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Review Article

Dentistry Section

Photobiomodulation and its Effect on Stability of Orthodontic Mini-implants: A Systematic Review and Meta-analysis of Randomised Controlled Trials

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ABSTRACT

Introduction: The influence of Photobiomodulation (PBM) on the field of orthodontics has been of recent interest. The PBM has a promising effect on acceleration of tooth movement, alleviation of pain during orthodontic treatment and Mini-Implant (MI) stability.

Aim: To systematically report on the effectiveness of PBM on the stability of orthodontic MI.

Materials and Methods: This systematic review was conducted during January 2021 and February 2021. Literature search was conducted in five electronic databases for human trials published between January 2000 to February 2021 on the effectiveness of PBM therapy for stability of orthodontic MI. Cochrane review manager software (Revman version 5.4) and Cochrane Risk Of Bias (ROB) 2 tool were used for bias assessment. The primary outcome measured was the stability of MI using Resonance Frequency Analysis (RFA) or Periotest Value (PTV). The secondary outcomes measured were pain and inflammation around the peri-implant area. Also, Interleukin-1β (IL-1β) was also measured in gingival crevicular fluid.

Results: A total of six Randomised Controlled Trials (RCTs) were included in the review. Out of the six studies, two showed low Risk Of Bias (ROB) whereas three showed some concerns and one showed high ROB. Quantitative analysis was done for four studies with a random effects model to assess the MI stability measured by periotest at 30 days and 60 days. A significant mean difference of -3.31 (95% Confidence Interval [CI]-5.15, -1.47) between PBM and controls for mini-implant stability at 30 days and a significant mean difference of -3.47 (95% CI-4.58, -2.36) between PBM and controls at 60 days with low heterogeneity was obtained. Three studies reported on the pain response after PBM and both groups showed no significant difference. A decrease in gingival inflammation was reported in one study whereas other study showed no significant change in IL-1β in gingival crevicular fluid.

Conclusion: Majority of the studies included in this review reported improved secondary stability with PBM. The low heterogeneous nature of the quantitative studies also supports the data obtained. However, the results should be concluded with caution.

Keywords: Bone implant interactions, Laser, Light accelerated orthodontia

INTRODUCTION

Stability of the MI is a critical factor that determines the clinical success of orthodontic treatment and is dependent on many factors. According to Baek SH et al., MI failures usually occur during the first week after loading. Therefore, enhancing early stabilisation could be an essential step in increasing the stability of MI [1]. Loading MI immediately after treatment does not give specific time for tissue healing [2]. An important factor responsible for the long-term clinical success of an implant is the quality of bone and its volume. The biomechanical stability of MI depends on bone formed at the bone-implant interface [2]. Mechanical retention in sufficiently dense bone provides sufficient primary stability for MI [3].

The PBM is a non invasive procedure used in orthodontics for accelerating tooth movement and alleviating pain during treatment. It is also known as Light Accelerated Orthodontia (LAO) therapy or Low-Level Light Therapy (LLLT) as it uses low energy light or laser in the red to near infrared range of about 600-1000 nm [4]. It induces a non thermal photochemistry effect on the cellular level following an increase of Adenosine Triphosphate (ATP) production in mitochondria [4].

Inflammation of the peri-implant region is one of the main reasons for failure and is manifested as redness, swelling of tissues around the neck of the screws [5]. Immediately after loading, the area of placement suffers from ischaemic injury, altered oxygen supply and lack of nutrients; which can lead to apoptosis of the injured cells in the peri-implant area [6]. The healing process involves inflammation, tissue formation, and tissue remodelling which in turn maintains tissue integrity [7]. However, inflammation can deteriorate the bone surrounding the neck of MI. PBM therapy has been proposed to show a beneficial effect on tissue growth and regeneration. It has been used in many areas such as wound healing, pain relief, antiinflammatory effect and accel-erating orthodontic tooth movement [8]. This therapy uses non ionising light sources in the visible and near infrared spectrum promoting non thermal biological processes over tissues [9]. This light is capable of affecting cell behaviour with significant heating effects, among other benefits [10]. PBM promotes an increase of the vascularisation; modulation of the inflammatory processes; proliferation of fibroblasts, keratinocytes, chondrocytes, and osteoblasts; and cytokine expression that induce matrix synthesis, improving the bone repair process [11-13].

