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Effective of Photobiomodulation in Periodontitis Treatment: A Systematic Review and Meta-Analysis

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Abstract

Aim: The aim of current study was evaluate the effective of photobiomodulation in periodontitis treatment.

Method: A search of the PubMed, Scopus, Web of Science, EBSCO and Embase electronic databases have been used to perform a systematic literature until August 2021. The quality of the randomized control trial studies included was assessed using the Cochrane Collaboration's tool. 95% confidence interval for mean difference with fixed effect model and Inverse-variance method were calculated. Meta-analysis was performed using Stata/MP v.16 software (The fastest version of Stata).

Result: In the initial review, duplicate studies were eliminated and abstracts of 531 studies were reviewed. The full text of 112 studies was reviewed by two authors, finally, nine studies were selected. Mean differences of wound healing between control group and photobiomodulation group was 1.05 (MD, 1.05 95% CI 0.70, 1.40. P=0.00). Risk ratio of bleeding on probing and Probing depth between test and control group was 0.24 (RR, 0.24 95% CI –0.10, 1.10.580. P>0.05) and 2.56 (MD, 2.56 95% CI 2.40, 2.72. P>0.05), respectively.

Conclusion: photobiomodulation can play an effective role on Wound healing, Wound epithelialization, bleeding on probing, probing depth, Loss of clinical attachment level.

Key words: photobiomodulation, periodontitis, low-level laser therapy

Introduction

Periodontitis is an infectious disease caused by pathogenic microorganisms in the mouth. The combined action of a strong host immune-inflammatory response regulated by several proinflammatory mediators causes debilitation of the periodontium(1). Intrinsic immunity is activated during the invasion of pathogens, including polymorphonuclear neutrophils(2). Any disturbance in chemotactic and phagocytic activity leads to the release of several harmful enzymes, including cytoplasmic granules and reactive oxygen and nitrogen species such as superoxide anion, hydrogen peroxide, and hydroxyl radicals(3, 4). Evidence suggests that intensification of the

oxidative cascade and functional conversion of polymorphonuclear neutrophils can lead to aggressive destruction and alter healthy periodontal structures(2, 5). Nonsurgical periodontal therapy is the multifactorial treatment of periodontal inflammatory lesions, whose main objective is to control and to eradicate such lesions(6). This treatment includes the inflammatory response and the potential to reduce the bacterial load(7). Also, can cause pain due to probing by damaging inflamed periodontal tissues(8, 9). On the other hand, can heal the tissue and wound.; Nonsurgical periodontal therapy acts like a double-edged sword(10). After periodontal surgery, wound healing is an important and vital factor in achieving optimal clinical results(11).
Photobiomodulation (PBM) therapy also known as low-level laser therapy is a phototherapy that employs low-level power light (12) and a treatment method using infrared or near-infrared light (600–1100 nm)(13); Evidence suggests that PBM therapy stimulates gingival fibroblast proliferation and improves its organization(14, 15).PBM therapy reduces the level of inflammatory mediators and through this can improve the release of oxygen in the tissue and thus increase the tissue repair process(16, 17). This therapy is a multifactorial process that releases endorphins and blocks the conduction of central and peripheral nerve fibers; also regulate collagen synthesis and accelerate tissue re-epithelialization(14). In dentistry, different oral applications of this treatment have been investigated for faster and optimal wound healing. Over the last 20 years, many studies and researches have been done in this field that have discovered the advantages and disadvantages of PBMT. The results of the research are contradictory, it is very important to review the results and provide comprehensive results, which can be reported through systematic review and meta-analysis.

Objective

The aim of current study was evaluate the effective of photobiomodulation in periodontitis treatment.

