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Original Article

Dentistry Section

Emerging Role of Photodynamic Therapy in Management of Periodontitis: A Systematic Review

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ABSTRACT

Introduction: Photodynamic Therapy (PDT) presents a non invasive avenue for treating various infections, including periodontal disease, offering an alternative to mechanical methods like scaling and root planing. Concerns about antibiotic resistance have fueled the exploration of PDT as an antimicrobial therapy. PDT combines low-power lasers with photosensitising drugs to eliminate microorganisms through the generation of cytotoxic reactive oxygen species upon light activation.

Aim: To evaluate the scope of PDT and its role in periodontology.

Materials and Methods: A comprehensive electronic search was conducted in major medical databases, including Google Scholar, PubMed, Cochrane Library, Scopus, Web of Science, Embase, and Wiley. A total of 43 studies from 2007 to 2023 were selected, focusing on PDT for the treatment of periodontal disease. The review included Randomised Controlled Trials (RCTs), case-control studies, and cohort studies involving human subjects, using Photosensitisers (PSs) or Indocyanine Green (ICG) for subgingival irrigation in chronic periodontitis patients after scaling and root planing, with follow-ups extending over one month. The outcomes measured were Probing Pocket Depth (PPD), Clinical Attachment Level (CAL), Plaque Index (PI), and Gingival Index (GI).

Results: In present review, after thorough analysis, a total of 21 studies were selected from databases including Google Scholar, PubMed, Cochrane Library, Scopus, Web of Science, Embase, and Wiley. The risk of bias assessment showed high-risk in 1 out of 128 studies (0.59%), low risk in 139 out of 168 studies (82.74%), and unclear risk in 28 out of 168 studies (16.67%). The results indicated significant clinical improvements when PDT was combined with conventional treatments.

Conclusion: The PDT in periodontology showcases varied roles, from antimicrobial action to tissue healing and the promotion of periodontal health. Its efficacy as an adjunctive treatment, especially in challenging cases or against resistant microbes, is evident, accentuated by its non invasive nature and minimal adverse effects, making it an appealing option in periodontal care.

Keywords: Antibiotic resistance, Microbial infections, Non invasive treatment, Oral health, Photochemical reaction, Photosensitiser drugs

INTRODUCTION

Periodontal diseases are a group of prevalent oral health conditions that affect the supporting structures of teeth, including the gums, periodontal ligament, and alveolar bone [1]. These diseases are primarily caused by the accumulation of dental plaque, a complex biofilm comprising bacteria and their by-products, which leads to inflammation, tissue destruction, and potential tooth loss if left untreated. Traditional methods of periodontal therapy involve mechanical scaling and root planing to remove bacterial deposits and promote tissue healing [2]. While effective, these approaches may have limitations in sites with difficult access and may not fully address the rising concerns of antibiotic resistance [3].

In recent years, PDT has emerged as a promising non invasive treatment approach for various infections, including periodontal diseases caused by dental plaque [4]. PDT utilises low-power lasers with specific wavelengths in combination with PSs drugs to selectively target and destroy microorganisms. The activation of photosensitising compounds by light initiates a photochemical reaction, leading to the production of cytotoxic reactive oxygen species, particularly singlet oxygen, which effectively kills bacteria [5].

The simplicity and high efficacy of bacterial killing with PDT have led to its extensive use as an antimicrobial therapy in various medical fields [6]. In periodontology, PDT offers a potential alternative to traditional mechanical methods, with the advantage of addressing concerns about bacterial resistance and providing an adjunct to non-surgical periodontal therapy [7].

The findings from this systematic review will contribute to a better understanding of the potential of PDT in periodontology, its limitations, and areas for further research. With the rising concerns of antibiotic resistance and the need for innovative and effective treatments, exploring PDT's role in periodontal disease management holds promise for revolutionising the way we approach the treatment of periodontal diseases and combating dental plaque-associated infections.

The present systematic review aimed to comprehensively assess the existing literature on the application of PDT in periodontology. By exploring the current evidence, authors aimed to evaluate the scope of PDT in periodontal disease management, its impact on clinical outcomes, factors affecting its efficacy, and potential safety considerations. Furthermore, authors will identify gaps in the literature and provide insights into future perspectives and recommendations for integrating PDT into clinical practice.

