Clinical Efficacy of Photobiomodulation on Dental Implant Osseointegration: A Systematic Review

Sara Mahmoud Zayed, Ahmed Adel Abdel Hakim

Department of Prosthodontics, Faculty of Dentistry, Alexandria University, Alexandria, Egypt

Background: Photobiomodulation (PBM) has been shown to have a positive effect on dental implant osseointegration Abstract and stability in in vitro and animal studies; however, its usefulness in dental implant clinical practice is yet unclear. Objective: The objective was to assess the clinical effectiveness of PBM on dental implants' osseointegration. Methods: Two reviewers independently conducted a comprehensive electronic search of articles published from inception up to January 10, 2020, in PubMed, Cochrane Library and Embase databases following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Randomized clinical trials (RCTs) and nonrandomized clinical studies that compared the effect of PBM on dental implant stability with control groups were included. Animals and in vitro studies studies as well as studies with confounders such as application of orthodontic were excluded. Risk of bias (using Cochrane Risk of Bias tool for RCTs and Risk of Bias in Non-Randomized Studies of Interventions tool for nonrandomized studies) was assessed by both authors. Owing to substantial heterogeneity, only a narrative synthesis of the included studies is presented. Results: Seven relevant clinical studies were included, and they used a variety of PBM parameters and devices. The posterior region of the jaw was found to be more frequently evaluated. For assessing the effect of PBM on implant stability, five studies used resonance frequency analysis and two used periotest; three studies additionally used biomarkers for assessment. Four studies found that PBM has a potential positive effect on the outcome of dental implant stability, whereas three studies reported that PBM has no effect on implant stability.

Conclusion: The findings of this systematic review suggest that postoperative application of PBM may potentially have some positive effect on dental implant's osseointegration and stability. However, additional studies are required with uniformity in methods to provide a more robust assessment of this effect.

Keywords: Dental implants, implant stability, low-level laser/light therapy, osseointegration, photobiomodulation

Address for correspondence: Dr. Sara Mahmoud Zayed, Department of Prosthodontics, Faculty of Dentistry, Alexandria University, Champlion Street, Azarita, Alexandria, Egypt. E-mail: dr_sara_23@hotmail.com

Submitted: 27-Sep-2019 Revised: 20-Oct-2019 Accepted: 04-Feb-2020 Published: 17-Apr-2020

INTRODUCTION

Developments in photonic technologies and an improved knowledge of light-tissue interactions have brought about

Access this article online						
Quick Response Code:	Mahaita					
	www.sjmms.net					
	DOI: 10.4103/sjmms.sjmms_410_19					

considerable advances in mainstream medicine. Using high-dose lasers and light devices in medicine and dentistry is nowadays common for various clinical applications.^[1-3]

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Zayed SM, Hakim AA. Clinical efficacy of photobiomodulation on dental implant osseointegration: A systematic review. Saudi J Med Med Sci 2020;8:80-6.

However, a less prevalent clinical application is the use of low-dosage biophotonics for therapy, referred to as photobiomodulation (PBM) or formerly as low-level laser therapy (LLLT), which is intended for relieving pain and inflammation, regulating immune responses as well as stimulating wound healing and tissue regeneration.^[3,4] In this manner, it presents an opportunity for a paradigmatic shift from conventional approaches to regenerative modalities in clinical dentistry. Although PBM initially received mixed responses,^[4] it is increasingly being recognized based on the accepted principles of photochemistry and cellular and molecular biology. The growing realization that PBM has a broad range of systemic and regional effects led to a striking increase in the number of its applications, with a special focus on its applications in dentistry.^[4-6]

In the field of oral implantology, research has been directed toward the potential of PBM to reduce the healing time following implant placement and to improve the potential of bone regeneration. Experimental studies have reported that PBM stimulates proliferation and differentiation of osteoblasts as well as it enhances bonding to titanium implant. In these studies, application of PBM in the early postoperative application was shown to improve the mechanical strength of the bone-implant interface and stimulate the bone matrix production.[7-11] However, the usefulness of PBM application in dental implant clinical practice is not yet clear. Thus, this systematic review was conducted to answer the following research question formulated based on the population, intervention, comparator and outcome (PICO) criteria: "In patients receiving dental implants, does postoperative application of PBM improve osseointegration?"

MATERIALS AND METHODS

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).^[12] Based on the research question, the population was adult patients who had received dental implantation, the intervention was postoperative application of PBM and the comparator was control group. The principal outcome was successful osseointegration of dental implants in terms of improved implant stability, and secondary outcomes were anti-inflammatory and accelerated healing effects.

