

Effectiveness of the photobiomodulation therapy using low-level laser around dental implants: A systematic review and meta-analysis

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Abstract

Background. The photobiomodulation (PBM) therapy has been applied in various fields. Its use in implant dentistry has been proven through various animal, in vitro, and recently also clinical studies. However, the cumulative data of its effect around dental implants in patients is limited.

Objectives. The purpose of the present study was to evaluate whether or not the PBM therapy has a positive effect around dental implants and on implant stability.

Material and methods. The studies included in the review and meta-analysis were selected according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and the PICOS criteria. The RoB 2 tool was used for assessing the risk of bias and the RevMan software, v. 5.0, was used for meta-analysis. Quantitative analysis was done considering the implant stability measurement as the outcome. The mean and standard deviation ($M \pm SD$) values for implant stability as well as the sample size were extracted from the articles, and the inverse variance method with random effects was used for meta-analysis. The forest plots for all time intervals were inspected to estimate the heterogeneity by assessing the I^2 statistic.

Results. A total of 148 articles were initially retrieved, out of which 81 remained after duplicate removal. Ten articles were included in the review after rejecting 68 on the basis of title and abstract. Seven were eligible for quantitative analysis. The meta-analysis showed non-significant differences in primary stability in control and laser groups at baseline ($p = 0.63$) and 3 months and above ($p = 0.06$). At 2 weeks, 1 month and 2 months, the results were statistically significant with $p = 0.01$, $p = 0.02$ and $p = 0.04$, respectively.

Conclusions. The PBM therapy showed a positive effect on implant stability during the early stages of healing and can be considered for patients with dental implants.

Keywords: photobiomodulation, implant stability, low-level laser, implant dentistry

Cite as

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Introduction

The most important factor to be considered in implant dentistry is the biologic union of the implant with the surrounding bone, which is termed osseointegration.¹ The cascade of phenomena that occur during osseointegration includes the formation of a blood clot, angiogenesis, the apposition of bone, and finally the remodeling of the woven bone in the peri-implant area.² Adequate implant stability plays a critical role in osseointegration. Both primary and secondary implant stability influences successful implant treatment, the former occurring due to the mechanical engagement of the implant into the bone, and the latter due to the remodeling and regeneration process during the healing phase.³ Various techniques have been advocated to improve implant stability as well as soft tissue healing around the dental implant, which in turn contributes to implant success.^{4,5}

Photobiomodulation (PBM) is a non-invasive, non-thermal therapy which through the use of low-level laser (LLL) stimulates cells to generate more energy and undergo self-repair. It involves the application of monochromatic light with a low energy density, which induces non-thermal photochemical effects on the cellular level.⁶ Photobiomodulation using low-level laser therapy (LLLT) with a low energy density stimulates the mitochondrial and cellular membrane photoreceptors to synthesize adenosine triphosphate (ATP), which in turn enhances the cell proliferation rate.⁷ It also increases the proliferation and differentiation of osteoblasts, thus having a bio-stimulatory effect on bone tissue.⁸ This potential role of PBM has been studied in the field of implant dentistry to improve implant stability, and overall hard and soft tissue healing around dental implants. Several in vitro and animal studies have suggested a positive effect of LLLT around the implant.^{9–14} However, considering human studies in the recent past, the effectiveness of the PBM therapy around dental implants has not been clearly shown. This systematic review and meta-analysis was conducted on the basis of clinical studies to evaluate the qualitative and quantitative effect of PBM on implant stability.

Material and methods

The systematic review was conducted in accordance with the guidelines provided in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.¹⁵ The review protocol was registered under PROSPERO International Prospective Register of Systematic Reviews (CRD42021249393). The review question was specifically constructed following the PICOS criteria:

- Population – male or female patients requiring the replacement of one or more missing teeth with dental implants;
- Intervention – the PBM therapy around dental implants;
- Comparison – patients who did not receive PBM or any other adjunctive therapy around dental implants;

- Outcome – the effect of the PBM therapy on implant stability; and
- Study design – randomized controlled trials (RCTs), clinical trials.

The review question was “Does the PBM therapy in patients receiving dental implants have an effect on implant stability?”