Many studies have reported increased stability of orthodontic MI with the use of PBM therapy [14-20]. The aim of the current systematic review is to systematically analyse the available literature and report on the effectiveness of PBM therapy for improving the stability of orthodontic MI.

MATERIALS AND METHODS

Protocol registration: The systematic review followed the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) statement [21]. This systematic review was conducted during January 2021 and February 2021. The review was registered with the PROSPERO database (CRD42020218813).

Search strategy: A systematic search of the medical literature produced from January 2000 to February 2021 was performed to identify all peer-reviewed articles potentially relevant to the review's question. The following databases were searched: PubMed, Cochrane library, Lilacs, Embase and Google Scholar. The search was attempted to gather all articles relevant to the study with no time and language restriction in order to eliminate bias [Table/Fig-1].

Search strategy	No. of articles	Keywords
PubMed	11	("orthodontic mini-implant*" (Title/Abstract) OR "orthodontic implant*" (Title/Abstract)) AND ("low level laser therap*" (Title/Abstract) OR "biostimulation" (Title/Abstract) OR "photobiomodulation" (Title/Abstract) OR "PBM" (Title/Abstract) OR "LED" (Title/Abstract) OR "low intensity laser" (Title/Abstract) OR "LLLT" (Title/Abstract) OR "laser biostimulation" (Title/Abstract) OR "semi conductor laser" (Title/Abstract) OR ("low level light therapy" (MeSH Terms) OR "low level light therapy" (MeSH Terms) OR "low level light therapy" (MeSH Terms) OR "low level light therapy" (MeSH Terms) OR "low level light therapy" (MeSH Terms))) AND ("orthodontic stability" (Title/Abstract) OR "orthodontic anchorage" (Title/Abstract))
Google Scholar	1440	Photobiomodulation OR Low level laser therapy AND Orthodontic Mini-implants OR Miniscrews OR Miniscrews AND stability
Embase	189	Photobiomodulation OR Low level laser therapy AND Orthodontic Mini-implants OR Miniscrews OR Miniscrews AND stability
Cochrane Library	600	Photobiomodulation in Title Abstract Keyword OR low level laser therapy in Title Abstract Keyword AND orthodontic mini-implants in Title Abstract Keyword OR orthodontic mini-screws in Title Abstract Keyword AND orthodontic stability in Title Abstract Keyword - (Word variations have been searched)
Lilacs	2	(Photobiomodulation) OR (Low level laser therapy) AND (Orthodontic mini-implants) OR (Miniscrews) AND (Stability)

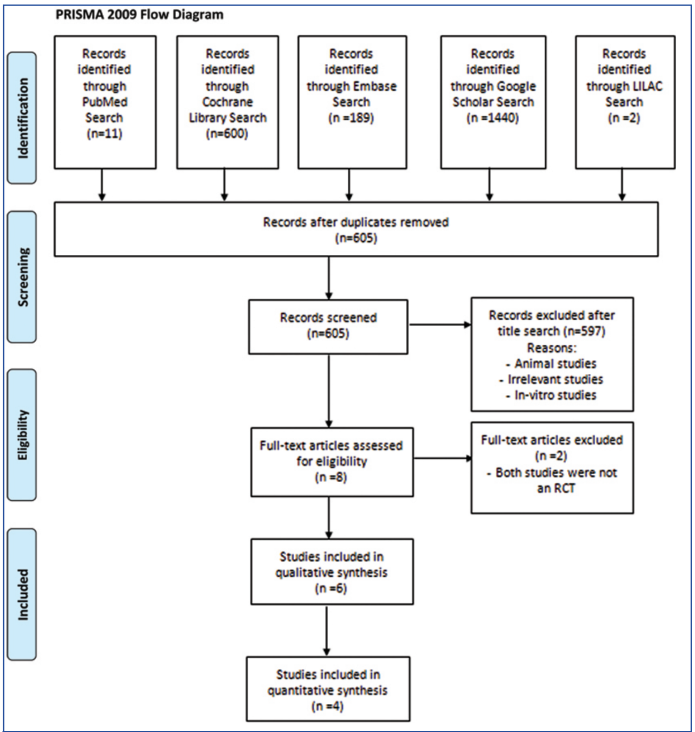
[Table/Fig-1]: Search strategy.