Search strategy

Two reviewers independently conducted an electronic search of PubMed, Cochrane Library and Embase for articles from inception up to January 10, 2020, using the following search terms: (dental implant OR dental implantology) AND (photobiomodulation OR low level laser therapy OR low level light therapy OR LLLT OR low intensity laser OR soft laser OR laser bio-stimulation) AND (osseointegration OR implant stability). No language filter was applied during the search. The title and abstracts of all articles in the searches were screened against the inclusion criteria to identify potentially eligible articles. Full texts of potential articles were read and assessed independently by the two reviewers. Any discrepancy was resolved through discussion until a consensus was reached. The inter-reviewers' reliability was calculated based on Cohen's kappa statistics. To detect any potential unidentified studies, bibliographies and reference lists of the included studies were also searched.

Inclusion/exclusion criteria

Randomized clinical trials (RCTs) and nonrandomized clinical studies that compared LLLT/PBM and other modalities such as ozone application on dental implant stability were included. Exclusion criteria were *in vitro* and animal studies, case reports, review articles, clinical studies on augmented implant sites and studies assessing a single type of treatment in the absence of a comparison group. In addition, to allow for reliable comparison, studies that applied orthodontic force on mini-implants were excluded to avoid its confounding effect on osseointegration and implant stability.

Data extraction

The two authors manually and independently extracted the data from each of the included studies; any disagreements in data extraction were resolved through discussion. The extracted data fields included first author name, year of publication, country where research was performed, study design, control group details, sample size, gender and mean age of patients, ethical approval, implant-related parameters (type, dimension and position), PBM parameters, number of PBM applications, analysis conducted, duration of follow-up and results.

Quality assessment

Methodological quality of the included studies was evaluated using the Cochrane Risk of Bias tool^[13] for RCTs and the Risk of Bias in Nonrandomized Studies-of Interventions (ROBINS-I) tool^[14] for nonrandomized studies.

RESULTS

The initial database search yielded a total of 202 articles. All relevant articles were only published in English. After removal of duplicates and applying the inclusion/exclusion criteria, full-text articles of 15 relevant studies were thoroughly evaluated independently by the two reviewers. Eight studies^[15-22] did not meet the eligibility criteria and were excluded [Table 1]. Eventually, seven studies were included for data synthesis [Figure 1].

The Cohen's kappa value for inter-investigator agreement on the selected studies was 0.85. Owing to inconsistent data and substantial heterogeneity in the included studies, a meta-analysis was not possible, and thus a narrative synthesis of the included studies is presented.

General characteristics of the included studies

Of the seven studies included, five^[23-27] were RCTs and two were prospective clinical studies.^[28,29] Three studies^[23-25] used the "split-mouth" experimental design, while the remaining studies separately included individuals as controls.^[26-29] All studies were conducted between 2012 and 2019. Two studies were conducted in Turkey;^[28,29] two in Iran;^[25,26] and one each in Serbia,^[24] Poland^[27] and Brazil.^[23] All the included studies were conducted in academic research institutions after ethical approval; only one study^[25] did not report the ethical approval. The

Table 1: List of articles excluded after full-text assessment and reason for exclusion

Study	Reason for exclusion
Sleem <i>et al.</i> , 2019 ^[15]	PBM combined with platelet-rich fibrin - which may influence PBM effect
Flieger <i>et al.</i> , 2019 ^[16]	Orthodontic mini-implants
Marañón-Vásquez et al., 2019 ^[17]	Orthodontic mini-implants
Arakeeb <i>et al.</i> , 2019 ^[18]	PBM combined with growth factors
Abohabib <i>et al.</i> , 2018 ^[19]	Orthodontic mini-implants
Mikhail <i>et al.</i> , 2018 ^[20]	PBM combined with Vitamin C,
	omega-3 and calcium therapy
Awad et al., 2017 ^[21]	Diabetic patients included in the study
Yanaguizawa <i>et al.</i> , 2017 ^[22]	Orthodontic mini-implants

PBM – Photobiomodulation



Figure 1: Flow diagram showing the screening and selection of articles

number of participants in the studies ranged from 8 to 25, while the age ranged from 20 to 64 years; one study^[25] did not report the mean age. Six studies enrolled healthy, nonsmoking patients with no systemic alterations, whereas the study by Gokmenoglu *et al.*^[28] did not exclude smokers. All the included studies evaluated the efficacy of PBM by comparing against a control group. Four studies^[23,24,26,27] compared laser PBM against control group; one study each compared laser PBM and light-emitting diode (LED) PBM against control group,^[28] and ozone therapy to laser PBM and control group [Table 2].^[29]

According to the Cochrane Risk of Bias tool, only two of the five randomized studies^[23,24] were of low risk of bias, while the other three studies^[25-27] were of moderate risk of bias [Table 3]. The risk of bias of the two nonrandomized trials^[28,29] was found to be moderate, according to the ROBINS-I tool [Table 4].