Search strategy

The search of electronic databases (PubMed, EBSCOhost, Cochrane, and Embase) was carried out by 2 investigators individually, without consulting one another. The following terms were searched in all databases: ‘dental implant’ OR ‘dental implants’ AND ‘photobiomodulation’ OR ‘low-level laser therapy’ OR ‘low-level laser’ OR ‘LLLT’ OR ‘laser therapy’ AND ‘primary stability’ OR ‘implant stability’ OR ‘dental implant stability’ OR ‘osseointegration’. Also unpublished data was searched on ClinicalTrials.gov. The electronic databases were searched for articles published till April 2021. The EndNote™ software, v. 8.0 (<https://endnote.com/downloads>), was used to remove duplicates. The same software was used for the initial screening of the articles on the basis of their title and abstract. Eligible articles fulfilling the inclusion criteria were further assessed by accessing their full text from relevant sources. This was done individually by the 2 investigators considering the inclusion and exclusion criteria. A detailed assessment of all the citations and references was done thoroughly to widen the search. Any discrepancy between the 2 investigators was resolved by a third investigator. The inter-investigator reliability was assessed using the Cohen’s kappa score.

Inclusion and exclusion criteria

Randomized controlled trials and clinical studies that evaluated the effect of PBM using LLL and a diode laser on the conventionally or immediately placed dental implants were selected for the review. The exclusion criteria were as follows: animal studies; in vitro studies; case reports; reviews; books; and studies that involved extensive grafting and adjunctive procedures during implant placement, systemically ill patients, or the use of orthodontic or mini implants.

Quality assessment

The risk of bias assessment for all the included studies was carried out using the RoB 2 tool.¹⁶ According to the RoB 2 tool, 5 domains were taken into consideration to evaluate each article in terms of risk of bias, namely the randomization process, deviation from the intended intervention, missing outcome data, the measurement of the outcome, and the selection of the reported results. Accordingly, the risk of bias of the particular articles was classified as low, high or unclear.

Meta-analysis

The Review Manager software (RevMan, v. 5.4; the Cochrane Collaboration, 2020) (<https://training.cochrane.org/online-learning/core-software/revman>) was used for the

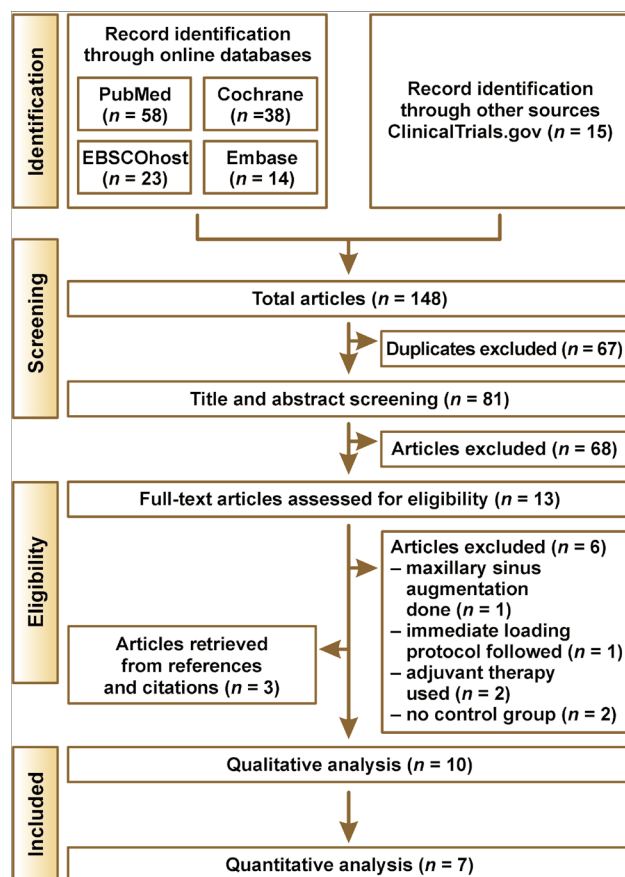


Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of the screening process

quantitative assessment of eligible articles. The mean and standard deviation ($M \pm SD$) values for implant stability as well as the sample size were extracted from the articles, and the inverse variance method with random effects was used for meta-analysis. Implant stability measurements were taken at baseline (immediately after implant placement), 14 days (1–2 weeks), 1 month (3–4 weeks), 2 months (5–8 weeks), and 3 months or more (9–12+ weeks) after implant placement. The forest plots for all time intervals were inspected to estimate the heterogeneity by assessing the I^2 statistic, where $I^2 > 50\%$ was moderate to high heterogeneity.¹⁷

Results

The initial search identified a total of 148 relevant articles from electronic databases, out of which 81 remained after the removal of duplicates. Out of this, 68 articles were excluded based on the exclusion criteria. At the end of the study selection, 10 articles were included for qualitative^{18–27} and 7 for quantitative analysis.^{18–20,22–24,27} The study screening and the selection of articles is explained in Fig. 1. The inter-investigator reliability in the selection of articles was statistically evaluated using Cohen's kappa analysis and a score of 0.97 was obtained.

