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Systematic Review

Photodynamic Therapy in Non-Surgical Treatment of Periodontitis: A Systematic Review and Meta-Analysis

Alessia Pardo [1], Andrea Butera [2,*], Angela Giordano [1], Simone Gallo [3,*], Maurizio Pascadopoli [3,*], Andrea Scribante [2,3] and Massimo Albanese [1]

[1] Dentistry and Maxillofacial Surgery Section, Department of Surgery, Dentistry, Pediatrics and Gynecology, University of Verona, 37121 Verona, Italy
[2] Unit of Dental Hygiene, Section of Dentistry, Department of Clinical, Surgical, Diagnostic and Pediatric Sciences, University of Pavia, 27100 Pavia, Italy
[3] Unit of Orthodontics and Pediatric Dentistry, Section of Dentistry, Department of Clinical, Surgical, Diagnostic and Pediatric Sciences, University of Pavia, 27100 Pavia, Italy
* Correspondence: andrea.butera@unipv.it (A.B.); simone.gallo02@universitadipavia.it (S.G.); maurizio.pascadopoli01@universitadipavia.it (M.P.)

Abstract: Aim: to evaluate the adjunctive effects of photodynamic therapy (aPDT) on nonsurgical mechanical treatment in patients with periodontitis. Materials and methods: The search strategy was conducted according to the PRISMA guidelines to answer research questions regarding the effectiveness of aPDT in association with non-surgical periodontal therapy. The mean values and standard deviations were collected by data extraction. A descriptive comparison between aPDT in association with periodontal treatment and periodontal treatment alone was performed, and meta-analyses of PPD were also performed. Both randomized controlled clinical trials (RCTs) and controlled clinical trials (CCTs) were included. Results: Out of 2059 records, 14 articles on adjunctive photodynamic therapy were included because they met the eligibility criteria. A comparison between the aPDT data and the control group showed improved PPD for photodynamic therapy (SMD −0.76, $p = 0.003$; $I^2 = 88\%$). Statistical analysis was then applied to the three PPD subgroups. The first group included studies that used indocyanine green in association with a wavelength of 810 nm (SMD −1.79, $p < 0.00001$, $I^2 = 88\%$). The second group included studies that used phenothiazine chloride at a wavelength of 660 nm (SMD −0.03, $p = 0.84$, $I^2 = 0\%$). The last group included studies that used methylene blue photosensitizers treated with a wavelength 628–670 nm were included (SMD −0.13, $p = 0.38$; $I^2 = 0\%$). Conclusions: despite the limited number of RCTs and the great heterogeneity between them, it can be concluded that aPDT in association with nonsurgical periodontal treatment improved the clinical parameters at 3 months.

Keywords: periodontitis; photodynamic therapy; photodynamic antimicrobial therapy; non-surgical periodontal treatment

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Citation: Pardo, A.; Butera, A.; Giordano, A.; Gallo, S.; Pascadopoli, M.; Scribante, A.; Albanese, M. Photodynamic Therapy in Non-Surgical Treatment of Periodontitis: A Systematic Review and Meta-Analysis. *Appl. Sci.* **2023**, *13*, 1086. https://doi.org/10.3390/app13021086

Academic Editors: Alberta Lucchese and Dario Di Stasio

Received: 4 December 2022
Revised: 1 January 2023
Accepted: 9 January 2023
Published: 13 January 2023

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1. Introduction

Ultrasonic scaling and root planing (US-SRP) is the most common nonsurgical periodontal treatment. However, residual pockets and periodontal pathogens bacteria are not eliminated, particularly in furcations, root concavities, interproximal areas, and sites with deep pockets that are inaccessible to periodontal instruments [1,2]. Clinical studies related to root planing [3,4] showed that the entire removal of subgingival calculus is usually difficult and that incomplete removal of dental plaque equals no plaque control [5]. It was also observed that complete removal of plaque and subgingival calculus is more difficult in deep pockets than in shallow pockets [5]. Therefore, much attention was posed on the evaluation of additional treatments in addition to SRP, reporting an antioxidant, antimicrobial, and immunostimulant action [6]. Mixed results were reported regarding the efficacy of adjunctive therapies, and there is no consensus on the method of choice to

improve mechanical treatment outcome [7,8]. However, the additional use of aPDT with SRP in reducing PD $\geq$ 5 mm and treating furcations was also not fully elucidated. In the last decades, the efficacy of aPDT in periodontal disorders were extensively studied [9,10]. The aPDT mechanism involves the stimulation of photosensitizing dye molecules by the application of the laser light of specific wavelengths that excites the dye molecule from the ground singlet state to the triplet state [11]. These molecules excited to the triplet state react with endogenous oxygen forming cytotoxic singlet oxygen, which facilitates the destruction of the bacterial cell [12]. However, the additional use of aPDT with SRP in reducing PD $\geq$ 5 mm and treating furcation was not fully elucidated. The following systematic literature review aimed to evaluate the efficacy of PDT in improving the clinical and microbiological parameters of photodynamic therapy in addition to non-surgical periodontal therapy.