MATERIALS AND METHODS

A comprehensive electronic search was conducted in major medical databases, including PubMed, Embase, and the Cochrane Library, to identify relevant studies published upto the date of this review. The following keywords and Medical Subject Headings (MeSH) terms were used: "Chronic Periodontitis," "Scaling and Root Planning," "Non Surgical Periodontal Therapy," "Subgingival," and "PDT," as shown in [Table/Fig-1]. After conducting a thorough analysis, duplicates were eliminated based on relevant databases, titles, authors, publication years, and abstracts. For present review article, a meticulous manual screening process was carried out to ensure the removal of duplicates.

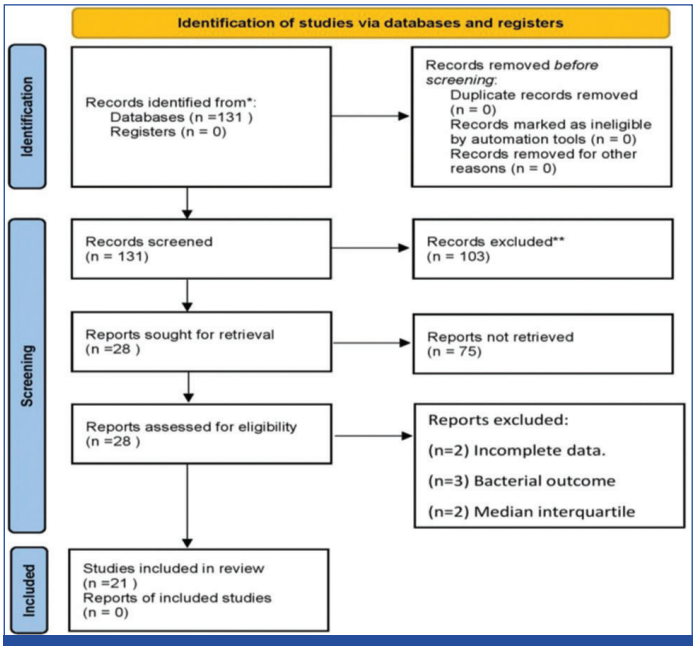
Variables	Population	Intervention	Comparison	Outcome	Study model
Key concepts	Chronic periodontitis	Photodynamic Therapy (PDT)	Test: SRP+PDT control: SRP	CAL/PPD/PI/GI	Clinical trials
MeSH terms	Chronic periodontitis	Photodynamic Therapy (PDT) Indocyanine Green (ICG) laser	Scaling and root planning	-	-
Free text terms	Adult periodontitis	SRP+aPDT	SRP+aPDT showed significantly greater reduction and gain compared to SRP alone at all time points, with no observed adverse affects of aPDT	Clinical Attachment Level (CAL) Probing Pocket Depth	-

[Table/Fig-1]: Showing the Patient/Population Intervention Comparison and Outcomes (PICOS) parameters.
SRP: Scaling and root planning; aPDT: Anti-microbial photodynamic therapy; PDT: Photodynamic therapy; CAL: Clinical attachment level; PPD: Probing pocket depth; PI: Plaque index; GI: Gingival index; MeSH: Medical subject headings

Inclusion criteria: Randomised Controlled Trails (RCTs), case-control studies, and cohort studies involving human subjects (both parallel and split-mouth designs) from 2007 to 2023 were included. Studies in which either PSs, ICG, or antimicrobial PDT (aPDT) was used for subgingival irrigation or subgingival application as an adjunct to scaling and root planning in chronic periodontitis patients were considered. Studies reporting outcomes such as probing pocket depth, Clinical Attachment Level (CAL), Plaque Index (PI), Gingival Index (GI), and other correlated outcomes were included.

Exclusion criteria: Animal studies, in-vitro studies, and studies in which patients were under systemic medication that may affect clinical outcomes were excluded. Additionally, studies that did not have proper follow-up and articles published in languages other than English were also excluded. Studies in which interventions were conducted using other antimicrobials were not considered.

In present review article, the included studies were selected from electronic databases covering the past 16 years, specifically from 2007 to 2023. After a complete analysis, duplicate entries were eliminated based on the titles and abstracts of the studies [Table/Fig-2].