All 10 articles raised some concerns as to the selection of the reported results (D5).^{18–27} Four studies showed a low risk of bias with regard to the randomization process (D1), deviation from the intended intervention (D2), missing outcome data (D3), and the measurement of the outcome (D4).^{18,20,24,27} The article by Memarian et al. showed an unclear risk of bias for all 5 domains (D1–D5).²¹ None of the articles in the review presented a high risk of bias (Fig. 2).

Unique ID	Study ID	Experimental group	Comparator	Outcome	Weight	D1	D2	D3	D4	D5	Overall
1	García-Morales et al.	LLLT	CONTROL	dental implant stability	1	+	+	+	+	!	!
2	Gokmenoglu et al.	LED PBM	CONTROL	dental implant stability	1	!	+	+	!	!	!
3	Mandić et al.	LLLT	CONTROL	dental implant stability	1	+	+	+	+	!	!
4	Memarian et al.	LLL and LED PBM	CONTROL	dental implant stability	1	!	!	!	!	!	!
5	Torkzaban et al.	LLLT	CONTROL	dental implant stability	1	!	+	+	!	!	!
6	Matys et al.	LASER	CONTROL	dental implant stability	1	!	+	+	!	!	!
7	Bittencourt Lobato et al.	LLLT	CONTROL	dental implant stability	1	+	+	+	+	!	!
8	Bakry et al.	LASER	CONTROL	crestal bone evaluation	1	+	+	+	!	!	!
9	Mohajerani et al.	LLLT and LED	CONTROL	dental implant stability	1	!	+	+	!	!	!
10	Gulali et al.	LLLT	CONTROL	crestal bone evaluation	1	+	+	+	+	!	!

⊕ low risk

! some concerns

⊖ high risk

D1 randomization process

D2 deviation from the intended intervention

D3 missing outcome data

D4 measurement of the outcome

D5 selection of the reported results

Fig. 2. Quality assessment of the included studies with the use of the RoB 2 tool

LLLT – low-level laser therapy; LED – light emitting diode; PBM – photobiomodulation; LLL – low-level laser.

Characteristics of the systematic review

All the articles included in the systematic review were clinical studies, and were published between 2012 and 2020. Three of the studies had a split-mouth design,^{18,20,21} while 7 had a case-control design.^{19,22–27} The studies were conducted in Brazil,^{18,24} Turkey,¹⁹ Serbia,²⁰ Iran,^{21,22,26} Poland,²³ Egypt,²⁵ and India.²⁷ A total of 381 dental implants were initially included in the studies, out of which 194 were in the laser group, while 187 acted as control. Males and females in the age group of 20–77 years were included. In 5 studies, implant placement was done in the mandible,^{18,21,23,25,27} while the maxilla was the implant site in 3 studies^{20,22,25}; for 2 studies, the implant site was not defined.^{19,24} Primary stability evaluation was the primary outcome of all but 2 studies, in which crestal bone loss was assessed.^{25,27} The Osstell® ISQ (implant stability quotient) device was used to measure implant stability in the majority of studies.^{18–20,22,24,26} In their study, Matys et al. calculated the periotest values (PTVs) for implant stability, and then inverted their signs to adapt them to the standard ISQ values used by other studies.²³ Crevicular biochemical markers, i.e., interleukin 1 beta (IL-1 β), transforming growth factor beta (TGF- β), prostaglandin E2 (PGE2), and nitric oxide were the secondary outcomes evaluated by Gokmenoglu et al.¹⁹ Alkaline phosphatase (ALP) and early implant success were evaluated by Mandić et al.,²⁰ while IL-1 β and PGE2 were recorded by Memarian et al.²¹ Bakry et al. assessed clinical parameters, including probing depth (PD) and the distance between the implant shoulder and the peri-implant mucosa (DIM).²⁵ The evaluation period was different for all studies, and ranged from baseline to 1 year (Table 1).