2. Materials and Methods

2.1. Focused Question

- In patients with untreated periodontitis, does the application of photodynamic therapy (aPDT) provide additional effects to traditional treatment with manual and mechanical instruments when comparing the patient's clinical parameters?
- In patients with untreated periodontitis, does the application of photodynamic therapy (aPDT) provide additional effects to traditional treatment with manual and mechanical instruments when comparing the patient's microbiological parameters?

2.2. Search Strategy

The current review was conducted according to the PRISMA guidelines [13]. The PICOS principle is constituted as follows: patients, adults with periodontitis having $\geq$5 mm PD; interventions, aPDT + SRP; comparators, SRP with or without placebo; outcomes, PD reduction; study design, and randomized clinical trials. Electronic and manual literature searches were conducted considering the following databases: MEDLINE, Embase, and Cochrane Central Register of Controlled Trials. Articles addressing the focused question were considered if published up to the end of December 2021. For the PubMed library, combinations of the following MeSH and free-text words were used: photodynamic therapy OR photochemotherapy OR diode OR photosensitizing agents AND periodontitis OR chronic periodontitis OR periodontitis, chronic OR adult periodontitis OR periodontitis, adult OR aggressive periodontitis OR peri-odontitis, aggressive OR periodontal disease OR attachment loss, periodontal OR alveolar bone loss OR periodontal pocket OR scaling, dental AND scaling, supragingival OR scaling, root OR scaling, subgingival OR root planing OR planning, and root OR periodontal debridement. The papers were screened by two independent reviewers, at first considering their titles and abstracts. Second, full-text papers fulfilling the eligibility criteria for inclusion were identified according to the study aims. The heterogeneity of the primary outcome across studies was determined based on the following factors: design of the study, evaluation period, medical and periodontal status of patients, number of patients, mean age and age range of patients, follow-up of the study, intervention type of aPDT, and type of photosensitizing agent used for photodynamic therapy. A summary of descriptive data was used; where appropriate, a meta-analysis was performed, and weight mean differences (WMD) were calculated using the Review Manager (RevMan) Version 5.4 for Windows. Copenhagen: The Nordic Cochrane Center, Cochrane Collaboration, 2003.

3. Results

3.1. Study Selection

A total of 2059 studies were initially identified, and after removing duplicates, 715 were identified. After applying the inclusion and exclusion criteria, 14 studies were selected and processed for data extraction. The study identification flowchart according to PRISMA, with reasons for the exclusion of articles, is shown in Figure 1.