[Table/Fig-2]: Preferred Reporting Items for Systemic Reviews and Meta Analyses (PRISMA) showing flow diagram for new systematic reviews which included searches of databases.

Study Procedure

Data assessment: The risk of bias for RCTs was assessed using the Cochrane Collaboration tool and performed with RevMan 2 software [8]. Risk of bias was evaluated by two independent reviewers for the RCTs included in the review, and discrepancies were resolved through discussion and consultation with a third reviewer. The domains for risk assessment were graded as high, unclear, or low risk based on selection bias, random sequence generation, allocation concealment, selective reporting, other bias, blinding of participants, blinding of outcome assessment, incomplete outcome data, and overall risk of bias. A study was assessed to have a low overall risk only if, all domains were found to have low risk; it was assessed to have a high overall risk if, one or more of the six domains were found to be at high-risk. An unclear risk assessment was assigned to studies when one or more domains were uncertain, provided none were at high-risk.

RESULTS

Risk of bias: RevMan software version 5.4 was used to analyse the risk of bias in the present study. Authors evaluated individual studies for various domains, including selection bias (creation of a random sequence), performance bias (blinding of cases and staff), attrition bias (incomplete results data), selective reporting (reporting bias), and other biases. Each study was classified as having low risk (+), high-risk (-), or unclear risk (?), as depicted in [Table/Fig-3] [9-29]. The present review of PDT in periodontology consolidated 43 articles into 21 relevant RCTs, as highlighted in [Table/Fig-3], providing a comprehensive summary of findings. Among these studies, the most concerning issues were the inadequacy or absence of randomisation, which resulted in a high-risk for 1 out of 168 trials (0.59%). In contrast, low risk was noted in 139 out of 168 trials (82.74%), and unclear risk was noted in 28 out of 168 trials (16.67%), as represented in [Table/Fig-4].

The assessment of study quality within the pool of 21 included studies was conducted using the Cochrane risk of bias tool, as detailed in [Table/Fig-4] [9-29]. Among the 21 studies, one study showed a high-risk of bias [13], and six of them were found to exhibit an overall unclear risk of bias [9,16,20,21,26,29]. Despite this unclear risk, the quality of these studies was deemed acceptable, suggesting that while they had some methodological limitations, they still provided valuable contributions to the research area.

In contrast, the majority of the studies, specifically 17 out of the 21, demonstrated an overall low risk of bias [9-29]. These studies were recognised for their robust methodology and study design, resulting in a classification of good quality. Their lower risk of bias underscores the reliability and trustworthiness of their findings within the context of the systematic review.

Study characteristics: In the present review, approximately 21 studies were included, which primarily focused on evaluating aPDT alongside traditional methods such as ultrasonic debridement and Scaling and Root Planing (SRP). Thirteen studies specifically compared these approaches, with five studies showing significant improvements in outcomes like Bleeding on Probing (BOP), Probing Pocket Depth (PPD), and Clinical Attachment Level (CAL) gain [17,19,21,22,26]. Two studies reported enhancements in BOP only [14,20]. However, five studies did not find notable differences between aPDT combined with conventional treatments and conventional treatments alone [10,13,15,16,28].

The aPDT protocols in the trials used various PSs like phenothiazine chlorine, methylene blue, toluidine blue, and Indocyanine Green (ICG). These were incubated for upto five minutes. Different light strategies were employed depending on the PS, with ICG treated at 810 nm and others at 628 to 680 nm. Light power ranged from 2 to 100 mW/cm^2, with energy levels between 20 and 320 J/cm^2 [10-15]. Moreover, the integration of ICG as a PS was consistently combined with conventional treatments in the studies, showing