Hypothesis

Effective of photobiomodulation on Wound healing
Effective of photobiomodulation on Wound epithelialization
Effective of photobiomodulation on bleeding on probing
Effective of photobiomodulation on probing depth
Effective of photobiomodulation on Loss of clinical attachment level

Material and Method

Search strategy

A search of the PubMed, Scopus, Web of Science, EBSCO and Embase electronic databases have been used to perform a systematic literature until August 2021.
MeSH used to search in PubMed database:
("Periodontal Diseases"[Mesh]) OR "Periodontitis"[Mesh]) AND "Wound Healing"[Mesh]) OR "Hypopigmentation"[Mesh]) OR "Gingivectomy"[Mesh]) AND "Low-Level Light Therapy"[Mesh]) AND "Pain"[Mesh]) OR "Periodontal Index"[Mesh]) OR "Dental Plaque Index"[Mesh].
Other databases were searched based on the following keywords:
Periodontal Diseases OR Periodontitis OR chronic periodontitis OR aggressive periodontitis AND Wound Healing AND pain after surgery AND photobiomodulation OR Low-Level Light Therapy

AND probing pocket depth AND loss of clinical attachment level AND bleeding on probing AND plaque index AND gingival index AND microbiological profile.

This systematic review has been conducted on the basis of the key consideration of the PRISMA Statement–Perfumed Reporting Items for the Systematic Review and Meta-analysis(18), and PICO strategy (Table1).

Table1. PICO strategy

PICO strategy	Description
P	Population: Periodontal diseases
I	Interventions: photobiomodulation
C	Comparison: Scaling and Root planning, Antimicrobial Photodynamic Therapy, other site
O	Outcome: plaque index, bleeding on probing and probing depth, pain after surgery and wound healing

Selection criteria

Inclusion criteria: patients with periodontal diseases, Age over 18, follow-up reported, in English. Case studies, case reports, animal studies, in vitro studies and reviews; Pregnancy were excluded from the study.

Study selection, Data Extraction and method of analysis

Studies data were reported by study, years, study design, age, Number of patients, Follow-up, Type of Periodontitis.

The quality of the randomized control trial studies included was assessed using the Cochrane Collaboration's tool(19). The scale scores for low risk was 1 and for High and unclear risk was 0. Scale scores range from 0 to 6. A higher score means higher quality.

For Data extraction, two reviewers blind and independently extracted data from abstract and full text of studies that included.Prior to the screening, kappa statistics was carried out in order to verify the agreement level between the reviewers. The kappa values were higher than 0.80.

95% confidence interval for mean difference and risk ratio with fixed effect model and Inverse-variance method were calculated. To deal with potential heterogeneity, random effects were used and I^2 showed heterogeneity. I^2 values less than 50% indicate low heterogeneity and above 50% indicate moderate to high heterogeneity. Meta-analysis was performed using Stata/MP v.16 software (The fastest version of Stata).

Result

In the review of the existing literature using the studied keywords, 543 studies were found. In the initial review, duplicate studies were eliminated and abstracts of 531 studies were reviewed. At this stage, 419 studies did not meet the inclusion criteria, so they were excluded, and in the second stage, the full text of 112 studies was reviewed by two authors. At this stage, 103 studies were excluded from the study due to incomplete data, inconsistency of results in a study, poor studies, lack of access to full text, inconsistent data with the purpose of the study. Finally, nine studies were selected (Figure1).

Characteristics

Nine studies (three parallel randomized controlled trial studies and six Split mouth randomized controlled trial studies) have been included in present article. The number of patients a total was 316. In all studies patients with chronic periodontitis were included (Table2). Table3 showed Photobiomodulation characteristics.

Bias assessment

According to Cochrane Collaboration's tool, two studies had a total score of 6/6, and two studies had a total score of 5/6 three studies had a total score of 4/6 and two studies had a total score of 3/6. Four studies had high quality or low risk of bias and five studies had moderate quality or moderate risk of bias (Table3).

