#### **REVIEW ARTICLE**



# Adjunctive photobiomodulation to Basic Periodontal therapy using different low-power laser application techniques: a systematic review and meta-analysis

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#### Abstract

To review current literature and synthesize clinical outcomes related to different low-level laser techniques as a complement to basic periodontal therapy (BPT). Electronic searches were conducted in PubMed, Cochrane, and Scopus, and clinical trials published from January 2013 to August 2023 using photobiomodulation as a complement to basic periodontal therapy, with a clear description of the laser technique, were included. The risk of bias was assessed using the Joanna Briggs Institute Critical Assessment Checklist. Estimates of interest were calculated using random effects meta-analyses. A total of 947 references were retrieved, and 22 studies were included for qualitative synthesis. Ten studies used intrasulcular laser techniques, with 89% using infrared wavelength, and 12 studies used transgingival techniques, with 61.5% using red wavelength. The frequency of photobiomodulation after BPT ranged from 1 to 9 sessions, with follow-up periods ranging from 5 days to 12 months. Risk of bias was considered low in 16 studies and moderate in six studies. Meta-analysis of 13 studies showed that BPT reduced probing depth at 4-, 12- and 24-weeks post-treatment, and improved clinical level attachment at 6-, 12- and 24-weeks post-treatment. Studies suggest that photobiomodulation may be a valuable complement in the treatment of periodontitis, especially using transgingival application technique.

Keywords Photobiomodulation · Low-level laser therapy · Periodontitis · Basic periodontal therapy

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# Introduction

Periodontitis is a chronic and progressive inflammatory condition that affects the tissues supporting the teeth, including the periodontal ligament and alveolar bone [1]. Tissue destruction is caused by the combination of host immune-inflammatory responses and the dysbiotic microbiota present in periodontal tissue. If not properly controlled and treated, periodontitis can lead to tooth loss and have negative impacts on both oral and systemic health [2].

Basic Periodontal Therapy (BPT) is a periodontal treatment protocol aimed at controlling gingival inflammation and halting the progression of periodontitis. It involves clinical and non-surgical interventions, including the mechanical removal of biofilm and dental calculus through scaling and root planning (SRP), followed by patient education on effective oral hygiene and guidance on maintaining proper home care [3]. BPT aims to reduce bacterial burden and restore a healthier oral environment, promoting the resolution of gingival inflammation and facilitating the stabilization of periodontal tissues [4]. In more advanced and complex cases, BPT may be complemented by adjunctive therapies, such as photobiomodulation [5].

Photobiomodulation, which was formerly known as lowlevel laser therapy (LLLT), is a therapeutic approach that utilizes low-intensity laser light to promote tissue regeneration and accelerate the resolution of periodontal inflammation [6]. During treatment, the emitted light penetrates the periodontal tissues, stimulating biochemical and biological processes such as ATP production, inflammation reduction, and cell proliferation [7, 8]. This can result in faster healing, reduced pain, and improved recovery following BPT, aiding in the regeneration of periodontal ligament and the reduction of periodontal pockets [9].

Clinical studies have been conducted in recent years to assess the anti-inflammatory and wound-healing effects of photobiomodulation. In a study that evaluated the use of LLLT as an adjunct to scaling and root planning in the treatment of periodontitis and compared it with SRP alone, significant improvements were observed in bleeding on probing (BOP), probing pocket depth (PPD), and clinical attachment level (CAL), along with a reduction in *Porphyromonas gingivalis* counts in the test group compared to the control group [10]. Furthermore, it was reported that patients with periodontitis who received photobiomodulation in conjunction with SRP had significantly reduced levels of interleukin 1 $\beta$  (IL-1 $\beta$ ) [10].

However, there is still no universally accepted or standardized protocol for the application of LLLT as an adjunct to BPT, especially concerning the laser application technique, whether intrasulcular (applied directly into the periodontal pocket with the aid of a fiber optic tip) or transgingival (placed on the gingival tissue). The use of LLLT in periodontics remains an evolving research area, and techniques and protocols vary among professionals and studies.

Thus, the aim of this literature review is to explore the current literature regarding clinical outcomes in the use of different low-level laser application techniques as adjuncts to basic periodontal therapy.

# Methods

## **Protocol and Registration**

The protocol of this review was developed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Checklist [11] and registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the identification number CRD42024516440.