Author and year	Place of the study	Study design	Aim	Treatment protocol/ follow-up	Dye used	Clinical parameters assessed	Results
Andersen R et al., 2007 [9]	USA	RCT	To compare the effectiveness of a photo disinfection process to that of scaling and root planing for non surgical periodontal treatment	Group 1-PD Group 2-SRP alone Group 3-SRP+PD 6 and 12 weeks	Methylene blue	BOP[1] PPD[2] CAL[3]	Significant results at 6 and 12 weeks in terms of BOP-71% and 73% in Group 1 CAL-0.92±0.62 and 0.86±0.61 in Group 2 PPD-1.16+0.39 and 1.11±0.53 in Group 2
Christodoulide N et al., 2008 [10]	Netherlands	Randomised control clinical trial	To evaluate the clinical and microbiological adjunctive uses of aPDT for non surgical periodontal treatment in chronic periodontitis	Group 1-SRP Group 2-aPDT+SRP 3 and 6 months	Methylene blue	FMPS[4] FMBS[5] BOP PPD	No significant differences were observed between the groups in terms of clinical parameters
Lulic M et al., 2009 [11]	Switzerland	Randomised control clinical trial	To evaluate possible added benefits of repeated adjunctive aPDT to conventional treatment of residual pockets in patients enrolled in periodontal maintenance	Group 1-Laser Group 2-aPDT 3, 6 and 12 months	Methylene blue	PPD CAL BOP	Significant results observed in test group; PPD reduction-6.08±1.19 to 5.41±1.09 at 6 months CAL gain-6.70±2.17 to 6.18±2.26 at 6 months BOP% decreased-97% to 67% at 6 months
Rühling A et al., 2010 [12]	Germany	Prospective, randomised, controlled, single-blind clinical study	Evaluate whether aPDT can reduce Probing Depth (PD) in persistent periodontal pockets, change the microbial composition, and decrease the total load of subgingival bacteria more than conventional mechanical debridement	Group 1-UST Group 2-aPDT 3 months	5% tolonium chloride (toluidine blue)	PD RAL[6] BOP	No significant differences were observed between the groups
Theodoro LH et al., 2012 [13]	Brazil	-	Evaluate the long-term clinical and microbiological effects of aPDT associated with non surgical periodontal treatment	Group 1-SRP group Group 2-SRP+aPDT 60, 80, 90 days	Toluidine blue	PI[7] BOP PD[8] GR[9] CAL	No significant differences were observed between the groups
Mongardini C et al., 2012 [14]	Italy	Single-blinded, split-mouth design, randomised parallel clinical trial	To study the potential adjunctive effect of microbiological/clinical photodynamic protocol using an Light Emitting Diode (LED) lamp (red spectrum) and to compare it to SRP	Group 1-SRP Group 2-toluidine blue+LED lamp 7 days	Toluidine blue	PPD BOP	Significant results in test group: BOP was reduced by 71% than control Group-27%
Balata ML et al., 2013 [15]	Brazil	Randomised, blinded, controlled clinical trial	To evaluate an aPDT protocol as an adjunct to ultrasonic debridement in patients with Severe Chronic Periodontitis (SCP)	Group 1-SRP Group 2-aPDT 1, 3 and 6 months	Methylene blue	PI GI[10] BOP PPD CAL	No significant differences were observed between the groups
Macedo GDO et al., 2013 [16]	Brazil	Randomised, controlled clinical trial	To evaluate the aPDT combined with non surgical periodontal and doxycycline on clinical and metabolic effects in patients that show type 2 diabetes mellitus	Group 1-SRP Group 2-SRP+aPDT, both the group in combination were given doxycycline (100 mg/day, for 2 weeks) 3 months	Phenothiazine chloride	PPD CAL BOP	No significant differences were observed between the groups in terms of clinical parameters. However, the test group exhibited greater differences in HbA1c between baseline and 3 months
Betsy J et al., 2014 [17]	India	Single-centered randomised and controlled clinical trial	To evaluate the potential of antimicrobial Photodynamic Therapy (aPDT) as an adjunct to Scaling and Root Planing (SRP) in the treatment of chronic periodontitis	Group 1-SRP Group 2-SRP+aPDT 1, 3 and 6 months	Methylene blue	PPD CAL GI GBI[11] PI	Significant results in test group PPD reduction-5.7 (5.0-6.0;1.0) to 3.0 (2.0-6.0;1.0) CAL gain-6.5 to 4.0 PI-2.0 to 1.0 GI-2.0 to 1.0 GBI-100 to 25
Carvalho VF et al., 2015 [18]	Brazil	Randomised controlled parallel-group clinical trial	Evaluate the clinical and microbiological effects of aPDT in the treatment of residual pockets of patients with chronic periodontitis subjected to supportive therapy	Group 1-saline solution Group 2-PS+light 3, 6 and 12 months	Methylene blue 0.01%	BOP PI PD CAL	No significant differences were observed between the groups
Moreira AL et al., 2015 [19]	Brazil	Split-mouth double-masked randomised controlled clinical trial	To study the efficiency of multiple sessions of aPDT in combination with SRP versus SRP in patients that show aggressive periodontitis	Group 1-SRP Group 2-SRP+aPDT 30 and 90 days	Phenothiazine chloride	BOP PD CAL GR PI	Significant results in test group PPD-5.32±0.34 to 2.91±0.45 CAL-5.38±0.93 to 3.85±0.91 GR-0.06±0.27 to 0.93±1.04 BOP-144 (60.00) to 22 (13.75)