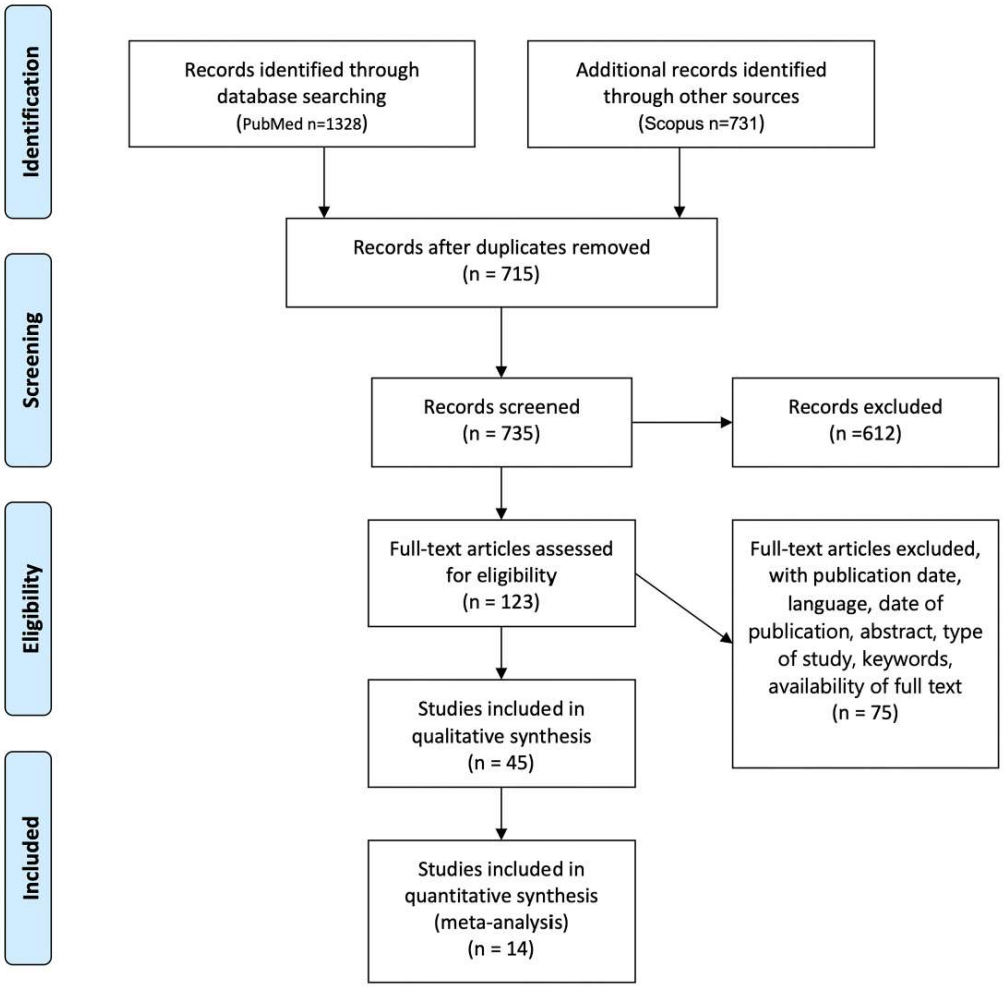


Figure 1. Preferred reporting items for systematic review and meta-analysis (PRISMA) flow diagram for studies retrieved through the searching and selection process.

3.2. Characteristics of Included Studies

The studies included in the systematic review were conducted in India, Australia, Germany, Thailand, Serbia, Iran, and Brazil, and were published between 2012 and 2022. These were comparative in vivo studies performed in periodontal patients to evaluate the adjunctive use of photodynamic therapy to SRP. In all the studies, the number of participants ranged from 16 to 50, with an age range of 18 to 75 years. The studies are summarized in Table 1 [14–27]. Different types of lasers with various parameters (power, energy, energy density, wavelength, application time, frequency, and emission mode) were used: an unspecified diode laser [14,15,19,20,24], AsGaAl diode laser [17,21,23], PAD Lit 600 [16], Periowave diode laser [18], Diode laser, Elexxion Claros pico [22], Picasso diode laser, AMD [26], and HELBO diode laser [25,27]. Among these, four studies used methylene blue photoactivator dye [14,17,18,24], five studies employed indocyanine green dye [15,21–23,26], two used toluidine blue photoactivator [16,19], and three used phenothiazine chloride dye [20,25,27]. All studies assessed parameters at baseline and at 3 months, six studies also performed an additional assessment at 1 month [15,17,18,20,22,27], and five other studies also performed a parameter measurement at 6 months [15,17,18,20,22,27]. All studies treated patients with chronic periodontitis, except one that treated patients with aggressive periodontitis [19].

Table 1. General characteristics of included studies.