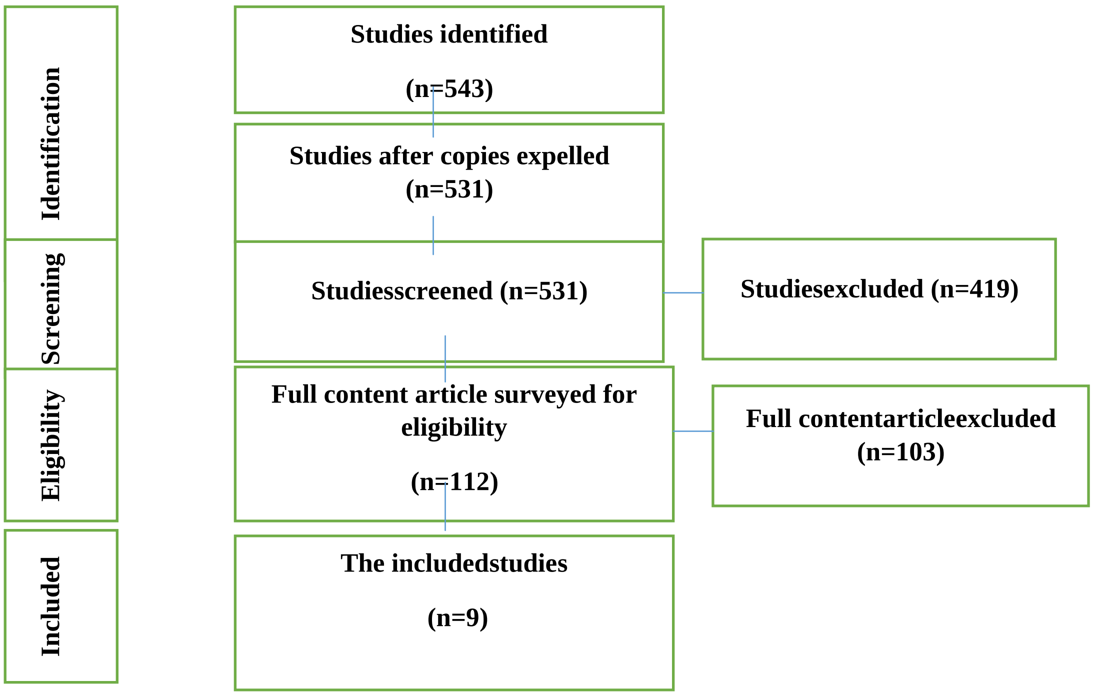

Figure 1. Study Attrition

Table2. Studies selected for systematic review and meta-analysis.

Study. Years	Study design	Number of patients	Type ofPeriodontitis	Mean of age	Follow-up (days/months)
Gandhi et al.,2019 (20)	RCT split-mouth	26	Chronic periodontitis	45.1	Baseline, 1, 3,6 and 9 months
Angiero et al.,2019 (21)	RCT split-mouth	40	Chronic periodontitis	48.4	Baseline and 3 months
Lingamaneni et al.,2019 (22)	RCT split-mouth	20	Chronic periodontitis	48.9	3, 7, 14 days
Kohale et	RCT split-	80	Chronic	51.2	3, 7, 30 days

al.,2018 (23)	mouth		periodontitis		
Isler et al.,2018 (24)	RCT	36	Chronic periodontitis	48.6	1, 2, 3, 7, 15, and 30
Mastrangeloet al., 2018(25)	RCT	30	Chronic periodontitis	48.	Baseline, 10 and 30 days
Mishra et al., 2018 (26)	RCT split-mouth	20	Chronic periodontitis	NR	Baseline, 1 and 3 months
Heidari et al.,2017 (27)	RCT split-mouth	24	Chronic periodontitis	41.1	7, 14, 21, 30 days
Ustaoglu et al., 2017 (28)	RCT	40	Chronic periodontitis	50	3, 7, 14, 21, 30 days