Pulikkoti SJ et al., 2016 [20]	Malaysia	Randomised split-mouth controlled clinical trial	To evaluate the efficacy of aPDT in reducing Aggregatibacter actinomycetemcomitans (Aa) in periodontitis patients	Group 1-NSPT Group 2-NSPT+PDT 7 days, 1 month and 3 months	Methylene blue	PD CAL BOP (PS%)	Significant results in test group: BOP decreased from 56.84±26.12 to 12.44±20.4
Shingnapurkar SH et al., 2016 [21]	India	Comparative split-mouth randomised clinical trial	To assess the effect of adjunctive Photodynamic Therapy (PDT) {using 810 nm diode laser and Indocyanine Green (ICG) as Photosensitisers (PSs)} in chronic periodontitis	Group 1-SRP Group 2-SRP+PDT 1 and 3 months	Indocyanine Green (ICG)	PI GI PPD RAL	Significant results in test group: PI-1.07+0.28 to 0.26+0.34 GI-1.72±0.56 to 0.18±0.27 PPD reduction-5.13±0.34 to 2.23±0.67 RAL-9.13±1.88 to 6.60±1.4
Raut CP et al., 2018 [22]	India	Randomised, single-blind, controlled clinical trial	To compare and evaluate the effects of photothermal therapy using ICG in the treatment of chronic periodontitis with Scaling And Root Planing (SRP)	Group 1-SRP Group 2-(SRP+ photothermal therapy) 6 months	Indocyanine Green (ICG)	PI BOP PPD CAL	Significant results in test group: BOP reduced from 100% to 10% PPD reduction-6.04±0.82 to 3.53±0.58 CAL gain-5.80±0.70 to 4.12±0.78
Cadore UB et al., 2019 [23]	Brazil	Double-blind, randomised, controlled, and split-mouth clinical trial	To evaluate the clinical effects and the subgingival microbiota after multiple sessions of aPDT associated with surgical treatment of Severe Chronic Periodontitis (SCP)	Group 1-multiple sessions of aPDT and surgical periodontal treatment (ST) Group 2-ST only 60, 150 days	Not mentioned	PD CAL GR BOP PI	Significant results in test group: PPD reduction-6.43±0.21 to 3.31±0.18 CAL gain-7.00±0.27 to 5.03±0.36
Borekci T et al., 2019 [24]	Turkey	Prospective controlled clinical study	To evaluate the microbiological and clinical effects of aPDT as an adjunctive tool to the non surgical periodontal protocol in patients that show aggressive periodontitis (agp)	Group 1-NSPT Group 2-NSPT+PDT 63 days	Toulidine blue	PI SBI[12] PPD RAL GR	Significant result in test group: SBI reduced from 3.51±0.73 to 0.96±3.41
Niazi FH et al., 2020 [25]	Saudi Arabia	Double-blind, RCT	To evaluate clinical periodontal and microbiological parameters after the treatment with adjunctive antimicrobial aPDT among Human Immunodeficiency Virus (HIV)-seropositive and seronegative patients with necrotising ulcerative periodontitis	Group 1-seropositive patients Group 2-Healthy 3 and 6 months	Methylene blue	FMPI[13] FMBOP[14] PD CAL	Significant results in test group: FMBOP%-69.7±22.5 to 14.8±9.2b PD-5.0±1.4 to 3.3±0.9b
Joshi K et al., 2020 [26]	India	Single centre split mouth randomised controlled clinical study	To assess the clinical efficacy of ICG, and PSs with better tissue absorption and low toxicity, as an aPDT adjuvant to Scaling and Root Planing (SRP)	Group 1-SRP Group 2-SRP+PDT 3 months	Indocyanine Green (ICG)	PI mSBI[15] PPD CAL	Significant results in test group: PPD reduction-5.56±0.55 to 3.20±0.54 CAL gain-5.68±0.61 to 3.34±0.62
Patyna M et al., 2021 [27]	Germany	Single-blinded, randomised, controlled clinical pilot study	To evaluate the microbiological and clinical effects of aPDT procedure alone or in combination with probiotics as an adjunct to non surgical periodontal treatment	Group 1-SD Group 2-SD+LAD Group 3-SD+LAD+ Probiotic 3 and 6 months	Toluidine blue	PPD CAL BOP GIs[16] PCR[17]	Significant result in Group 3: BOP-34.00 (±25.30) to 4.88 (±6.72) GIs-29.09 (±25.12) to 3.18 (±5.33)
Alshibani N et al., 2022 [28]	Saudi Arabia	Parallel-armed RCT	To assess the effect of Non surgical Periodontal Therapy (NSPT) with adjunct Photodynamic Treatment (PDT) for the management of periodontal inflammation in young Electronic cigarette (E-cig) users	Group 1-NSPT+PDT Group 2-NSPT alone 6 months	Not mentioned	PI BI CAL PD	No significant differences were observed between the groups
Skalerič E et al., 2023 [29]	Slovenia	RCT	To compare the long-term results of antimicrobial PDT (aPDT) and antibiotic therapy as an adjunct to conventional non-surgical therapy in patients with aggressive periodontitis	Group 1-NSPT+aPDT Group 2-NSPT+ antibiotics (amoxicillin 500 mg and metronidazole 400 mg, 7 days) 6, 9 and 12 months	Methylene blue	PD CAL BOP	No significant differences were observed between the groups