Investigators	Study Design	Lasers and Fotosensitizing	Patients	Parameters Involved	Follow up (Weeks)
Pulikkotil SJ et al. [14]	RCT-split mouth	Methylene blue; wavelength 628 nm; Diode laser	16 patients; CP; average age 39 ± 21 years	CAL; PPD; BOP *A. actinomycetemcomitans*	Up to 12
Shingnapurkar et al. [15]	RCT-split mouth	Indocyaine green (IGC); wavelength 810 nm; Diode laser	33 patients; chronic periodontitis; average age 40 ± 15 years	PPD; PI; GI; RAL	Up to 12
Raj et al. [16]	RCT-Full mouth	Toluidine blue, wavelength of 635 nm; PAD [Lit 600], Apoza, Taiwan	20 patients; chronic periodontitis; average age 42.5 ± 7.5 years	CAL; PPD *P. gingivalis, T. forsythia, T. denticola*	Up to 12
Balata et al. [17]	RCT-split mouth	Methylene blue, wavelength 660 nm; AsGaAl diode laser	22 patients; CP; average age 46.5 ± 15.5 years	CAL; PPD; BOP	Up to 24
Berakdar et al. [18]	RCT-split mouth	Methylene blue, wavelength of 670 nm; Diode laser Periowave	22 patients; CP; average age 56 ± 18 years	PPD: BOP	Up to 24
Chitsazi et al. [19]	RCT-split mouth	Blu-toluidine; wavelength of 670–690 nm; Diode laser	24 patients; AgP; average age 29 years	CAL; PPD BOP; GI; REC *A. actinomycetecommitans*	Up to 12
Bundidpun et al. [20]	RCT-split mouth	Phenothiazine chloride (HELBO Blue); wavelength of 660 nm; Diode laser	20 patients; CP; average age 52.5 ± 17.5 years	CAL; PPD; BOP; PI; GI	Up to 24
Raut et al. [21]	RCT Full mouth	Indocyain green (IGC), wavelength of 810 nm; AsGaA Diode laser	50 patients; CP; NA	CAL; PPD; BOP; PI	Up to 24
AlSarhan et al. [22]	RCT-split mouth	Indocyanine green; wavelength of 808 nm +/− 10 nm. Diode laser Elexxion Claros peak; Elexxion AG	20 patients; CP, average age 54 years	CAL; PPD; BOP; PI; REC	Up to 12
Wadhwa et al. [23]	RCT Split Mouth	Indocyanine green; wavelength 810 nm. AsGaA Diode laser	30 patients; CP; average age 46 ± 10 years	PPD; BOP; PI; GI;	Up to 24
Aabed et al. [24]	RCT Full mouth	Methylene blue (MB) (0.005%), wavelength 660 nm and 150 mW, Diode laser	44 patients; CP; NA	CAL; PPD; PI; GI *A. actinomycetemcomitans, P. gingivalis*	Up to 12
Arsic Z et al. [25]	RCT Split Mouth	Phenothiazine chloride (HELBO Blue); wavelength of 660 nm; Diode laser, HELBO	25 patients; CP; average age 50 ± 20 years	CAL; PPD; BOP; PI *A. actinomycetemcomitans, P. gingivalis, T. denticola*	Up to 12
Karmakar et al. [26]	RCT Split Mouth	Indocyanine green (IGC); wavelength of 810 nm. Diode laser Picasso, AMD	20 patients; CP; average age 45 ± 10 years	CAL; PPD *P. gingivalis, T. forsythia*	Up to 12
Ahad et al. [27]	RCT Split Mouth	Phenothiazine chloride (HELBO Blue); wavelength of 660 nm; Helbo diode laser	30 patients; CP; average age 38.67 ± 10.52 years	CAL; PPD; BOP; PI	Up to 12

AgP, aggressive periodontitis; CP, chronic periodontitis; NA, not available; PPD, probing pocket depth; BoP, bleeding on probing; GI gingival index; PI plaque index; CAL clinical attachment level; RCT, randomized control trial; and SRP, scaling and root planing.

3.3. Main Outcome of the Study

All 14 articles evaluated the probing pocket depth (PPD) at baseline and follow-up, and found a significant difference in PPD in the test group compared to the control one. Clinical periodontal parameters (PPD) are shown in Table 2, in association with the type of laser, wavelength, and photosensitizer. All studies reported an improvement in PPD when using aPDT in association with US-SRP; in five studies, the improvement

was statistically significant with respect to the control group, and three studies [18,20,21] performed an additional follow-up at 6 months, and all agreed that the greatest reduction in PPD, achieved by a combination of SRP/aPDT, was statistically significant after this period. In the rest of the studies, after treatment, an improvement was observed in both groups without a significant statistical difference, even if we found a slightly greater improvement in favor of SRP+PDT.

Table 2. Outcomes (PPD) of the research articles included in the current review.