## **Eligibility criteria**

The acronym "PICOS" was used to consider the eligibility of studies to be included or excluded from the review, which aims to answer the following question: In patients with periodontitis, can the application of different low-level laser protocols adjunctive to basic periodontal therapy in patients with periodontitis, compared to scaling and root scaling, improve clinical periodontal parameters?

- Population (P) Patients with periodontitis;
- Intervention (I) Low-level laser therapy;
- Comparison (C) Scaling and root planning;
- Outcomes (O) Clinical periodontal parameters;
- Study design (S) Clinical trials.

## Inclusion criteria

Randomized and non-randomized clinical trials, in any language, reporting clinical and/or radiographic outcomes of photobiomodulation as an adjunct treatment to basic periodontal therapy, were included. The search was limited to studies that, in their design, included at least one control group receiving conventional treatment (SRP), and explicitly described the technique used for low-level laser application, whether intrasulcular or transgingival. Additionally, studies were required to provide details regarding patient selection criteria, patient allocation method, treatment performed, laser settings, number of laser applications, and patient follow-up duration.

#### **Exclusion criteria**

Studies that did not meet the inclusion criteria were excluded, along with secondary studies (reviews) and publications in which photobiomodulation was used in combination with another adjunct therapy.

## Information sources and search strategy

An electronic search was conducted in the Pubmed, Cochrane, and Scopus databases, with the latest search performed on September 27, 2023. The search strategy used was as follows: (periodontitis or "periodontal disease" or "periodontal therapy" or "periodontal treatment") AND (photobiomodulation or "low-level laser therapy"). The established publication time limit was 10 years, and studies published from January 2013 to August 2023 were included in the search. The reference lists of the included articles were also assessed to include potential studies that were not retrieved by the electronic search.

## **Selection process**

Studies were initially selected by independently reviewing titles and abstracts by two reviewers, with reasons for exclusion recorded. Subsequently, an agreement test between reviewers was conducted using the Kappa coefficient. In case of disagreement, a third reviewer was consulted for decision-making. Then, full-text articles were examined to determine if they met the inclusion criteria for this review.

### Data Collection process and data items

The main variables extracted from the studies, independently by the same two reviewers, included patient sex and age, sample size, periodontal diagnosis, clinical variables, low-level laser settings, number of laser applications, laser application technique, follow-up time, and key outcomes. These variables were compiled into a table for better identification and subsequent analysis and description of the current literature regarding clinical outcomes associated with the use of different low-level laser application techniques as adjuncts to basic periodontal therapy.

## **Study risk of Bias Assessment**

The risk of bias in the studies included was assessed using the Joanna Briggs Institute Critical Assessment Checklist for randomized and non-randomized clinical trials [12]. The included articles were judged as "high risk," "moderate risk," and "low risk" when the domains with "yes" answers represented 0–49%, 50–69%, 70% or more, respectively, of the other domains.

## **Statistical analyses**

#### Effect measures and synthesis methods

Clinical level attachment and probing depth were the outcomes assessed in qualitative synthesis. The number of patients was considered as the sampling unit for the analysis since it was the only common measure among them. As data were presented as continuous variables and in the same unit of measurement for each outcome, the difference between means (MD) was then calculated between the two groups of interest.

A meta-analysis was conducted using a random-effects model, weighted by the inverse variance method. The variance was estimated by the Tau-squared value, calculated using the DerSimonian-Laird estimator, and heterogeneity was assessed by the Higgins inconsistency index (I<sup>2</sup>). The significance level was set at 5%. All analyses and graphics were performed using the integrated development environment RStudio, version 1.2.1335 (Rstudio Inc., Boston, USA), for the R programming language.

#### **Reporting bias assessment**

To assess publication bias, funnel plot asymmetry was evaluated, and the Egger test was also performed for each outcome, considering a significance level of 5%.

# Results

## **Study selection**

The study identification flowchart is presented in Fig. 1. The electronic search in the databases resulted in a total of 947 articles. After removing duplicates, 758 studies remained for the title and abstract screening. In phase I, 725 articles were excluded. The main reasons for exclusion at this stage included articles with designs other than clinical trials, laser application for purposes other than periodontal therapy (dentin hypersensitivity, analgesia, temporomandibular dysfunction, among others), surgical therapies, combined use of adjunct therapies, cohort studies, and photodynamic therapy. Subsequently, 33 references were selected for full-text evaluation. After excluding 11 articles (exclusion reasons listed in Table 1), a total of 22 studies published from January 2013 to August 2023 were included.