Table3. Photobiomodulation characteristics

Study. Years	Wavelength (mm)	Power Output (W)	Energy density (J/ cm^2)
Gandhi et al.,2019 (20)	810	0.1	NR
Angiero et al.,2019 (21)	645	2.5	10
Lingamaneni et al.,2019 (22)	810	0.1	NR
Kohale et al.,2018 (23)	940	0.1	4
Isler et al.,2018 (24)	970	2	5.25
Mastrangelo et al., 2018 (25)	600–1000	NR	0.04–60
Mishra et al., 2018 (26)	810	0.5	7.64
Heidari et al.,2017 (27)	660	0.2	4
Ustaoglu et al., 2017 (28)	940	3	8.6

Table4. Risk of bias assessment (Cochrane Collaboration's tool(19))

study	Random sequence generation	allocation concealment	blinding of participants and personnel	blinding of outcome assessment	incomplete outcome data	selective reporting	Total score
Gandhi et al.,2019 (20)	-	-	+	+	+	+	4
Angiero et al.,2019 (21)	+	+	+	+	+	+	6
Lingamaneni et al.,2019 (22)	+	+	+	+	+	+	6

Kohale et al.,2018 (23)	?	+	-	?	+	+	3
Isler et al.,2018 (24)	+	+	+	?	+	+	5
Mastrangelo et al., 2018 (25)	?	-	+	+	+	-	3
Mishra et al., 2018 (26)	-	-	+	+	+	+	4
Heidari et al.,2017 (27)	+	+	+	+	-	+	5
Ustaoglu et al., 2017 (28)	+	+	-	+	+	-	4

Low (+), unclear (?), high (-)

Wound healing

Mean differences of wound healing between control group and photobiomodulation group was 1.05 (MD, 1.05 95% CI 0.70, 1.40. P=0.00) among two studies with low heterogeneity (I^2=46.25%; P =0.17), there was significant difference about Wound healing between control group and photobiomodulation group(Figure2).

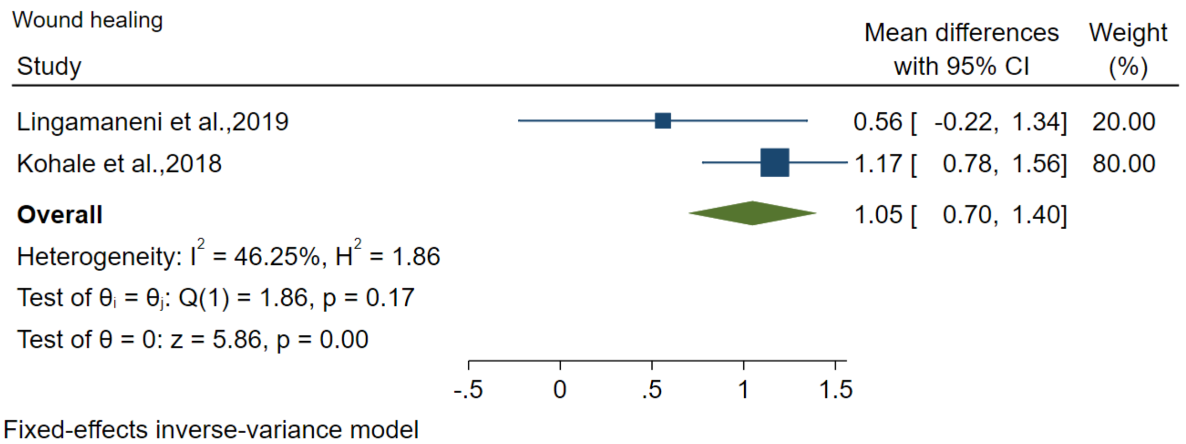

Figure2. Forest plot showed Wound healing as outcome between test and control group (7th postoperative day)

Wound epithelialization

Risk ratio of wound epithelialization between control group and photobiomodulation group was 3.73 (MD, 3.73 95% CI -0.03, 7.48. P=0.05) among three studies with low heterogeneity (I^2=0%; P =0.99), there was significant difference about wound epithelialization between control group and photobiomodulation group (Figure3).

