming) and its miraculous bactericidal properties, as well as other antibiotics (1940–1990) impeded the progresses made in aPDT.[8]

In April 2014, the WHO warned that we are on the cusp of a "post-antibiotic era." The growing resistance to many antibiotics in recent years and emergence of multidrug-resistant bacteria has diverted the attention toward alternative antibacterial therapies such as aPDT.[9]

Components of PDT

PDT involves three components as shown in Figure 2, such as visible light, a non-toxic PS, and oxygen.[10]

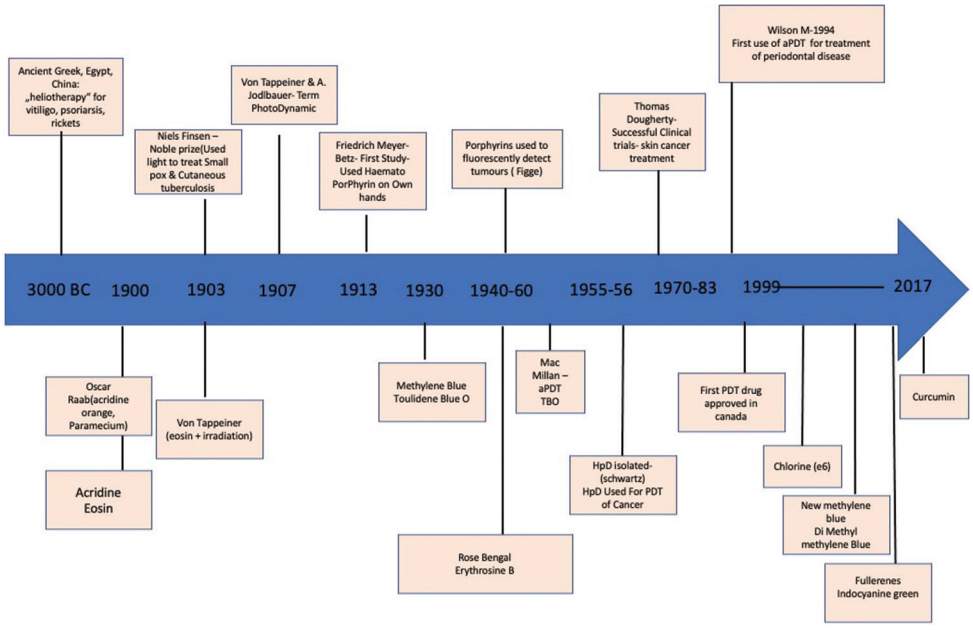

Figure 1: History of aPDT

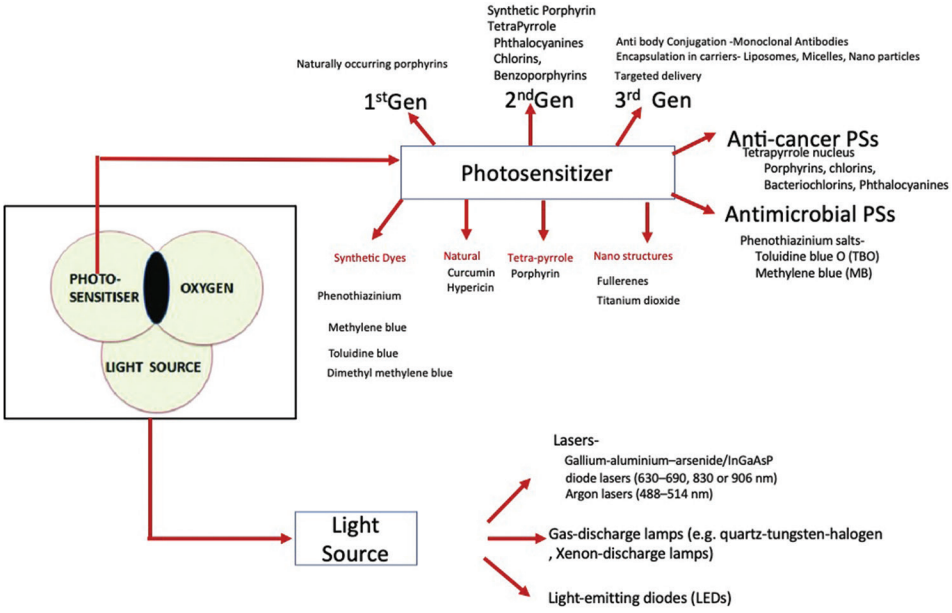

Figure 2: Components of aPDT

Light

Low-power light source of specific wavelength, as shown in Figure 2, is required for activation of the PS. Mostly, the PSs are triggered by red wavelength light between 630 and 700 nm, which corresponds to depth of light infiltration from 1.5 cm (700 nm) to 0.5 cm (at 630 nm), which is sufficient for periodontal treatment.[10]