Investigators	Changes in PPD (mm) Comparing Test and Control Groups	
Pulikkotil SJ et al. [14]	aPDT + SRP (≥5 mm) T0: 4.66 ± 0.39 Follow-up:3.56 ± 0.69 *	SRP (≥5 mm) T0: 4.95 ± 0.95 Follow-up: 3.93 ± 0.23 *
Shingnapurkar SH et al. [15]	aPDT + SRP (≥5 mm) T0: 5.13 ± 0.34 Follow-up:2.23 ± 0.67 *	SRP (≥5 mm) T0: 5.27 ± 0.069 Follow-up: 3.67 ± 0.75 *
Raj KR et al. [16]	aPDT + SRP (≥5 mm) T0: 6 ± 1.1 Follow-up: 3.5 ± 0.8	SRP (≥5 mm) T0: 5.9 ± 0.99 Follow-up: 3.5 ± 0.6
Berakdar M et al. [18]	aPDT + SRP (≥5 mm) T0: 6.0 ± 1.1 Follow-up: 4.3 ± 0.94 *	SRP (≥5 mm) T0: 5.9 ± 0.99 Follow-up: 5 ± 0.66 *
Chitsazi MT et al. [19]	aPDT + SRP (≥4 mm) T0: 5.79 ± 1.06 Follow-up: 4.29 ± 0.95	SRP (≥4 mm) T0: 5.45 ± 0.77 Follow-up: 4.54 ± 0.88
Bundidpun P, et al. [20]	aPDT + SRP (≥6 mm) T0: 4.96 ± 1.11 Follow-up: 3.54 ± 0.94	SRP (≥6 mm) T0: 4.91 ± 1.02 Follow-up: 3.5 ± 1
Balata ML et al. [17]	aPDT + SRP (≥5 mm) T0: 5.11 ± 0.56 Follow-up: 2.83 ± 0.47 *	SRP (≥5 mm) T0: 5.15 ± 0.46 Follow-up: 2.83 ± 0.4 *
Raut CP et al. [21]	aPDT + SRP (≥5 mm) T0: 6.04 ± 0.82 Follow-up: 3.53 ± 0.58 *	SRP (≥5 mm) T0: 6.08 ± 0.73 Follow-up: 5.08 ± 0.66 *
AlSarhan MA et al. [22]	aPDT + SRP (≥5 mm) T0: 4.71 ± 0.863 Follow-up: 2.27 ± 1.024 *	SRP (≥5 mm) T0: 5.22 ± 0.924 Follow-up: 3.28 ± 0.749 *
Wadhwa A et al. [23]	aPDT + SRP (≥5 mm) T0: 3.37 ± 0.47 Follow-up:1.3 ± 0.36 *	SRP (≥5 mm) T0: 3.37 ± 0.46 Follow-up: 2.19 ± 0.48 *
Arsić, Z., et al. [25]	aPDT + SRP (≥5 mm) T0: 3.75 ± 0.7 Follow-up: 2.79 ± 0.61 *	SRP (≥5 mm) T0: 3.78 ± 0.75 Follow up: 2.92 ± 0.61 *
Karmakar S., et al. [26]	aPDT + SRP (≥5 mm) T0: 6.5 ± 0.61 Follow-up: 3.7 ± 0.86	SRP (≥5 mm) T0: 6.4 ± 0.75 Follow-up: 4.8 ± 0.77
Ahad, A., et al. [27]	aPDT + SRP (≥5 mm) T0: 7.9 ± 1.71 Follow-up: 5.43 ± 1.36	SRP (≥5 mm) T0: 7.53 ± 1.31 Follow-up: 5.37 ± 0.85
Aabed K et al. [24]	aPDT + SRP (≥5 mm) T0: 4.7 ± 0.2 Follow-up: 1.3 ± 0.2	SRP (≥5 mm) T0: 4.5 ± 0.07 Follow-up: 1.5 ± 0.1

aPDT, antimicrobial photodynamic therapy; SRP, scaling and root planing. The asterisk "*" indicate the presence of a statistically significant difference from baseline to the follow-up ($p < 0.05$).

Concerning the clinical attachment level (CAL) out of eleven studies evaluated this parameter, two studies noted a statistically significant improvement after three months in the test group compared to the control group, Karmakar et al. [26] (test 1.8 mm ± 0.88 vs. control group 2.9 mm ± 0.7), AlSarhan et al. [22] (test: 3.06 ± 1.756 vs. control: 4.06 ± 1.725). In most articles (nine) we found no significant difference in parameters between the test group and the control one [14,16,17,19–21,24,25,27]. However, in the study by Raut et al. [21], there was a further increase in CAL after six months in the test group compared to the control one. Regarding the gingival bleeding index out of ten articles that took BOP into consideration, we found five articles that identified an improvement in the test group (SRP+PDT) compared to the control group (SRP). In the study by Pulikkotil et al. [14], a reduced BoP was identified, at 3 months, of less than 20%, the values in the test group at follow up were 12.44% ± 20.45 while in the control group 19.54% ± 23.35. AlSarhan et al. [21], at three months, found 36.30% of sites with positive Bop in the test group against the control group, which presented 54.16%. Wadhwa A et al. [23], showed a better result in the test group 0.91 ± 0.25 than the control 1.69 ± 0.28; in the study by Ahad et al. [27], at 3 months there was a significant difference in the Bop of the test group 0.31 ± 0.30 compared to the control group 0.46 ± 0.27, and Bundidpun P., et al. [20] found a slight improvement in the test group with values of 30% compared to the control group 38.10%. In four articles, we found no significant difference between the test group and the control group at three months after application [17,18,21,25]; of the latter, three found an improvement in the Bop score at 6 months [18,20,21]. Out of eight articles that evaluated the plaque index (PI), only in the article Wadhwa A., et al. [23] we found a significant difference in PI in the test group compared to the control group (test 0.72 ± 0.27 vs. control 1.25 ± 0.23). In all studies, there was a significant reduction in PI values in both groups from the baseline to follow-up visits, which can be attributed to the reduction in supragingival plaque following SRP and oral hygiene instructions received during the preliminary visits. Out of five articles evaluating the gingival inflammation index (GI) only in the study by Wadhwa A., et al. [23] the test sites showed a significantly greater improvement than the control group (test 0.65 ± 0.21 vs. control 1.18 ± 0.25).