Data collection process: PICO (patient/population, intervention, comparison and outcomes) analysis along with eligibility criteria is mentioned in [Table/Fig-2]. All studies meeting the selection criteria were included in the review. The selection process of included studies was reported in the PRISMA flow chart [Table/Fig-3]. A table for describing the 'study characteristics' of the included articles was made that included the following information: first author, year of publication, study design, sample size, control group, intervention group, outcomes in the studies (i.e., stability, displacement, pain assessment, etc.,), parameters assessed and the statistical tests done.

	Inclusion criteria	Exclusion criteria
P	RCTs reporting on use of Mini screws for Anchorage	Other studies like animal studies, in-vitro studies
I	Application of Photobiomodulation	Other methods to improve stability; e.g., surface treatments/coatings on Mini screws, etc.,
C	No treatment/placebo effect	
O	Primary Outcome: MS stability Secondary Outcome: Inflammation and pain in the peri-implant area	

[Table/Fig-2]: Eligibility criteria based on PICO analysis.

Risk of Bias (ROB): The ROB was assessed using Cochrane ROB-2 tool [22]. The risk of the included studies are assessed in five domains according to the tool- bias due to randomisation process, deviations from intended intervention, missing outcome data, measurement of outcome and selection of reported results. Each RCT was assigned at high risk (>1 domains showed high), some concerns (>1 domains showed some concerns) or low risk (no domains showed high or some concerns). Two authors (RM and RKJ) performed the ROB independently and a third author (ABS) resolved the disparities. The Cohen's kappa test (κ) test was used to assess the level of agreement between the reviewers.



[Table/Fig-3]: PRISMA flowchart.

Quantitative assessment: Meta-analysis was performed on studies reporting the stability of MI that were assessed by PerioTest Value (PTV) units at 30 days and at 60 days using random effects model where heterogeneity was high [I^2 >50%]. Cochrane review manager software (Revman version 5.4) was used for meta-analysis and the studies involving both RFA groups were not taken into consideration as one study measured mobility in Hertz and the other measured it in Implant Stability Quotients (ISQ) grading.

Level of evidence: The certainty of the scientific evidence was assessed using the GRADEpro (Grading of Recommendations Assessment, Development, and Evaluation) guidelines [23]. The stability of MI between the two groups after 30 and 60 days of loading in the studies involved for quantitative analysis were assessed for their study design, ROB, inconsistency, indirectness, imprecision and publication bias if any.

RESULTS

Search strategy: The electronic search identified a total of 2,242 studies. After removal of duplicates, there were a total of 605 articles, which were then subjected to further screening. After screening through titles and abstracts, a total of eight articles were assessed for eligibility. From this, based on the inclusion criteria, two articles were excluded. Only six relevant studies were identified and were included for the qualitative analysis. Total of four studies out of six were included for quantitative analysis. The results of the search are illustrated in the PRISMA flow chart [Table/Fig-3].

The studies included were all of the split mouth design. A total of 104 participants were involved, all of whom were treated with PBM or LLLT on the experimental side.

Characteristics of the intervention: All included studies assessed the effect of PBM on the stability of MI and their information is given in [Table/Fig-4] [14-19].