The kappa value for agreement between reviewers for the selection of titles and abstracts and for full-text evaluation was 0.95.

## **Study characteristics**

The main data from the articles were divided and described in two tables, according to the low-level laser application technique used: intrasulcular (Table 2) and transgingival (Table 3). The data include study design, participant gender and age, intervention groups, follow-up, and main results.

Considering the 22 clinical trials that evaluated the effect of photobiomodulation as an adjunct therapy to SRP, ten studies applied low-level laser therapy intrasulcularly (inside the periodontal pocket), and 12 applied it transgingivally (externally to the gum). In total, the included studies recruited 856 patients, with a higher prevalence of male participants.

Thirteen studies included participants with a diagnosis of generalized moderate to severe chronic periodontitis or chronic periodontitis [10, 24–28, 32, 33, 36, 37, 39, 40, 43]. The other studies also included patients with periodontitis and type 2 diabetes mellitus (T2DM) [34, 35, 38, 41, 42], periodontitis stage II/Grade B and tobacco chewers [4],



**Table 1** Excluded articles and reasons for exclusion (n = 11)

Author, year	Reason for exclusion
Ahmadinia & Staji, 2023 [13]	1
Bunjaku et al., 2017 [14]	
Freire et al., 2020 [15]	
Singh et al., 2014 [16]	
Lessang et al., 2018 [17]	2
Mastrangelo et al., 2018 [18]	
Ezber et al., 2022 [19]	3
Malgikar et al., 2016 [20]	
Obradović et al., 2013 [21]	4
Sudhakar et al., 2015 [22]	
Obradović et al., 2012 [23]	5

(1) Studies that did not perform only SRP in control groups (n=4); (2) Studies that did not clearly describe the low-level laser application technique (n=2); (3) Studies that used a combination of adjunctive therapies in the same group (n=2); (4) Studies that did not evaluate clinical periodontal parameters (n=2); (5) Studies that did not meet the established time limit for the research (n=1)

periodontitis following myocardial infarction [31], as well as patients in periodontal maintenance [30] or with residual periodontal pockets [29].

For the intrasulcular technique, the application time varied from 20 s [41] to 2 min [32], with one study having no time restriction for laser activation [30]. The application movements varied from vertical and horizontal sweeping motions apically along the long axis of the root surface until the desired depth was reached, to apical-to-coronal sweeping of the fiber.

Transgingival applications occurred mostly at a distance of 1 mm [33] to 15 mm [4] from the gingival surface. The application time for this technique ranged from 5 s per point with 4 points per tooth [43] to 4 min [37]. In general, when described, the application movement was from apical to coronal.

Regarding the wavelength of the laser, one study (11%) using intrasulcular technique [24], and five (38,5%) studies using transgingival technique [33, 34, 37, 38, 41] operated

 Table 2
 Main characteristics of clinical studies included in the review using the intrasulcular laser application technique