Characteristics of treatment and methods used

In terms of the implant systems used, two studies each used XiVE[®]-s (Dentsply, USA)^[23,28] and DIO implant (South Korea),^[25,26] and one study each used BlueSKY (Bredent, Germany),^[24] DTI implant system (Turkey)^[29] and Superline (Dentium, South Korea).^[27] Nevertheless, the implant dimensions used were very close; the length ranged from 10 to 12 mm and the diameter from 3.8 to 4.5 mm. Only one study^[25] did not report the implant dimensions used.

Mostly, the gallium aluminum arsenide^[23,24,29] and semi-conductor diode^[25-27] lasers were used, and LED was used in one study.^[28] A comparison between LED and diode was done in the study by Memarian *et al.*^[25]

Most studies used lasers in the near-infrared spectrum; however, the wavelengths differed: two studies used $830 \text{ nm}^{[23,29]}$ and one study each used $810 \text{ nm}^{[25]}$ and 940 nm.^[26] Three studies used visible-range lasers with wavelengths of 626 nm and 637 nm.[24,27,28] Follow-up period varied from 6 to 24 weeks, and the number of PBM applications ranged from 5 to 9. In terms of the jaw regions evaluated, three studies were performed on the posterior area of the mandible,^[23,27,29] two on the maxillary posterior^[24,26] and one on the anterior mandible;^[25] one study did not state the specific irradiated area.^[28] Five studies examined the effect of PBM in terms of implant stability quotient by resonance frequency analysis (RFA),^[23,24,26,28,29] whereas the remaining two studies used periotest.[25,27] Three studies additionally examined biomarkers to augment their results.[24,25,28]

Point of				Author			
comparison	García-Morales <i>et al.</i> , 2012 ^[23]	Mandić <i>et al.</i> , 2014 ^[24]	Memarian <i>et al.</i> , 2017 ^[25]	Torkzaban <i>et al.</i> , 2018 ^[26]	Matys <i>et al</i> ., 2019 ^[27]	Gokmenoglu <i>et al.</i> , 2014 ^[28]	Karaca <i>et al.</i> , 2018 ^[29]
Country Study design	Brazil Split mouth (RCT)	Serbia Split mouth (RCT)	Iran Split mouth (RCT)	Iran Different individuals (RCT)	Poland Different individuals (RCT)	Turkey Different individuals (non-RCT)	Turkey Different individuals (non-RCT)
Control Sample size	Placebo 8	Placebo 12	Placebo 12	Placebo 19	Placebo 24	Placebo 15	Placebo 25
Gender	2 males 6 females	6 males 6 females	Not reported	9 males 10 females	16 males 8 females	9 males 6 females	11 males 14 females
(years), range	30, 20-55 Yes	01.28, 00-70 Yes	Not reported	Female: 43	40.7±8.7	LED: 50.43+9.25	31.2±2.3, 30-04
Implant type and dimensions	XiVE-S implants (Dentsply, Germany) Diameter: 3.8 mm Length: 11 mm	Self-tapping implants BlueSky [®] (Bredent, Germany) Diameter: 4 mm Length: 10 mm	DIO implants (invasive fungal infectionstissue level) with resorbable blast media surface (Korea) Dimensions not reported	DIO UF implants (Korea) Diameter: 4-4.5 mm Length: 10-11.5 mm	Superline (Dentium, Korea) Diameter: 4.5 mm Length: 10-12 mm	XiVE-S implants (Dentsply, Germany) Control diameter: 3.8 (3.5-4.5) mm Length: 11 mm LED: Diameter: 4.5 (3.8-4.5) mm Length: 11.0 (10.6-11.0)	DTI Implant Systems (Turkey) Diameter: 4-4.5 mm Length: 10 mm
Implant position	Posterior mandible	Posterior maxilla	Anterior mandible	Posterior maxilla	Posterior mandible	Not reported	Posterior mandible
Laser type and wavelength	GaAlAs 830 nm	GaAlAs 637 nm	Diode 810 nm, LED 626 nm	Diode 940 nm	Diode 635 nm	LED 626 nm	GaAlAs 830 nm
PBM parameters	86mW, CW 0.25 J, 3s/ point, 20 points 0.0028 cm ² , 3.71 W/cm ² 92.1 J/cm ² , in contact	40mW, CW, 6.26 J/cm ² per implant Noncontact (1 cm)	50mw, CW 50 mw/cm ² 20 J/cm ² In contact 185 mW, 38.5 mW/cm2, 46.2 J/cm ² Transcutaneous	100 mw, CW 354.6 mw/cm², 14.18 J/cm² In contact	100 mw, CW 0.5 cm ² 199.04 mW/cm ² 8 J/cm ² In contact	185 mW; 222 J; 20 min 38.5 mW/cm²; 46.2 J/cm² Transcutaneous	86 mW, CW 0.0028 cm2, 0.25J per point, 3.71 W/cm ² 92.1 J/cm ² , in contact
Number of applications	7	7	5	6	6	9	7
Analysis conducted	ISQ assessed by RFA	ISQ by RFA+ALP activity and early implant success rate	Implant stability By periotest + IL1β, PGE2	ISQ assessed by RFA	Implant stability By periotest & Bone Density by CBCT	ISQ by RFA and IL-1β, TGF-b, PGE2, NO levels in peri-implant crevicular fluid	ISQ assessed by RFA
Follow up Results	12 weeks No effect on implant stability	6 weeks No significant influence on osseointegration of self-tapping Implants placed into low-density bone	8 weeks Positive effect on the stability of the implants 3 weeks and no effect on the level of IL1β and PGE2 in 4 and 8 weeks	12 weeks No significant effect on dental implant stability	12 weeks PBM enhanced secondary implant stability and bone density	12 weeks Positive effect on osseointegration and implant stability In LED group, a negative correlation found between PGE2 and ISQ values	6 months Positive effect on dental implant stability