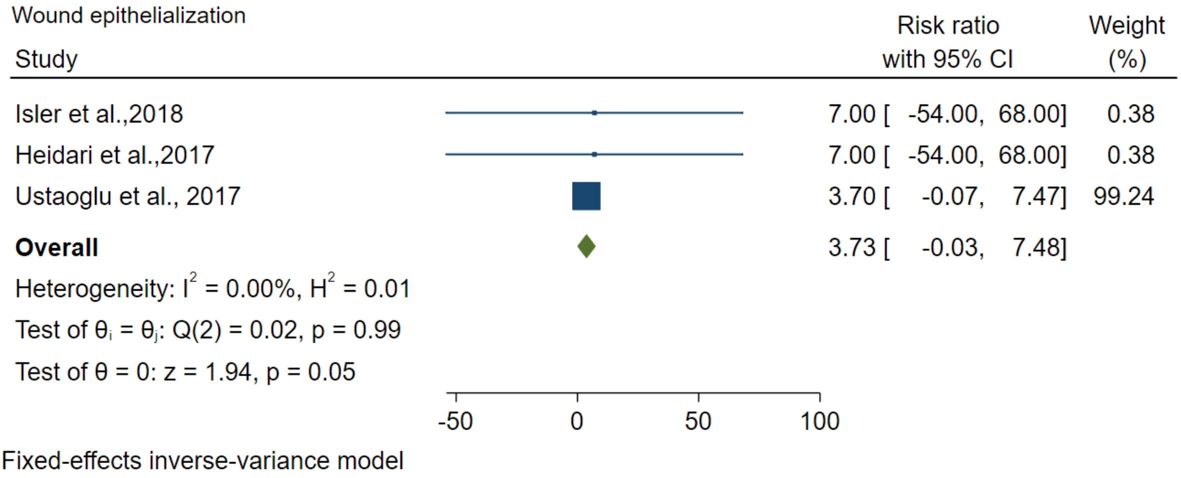

Figure2. Forest plot showed wound epithelialization as outcome between test and control group (14th postoperative day)

Bleeding on probing

Risk ratio of bleeding on probing between test and control group was 0.24 (RR, 0.24 95% CI –0.10, 1.10.580. P>0.05) among two studies with low heterogeneity (I^2<0%; P =0.70), there was no significant difference between two groups (Figure4).

Probing depth

Mean difference of probing depth between test and control group was 2.56 (MD, 2.56 95% CI 2.40, 2.72. P>0.05) among four studies with low heterogeneity found (I^2<0%; P =0.70), there was significant difference between two groups (Figure5).