Author	Design	Sex (M/F)	Age (years)	Intervention groups	Follow-up	Main results
Alzoman & Diab, 2016 [24]	Parallel	11/19	48.4	G1: SRP G2: SRP+PBM	Baseline, 2 months	The laser group showed improvements in GI, BOP, PPD, and gingival index compared to the control group ( $p < 0.05$ ). There was a significant change in the percentage of sites positive for Pg only in the test group (from $80-20\%$ ).
Dukić et al., 2013 [25]	Split mouth	21/14	30	G1: SRP G2: SRP+PBM	Baseline, 6 and 18 weeks	There were reductions in PPD, CAL, BOP in deep pockets, and PI in both groups ( $p < 0.05$ ), with no differences between them. The test group showed a significant reduction only in moderate pockets (4–6 mm) compared to the control group.
Gandhi et al., 2019 [10]	Split mouth	30	30–60	G1: SRP G2: SRP+PBM G3: SRP+aPDT	Baseline, 1, 3, 6 and 9 months	Reductions in BOP, CAL, PPD, GI, and counts of Pg and Aa were observed in the test groups compared to the control group at all follow-up time points ( $p < 0.05$ ).
Gupta et al., 2021 [26]	Split mouth	7/3	M:38.43 F:37.33	G1: SRP G2: SRP+PBM	Baseline, 6 weeks, 3 and 6 months	Reductions in BOP and CAL ( $p < 0.001$ ), as well as in levels of GCF and aspartate aminotransferase ( $p < 0.001$ ) were observed in the test group sites compared to the control group.
Katsikanis, Strakas & Vouros, 2020 [27]	Split mouth	21	48.2	G1: SRP G2: SRP+PBM G3: SRP+aPDT	Baseline, 3 and 6 months	All treatment modalities resulted in statistically significant improvements in the evaluated clinical parameters at both 3 and 6 months compared to the baseline. There was no statistically significant difference in terms of PD and BOP between the groups.
Kaur, 2021 [28]	Split mouth	25	38.08	G1: SRP G2: SRP+PBM	Baseline, 1 and 3 months	Statistically significant reductions in PPD, BOP, CAL, GI, and gingival index in the test group compared to the control group ( $p < 0.001$ ) at 1 and 3 months.
Lu et al., 2023 [29]	Parallel	G1:11/19 G2:14/15	38	G1: SRP G2: SRP+PBM	Baseline, 4, 12 and 24 weeks	Both groups exhibited significant improvements in PD, CAL and BOP by the end of the study compared to baseline. The test group demonstrated greater reductions in PD, CAL, and BOP when compared to the control group ( $p < 0.05$ ).
Nguyen et al., 2015 [30]	Split mouth	13/9	61.8	G1: SRP G2: SRP+PBM	Baseline, 3 months	Reductions in BOP, CAL, and PPD were observed in both groups ( $p < 0.05$ ), with no differences between the two therapies. No differences in IL- $\beta$ levels from baseline to post-treatment between the groups were found.
Samulak et al., 2021 [31]	Parallel	29/7	56.3	G1: SRP G2: SRP+PBM	Baseline, 2 weeks and 3 months	The test group achieved a significant reduction in pockets with PPD $\geq$ 7 mm, but not for CAL, BOP, and PBI. Additionally, there was a decrease in the total bacterial count at 3 months ( $p < 0.05$ ).
Sopi et al., 2020 [32]	Parallel	80	>18	G1: SRP G2: SRP+PBM G3: SRP+surgi- cal periodontal therapy	Baseline, 3 and 6 months	The PBM group exhibited reductions in the evaluated periodontal parameters (CAL, PD, BOP, PPD, GI, mobility), along with a decrease in MMP-8 levels and radiographic bone loss compared to the other treatment groups ( $p < 0.05$ ).

M: Male. F: Female. SRP: Scaling and root planning. APDT: Antimicrobial photodynamic therapy. PBM: Photobiomodulation. PPD: Probing pocket depth. CAL: Clinical attachment level. PI: Plaque index. BOP: Bleeding on probing. Pg: *Porphyromonas gingivalis*. Aa: *Aggregatibacter actinomycetemcomitans*. GR: Gingival recession. MMP-8: Matrix metalloproteinase 8. MMP-9: Matrix metalloproteinase 9

with red laser, with the majority using the infrared wavelength range (810–980 nm). Table 4 summarizes laser settings and the frequency of application.

The mean follow-up time of the evaluated studies was 3 months, ranging from 5 days [40] to 12 months [34]. None of the studies assessed the effects of photobiomodulation as an adjunctive to basic periodontal therapy in the long term, nor did they use pain and quality of life questionnaires as evaluation tools.

## **Risk of Bias in studies**

Sixteen studies were classified as having a low risk of bias [10, 24, 25, 27–30, 32–36, 39, 40, 42, 43], and six were classified as having a moderate risk of bias [4, 26, 31, 37, 38, 41]. As for the methodological weaknesses of the randomized clinical trials, questions related to participants' and operators' (those who performed SRP) awareness regarding the treatment assignment stood out. Figure 2 describes the detailed characteristics of the risk of bias assessment.