The type of laser and protocol used for PBM is presented in Table 2. Diode lasers were used in all studies with a wavelength range of 626–980 nm. In their study, Memarian et al. used 2 diode lasers, one with a wavelength of 810 nm and the other with a wavelength of 626 nm, and compared the experimental groups with the control group.²¹ The time of laser application differed in the studies, ranging from immediately after implant placement to 24 days after implant placement. However, in the studies by Matys et al.²³ and Bakry et al.,²⁵ PBM was applied 1 day and 2 weeks before implant placement, respectively.

Meta-analysis

A meta-analysis was performed to evaluate the effect of the PBM therapy using LLL on implant stability. The analysis was divided into subgroups depending on the time of implant stability evaluation (Fig. 3). All the 7 studies included in the meta-analysis evaluated implant stability at baseline (immediately after implant placement), for which the result was statistically non-significant ($p = 0.63$).^{18–20,22–24,26} Implant stability evaluation at 2 weeks, 1 month and 2 months was done by all^{18–20,22,23,26}

but Bittencourt Lobato et al., who evaluated implant stability at baseline and after 3 months only.²⁴ The overall effect of the analysis calculated for all 3 subgroups was statistically significant with $p = 0.01$, $p = 0.02$ and $p = 0.04$, respectively. However, the analysis at 3 months showed statistically non-significant data ($p = 0.06$).

Heterogeneity was assessed for all time intervals. For implant stability at baseline, heterogeneity was non-significant ($p = 0.50$; $I^2 = 0\%$). Similarly, for 2 weeks, 1 month, 2 months, and 3 months there was non-significant heterogeneity with $p = 0.11$; $I^2 = 44\%$, $p = 0.16$; $I^2 = 37\%$, $p = 0.15$; $I^2 = 38\%$, and $p = 0.21$; $I^2 = 31\%$, respectively (Fig. 3).

Discussion

There have been systematic reviews and meta-analyses evaluating the effect of the PBM therapy on osseointegration, crestal bone loss, and implant stability around orthodontic or mini implants, and even evaluating PBM as surface treatment around dental implants. However, reviews assessing the efficacy of LLLT or the PBM therapy around conventional dental implants in terms of implant stability are very few.^{28–30} This review was conducted to evaluate the effect of the PBM therapy on implant stability. Various methods are used to assess implant stability, such as insertion torque values, the reverse torque test, the percussion test, ISQ, and PTVs.³¹ Among these, the most reliable are ISQ and PTVs, which were used in the studies included in the present meta-analysis.^{18–20,22–24,26}

The PBM therapy using LLL has shown positive effects in studies done on implants in animals.^{9–14} This review focused on clinical trials only. Five out of 10 studies in the review concluded that the PBM therapy had no effect around dental implants.^{18,20,22,24,25} Statistically non-significant differences were observed for implant stability as well as ALP activity around dental implants in the study by Mandić et al.²⁰ However, when evaluating the recorded outcome variables in this study, the laser group had higher values at the end of the study for both implant stability and ALP activity.²⁰ This phenomenon can be correlated with the relationship between LLLT stimulation and the tissue stem cells reacting to it, inducing the new formation and healing of the peri-implant soft tissues and the peri-implant bone.³² Similar results were found in the studies by Torkzaban et al.²² and Bittencourt Lobato et al.,²⁴ even though the observed differences were not statistically significant. The pooled result of all the studies included in the meta-analysis showed a positive effect of the PBM therapy on dental implant stability in contrast to the other systematic review results. Crestal bone loss was evaluated by 2 studies; Bakry et al. concluded that the PBM therapy had no effect,²⁵ while Gulati et al. showed a positive effect.²⁷

No homogeneity was found in the laser parameters used in the different studies included in the review. This may be one of the reasons for the discrepancy in the results of the studies.