In the included studies of this review, the protocol of laser application was different. In the study by Ekizer A et al., PBM with energy density of 20 mW/cm^2 was applied on the test side and pseudo application was done on the placebo side for a period of 21 successive days (20 minutes per day) [16]. The primary stability was assessed with RFA using an Osstell ISQ RFA device. Flieger R et al., in their study used a 635 nm laser with a dose of 10 J for 100 seconds at two points each (buccal and palatal side of the alveolus/implant) [14].

Study	Study design	Sample size	Intervention	Control	Outcomes	Parameter assessed	Statistics
Ekizer A et al., 2016 [16]	RCT	20 patients (13 girls, 7 boys)	LPT was applied with an energy density of 20 mW/cm²	Placebo application on one side	- Assess effect of LPT on the rate of orthodontic tooth movement	Superimposed 3D models	- Paired samples t-test - ANOVA
					- Measuring stability of MI	- ISQ values using RFA measured at insertion of MI T0, T1 (1st month T), T2 (2nd month), and T3 (3rd month) of treatment	
					- Interleukin -1b levels in gingival and peri-implant crevicular fluid after LPT	GCF and PICF samples were collected and evaluated	
Flieger R et al., 2020 [14]	Split mouth-RCT	20 subjects (13 women and 7 men; age: 32.5±6.1 years); 40 MI	Irradiated with 635nm diode laser	No laser irradiation on one side	- MI stability in orthodontics	PTV using Periotest for stability measured at 0, 3, 6, 9, 12, 15, and 30 days after placement	- Kolmogorov-Smirnov test - Dependent sample Student's t-test
					- Pain level after the treatment.	- NRS-11 scale for pain assessment	
Matys J et al., 2020 [15]	Split mouth-RCT	22 patients ; 14 women, 8 men; 44 MI	Irradiated with 808 nm laser at palatal and buccal part of the peri-implant area (n=22)	No laser irradiation (n=22)	- Effect of a 808 nm wavelength on orthodontic MI stability - Pain assessment	- PTV values using Periotest measured immediately, 3, 6, 9, 12, 15, and 30 days post the implantation - NRS-11 for pain score	- Kolmogorov-Smirnov analysis - ANOVA repeated measures with a Bonferroni post hoc test
Osman A et al., 2017 [18]	Split mouth-RCT	12 patients, six males and six females; Twenty-four MI	Application of LLLT (n=12)	No laser irradiation; Placebo used as control (n=12)	- Stability of immediately loaded MI - Degree of peri-implant gingival inflammation	- PTV values using Periotest for stability measured at days 0, 7, 14, 21, 30, and 60 - Gingival index.	- Kolmogorov- Smirnov test for normality - Unpaired t test (parametric test) for comparison of means
Matys J et al., 2020 [19]	Split mouth-RCT	15 subjects, 30 MI	-Irradiated with the laser at palatal and buccal part of peri-implant area (n=15)	No laser irradiation (n=15)	- Effect of a 635 nm wavelength on orthodontic MI stability - Pain assessment	- PTV values using Periotest measured 0, 3, 6, 9, 12, 15, 30 days after placement. - NRS-11 scale	- Kolmogorov-Smirnov analysis - ANOVA repeated measures with a Bonferroni post hoc test - Dependent sample Student's t-test for pain assessment
Abohabib AM et al., 2018 [17]	Split-mouth RCT	15 subjects with mean age 20.9 (±3.4) years; 30 MI	Application of LLLT with a wavelength of 940 nm	Placebo application on one side	- Stability of immediately loaded MI - Clinical success and failure rates of MI	- ISQ values using RFA for stability measured at 0, 7, 14, 21 days - Mobility was checked for success and failure rates	- Mean and SD - Kolmogorov- Smirnov test for normality - Paired t-test - ANOVA followed by Tukey's post-hoc test were used to study the changes of time in each group