[Table/Fig-3]: Randomised Controlled Trials (RCT) on PDT [9-29].
[1]BOP: Bleeding on probing; [2]PPD: Pocket probing depth; [3]CAL: Clinical attachment loss; [4]FMPS: Full mouth plaque score; [5]FMBS: Full mouth bleeding score; [6]RAL: Relative attachment loss; [7]PI: Plaque index; [8]PD: Probing depth; [9]GR: Gingival recession; [10]GI: Gingival index; [11]GBI: Gingival bleeding index; [12]SBI: Sulcular bleeding index; [13]FMPI- full mouth plaque index; [14]FMBOP: Full mouth bleeding on probing; [15]mSBI-modified sulcular bleeding index; [16]GI: Gingival index simplified; [17]PCR: Plaque control record

Author and year	Random sequence generation	Allocation concealment	Selective reporting	Other bias	Blinding of participants	Blinding of outcome assessment	Incomplete outcome data	Overall risk of bias
Andersen R et al., 2007 [9]	Unclear	Low	Low	Low	Low	Unclear	Low	Unclear
Christodoulide N et al., 2008 [10]	Low	Unclear	Low	Low	Low	Low	Low	Low
Lulic M et al., 2009 [11]	Low	Low	Low	Low	Low	Low	Low	Low
Rühling A et al., 2010 [12]	Low	Unclear	Low	Low	Low	Low	Low	Low

Theodoro LH et al., 2012 [13]	Unclear	Unclear	Low	Low	Unclear	Unclear	Low	High
Mongardini C et al., 2012 [14]	Low	Unclear	Low	Low	Low	Low	Low	Low
Balata ML et al., 2013 [15]	Low	Low	Low	Low	Low	Low	Low	Low
Macedo GDO et al., 2013 [16]	Low	Unclear	Low	Low	Low	Low	Unclear	Medium
Betsy J et al., 2014 [17]	Low	Low	Low	Low	Low	Low	Low	Low
Carvalho VF et al., 2015 [18]	Low	Low	Low	Low	Low	Low	Low	Low
Moreira AL et al., 2015 [19]	Low	Low	Low	Low	Low	Low	Low	Low
Pulikkoti SJ et al., 2016 [20]	Low	Unclear	Low	Low	Low	Unclear	Low	Medium
Shingnapurkar SH et al., 2016 [21]	Low	Unclear	Low	Low	Unclear	Unclear	Low	Medium
Raut CP et al., 2018 [22]	Low	Unclear	Low	Low	Low	Low	Low	Low
Cadore UB et al., 2019 [23]	Low	Low	Low	Low	Low	Low	Low	Low
Borekci T et al., 2019 [24]	Low	Unclear	Low	Low	Low	Low	Low	Low
Niazi FH et al., 2020 [25]	Low	Low	Low	Low	Low	Low	Low	Low
Joshi K et al., 2020 [26]	Low	Unclear	Low	Low	Low	Unclear	Low	Unclear
Patyna M et al., 2021 [27]	Low	Low	Low	Low	Low	Low	Low	Low
Alshibani N et al., 2022 [28]	Low	Low	Low	Low	Low	Low	Low	Low
Skalerič E et al., 2023 [29]	Low	Low	Low	Low	Unclear	Unclear	Low	Medium