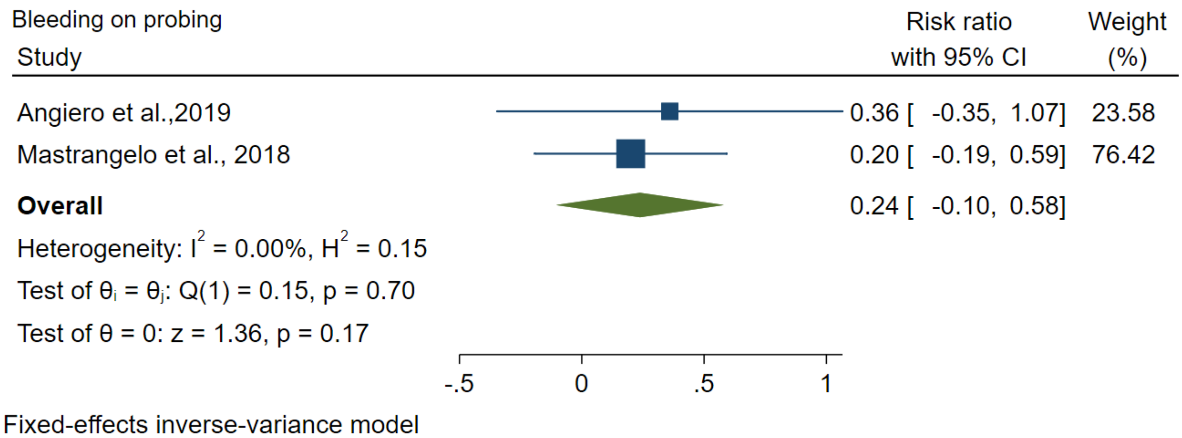

Figure4. Forest plot showed Bleeding on probing

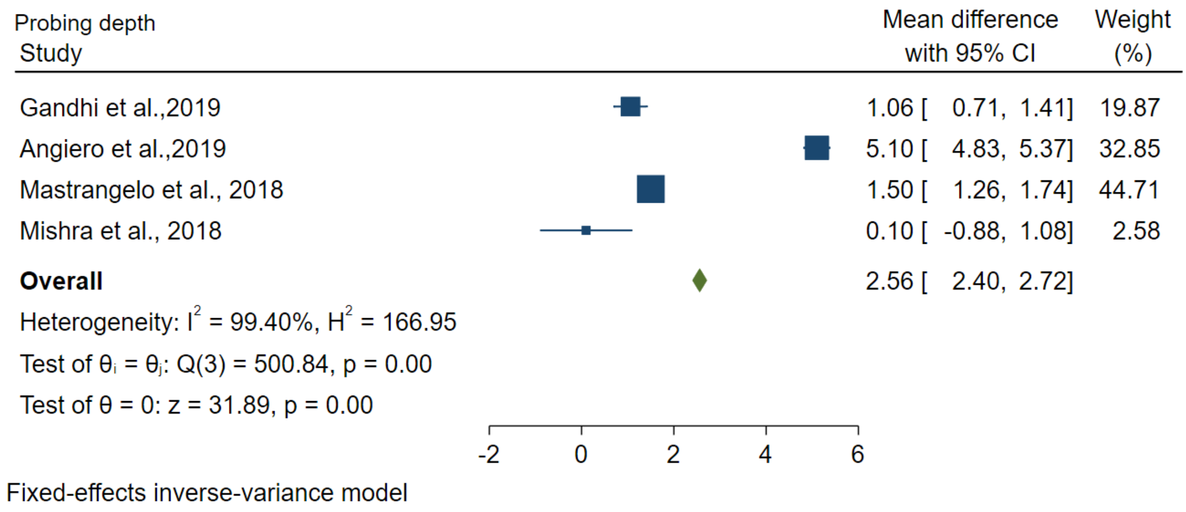

Figure5. Forest plot showed Probing depth

Loss of clinical attachment level

Mean difference of Loss of clinical attachment level between test and control group was 0.90 (MD, 0.90 95% CI 0.78, 1.01 P<0.05) among two studies with low heterogeneity found (I^2<0%; P =0.38), there was significant difference between two groups (Figure6).