Table 3	Main characteristics	of the clinical studi	es included in the	review using	the transgingival l	aser application technique	
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Author	Design	Sex (M/F)	Age mean (years)	Intervention groups	Follow-up	Main results
Al-Rabiah et al., 2020 [4]	Parallel	64 (M)	46.5	G1: SRP G2: SRP+PBM	Baseline, 3 and 6 months	At 3 and 6 months, PPD, CAL, and BOP significantly reduced in the test group compared to the control group. There was no statistically significant difference in GI and radiographic marginal bone loss between the patients in both groups.
Angiero et al., 2019 [33]	Split mouth	10/10	38.25	G1: SRP G2: SRP+PBM	Baseline and 3 months	Both groups had statistically significant reductions in clinical parameters (PPD, BOP, CAL, and GCF level) at 3 months of follow-up, with no differences between them.
Castro dos Santos et al., 2019 [34]	Split mouth	5/14	52.26	G1: SRP G2: SRP+PBM	Baseline, 3, 6 and 12 months	The frequency of pockets with PPD of 5–6 mm was signifi- cantly lower in the test group than in the control at 6 months. Reductions in deep pockets (PPD $\geq$ 7 mm) were significant in the test group at 3, 6, and 12 months, while in the control, it was only significant between baseline and 6 months. At 12 months, there was no statistically significant difference in the mean PPD and CAL between the groups.
Demirturk- Gocgun et al., 2017	Split mouth	7/15	50.50	G1: SRP G2: SRP+PBM	Baseline, 1 and 3 months	Significant improvement in PPD and CAL in deep pockets at 1 month in the test group compared to the control. No significant differences between the groups for BOP, GI, and CAL.
Gündoğar et al., 2016 [36]	Split mouth	9/16	40.44	G1: SRP G2: SRP+PBM	Baseline, 1, 3 and 6 months	The test group showed a significant reduction ( $p < 0.05$ ) in PPD compared to the control group at 1 month. There was no statistically significant difference in the other evaluated parameters (GI, BOP, CAL, and GCF cytokines) at 1, 3, and 6 months.
Ismaili & Bokonjic, 2014 [37]	Parallel	19/17	51.6	G1: SRP G2: SRP+PBM	Baseline, 10 days	For patients in periodontal maintenance, there was a significant reduction in PPD, CAL, and BOP in both groups, with no differences between them. PBM reduced the levels of IL-1 $\alpha$ and IL-1 $\beta$ in GCF ( $p < 0.05$ ), but not MMP-9.
Kamatham & Chava, 2022 [38]	Parallel	28/32	G1: 47.5 G2: 43.8 G3: 46.4 G4: 45	Non-diabetic patients G1: SRP G2: SRP+PBM T2DM patients G3: SRP G4: SRP+PBM	Baseline, 8 weeks	The evaluated clinical parameters (PPD, CAL, BOP, and GI) showed significant differences in all groups. Only PPD, CAL, and salivary calprotectin levels had significant differences for the laser groups ( $p < 0.05$ ).
Pamuk et al., 2017 [39]	Split mouth	60	-	Non-smokers patients G1: SRP G2: SRP+PBM Smoker patients G3: SRP G4: SRP+PBM	Baseline, 30 days	Significant decreases in all clinical parameters were noted from baseline to day 30 following SRP treatment in both the LLLT and placebo groups ( $p < 0.001$ ). There were no notable differences between the LLLT and placebo groups, regardless of whether the individuals were smokers or non-smokers.
Petrović et al., 2018 [40]	Parallel	G1:11/19 G2:13/17	G1:42.03 G2:37.97	G1: SRP G2: SRP+PBM	Baseline, 5 days and 1 month	Statistically significant decrease in the prevalence of Tf, Td, Pg, Aa, and Pi bacteria after SRP in the laser group compared to the control group. The test group achieved reductions in PPD and GI at 5 days and 1 month, and in CAL at 1 month compared to the control group ( $p < 0.05$ ).
Pulivarthi & Chava, 2022 [41]	Parallel	28/32	G1: 47.5 G2: 43.8 G3: 46.4 G4: 45	Non-diabetic G1: SRP G2: SRP+PBM T2DM G3: SRP G4: SRP+PBM	Baseline, 8 weeks.	All groups showed reductions ( $p < 0.05$ ) in PPD, CAL, BOP, GI, and salivary TNF- $\alpha$ levels at 8 weeks of follow-up.