Table 1. Characteristics of the included studies

Study	Country	Study design	Number of implants	Average age [years]	Sex		Implant site	Implant producer	Bone type	Outcome	Evaluation time	Study conclusion
					M	F						
García-Morales et al. 2012	Brazil	SM	29 LG (15) CG (14)	36	2	6	posterior mandible	Dentsply, Mannheim, Germany	–	implant stability (Osstell ISQ device)	immediately, 10 days, and 3, 6, 9, and 12 weeks postoperatively	no effect
Gokmenoglu et al. 2014	Turkey	CC	22 LG (10) CG (12)	48	9	6	–	Dentsply, Mannheim, Germany	type 2 or 3	implant stability (Osstell ISQ device) IL-1 β , TGF- β , PGE2, and nitric oxide	immediately, and 2, 4, 8, and 12 weeks postoperatively 4 and 12 weeks postoperatively	positive effect
Mandić et al. 2015	Serbia	SM	40 LG (20) CG (20)	61	6	6	posterior maxilla	Bredent, Senden, Germany	–	implant stability (Osstell ISQ device) PICF early implant success	immediately, and 1, 2, 3, 4, 5, and 6 weeks postoperatively 7, 14, 21, and 28 days postoperatively 6 weeks postoperatively	no effect
Memarian et al. 2018	Iran	SM	36 LG (12) LG (12) CG (12)	–	–	–	anterior mandible	Dio, Busan, South Korea	type 2 or 3	implant stability (PTVs) inflammatory biomarkers	at the day of surgery, and 3, 4 and 8 weeks after surgery 4 and 8 weeks postoperatively	positive effect
Torkzaban et al. 2018	Iran	CC	80 LG (40) CG (40)	42	9	10	maxilla	Dio, Busan, South Korea	D3 and D4	implant stability (Osstell ISQ device)	immediately, 10 days, and 3, 6 and 12 weeks postoperatively	no effect
Matys et al. 2019	Poland	CC	40 LG (18) CG (22)	47	16	8	posterior mandible	SuperLine Dentium, Cypress, USA	D2	implant stability (PTVs)	immediately, 2 and 4 weeks, and 2 and 3 months postoperatively	positive effect
Bittencourt Lobato et al. 2019	Brazil	CC	46 LG (23) CG (23)	51	–	–	–	Straumann Basel, Switzerland	–	implant stability (Osstell ISQ device)	immediately and at the abutment selection phase	no effect
Bakry et al. 2020	Egypt	CC	12 LG (6) CG (6)	40	–	–	posterior maxilla	Zimmer Dental, Carlsbad, USA	–	crestal bone level (RVG) clinical parameters	immediately, and 2, 12 and 26 weeks postoperatively immediately, and 2, 12 and 26 weeks postoperatively	no effect
Mohajerani et al. 2020	Iran	CC	56 LG (28) CG (28)	38	32	26	posterior mandible	Zimmer Dental, Carlsbad, USA	–	implant stability (Osstell ISQ device)	immediately, and 10, 21, 42, and 63 days postoperatively	positive effect
Gulati et al. 2020	India	CC	20 LG (10) CG (10)	35	13	7	posterior mandible	Adin Dental, Bielsko-Biała, Poland	type 2 or 3	crestal bone level (IOPA) CBCT	immediately, 6 weeks and 6 months following prosthesis loading, and at 1 year immediately and at 1 year	positive effect

M – male; F – female; SM – split-mouth; CC – case-control; LG – laser group; CG – control group; ISQ – implant stability quotient; IL-1 β – interleukin 1 beta; TGF- β – transforming growth factor beta; PGE2 – prostaglandin E2; PICF – peri-implant crevicular fluid; PTVs – periosteal values; RVG – radiovisiography; IOPA – intraoral periapical radiograph; CBCT – cone-beam computed tomography.