3.4. Microbiological Outcome of the Study

In two articles, we found an improvement in microbiological parameters in the test group compared to the control group. The main microorganisms involved in the studies and reduced as a result of photodynamic therapy were *P. gingivalis*, *T. denticola*, and *A. actinomycetemcomitans*. In the study by Raj KR et al. [16], there was a significant reduction in microbial levels in test groups for *T. denticula* (test: 0.3 ± 0.50, control: 0.6 ± 0.51) (test: 0.2 ± 0.42, control 0.7 ± 0.48) and *T. forsythia* (test: 0.2 ± 0.42, control: 0.7 ± 0.48), this could be due to highly reactive oxygen species, particularly singlet oxygen, which can damage a wide variety of proteins, lipids, and carbohydrates. According to Arsić et al. [25], the test group had a significantly higher reduction in the number of microorganisms than the control groups *A. actinomycetemcomitans* (test 4.0% vs. control 18.0%), *P. gingivalis* (test 8% vs. control 40%), and *Treponema denticula* (test 24% vs. control 67.3%). In three articles there was an improvement of all microbiological parameters in both groups but without a significant difference, Chitsazi et al. [19] showed a significant reduction in *A. actinomyceticomitans* count at 3 months compared to baseline, Karmakar S et al. [26] showed a reduction in all organisms tested, *T. denticola*, *P. gingivalis*, and *T. forsythia*, at the sites of both treatment groups at 3 months post-treatment; in the study by Aabed et al. [24] *A. actinomycetemcomitans* and *P. gingivalis* were identified in significantly fewer patients at follow-up in both groups than their respective baseline values. In the study by Pulikkotil et al. [14], it was found that all subjects had the presence of *A. actinomycetemcomitans* at the sites sampled in all phases of the study, and that no reduction was observed either at 7 days or at 3 months after the respective treatments compared to baseline.

3.5. Meta-Analysis

Thirteen studies were included, and we performed three subgroups to evaluate the outcome of adjunctive aPDT on deep PD (≥5 mm) reduction based on the type of sensitizing and wavelength lasers. Figure 2 provides a summary of the meta-analysis outcomes. In all instances, the baseline scores were not statistically different.