#### Table 3 (continued)

Author	Design	Sex (M/F)	Age mean (years)	Intervention groups	Follow-up	Main results
Özberk et al., 2020 [42]	Split mouth	10/12	45.32	G1: SRP G2: SRP+PBM	Baseline, 1, 3 and 6 months	PPD reduced in the test group sites compared to the control group at all three evaluation times, as well as GI at 3 and 6 months, CAL at 6 months, GCF at 1 week, 1, 3, and 6 months, and IL-1 $\beta$ at 3 months ( $p < 0.05$ ). There were no significant differences between the treatment groups for PPD.
Özdemir et al., 2021 [43]	Paralel	29/31	G1:38.7 G2:36.4 G3: 37.7 G4: 35.2	Non-smokers G1: SRP G2: SRP+PBM Smokers G3: SRP G4: SRP+PBM	Baseline, 6 weeks	PBM + SRP resulted in a significant reduction in PPD and CAL, but no significant changes in GI and PI compared to SRP alone. Clinical outcomes at six weeks after treatment were similar for both smokers and nonsmokers.

M: Male. F: Female. SRP: Scaling and root planning. PBM: Photobiomodulation. PPD: Probing pocket depth. BOP: Bleeding on probing. CAL: Clinical attachment level. GI: Gingival index. GCF: Gingival crevicular fluid. Tf: *Tannerella forsythia*. Td: *Treponema denticola*. Pg: *Porphyromonas gingivalis*. Aa: *Aggregatibacter actinomycetemcomitans*. Pi: *Prevotella intermedia*. T2DM: Type 2 diabetes mellitus

Table 4 Laser parameters and frequency of application

Author	Wave-	Average	Power den-	Treat-	Flu-	Total	Fiber diam-	Laser therapy frequency
	length (nm)	power	sity (W/ $am^2$ )	ment time	ency	energy	eter (μm) / Fiber spot	
	(iiii)	(**)	ciii )	(seconds)	$cm^2$ )	(3)	size (cm <sup>2</sup> )	
Intrasulcular								
Alzoman & Diab, 2016 [24]	685	4	-	20	1.6	-	400	1x (after SRP)
Dukić et al., 2013 [25]	980	0.66	-	20	-	-	300	3x (after 1, 3 and 7 days)
Gandhi et al., 2019 [10]	810	0.1	-	120	-	-	-	1x (after SRP)
Gupta et al., 2021 [26]	980	2.5	-	30	-	-	400	2x (after SRP, 60-second interval)
Katsikanis et al., 2020 [27]	940	2	2.831	30	-	-	300	3x (after 2, 7 and 14 days)
Kaur, 2021 [28]	810	0.4	-	-	2	-	400	3x (after 1, 2 and 7 days)
Lu et al., 2023 [29]	810	1.5	-	40	-	-	-	1x (after SRP)
Nguyen et al., 2015 [30]	940	0.8	-	Not restricted	-	-	-	1x (after SRP)
Samulak et al., 2021 [31]	980	1	3184.7	40	640	20	200	3x (after SRP, 5 and 7 days)
Sopi et al., 2020 [32]	980	0.1	-	60	-	-	-	1x (after SRP)
Transgingival								
Al-Rabiah et al., 2020 [4]	940	0.3	-	20	3.41	-	1.76	1x (after SRP)
Angiero et al., 2019 [33]	645	2.5	0.125	80	10	20	0.5	4x (after SRP, 1, 3 and 7 days)
Castro dos Santos et al., 2019 [34]	660	0.03	1.1	20	22	0.6	0.028	1x (after SRP)
Demirturk-Gocgun et al., 2017 [35]	808	0.25	0.89	20	4.46	-	0.28	3x (after 1, 2 and 7 days)
Gündoğar et al., 2016 [36]	980	0.4	-	15	7.64	-	0.785	4x (after SRP, 1, 3 and 7 days)
Ismaili e Bokonjic, 2014 [37]	635	2.5	1	240	-	-	-	9 consecutive days
Kamatham & Chava, 2022 [38]	670	4	-	-	-	-	-	1x (after SRP)
Pamuk et al., 2017 [39]	940	0.3	-	20	3.41	-	1.76	3x (after SRP, 2 and 7 days)
Petrović et al., 2018 [40]	980	0.2	-	30	6	-	0.95	1x (after SRP)
Pulivarthi & Chava, 2022 [41]	630–670	4	-	15	-	-	-	1x (after SRP)
Özberk et al., 2020 [42]	980	0.4	-	15	0.5	-	0.785	4x (after SRP, 1, 3 and 7 days)
Özdemir et al., 2021 [43]	820	5	1.59	5	7.96	0.25	0.0314	3x (after SRP, 1, 2 and 3weeks)