[Table/Fig-4]: General characteristics of included studies [14-19].
RCT: Randomised control trial; LPT: Light-emitting diode-mediated- photobiomodulation therapy; MI: Mini-implant; ISQ: Implant stability quotient; RFA: Radio-frequency analysis; PTV: Periotest value; GCF: Gingival crevicular fluid; PICF: Peri-implant crevicular fluid; NRS: Numeric rating scale; LLLT: Low level laser therapy; SD : Standard deviation; LPT: Light-emitting diode-mediated- photobiomodulation therapy

The total energy per session was 20 J/cm². The laser application was done on 0, 3, 6, 9, 12, 15, and 30 days after implant placement and the total energy for all therapeutic sessions together was 140 J. The implant stability was measured using a Periotest device (PTV). Matys J et al., in their two studies used two different laser emission parameters that is 635 nm [19] and 808 nm [15]. In both the studies, they irradiated with diode laser at two points (palatal and buccal peri-implant area) with 4 J energy per point for 40 seconds. The total energy applied was 56 J after all the sessions. The periotest device was used to assess the stability of the implant. Osman A et al., used a 910 nm diode laser using 0.7 watts for 60 seconds over the MI insertion area without any contact with the mini-screw [18]. The stability was assessed before and after loading at different time periods (immediately, 7, 14, 21, 30, and 60 days) with a PTV device. Abohabib AM et al., used a diode laser with 940 nm wavelength at 0, 7, 14 and 21 days after the placement of the MI, where the stability was measured using RFA [17].

The results of most of the included studies have shown an increase in the implant stability after 30 days of loading of the MI, except for Osman A et al., who demonstrated no significant difference in improvement of MI stability after application of PBM [Table/Fig-5] [14-19].

Study	Parameters	Results			Inference
		Mean±SD		p-value	
Ekizer A et al., 2016 [16]	ISQ values for stability	LPT (T0) Control (T0)	69.05±5.19 69.21±4.21	0.927	No significant difference
		LPT (T2) Control (T2)	71.75±4.55 68.35±2.20	0.002**	MIs in PBM groups were more stable
		LPT (T3) Control (T3)	70.85±5.69 66.55±3,41	0.001**	MIs in PBM groups were more stable
	Tooth movement by 3D model superimposition	LPT (T1-T0) Control (T1-T0)	1.47±0.51 0.93±0.40	<0.001*	Increased tooth movement on the LPT side
		LPT (T2-T1) Control (T2-T1)	1.37±0.79 1.13±1.11	<0.05*	Increased tooth movement on the LPT side
		LPT (T3-T2) Control (T3-T2)	0.93±0.60 0.71±0.5	<0.001*	Increased tooth movement on the LPT side

Flieger R et al., 2020 [14]	PTV for stability	PBM (baseline) Control (baseline)	−2.74±0.70 −2.53±0.58	0.1231	No statistical significance
		PBM (30 days) Control (30 days)	6.18±5.30 9.17±8.25	0.0003*	MIs in PBM groups were more stable
		PBM (60 days) Control (60 days)	1.51±2.25 5.00±3.24	0.0001*	MIs in PBM groups were more stable
Matys J et al., 2020 [15]	PTV for stability	PBM (baseline) Control (baseline)	-1.25±2.65 −1.08±2.34	0.824	No statistical significance
		PBM (30 days) Control (30 days)	6.32±3.62 11.34±5.76	0.004*	MIs in PBM groups were more stable
		PBM (60 days) Control (60 days)	6.55±4.66 10.95±4.77	0.009*	MIs in PBM groups were more stable
Osman A et al., 2017 [18]	PTV for stability	PBM (baseline) Control (baseline)	1.26 (3.98) 2.27 (4.23)	0.6792	No statistical significance
		PBM (30 days) Control (30 days)	2.60 (1.90) 4.32 (2.65)	0.2254	No statistical significance
		PBM (60 days) Control (60 days)	2.02 (2.60) 4.29 (2.57)	0.1592	No statistical significance
Matys J et al., 2020 [19]	PTV for stability	PBM (baseline) Control (baseline)	-0.44+1.67 -1.25+2.48	0.2819	No statistical significance
		PBM (30 days) Control (30 days)	6.12+4.78 10.88+5.89	0.0218*	MIs in PBM groups were more stable
		PBM (60 days) Control (60 days)	5.7+3.39 10.55+4.81	0.0037*	MIs in PBM groups were more stable
Abohabib AM et al., 2018 [17]	ISQ values for stability	PBM (baseline) Control (baseline)	5188.8+339.3 5050.0+422.0	0.433	No statistical significance
		PBM (4 weeks) Control (4 weeks)	4417.5+565.4 3980.0+743.4	0.047*	MIs in PBM groups were more stable
		PBM (8 weeks) Control (8 weeks)	4411.3+645.3 3912.5+799.2	0.037*	MIs in PBM groups were more stable