In the past, a range of light origins such as argon lasers, potassium titanyl phosphate, and Nd: YAG was used for PS activation. At present, most commonly applied light sources in PDT are helium neon lasers (633 nm) and Ga-Al-As diode laser (630–690 nm, 830 nm, or 906 nm). Among the above, diode lasers which have a number of advantages such as cost-effectiveness, portability, easy handling, precision, and user friendliness are used predominantly.[7]

Non-coherent light sources such as quartz halogen, tungsten filament, phosphor-coated sodium lamps, and xenon arc are utilized to treat larger areas. Non-laser light sources such as light-emitting diodes (LEDs) have been utilized recently due to their portability, cost-effectiveness, and light weight properties, however, due to lack of literature, their efficiency cannot be exactly determined.[10]

PS and Generations

Photosensitizing agents/PSs are dyes molecules which can absorb light power and use it in promoting chemical reactions in tissues and cells.[11]

Among different PSs, as shown in Table 1, porphyrins, the first PSs, were discovered about 70 years back and commonly known as the first-generation PSs. The second generations refer to porphyrin derivatives and synthetics who are more efficient in producing singlet oxygen. In the third generation, PSs became modified by the incorporation of a photo bleaching capability, antibody conjugates (more effectively cleared from the circulation, which decreases their toxic effect to healthy tissues), or protein/receptor system, liposome nano species.[12]

Antimicrobial action of PS

The ideal PS structure is very dissimilar between antimicrobial and anticancer PSs. Anticancer PSs are with little or no overall charge (either positive or negative) is more likely to be lipophilic, whereas antimicrobial PSs tend to have marked cationic charges, and in most of the cases, more the charge the better the dye particularly for aiming at Gram-negative bacteria. Anticancer PSs commonly have absorption bands infrared or near-infrared (long wavelength) bands for enhanced tissue permeation of the stimulating light, however for antimicrobial PSs, the above quality is of lesser importance as infections treated by PDT are more likely superficial in nature.[12]

The two most popular phenothiazinium dyes, that is, MB and TBO with wavelengths of absorption of 600–660 nm have been widely studied for antimicrobial applications and less often for anticancer.[12]

Mechanism of PDT

Photodynamic reaction has mainly two mechanisms. Both of them are closely related to molecular oxygen inside the cells. Both the mechanisms share similar first stage. Each PS has an absorption spectrum. A PS, after entering the cell, when irradiated with this wavelength, absorbs a photon and gets transformed from its singlet basic energy state S° to the excited singlet state S1 because of the photon absorption. In its excited state, PS molecule loses part of its energy through radiating a considerable amount of fluorescence, and with the remaining

Table 1: Generation and types of photosensitizers

Type and generation of photosensitizers	
Generation	**Photosensitizers**
First	Porphyrins • Photofrin • Hematoporphyrin • Hematoporphyrin derivatives (HPDs) -Porfimer sodium
Second	Porphyrins
Non-porphyrins	• Metalloporphyrins
• Psoralen	• Porphycenes
• Anthracyclines	• Pheophorbides
• Chalcogenopyrylium	• Purpurin
• ADPMs	Tinethyletiopurpurin (SnET2)
• Cyanines	• Chlorins
• Phenothiazium dyes	Mono-L-aspartyl chlorin e6
Methylene blue	• Phthalocyanines
Toluidine blue	Aluminum disulfonated phthalocyanine
• Xanthenes	Naphthalocyanine
Erythrosine	• 5-Aminolevulinic acid (ALA)
• Monoterpene	• Benzoporphyrin derivative (BPD)
Azulene	• Texaphyrin
	• Meta-Tetra (hydroxyphenyl) porphyrins (mTHPP)
	• Talaporfin sodium (LS11) mTHPC
Third	2nd generation plus biologic conjugates (e.g., antibody conjugate, liposome conjugate)

energy, the molecule is directed to the excited triplet state T1. T1 is the suitable therapeutic form of the PS.[13]