# **Results of Individual studies**

Among the ten studies that used the intrasulcular technique, three parallel [24, 29, 32] and three split-mouth studies [4, 26, 28] showed significant improvements in the evaluated periodontal clinical parameters (PPD, CAL, PI, GI, GCF level, and bacterial counts) for groups that received photobiomodulation as an adjunct to SRP compared to basic periodontal therapy alone. One parallel study found a significant reduction in PS in the test group compared to the



Fig. 2 Risk of bias assessment of the clinical trials. (A) Risk of bias graph of randomized clinical trials, (B) Risk of bias graph of non-randomized clinical trial

control group in deep pockets but not for BOP and CAL [31]. Only in two split-mouth publications, a reduction in PI, BOP, PPD, CAL, GCF level, and IL-1 $\beta$  was observed over the follow-up periods for all treatment groups, with no significant differences between them [25, 30].

For the studies using the transgingival technique, the majority of included studies showed additional benefits in using photobiomodulation as an adjunct to SRP in the short and medium term, both in terms of reductions in PPD, BOP, CAL, and bacterial counts, compared to SRP alone [4, 34–36, 38, 40, 42]. However, several studies also showed no significant differences between treatment groups during follow-up periods for some clinical parameters, such as PPD and CAL [4, 33–38, 41].

Only two studies included in this review performed radiographic examination as one of the evaluation methods [4, 32]. The study that used the intrasulcular technique observed significant improvements in radiographic bone

loss for the laser group compared to the SRP group [32]. On the other hand, the study that used the transgingival technique did not find significant differences in mesial and distal marginal bone loss (measured as a straight line 2 mm below the cementoenamel junction to the bone crest) in either treatment group at both 3 and 6 months [4].

## **Results of synthesis**

A total of 13 studies were included in the meta-analysis for the outcomes of periodontal probing depth and clinical attachment level at 4, 6, 8, 12, and 24 weeks.

When considering the 4-week period, significance was found only for clinical attachment level, showing a decrease in values for the experimental group [MD = -0.57; 95% CI = -1.06 to -0.08;  $I^2 = 84\%$ ]. However, the lower limit of the confidence interval of the overall estimate was located near the null line, indicating a small effect size (Fig. 3).



Fig. 3 Forest plot for four weeks post-intervention: (A) Probing depth -4 weeks post-intervention; (B) Clinical attachment level -4 weeks post-intervention



**Fig. 4** Forest plot for six- and eight-weeks post-intervention: (**A**) Probing depth -6 weeks post-intervention; (**B**) Clinical attachment level -6 weeks post-intervention; (**C**) Probing depth -8 weeks post-intervention; (**D**) Clinical attachment level -8 weeks post-intervention

For the 6-week period, only studies that used the transgingival technique showed significance for both outcomes. There was a global decrease of 0.89 in probing depth in favor of the intervention group [95% CI=1.58 to -0.20;  $I^2=92\%$ ]. No differences were observed between the control and experimental groups for the 8-week period (Fig. 4).

For the 12- and 24-week post-intervention period, photobiomodulation improved probing depth and clinical level attachment, with emphasis on studies that performed the transgingival technique. However, a small effect size was also observed, with the lower limit of the confidence interval located near the null line for all comparisons (Fig. 5).

## **Reporting biases**

No funnel plot asymmetry was detected, as confirmed by both through graphical analysis and Egger's test (p > 0.05) (Figure S1).

#### Discussion

Based on the analysis of the included studies in this review, it is evident that there is heterogeneity regarding the lowlevel laser therapy application protocols, along with a lack of comparative studies among them. Variable parameters, in addition to the laser application technique, include wavelength, laser power, application time, and therapy frequency immediately after scaling and root planning.