[Table/Fig-5]: Results of the included studies [14-19].
LPT: Light-emitting diode-mediated-photobiomodulation therapy; MI: Mini-implant; ISQ: Implant stability quotient; RFA: Radio-frequency analysis; PTV: Periotest value; LLLT: Low level laser therapy; SD: Standard deviation; *Significant

Risk Of Bias (ROB) of the included studies [Table/Fig-6]: Out of the six studies, only two had a low ROB [16,17] whereas one showed high risk [18] and three showed some concerns [14,15,19]. Flieger R et al., Matys J et al., and Matys J et al., had not mentioned how they had blinded their participants and personnel showing bias in the randomisation process. In the study by Matys J et al., reporting bias was observed. One microimplant in the control group was lost during the 60 day frame and the results still included the failed microimplant group [14,15,19]. The study by Osman A et al., showed bias due to deviation from intended interventions and outcome measurement [18].

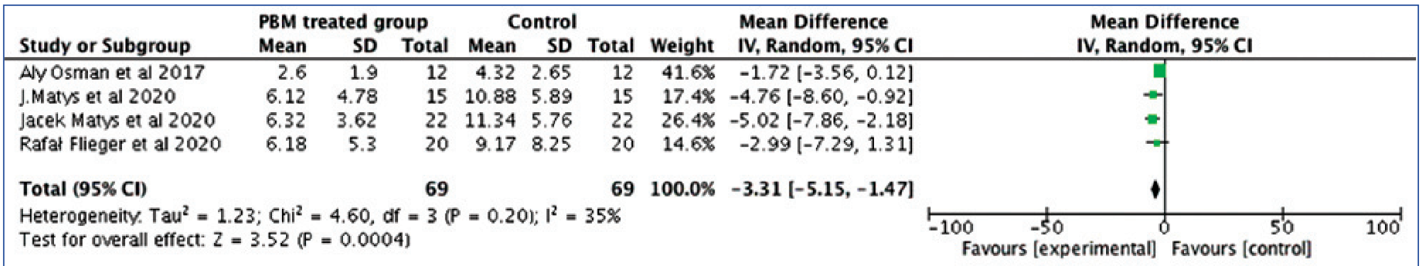
Studies	D1	D2	D3	D4	D5	Overall
Ekizer A et al., 2016 [16]	Low	Low	Low	Low	Low	Low
Flieger R et al., 2020 [14]	Low	SC	Low	High	Low	High
Matys J et al., 2020 [15]	Low	Low	Low	Low	Low	Low
Osman A et al., 2017 [18]	SC	SC	Low	Low	Low	SC
Matys J et al., 2020 [19]	SC	SC	Low	Low	Low	SC
Abohabib AM et al., 2018 [17]	SC	Low	Low	Low	Low	SC

[Table/Fig-6]: Risk of Bias (ROB) using Cochrane ROB-2 tool [22].
D: Domain; SC: Small concerns

Meta-analysis: The results of the meta-analysis for mini-implant stability after 30 days of loading between PBM and control group showed significant (p-value=0.0004) mean difference of -3.31 (95% CI -5.15, -1.47) and a low heterogeneity (I^2=35%) in the included studies [Table/Fig-7].