Type I Mechanism of Photodynamic Reaction

The PS in its excited state, that is, triplet T1 transmits energy directly to its surrounding biomolecules producing free radicals and radical ions through electron transfer reactions or hydrogen-atom abstraction. These extremely reactive free radical species further cointeract with endogenic molecular oxygen to create ROS such as hydrogen peroxide, superoxide, and hydroxyl radicals.[13]

Type II Mechanism of Photodynamic Reaction

PS (excited triplet state) transports energy directly to the oxygen molecule present in their basic triplet state (basic energetic state) producing singlet oxygen. Singlet oxygen is lethal to various microorganisms including bacteria, protozoa, viruses, and fungi causing oxidative injury to the bacterial cell membrane. Due to a brief lifetime and very short radius of action, the effect is localized without any effects on the distant, cells, molecules, or organs.

Type II photo route of aPDT is commonly recognized as the key path in microbial cell injury and singlet oxygen is the major cytotoxic agent which is liable for the biological consequences of the photo-oxidative process.[12-14]

The ROS reacts with proteins, organelles, nucleic acids, and lipids which are the cellular components and cause irreversible damage by modifying the respiratory chain and increasing the membrane permeability ultimately leading to cell death.[12]

PDT in the Treatment of Oral Diseases

PDT applications in dentistry are as under: [7,10,11]

- Diagnosis of malignant oral lesions
- Treatment of premalignant superficial oral lesions such as oral erythroleukoplakia, oral leukoplakia, and lichen planus oral verrucous hyperplasia
- Treatment of oral cancerous lesions
- Treatment of bacterial, viral, and fungal infections (candidiasis) of the oral cavity
- Disinfection of cavity post-caries excavation
- As an aide to conventional endodontic disinfection treatment of the canal
- As an adjunct to periodontal therapy.

Application of PDT in periodontal therapy

- As an adjunct to non-surgical periodontal therapy in the management of
  - Chronic periodontitis
  - Aggressive periodontitis (AgP)
  - Refractory periodontitis
  - Peri-implant mucositis
  - Peri-implantitis
  - Chronic periodontitis in diabetic patients
  - Chronic periodontitis in smokers
- As an adjunct to surgical periodontal therapy in the management of chronic periodontitis
- Disinfection of implant site ostectomy

PDT in Periodontitis

Although PDT is more widely known for its application in the treatment of neoplasms, there is an interest in antimicrobial PDT, because a large number of microorganisms (including oral species) were reported to be killed *in vitro* by this approach.[9] Further, the potential of some key virulence factors (lipopolysaccharide and proteases) was shown to be reduced by photosensitization.[10]

In the periodontology antimicrobial PDT, various PSs have been used in various concentrations, as shown in Table 2, for example, TBO (concentration – 0.1 mg/ml, 100 ug/ml) or tolonium chloride (5%), MB (concentration – 10 mg/ml, 1%, 0.01%, 0.03%), phenothiazine chloride (100 ug/ml), or indocyanine green. PSs have been placed in periodontal pockets from time ranging from 1 to 3 min and laser wavelength ranges from 660 to 690 nm.[15]

Studies have used different frequency of aPDT application ranging from 1 to 4 times.[16]

Follow-up duration of the included studies, as shown in Table 2, was limited ranging from 12 to 24 weeks.[16-18]

Majority of studies have applied a split-mouth approach as shown in Table 2, barring a few,[17] also majority of the studies

Table 2: Clinical studies on the use of antimicrobial Photodynamic therapy adjunctive to SRP in the Management of chronic periodontitis