The occurrence of clinical effects in photobiomodulation therapy directly depends on the absorption of light by the tissues. Reflected, transmitted, or scattered light doesn't trigger any effect. The absorption of laser light relies on the quantity of chromophore in the tissue and how well the wavelength matches the absorption traits of this chromophore [44]. Within periodontal tissues, cytochrome C oxidase, found in mitochondria, acts as the primary photoreceptor driving the effects of biomodulation [45].

Both wavelength ranges that can be used in photobiomodulation, red or infrared, offer benefits to human tissues,



Fig. 5 Forest plot for twelve- and twenty-four-weeks post-intervention: (A) Probing depth -12 weeks post-intervention; (B) Clinical attachment level -12 weeks post-intervention; (C) Probing depth -24 weeks post-intervention; (D) Clinical attachment level -24 weeks post-intervention;

such as stimulating cellular metabolism, reducing inflammation, and increasing blood circulation. The choice depends on treatment objectives and desired tissue penetration depth. Infrared light has a greater ability to penetrate soft tissues, reaching deeper areas like the alveolar bone, stimulating cellular metabolism, and promoting healing and cellular regeneration in these regions. In contrast, red light primarily affects superficial tissue layers [46].

The insertion of the fiber optic tip into periodontal pockets can deliver light directly to the pocket's epithelium and base, while applying it on the gum's surface, at the depth of probing, can reach the gum and bone tissues. Therefore, in the first case, both wavelength ranges can be used to provide additional benefits to SRP, while in the second case, using a longer wavelength (near-infrared) may be preferable [46].

The analysis of different laser application techniques concerning the follow-up time, in weeks, revealed that for probing depth, at 4 and 8 weeks, there were no significant differences compared to the baseline for both techniques. Although significant global differences were found at 6, 12, and 24 weeks, when evaluating subgroups, the results of the transgingival technique stand out. As for the clinical attachment level, there are positive results in favor of the photobiomodulation group at 4, 12, and 24 weeks, while at 6 weeks, only for the transgingival technique. One point to consider is the multiple application of laser in studies that used the intrasulcular technique [25–27, 31]. The insertion of the optical probe into healing periodontal tissues could

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lead to bleeding in the region, increasing the concentration of hemoglobin, another important chromophore that can absorb the light applied in therapy, potentially reducing its effectiveness [27, 45].

Taking into consideration the diffusion and refraction of light, studies in the transgingival group positioned the laser tip about 1 to 15 mm away to avoid excessive concentration in a specific area and achieve more uniform light diffusion [34, 39]. For both laser application techniques, most studies used slow and steady movements, both apical-coronal and coronal-apical, to distribute the light and its effects throughout the periodontal pocket tissue [25, 33].

Concerning the number of laser applications after SRP, no conclusive evidence could be obtained regarding the best approach. The frequency varied widely from one study to another, ranging from a single application [4, 10, 24, 29, 30, 32, 38, 41] to nine consecutive days of therapy [37]. Clinical, biochemical, and bacteriological outcomes also varied among studies with the same application frequencies.

The results observed in studies involving patients with periodontitis and type 2 diabetes [34, 35, 38, 42] showed significant reductions in clinical periodontal parameters (BOP, CAL, PPD, GCF levels, frequency of deep pockets) and biochemical markers (IL-1 $\beta$  and calprotectin) compared to scaling alone. All these studies utilized laser therapy transgingivally.

Similarly, the study evaluating the adjunctive effect of photobiomodulation using intrasulcular laser therapy in the

treatment of periodontitis in patients who had a heart attack observed a significant reduction in the number of deep pockets [31]. Therefore, photobiomodulation may benefit systemically compromised patients, regardless of the laser application technique.

Given the limitations of this review, the results should be interpreted with caution due to the heterogeneity of the protocols used, the different assessment methods, and the aspects related to the risk of bias in the included studies. In this context, there is a need for randomized clinical trials comparing protocols of photobiomodulation to improve the outcomes of basic periodontal therapy.

# Conclusion

Current evidence suggests that the use of adjunctive low-level laser therapy in the treatment of periodontitis, especially in transgingival application, may enhance the outcomes of basic periodontal therapy. However, caution is warranted in interpreting the results of the present study due to the small effect size observed.

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## **Declarations**

Ethical approval Not applicable for this type of study.

**Conflict of interest** The authors have no relevant financial or non-financial interests to disclose.

**Standards of reporting** The authors adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) for conducting this review.

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