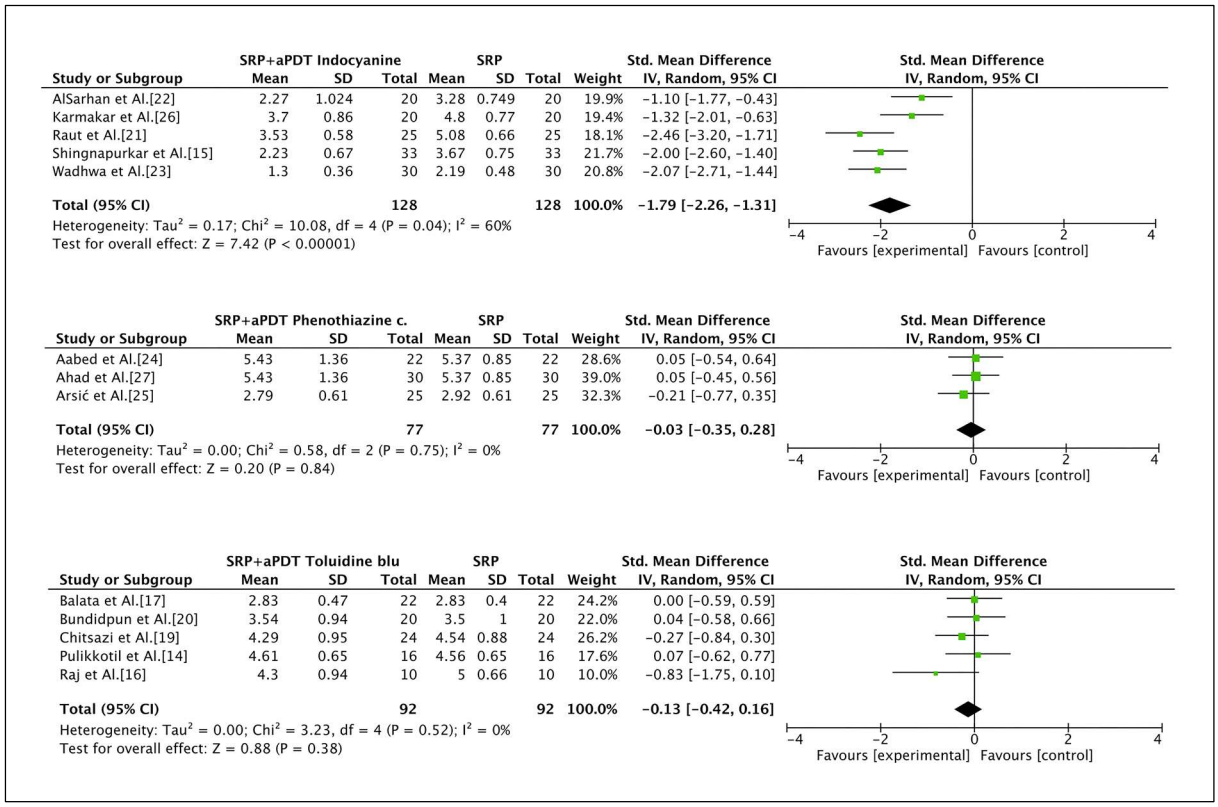


Figure 2. Forest plot showing post therapy PPD (≥5 mm) comparing the effect of adjunctive antimicrobial photodynamic therapy (aPDT) vs. scaling and root planing (SRP) divided into subgroups.

In the first group, we grouped together the studies that used indocyanine green dye and a wavelength of 810 nm [15,21–23,26]. End scores only showed a significant effect in the aPDT-SRP group compared with the SRP group [WMD: −1.79, 95% CI (−2.26–1.36); test for heterogeneity, $p = 0.004$; $I^2 = 60\%$].

The second group shows us comparing studies that used phenothiazine chloride [24,25,27] wavelength 660 nm, and we note a standardized mean difference [WMD −0.03 (95%−0.35, 0.28), with statistical significance ($p = 0.75$) and $I^2 = 0\%$. This type of dye appears to have a weaker beneficial effect than indocyanine green. In the last group, we compared the studies that used photosensitizers, methylene blue, treated with wavelengths of 628–670 nm [14,17,18,24], toluidine blue, treated with a wavelength of 636–670 nm [16,19], and found a standardized mean difference [WMD −0.13 (95%−0.42−0.16), statistical significance ($p = 0.52$), and $I^2 = 0\%$; from what we deduce from the comparison with the first two groups, a better result was found in the studies using indocyanine green and a higher wavelength of 810 nm.

4. Discussion

The recourse to non-surgical system for the treatment of periodontal/periimplant disease represents a trend topic in dental research nowadays [28]. The limitations of the conventional treatment scaling and root planing (SRP), required the necessity to test adjunctive protocols. Previous recent research was conducted to evaluate the efficacy

of systems reporting an antimicrobial, antioxidant, and immunostimulant activity, such as ozone therapy [29–31], probiotics [32], paraprobiotics [33–35], postbiotics [36,37], and photodynamic therapy [38].

The purpose of the current systematic review is to study the additional effects of aPDT application in nonsurgical periodontal therapy in patients with untreated periodontitis after a 3-month follow-up period. Additionally, based on the great heterogeneity observed among the studies selected, particularly in terms of laser type, tip diameter, wavelength, photosensitizer, periodontal treatment modality, number of sites treated, population, and different possible combinations of these parameters, a careful attempt to conduct a meta-analysis was made only when the changes in PPD, BOP, and CAL between the baseline and 3-month follow-up were reported in the original articles using the same measurement indices and performing statistical searches by dividing them into subgroups according to the type of photosensitizer. For the reduction in pocket depth (PPD), all 14 articles included in the review evaluated the probing depth at baseline and follow-up, and in five of these articles, we found a significant difference in PPD in the test group with respect to the control group [15,21–23,26]. All studies used indocyanine green as a photo activator; in the rest of the studies, an improvement was observed after treatment in both groups without a significant statistical difference, although we found a slightly greater improvement in favor of SRP+aPDT. Three studies [18,20,21] performed an additional follow-up at six months, and all agreed that a greater reduction in PPD, achieved by a combination of SRP/aPDT, was statistically significant after this period. The results of this systematic review agree with those found in studies by Azaripour et al., 2018 [39], and Akram Z., 2018 [40], who stated that aPDT, in addition to SRP, provides a significant reduction in PPD at 3 and 6 months. The results of the present analysis partially agree with a previous review by Atieh [41], which found a significant reduction in PD at 3 months when PDT was also used, but no significant CAL gain after 3 months. According to the RCTs that performed microbiological evaluation, in two articles, we found an improvement in microbiological parameters in the test group compared to the control group [16,25]. In three articles, there was an improvement in all microbiological parameters in both groups, but without a significant difference [19,25,26]. In the study by Pulikkotil et al. [14], no differences were found between the two groups at baseline and follow-up. Thus, we conclude that, as reported by Akram et al. [40], the bactericidal efficacy of aPDT in addition to SRP against periodontal pathogens in periodontal disease remains questionable. Reviewing the data obtained, the best results were obtained in the studies that used photosensitizing green indocyanine for BOP [23] for PPD [15,21–23,26], probably because of its efficacy in reducing bacterial load, as shown by Topaloglu et al., 2013 [42] and the study by Sukumar K et al., 2020 [43]. An analysis of studies suggests a short-term benefit of aPDT in addition to SRP, in terms of clinical parameters. However, evidence regarding its long-term efficacy is lacking and no significant effect was confirmed in regard to the CAL gain at 3 months. These encouraging results can be partly attributed to the deactivation and detoxification of periodontal pathogens and their products by the additional use of aPDT in those areas that are inaccessible to mechanical instruments, such as deep pockets or root concavities, which act as a reservoir for periodontal pathogen microorganisms, leading to the recolonization of bacteria; aPDT can overcome these difficulties, thus promoting the achievement of better clinical outcomes by photoactivating the remaining periodontal pathogens. Moreover, photodynamic periodontal treatment has further positive aspects, such as the reduced treatment time, the absence of required local anesthesia, and no damage to the surrounding soft tissues. In addition, the recourse to aPDT was not affected by increasing bacterial resistance caused by the clinician's reckless prescription of antibiotics. Scaling and root planning (SRP) are essential to establish a biologically compatible subgingival environment for the promotion of periodontal health. Therefore, regular oral hygiene instructions should be provided to patients undergoing periodontal treatment to improve their clinical outcomes. Considering the limitations of this review, including the heterogeneity of the studies selected especially in regard to the parameters considered for the photodynamic