[Table/Fig-4]: Assessment of study quality [9-29].

clinical improvements. Follow-up durations ranged from seven days to 12 months, allowing for the assessment of both short-term and long-term effects.

DISCUSSION

The systematic review on PDT in periodontology has provided valuable insights into the potential of this innovative treatment approach for managing periodontal diseases caused by dental plaque. This discussion will delve into the key findings, implications, and future perspectives identified in the review, shedding light on the current evidence and its significance in the field of periodontal therapy.

Effectiveness of PDT in periodontal disease management: The review demonstrated that PDT, when used as an adjunct to conventional periodontal treatments, can lead to significant clinical improvements. The ability of PDT to target and kill microorganisms through the generation of cytotoxic reactive oxygen species, particularly singlet oxygen, provides a promising alternative to traditional mechanical approaches for eliminating bacterial deposits [30,31]. These findings suggest that PDT has the potential to enhance the outcomes of non-surgical periodontal therapies and address the limitations of conventional methods in sites with difficult access.

Effectiveness of PDT in various test groups: Similarly, another study introduced a test group infused with probiotics in conjunction with PDT and SRP. The outcomes reported by Patyna M et al., favoured this combination, resulting in significant clinical improvements and a microbiological achievement marked by a substantial reduction of specific pathogens [27].

The review also included two studies that explored the implications of repeated applications of PDT in supportive periodontal therapy. The outcomes of these studies underscored the potential for multiple applications of adjunctive PDT to yield improved clinical results in residual pockets among maintenance patients [11,12].

Furthermore, a comparison between PDT and antibiotics in the context of scaling and root planing revealed comparable long-term improvements in periodontal parameters for both interventions. Another investigation examined the adjunctive effect of PDT in surgical periodontal therapy, showing significant reductions in probing depth and gains in clinical attachment level for the PDT group. Notably, changes in the subgingival microbiota were consistent across both groups; however, the PDT group exhibited a higher concentration of bacteria associated with periodontal disease at the conclusion of the study [29].

Andersen R et al., and Christodoulides N et al., employed more complex methodologies in their investigations, each characterised by three distinct study arms. One study introduced a supplementary experimental group exclusively undergoing PDT, with three study arms designed to comprehensively investigate the effects of different interventions. Each arm represented a unique aspect, enhancing internal validity and providing insights into the effectiveness of the interventions. In a prior investigation, patients underwent SRP before being randomised into either a no further treatment arm or an adjunctive PDT arm [9,10].

Variability in study outcomes: While the majority of studies demonstrated favourable outcomes, it is important to acknowledge the variability in the results. Some studies did not observe significant differences between PDT in combination with conventional treatment and conventional treatment alone [10,13,15,16,28]. This variability could be attributed to several factors, including differences in study design, patient populations, PDT protocols, PSs used, and light parameters. These variations highlight the need for standardisation and consistency in future research to obtain more robust and generalisable results.

In the analysis of the 21 studies included in present review, it is noteworthy that one study was identified as having a high-risk of bias, as indicated by the risk of bias assessment tool utilised [13]. This finding emphasises the importance of critically evaluating the methodological quality of studies in research synthesis, as studies with a high-risk of bias may introduce substantial uncertainty and potential inaccuracies in the conclusions drawn. Additionally, the discovery that six studies demonstrated an overall unclear risk of bias further underscores the need for transparent reporting and robust methodological approaches in future research endeavours. Addressing and minimising bias in study design, conduct, and reporting are imperative to enhance the reliability and validity of research outcomes, ultimately contributing to evidence-based decision-making in healthcare and clinical practice.