Table 2. Specifications of the lasers used in the included studies

Study	Laser	Laser specifications	Dosage
García-Morales et al. 2012	GaAlAs diode LLL Thera Lase Surgery; DMC, São Carlos, Brazil	wavelength: 830 nm mode: contact mode power: 86 ± 2 mW laser spot size: 0.0028 cm^2 energy density: 92.1 J/cm^2 irradiation time per point: 3 s total points: 20 points (9 at the vestibular, 9 at the lingual, 1 at the distal, and 1 at the mesial region of the implant) total energy per session: 8 J	immediately, and 2, 4, 6, 8, 10, 12, and 14 days postoperatively
Gokmenoglu et al. 2014	Osseopulse AR 300; Biolux Research, Vancouver, Canada	wavelength: 626 nm mode: contact mode (extraoral) power: 185 mW laser spot size: 4.80 cm^2 energy density: 46.2 J/cm^2 average intensity: 38.5 mW/cm^2 irradiation time: 20 min total energy per session: 222 J	immediately, and 1, 2 and 3 weeks (3 times per week) postoperatively
Mandić et al. 2015	GaAlAs laser Medicolaser 637; Technoline, Belgrade, Serbia	wavelength: 637 nm mode: non-contact mode (extraoral) power: 40 mW energy density: 6.26 J/cm^2	every 24 h for 7 days postoperatively
Memarian et al. 2018	diode laser Doctor Smile; Lambda, Brendola, Italy	wavelength: 810 nm mode: contact mode power: 50 mW laser spot size: 1 cm^2 irradiation time: 400 s	immediately, and 3, 7, 10, and 14 days postoperatively
	Osseopulse AR 300; Biolux Research, Vancouver, Canada	wavelength: 626 nm mode: contact mode (extraoral) power: 185 mW laser spot size: 4.80 cm^2 energy density: 46.2 J/cm^2 average intensity: 38.5 mW/cm^2 irradiation time: 20 min	immediately, and 3, 7, 10, and 14 days postoperatively
Torkzaban et al. 2018	Epic 10; Biolase, Irvine, USA	wavelength: 940 nm mode: contact mode power: 100 mW laser spot size: 0.2826 cm^2 average energy density: 14.18 J/cm^2 average power density: 354.6 mW/cm^2 irradiation time per point: 40 s total points: 2 points (at the buccal and palatal sites of the implant) total energy per session: 8 J	2, 4, 6, 8, 10, and 12 days postoperatively
Matys et al. 2019	red diode laser Smart M; Lasotronix, Piaseczno, Poland	wavelength: 635 nm mode: contact mode power: 100 mW laser spot size: 0.5024 cm^2 average power density: 99.04 mW/cm^2 irradiation time per point: 40 s total points: 2 points (at the buccal and lingual sites of the implant) total energy per session: 8 J	1 day preoperatively, immediately, and 2, 4, 7, and 14 days postoperatively
Bittencourt Lobato et al. 2019	GaAlAs diode laser Therapy XT; DMC, Sao Carlos, Brazil	wavelength: 808 nm power: 50 mW laser spot size: 0.4 cm^2 irradiation time per point: 1.23 min total points: 6 points (2 at the labial, 2 at the lingual and 2 at the occlusal site of the implant) total energy per session: 66 J	immediately after implant placement
Bakry et al. 2020	diode laser Smart M Pro; Lasotronix, Piaseczno, Poland	wavelength: 980 nm mode: contact mode power: 2 W irradiation time: 5 min frequency: 300 Hz	2 weeks before implant placement, and 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24 days postoperatively
Mohajerani et al. 2020	–	wavelength: 830 nm (laser) + 632 nm (LED) power: 10 mW laser spot size: 0.0015 cm^2 irradiation time: 20 min	every day for 10 days postoperatively
Gulati et al. 2020	Photon Plus; Zolar Technology & Mfg Co. Inc., Mississauga, Canada	wavelength: 980 nm power: 0.1 W laser spot size: 0.25 cm^2 energy density: 4 J/cm^2 irradiation time per point: 10 s total points: 6 points (at the mesiobuccal, distobuccal, midbuccal, midlingual, mesial, and distal areas) total energy per session: 6 J	immediately following osteotomy and prior to implant placement, and 3, 7 and 14 days postoperatively

GaAlAs – gallium aluminum arsenide.