The results of the meta-analysis for mini-implant stability after 60 days of loading between PBM and control group showed significant (p-value <0.00001) mean difference of -3.47 (95% CI -4.58, -2.36) and no heterogeneity (I^2=0%) in the included studies [Table/Fig-8].

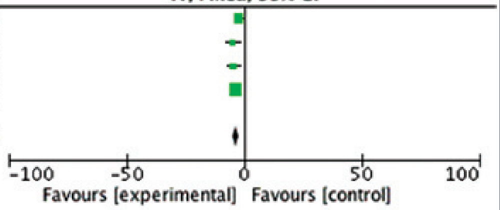
Assessment of certainty of evidence [Table/Fig-9]: The quality of available evidence of MI stability between the groups after loading at 30 days and 60 days was assessed using GRADEpro [23]. The certainty of evidence on the effect of PBM on MI stability after 30 and 60 days of loading was found to be 'low' owing to the high ROB associated with one study [18] and some concerns with three studies [14,15,19] included for the quantitative analysis. Also, a small sample size and fewer number of studies contribute to risk of imprecision which further downgrades the level of evidence from the RCTs.



[Table/Fig-7]: Forest plot - Comparison of MI stability between groups after 30 days of loading [14,15,18,19].

Study or Subgroup	PBM treated group Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Aly Osman et al 2017	2.02	2.6	12	4.29	2.57	12	29.0%	-2.27 [-4.34, -0.20]
J.Matys et al 2020	5.7	3.39	15	10.55	4.81	15	14.0%	-4.85 [-7.83, -1.87]
Jacek Matys et al 2020	6.55	4.66	22	10.95	4.77	21	15.6%	-4.40 [-7.22, -1.58]
Rafał Flieger et al 2020	1.51	2.25	20	5	3.24	20	41.5%	-3.49 [-5.22, -1.76]
Total (95% CI)			**69**			**68**	**100.0%**	**-3.47 [-4.58, -2.36]**

Heterogeneity: $Chi^2 = 2.54$, $df = 3$ ($P = 0.47$); $I^2 = 0\%$
Test for overall effect: $Z = 6.11$ ($P < 0.00001$)



[Table/Fig-8]: Forest plot - Comparison of MI stability between groups after 60 days of loading [14,15,18,19].

Certainty assessment							Summary of findings				
							No.of patients		Effect		
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PBM group	Control	Relative (95%CI)	Absolute (95% CI)	Certainty
MI Stability after 30 days of loading											
4	RCT	Serious (a)	Not serious	Not serious	Serious (b)	None	69	69	-	SMD 0.75 lower (1.1 lower to 0.4 lower)	Low
MI Stability after 60 days of loading											
4	RCT	Serious (a)	Not serious	Not serious	Serious (b)	None	69	68	-	SMD 1.04 lower (1.4 lower to 0.68 lower)	Low

[Table/Fig-9]: Grade pro-assessment [23].

DISCUSSION

Summary of evidence: This systematic review included six RCTs which assessed the stability of the orthodontic mini-implants after low level laser diode application. All included studies [14-19] reported higher mini-implant secondary stability after application of PBM in the peri-implant area and a statistically significant increase in the stability was noted in five [14-17,19] of the six studies. None of the studies reported significant reduction in pain experience after laser application. All of the six studies were split mouth RCTs, the laser application protocols and dosages varied among the studies. Since, one of the included studies had reported a high ROB [18] and three showed some concerns [14,15,19], a higher mini-implant stability following treatment with PBM should be carefully considered. In the present review, meta-analysis to assess the MI stability reported a significant mean difference of -3.31 and -3.47 between PBM and control groups concluding a significantly improved mini-implant stability after subjecting to PBM at 30 days and 60 days. A low heterogeneity of the included studies was noted at both 30 and 60 days.