Factors affecting PDT efficacy: The review identified various factors that can influence the efficacy of PDT in periodontal disease management. One crucial aspect is the selection of appropriate PSs and their concentrations. The PSs should possess the following properties: a high binding affinity for the target microorganism, a broad spectrum of action, a low binding affinity for mammalian cells to avoid the risk of photodestruction of host tissues, a low propensity for selecting resistant bacterial strains, a minimal risk of promoting mutagenic processes, and low chemical toxicity [32].

Different PSs exhibit varying levels of bacterial selectivity and activation wavelengths, which can impact the overall effectiveness of PDT. Generally, Gram-positive bacteria are susceptible to photo-inactivation, whereas Gram-negative bacteria are often resistant unless the permeability of their outer membrane is modified. This is connected to the difficulties encountered by PSs in penetrating gram negative bacterial cells. Antimicrobial PSs such as porphyrins, phthalocyanines, and phenothiasines (e.g., methylene blue and toluidine blue O) have been reported to penetrate both gram-positive and gram negative bacteria. The positive charge seems to promote the binding of the PSs to the gram negative bacterial membrane, leading to localised damage and resulting in increased permeability. Hence, toluidine blue O and methylene blue are commonly used in antimicrobial photodynamic therapy (aPDT). The hydrophilicity, low molecular weight, and positive charge of methylene blue facilitate its passage across the porin-protein channels in the gram negative outer bacterial membrane. Methylene blue's interaction with the anionic lipopolysaccharide macromolecule of gram negative bacteria results in the generation of methylene blue dimers, which participate in the photosensitisation process [32,33].

Moreover, the choice of light sources and their parameters, including light intensity and exposure time, can also influence the photodynamic reaction [34]. Therefore, optimising these parameters is essential for achieving consistent and reproducible outcomes in PDT-based periodontal therapies.

Safety and adverse effects: The safety profile of PDT in periodontology was explored in the review. PDT is generally considered safe, with minimal adverse effects reported in the selected studies [35-38]. However, like any medical procedure, PDT is not entirely devoid of risks. Potential adverse effects may include mild discomfort, tissue sensitivity to light, and transient post-treatment inflammation [39]. Nonetheless, the incidence of serious complications is low, indicating that PDT can be considered a safe treatment modality when appropriately administered. Long-term studies with larger sample sizes would be beneficial to further assess the safety and potential long-term effects of PDT in periodontal patients.

Future perspectives and recommendations: The systematic review has highlighted the potential of PDT as a valuable addition to periodontal disease management. However, several avenues for future research and improvements in PDT's clinical application have been identified. Further investigations are needed to establish the long-term efficacy of PDT and to identify optimal treatment protocols, including the most suitable PSs and light parameters [40]. Large-scale randomised controlled trials and comparative studies can provide stronger evidence for the effectiveness of PDT and enable the identification of specific patient populations that may benefit the most from this therapy. Additionally, exploring the use of PDT in combination with other emerging periodontal treatments or technologies may offer further benefits and enhance its efficacy.

Limitation(s)

Studies on PDT in periodontology may vary widely in terms of study designs, patient populations, intervention protocols, and outcome measures, making it challenging to draw direct comparisons or generalise findings and many studies may have short-term follow-up periods, which limits the assessment of the long-term efficacy and safety of PDT in periodontal treatment.

CONCLUSION(S)

The PDT presents a promising scope in periodontology, showcasing varied roles ranging from antimicrobial action to tissue healing and periodontal health development. Its efficacy as an adjunctive treatment, especially in challenging cases or against resistant microbes, is evident. This is further accentuated by its non invasive nature and minimal adverse effects, making it an appealing option in periodontal care. Despite these advantages, PDT's full potential remains untapped due to challenges such as protocol standardisation, optimising light sources, and identifying ideal PSs, which necessitates further investigation. Moreover, addressing cost-effectiveness and accessibility concerns is pivotal for the widespread adoption of PDT. In essence, PDT offers a pathway for advancements in periodontal therapy. Ongoing research and trials are vital to unravel its mechanisms, improve protocols, and solidify its role in enhancing periodontal treatment outcomes.

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