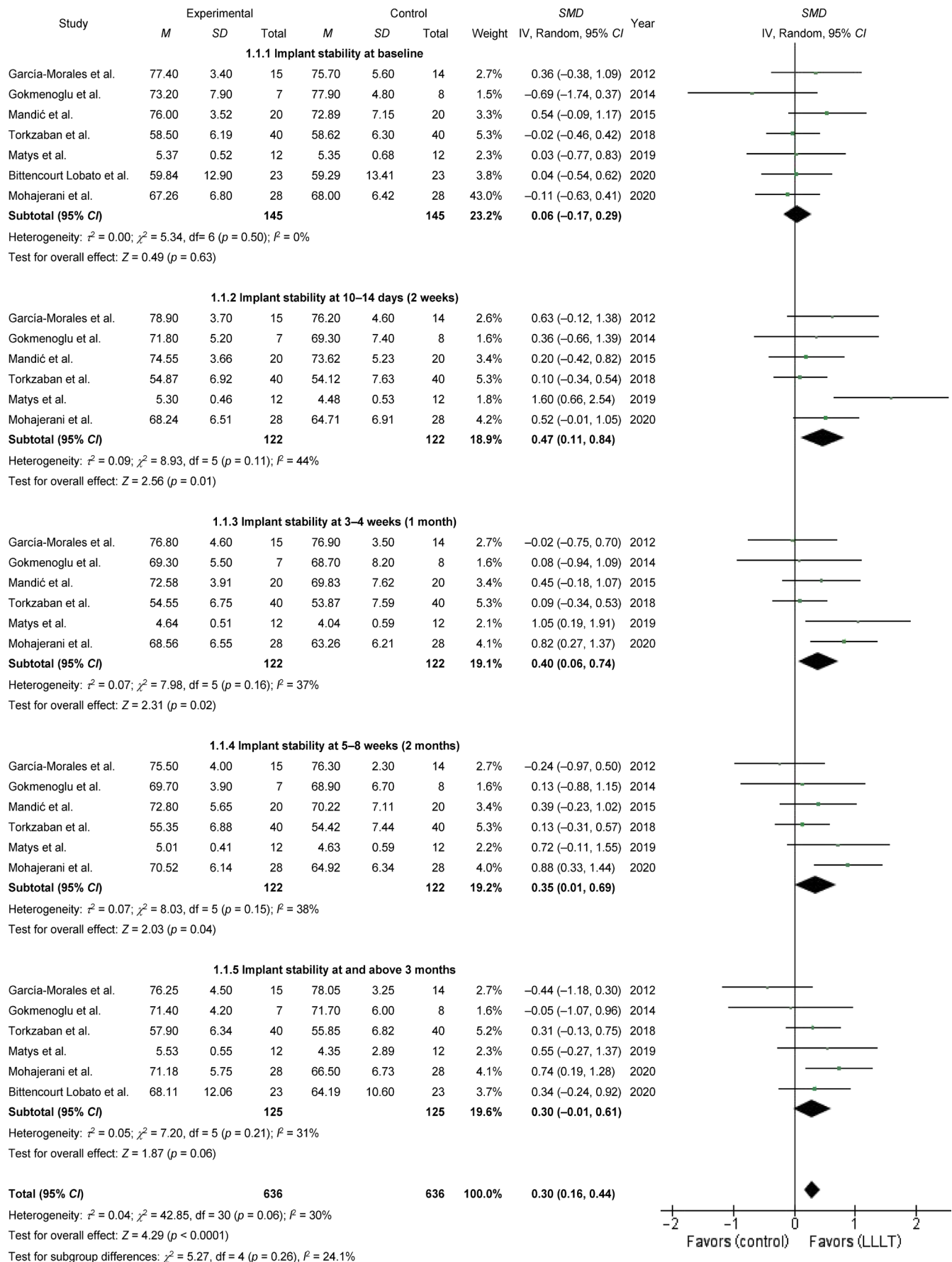


Fig. 3. Forest plots of dental implant stability for experimental (laser) and control groups at baseline, 2 weeks, 1 month, 2 months, and 3 months and above M – mean; SD – standard deviation; SMD – standardized mean difference; CI – confidence interval; df – degrees of freedom.

A laser of a higher wavelength benefits, as it penetrates deeper into the tissues and has a positive osteogenic effect.³³ Considering all the studies included in this review and their results, a standardized protocol for the PBM therapy using LLL around dental implants must be implemented.

Limitations

The current review consisted of 10 articles which were eligible for qualitative analysis, and 7 out of them were selected for quantitative analysis. This number is relatively small for a review, which is due to the fact that the topic is new and still under modification. Future research in this field should be considered for a review in the future.

Conclusions

The PBM therapy using LLL shows a positive effect on implant stability at different intervals, especially during the early stages of healing, and is worth considering for patients with dental implants. The need of the hour is to develop and test a standardized laser protocol for the PBM therapy to improve tissue around dental implants. With laser becoming one of the most popular modalities in clinical dentistry and being available to many clinical setups now, its use to enhance implant stability and healing can be of great benefit in implant dentistry.

Ethics approval and consent to participate

Not applicable.

Data availability


All data analyzed during this study is included in this published article.


Consent for publication

Not applicable.

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