Costa ACF et al., has recently published a systematic review on the stability of MIs when subjected to PBM [24]. They have included both randomised and non randomised trials in their SR and have reported that two studies had low ROB and three had unclear ROB. In this review a high ROB was noted in 1 study [18] and some concerns in three studies [14,15,19]; and it is supported by the inter-reviewer agreement. Also, the method of conversion of PTVs to RFA values as mentioned by Costa ACF et al., in their review is questionable as it is just a plain inversion of values whereas a method of proper conversion is reported in the literature [25]. In this review, meta-analysis of only the PTV values reported in 4 of the articles included was done.

All studies included in this review [14-19] have reported using 8-10mm long and 1.5 mm diameter implants. The loading protocol is one important factor which influences the stability of mini-implants. It was uniform in all the six studies included in the review and a delayed loading after two weeks was done. The site of placement is also an important factor affecting mini-screw stability and all the studies reported placement in the attached gingiva between second premolar and first molar in maxilla [14-19]. In none of the studies, stent was used for placing mini-implants. Hence, many factors affecting the stability of mini-implants were matched and standardised. The measurement tool used to assess the stability of the mini-screws was either RFA or Periotest. Both these are established methods for analysing implant stability and a significant correlation between the two has been reported in the literature [26].

All of the included studies reported a higher mini-implant stability following administration of PBM except for the study by Osman A et al., which reported a non significant reduction in the mobility of the mini-screws after PBM therapy when compared to untreated controls [18]. On bias assessment, this study reported a high ROB due to deviation from intended interventions and outcome measurements. The authors did not mention the method of mini-screw placement and the total energy dosage of laser application. Since, there are some methodological deficiencies reported in the study, the results of the study should be considered with caution.

Three studies had reported on the pain response of patients after mini-implant placement in both control and study groups [14,19,27]. No significant differences in pain experience between the both groups were reported. All subjects experienced pain after the first 2-4 hours following placement of the MIs. The initial pain remained over the first 24 hours then subsided over the week. The efficacy of laser application for relieving pain after MI placement is not significant in the three studies. However, since the three studies are conducted by the same authors the results should be considered with caution.

Gingival inflammation was reported in the study by Osman A et al., They reported less inflammatory changes in the PBM treated group [18]. In the control group, they reported inflammation in three patients by the end of one month. This was resolved with proper oral hygiene instructions. However, the gingival inflammation increased by the end of two months in the control group; whereas the experimental group showed no signs of inflammation throughout treatment. The results by Osman A et al., suggested that laser therapy seems to modulate the inflammatory response which in turn increases the inflammatory cytokines which reabsorb the traumatised bone and improves bone metabolism [18]. These results are consistent with an animal study by Yanaguizawa MS et al., where they suggested that the lack of gingival inflammation observed in the lower level laser therapy group could be attributed to the decreasing level of IL-8 on laser therapy stimulation [28]. Boyce B et al., study has shown that IL-1 and tumor necrosis factor played an important role during bone remodelling by osteoclast formation and activation [29]. Studies have shown that IL-1ß levels are involved with bone resorption and inhibition of apposition during orthodontic movement of teeth [30-32]. Ekizer A et al., suggested that PBM treatment had no effect on IL-1 levels in the gingival crevicular fluid of tooth and peri-implant crevicular fluid during canine distalisation [16].

Limitation(s)

The limitations of this review include different laser application protocols reported in the selected studies which can affect the results. Inclusion of a small number of studies for the meta-analysis can also be considered a limitation. The quality of the included studies was moderate thus, limiting the clinical application of the review findings. Therefore, considering all these limitations further clinical trials with better methodology are required.

CONCLUSION(S)

Based on the evidence provided by this systematic review, it is suggested that PBM therapy is effective in enhancing the primary stability of MIs. It is also observed that PBM has no effect on pain experience after MI placement. However, due to the low quality evidence, we recommend well-designed studied with standard protocols to be conducted in the near future.

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