therapy, and based on the paucity of studies reporting the efficacy of PDT combined with SRP for a longer follow-up period (>3 months) in the literature, it is currently not possible to draw a definitive conclusion regarding its medium- or long-term effects. Future randomized clinical trials should be performed in order to completely clarify the role of photodynamic therapy for the non-surgical treatment of periodontal disease, as well as to compare its efficacy with other innovative non-surgical protocols adjuvant to SRP, such as ozone therapy and the use of probiotics. It could also be interesting to further evaluate the effect of periodontal treatment through photodynamic therapy on glycemic control, as well as to evaluate other outcomes of those systemic conditions which are shown to be related to the periodontal status [44–55].

5. Conclusions

The following three question were addressed in this systematic review:

- The first question that this systematic review aims to answer is whether there is sufficient evidence to justify the use of photodynamic therapy as an adjunct to conventional nonsurgical periodontal therapy using manual or mechanical instruments. A PDT emerged as a beneficial treatment option for periodontitis. The results of many studies indicated that aPDT combined with SRP has a slight advantage in the treatment of periodontitis. Despite a wide range of heterogeneity, all the included studies indicate that aPDT has the potential to be an effective adjuvant in the treatment of periodontitis. Scaling and root planing (SRP) remains essential for the promotion of a healthy subgingival environment.
- The second question was whether photodynamic therapy (aPDT) provides additional effects to traditional treatment with manual and mechanical instruments when comparing the patient's clinical parameters. The analysis of the studies suggests a short-term benefit of PDT in addition to SRP in terms of clinical outcome variables; however, the evidence regarding its long-term efficacy is still insufficient, and no significant effect was confirmed in terms of CAL gain at 3 months.
- The third question concerned was whether in patients with untreated periodontitis the application of photodynamic therapy (aPDT) provides additional effects to the traditional treatment with manual and mechanical instruments when comparing the microbiological parameters of the patient. The bactericidal effect of aPDT as an adjunctive treatment to SRP against periodontopathogens in periodontal disorders remains questionable.

Although the short-term clinical benefit of aPDT as an adjunct to SRP was confirmed in this systematic review and meta-analysis, some questions still remain to be answered. Future RCTs should focus on the difference between split-mouth and parallel designs in their protocols. Furthermore, the optimal combination of photosensitizers and laser parameters should be determined with high-quality studies. Clinicians are looking for an efficient and safe treatment modality, both as an alternative and in addition to standard therapies. Photodynamic therapy, as evidenced by the results of this meta-analysis, has the potential to improve some clinical parameters in the short term.

Author Contributions: Conceptualization, A.P., A.G. and M.A.; methodology, A.P., A.G. and M.A.; software, A.P., A.G. and M.A.; validation, A.B. and S.G.; formal analysis, A.P., A.G. and M.A.; investigation, A.P., A.G. and M.A.; resources, A.P.; data curation, A.G. and M.A.; writing—original draft preparation, A.P., A.G. and M.A.; writing—review and editing, S.G.; visualization, M.P. and A.S.; supervision, A.B.; project administration, A.S.; funding acquisition, A.B. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data are available at the corresponding authors upon reasonable request.

Conflicts of Interest: The authors declare no conflict of interest.

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