Author and year	Type of study	Light	Photosensitizer, time of application	Light parameters and time of exposure method of irradiation	Purpose of application (period of observation)	Findings
Yilmaz *et al*., 2002[25]	RCT	Diode laser (685 nm)	MB	30 mW (5 Hz), pulsed 71 s per each papillary region over gingiva	32 days	No additional clinical and microbiological improvement
Andersen *et al*., 2007[62]	RCT	Diode laser (670 nm)	MB	150 mW, CW 60 s per site into periodontal pockets	3 months	Significant clinical improvements over SRP
Christodoulides *et al*., 2008[26]	RCT	Diode laser (670 nm)	MB	75 mW 60 s per tooth into periodontal pockets	6 months	PD reduction and CAL gain comparable to SRP significantly higher reduction in BOP than SRP
Braun *et al*., 2008[37]	RCT	Diode laser (660)	100 µg/ml phenothiazine chloride	100 mW/cm^2 10 s	3 months	Significant improvement of PD reduction and CAL gain in favor of SRP+aPDT after 3 months (P<0.05). No difference in REC.
Ge *et al*., 2010[36]	RCT	670 nm	0.01% methylene blue	140 mW/cm^2 21 J/cm^2 60 s	3 months	PD reduction and CAL gain comparable to SRP significantly higher reduction in BOP than SRP
Campos *et al*., 2013[63]	RCT	Diode laser (660)	MB	60 mW 60 s per tooth into periodontal pocket	3 months	Significantly higher PD reduction and CAL gain compared to the sites treated by conventional SRP alone
Bassir *et al*., 2013[23]	RCT	Diode laser (625–635 nm)	Toluidine blue O 0.1 mg/ml	LED lamp 2000 mW/cm^2 - 60 J/cm^2 - 1 min	3 months	No significant improvements for any clinical parameter in favor of SRP+aPDT
Luchesi *et al*., 2013[31]	RCT	Diode laser (660 nm)	MB	60 mW 1 min per site into periodontal pocket	6 months	No clinical benefits for class II furcation, but reduction in pro-inflammatory cytokines and a reduction in periodontopathogens
Balata *et al*., 2013[30]	RCT	Diode laser (660 nm)		100 mW/cm^2 60 s per tooth into periodontal pocket	6 months	No significant improvements in any clinical parameter in favor of SRP+aPDT
Betsy *et al*., 2014[47]	RCT	Diode laser (655 nm)	MB	60 mW 60 s into periodontal pocket	6 months	Significant reduction in PD and gain in CAL
Berakdar *et al*., 2012[41]	RCT	Diode laser (670 nm)	0.005% Methylene blue	150 mW 1 min	6 months	Significant improvement of PD reduction and CAL gain in favor of SRP+aPDT after 6 months (P=0.007). No significant difference in CAL gain.
Cappuyns *et al*., 2012[39]	RCT	Diode laser (660 nm)	100 µg/ml phenothiazine chloride	40 mW/cm2–9 J/cm^2 - 1 min	6 months	No significant differences between SRP, soft laser, and adjunctive aPDT after 6 months. The risk for a site to remain >4 mm with BOP was after SRP+aPDT significant lower than after SRP alone or soft laser treatment
Pourabbas *et al*., 2014[24]	RCT	Diode laser (638 nm)	Toluidine blue O	8–10 J/cm^2 120 s	3 months	No significant differences for PD reduction, CAL gain, and inflammatory markers were observed in between-group comparisons
Carvalho *et al*., 2015[32]	RCT	Diode laser (660 nm)	MB	40 mW 90 s per site in to periodontal pocket	9 months	No significant differences between test and control groups
Sigusch *et al*., 2010[53]	RCT	Diode laser (670 nm)	100 µg/ml phenothiazine chloride	60 mW/cm^2 60 s	3 months	Significant reductions in reddening, BOP, PD, and CAL, were observed during the follow-up in respect to controls. PD reduction and CAL gain showed significant differences from baseline values and from those of the control groups, at 1 and 3 months after adjunctive aPDT treatment

used aPDT as adjunctive approach to NSPT excluding a few who used it as a monotherapy[16,18] with promising outcome on application of aPDT.

Power output, energy fluence, and duration of irradiation, as shown in Table 2, were frequently around 75 mW (milliWatts), 212.23 Jcm^2 (joules per square centimeters), and 60–120 s, respectively.[16,18]

In majority of studies, patients with systemic conditions, pregnant or lactating women and patients who had taken antibiotics in the past 3–12 months, and smokers were excluded from the study.[16-18]

Various commercial aPDT systems are available in the market, such as "Fotosan 630™" (CMS Dental, Copenhagen), in which TBO in a 0.01% solution and a LED light source with a wavelength of 630 nm are used, another system called "Helbo™" (Bredent™ Medical), uses a 1% MB solution and a 660 nm wavelength laser, "PadPlus™" system (Orange Dental) uses tolonium chloride in a 0.00127% solution and a light source with a wavelength of 635 nm, and "PACT™" (Cumdente GmbH) uses TBO in a 0.005% solution and a laser with a wavelength of 635 nm. Adjunct H_2O_2 application with aPDT has also been tried in literature with some success.[10,16,18]