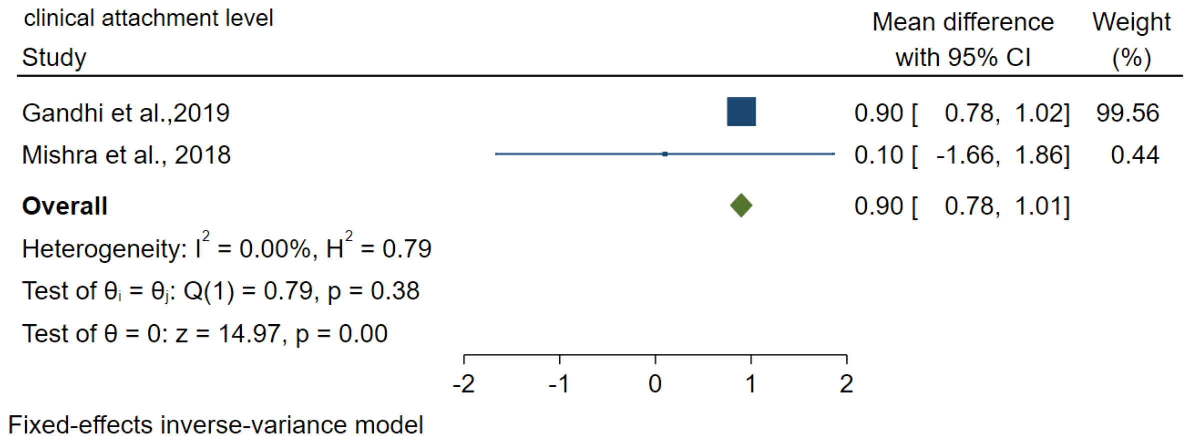

Figure6. Forest plot showed Probing depth

Discussion

Periodontitis is the most common cause of tooth loss, especially in adults, and the sixth most common disease in the world(29).The use of lasers to manage and treat periodontal disease is one of the most useful treatment methods in recent decades(16). The aim of current Systematic Review and Meta-Analysis was evaluate effective of photobiomodulation in periodontitis treatment. The results of studies that selected in present systematic review have shown that PBMT can reduce clinical signs of inflammation, including BOP. It also plays an effective role in reducing PPD and CAL. The results report statistically significant differences between the findings of clinical parameters, which should be addressed in future studies. In animal studies examining the effect of PBM, it was found that this treatment improves tissue healing faster and also facilitates bone regeneration during the periodontium repair process(30). Studies have shown statistically significant improvements in levels of inflammatory biochemical markers after PBMT(21, 25, 31). Qadri et al., reported that PBMT could significantly improve bone density(32). The results of a study by Lai et al., Refute these findings(33). Evidence suggests that PBMT cannot completely eliminate pathogens; therefore, the role of PBMT in reducing bacterial load, if any, should be analyzed. Different findings are observed to evaluate pain, although in most studies the VAS score was lower in the PBMT group, however, no statistically significant difference was observed. Because of this, no meta-analysis was performed for pain. There were many discrepancies in the methods of evaluating the effectiveness of PBMT between studies, which are among the limitations of the present study, such as low sample size, different follow-up period, and failure to report the severity of the disease. Also, in some studies, smokers were studied, but in other studies, this variable was not reported. A study showed that in smokers, PBMT was significantly effective on BOP, PPD and CAL(34). One of the most common challenges in achieving optimal treatment is not using the right laser parameters. According to Table 3, the PBM parameters are not the same in the studies, this is a serious limitation. Chen et al., 2020 showed LED-PBMT can play an effective role on PPD and CAL.

Findings from some studies have shown that PBM can facilitate the speed and quality of wound healing(35). Zhao et al., 2020 in a systematic review and meta-analysis showed PBM can have a positive effect on primary or secondary wound healing, although the type of effect on primary and secondary wound is different(36). This may be due to different healing mechanisms and cellular and molecular events between secondary and primary wound healing. Another limitation of the present study was the methodological changes that could affect the results of the meta-analysis, although there was not much heterogeneity between the studies.Almost all studies had a low to moderate risk of bias and a study with a high risk of bias was not included in present study. According to the results of studies, the use of PBM is a suitable option for the healing of secondary wounds after periodontal surgery.

Conclusions

Due to the reported limitations and few studies in this field, the findings showed that photobiomodulation can play an effective role on Wound healing, Wound epithelialization, Bleeding on probing, Probing depth, Loss of clinical attachment level. photobiomodulation can also be used as a complementary treatment to promote wound healing after periodontal soft tissue surgery.

FUTURE EXPECTATIONS

Due to the fact that the results of the studies were not the same, the results of the present study can be used in future research. More RCTs with the same sample size and the same follow-up time require the same methodology, and longer follow-ups can provide stronger evidence. The study of the role of parameters can also play an important role in the results, which is suggested to be studied in future studies.

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