The results of several *in vitro* and animal studies have demonstrated the effectiveness of aPDT in the reduction of periodontopathic bacteria. Using histomorphometric analysis, studies have also evaluated the effects of aPDT in the control of alveolar bone loss and the extension of the inflammatory process in experimentally induced periodontitis in animals. These studies have demonstrated that aPDT is an effective therapy for controlling and treating periodontal disease.[19-22]

In the past two decades, several clinical studies on humans have evaluated the effect of aPDT as an adjunctive therapy in the treatment of chronic periodontitis.[23-42]

Studies evaluating clinical parameters do not give clear picture of role of PDT as an adjunct to the gold standard mechanical debridement, that is, SRP.

The notion of repetitive appliance and light activation of the PS has been attended in only few of the studies, where up to four aPDT applications were utilized.[43] In a trial,[25] application of three rounds of PDT within a time period of 1 week had insignificant effect on microbiological and clinical parameters,[44] however, systematic reviews have analyzed the literature and stated multiple application produced no statistical differences compared to single application.[15,45,46]

Studies, as shown in Table 2,[26,37,47] have shown a significant reduction in BOP when aPDT used as an adjunct to NSPT, while other studies have shown no significant differences.[23-25]

Similarly, for other clinical parameters, that is, pocket probing depth PPD, CAL[13,19,21,37,41,48-50] found significant improvements, contrary to these[26,30,51] reported that aPDT provided no additional benefits in PPD reduction and CAL.

In comparison to clinical parameters, evaluation of microbial parameters has been evaluated in fewer studies.[31,33,52] Many of the studies have reported the microbial parameters evaluating around 40 different bacterial species such as *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Tannerella forsythia*, *Treponema denticola*, *Prevotella intermedia*, *Fusobacterium nucleatum*, *Eubacterium nodatum, Capnocytophaga* spp., and *Parvimonas micra* to name a few.[19-21,31,42,49,53]

aPDT as an adjunct to SRP in the management of AgP was compared to the adjunct use of systemic antibiotics, however, the use of antibiotics showed significantly better outcome as compared to aPDT. However, the authors of the studies mentioned that aPDT in contrast to the use of antibiotics has the advantage of repeated applications as bacterial resistance to aPDT has not been reported.[54] In a study comparing the localised application of antibiotics and aPDT in the management of perimplantitis, the clinical outcomes were comparable.[55] Other studies also showed a statistically significant decrease in *P. gingivalis* and *T. forsythia* in the PDT group.[22,31] On the other hand, PDT protocol presented inferior frequency of *P. gingivalis* at 3 months when compared with the other therapies similarly PDT failed to show superior pathogen load reduction.[32,56]

There are inadequate data in the literature about the effect of PDT on the modulation of immune biomarkers, that is, interleukin (IL-1β), tumor necrosis factor (TNF-α), transforming growth factor (TGF-b), and matrix metalloproteinase (MMP-8) levels in GCF. Three studies[31,36,43] reported lower IL-1β levels in the GCF of patients treated with adjunct aPDT to SRP while two studies,[24,38] there was no significant difference in the IL-1β concentrations. Levels of TNF-α were explored in two studies,[24,43] out of which, one study[24] reported lower levels of TNF-α in the GCF of patients treated with aPDT compared to SRP alone and one study[43] reported no significant difference. Two studies[36,57] reported significantly lower MMP-8 levels in GCF adjunct aPDT groups compared to SRP while another study[24] identified comparable MMP-8 and MMP-9 levels. Similarly, another study identified similar IL-10 concentration in GCF and gingival tissue among patients receiving SRP or SRP with adjunctive aPDT up to 12 weeks follow-up.[43] One study reported lower TGF-β1 levels after aPDT adjunct to SRP compared to SRP alone.[17]

aPDT when used as an adjunct to surgical periodontal treatment, there were more remarkable reductions than those observed in studies in which used non-surgical techniques.[26] A possible explanation for the large reductions is that surgical debridement itself contributes to reducing PD, moreover, surgical access can enhance the penetration of photosensitizing agents into epithelial and connective tissues, thus eliminating periodontopathogens found therein.[35] Furthermore, there could be a bio modulatory effect triggered by low-power laser on local cells during tissue healing, improving tissue repair, and reducing periodontal inflammation.

The above reported findings in the studies showed significant heterogeneity, possibly due to heterogeneous demographic factors, such as severity of chronic/AgP, as the initial PD varied widely, sample size, inclusion of smokers or not, and different follow-up procedures.[15,34] Differences in aPDT protocols, such as number of cycles of aPDT, laser settings, and the PS applied (type, concentration, and incubation time) may contribute further to heterogeneity, and moreover, in some studies, aPDT

protocols were not even reported. Fiber thickness influences the energy output and power density during aPDT and can alter the definite measure of energy discharged during the procedure, possibly affecting the antimicrobial efficiency of PDT. Furthermore, the frequency of aPDT application varied from four applications to just one which could have influenced the overall efficacy of aPDT in the studies. In majority of studies, aPDT was applied without a time lag after mechanical instrumentation, however, few studies reported aPDT that is after 24 h or 1 week.[15]

Frequency of oral hygiene instructions and/or professional prophylaxis also varied ranging from 1, 3, to 6 months in few studies[29] and in weekly to monthly intervals in one study.[41]

Furthermore, the presence of confounding factors has not been explained in many of the studies, one, for example, of the confounders was the number of a PDT cycles, which was only considered in two studies with more than 1 treatment arms, both showed that repeated aPDT applications did not result in further clinical improvement.[53] Another confounder was the use of indocyanine as PS, in some studies, because its antimicrobial effects are based on photothermal destruction of bacterial membranes rather than ROS induction.[15] Some studies also evaluated carry-across effect by leakage of PS in split-mouth studies, though some differences in effect size and heterogeneity between studies were found but these differences disappeared after removing outliers, therefore, a carry-across effect seems unlikely.

Although there is a variability of data available in the literature, almost all of them have pointed out advantages of PDT in periodontal therapy such as

Few advantages of PDT in periodontal therapy

- Relatively short treatment time
- Minimally invasive technique with least collateral damage to normal cells enhances results and superior healing
- No need for anesthesia
- Precise direction of laser light using optical fiber
- No total dose limitations thus repetitions can be done
- Exceedingly efficient broad spectrum of action
- Effectiveness not dependent on the antibiotic resistance of the microbial strain
- Repetitive application does not cause resistance.
- Eradication of pathogens in non-accessible spaces of periodontal pockets
- The treatment also does not produce any adversarial effects such as sloughing, ulcers, or charring of tissues
- No thermal damage to the root surface and gingival tissues
- In supplement to the bactericidal effect, aPDT stimulates the photobiological influence such as improved wound healing, anti-inflammatory, and also pain-relieving efficiency.
- The oral cavity is particularly apt for PDT since it is quite easily reachable to illumination.[7,10,11,15,16,18]

Drawbacks of PDT

- Most of the PS dyes firmly adhere to the soft-tissue surface of the periodontal pocket, even when applied for a short time period, may be temporarily unesthetic for patients
- Cannot be used in individuals sensitive to porphyrins
- Lack of precise dosimetry.[15-18]

Future developments

Lately, to enhance PS uptake by microorganisms using the PDT approach, these molecules have been encapsulated, laden, or linked in variety of drug delivery systems in nano- and micro-particles forms to increase the to increase the antibiofilm effectiveness.[58,59]

Dentine, dentinal matrix, pulp tissue, bacterial lipopolysaccharides, and bovine serum albumin were found to significantly decrease PDT antimicrobial efficacy.[60] Additional efforts comprise the use of photo-activated functionalized chitosan nanoparticles or a PS solvent efflux pump inhibitor[60] for stabilization and disinfection of the dentine matrix.[61]

Conclusion

A variability of data on PDT exists in literature, however, almost all of them have pointed out few advantages of PDT in periodontal therapy such as relatively short treatment time, no need for anesthesia, selective uptake of PSs, precise direction of laser light using optical fibers, no antimicrobial resistance, and no total dose limitations.

The need of the hour is to develop a standardized protocol to assess a PDT and compare the existing studies in terms of concentrations of dyes, resident time of PSs, energy, application time, modes of irradiation, power settings, and laser types. Further clinical trials with proper PDT protocol, large sample size, and standardized clinical, biochemical, and microbiological assessment may be undertaken, to determine the efficacy of adjunctive effect of PDT with SRP.

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