Table 2: Description of the included studies

RCT – Randomized clinical trial; LED – Light-emitting diodes; ISQ – Implant stability quotient; RFA – Resonance frequency analysis; IL-1β – Interleukin-1β; TGF-β – Transforming growth factor-β; PGE2 – Prostaglandin-E2; NO – Nitric oxide; ALP – Alkaline-phosphatase;

CBCT – Cone-beam computed tomography

Table 3: Risk-of-bias assessment of the included r	randomized clinical	trials according to	Cochrane R	lisk of Bias	Assessment Too	I

Domain	Authors						
	García-Morales et al., 2012 ^[23]	Mandić <i>et al.</i> , 2014 ^[24]	Memarian <i>et al.</i> , 2017 ^[25]	Torkzaban et al., 2018 ^[26]	Matys <i>et al.</i> , 2019 ^[27]		
Random sequence generation (selection bias)	+	+	+	+	+		
Allocation concealment (selection bias)	+	+	?	?	?		
Blinding of participants and personnel (performance bias)	+	+	?	?	?		
Blinding of outcome assessment (detection bias)	+	+	?	?	?		
Incomplete outcome data (attrition bias)	+	+	+	+	+		
Selective outcome reporting (reporting bias)	+	+	+	+	+		
Other potential threats to validity	+	+	?	+	+		
Risk of bias	Low	Low	Unclear	Unclear	Unclear		

+ - Low risk of bias; ? - Unclear risk of bias

ROBIN-I item	Study				
	Gokmenoglu et al., 2014 ^[28]	Karaca <i>et al.</i> , 2018 ^[29]			
Bias due to confounding	Moderate	Moderate			
Bias in the selection of participants	Moderate	Low			
Bias in the classification of interventions	Low	Low			
Bias due to deviations from intended interventions	Low	Low			
Bias due to missing data	Moderate	Low			
Bias in the measurement of outcomes	Moderate	Moderate			
Bias in selection of the reported result	Low	Low			
Overall bias	Moderate	Moderate			

Table	4: Risk-of-bias	assessment of	f the included	nonrandomized	clinical tria	ls with th	e ROBINS-I	too
-------	-----------------	---------------	----------------	---------------	---------------	------------	------------	-----

Outcomes

Four studies^[25,27-29] reported that PBM application had a potential positive effect on the outcome of dental implant stability. On the other hand, three studies^[23,24,26] reported no significant influence, and there were no reports of adverse or negative effects of PBM. Therefore, a significant positive influence of PBM on osseointegration clinically was not established [Table 2].

DISCUSSION

Dental implant stability depends on the implant's capacity to successfully osseointegrate, that is, successful bone-to-implant union while preserving the structural and functional integrity of the host site.[30-32] PBM is increasingly being acknowledged in the literature for its potential beneficial effects in medicine and dentistry.^[3,4,33] Experimental studies have evaluated the use of PBM to stimulate osteoblast activity in vitro and concluded that PBM enhances the stability of dental implants. Furthermore, it was found to be capable of boosting the healing process around the surgical site by increasing adenosine triphosphate synthesis and angiogenesis, in addition to increasing the proliferation of osteoblast and reducing inflammation.^[31-33] Conversely, other articles had reported contradictory results.^[34,35] Such discrepancies may be attributed to variations in the irradiation protocols and/ or the experimental models used.^[4,6,36] However, given that humans have a different and more complex biological nature than experimental models, results from in vitro and animal models may not necessarily apply clinically.^[33] Accordingly, the current systematic review was envisioned to address a focused research question related to the clinical efficacy of PBM on dental implant osseointegration and stability.

Three studies used the split-mouth study design.^[23-25] Of these, García-Morales *et al.*^[23] reported that there was no evidence of PBM influencing the dental implant stability when measured by RFA. Nonetheless, the authors attributed the high primary stability and favorable bone quality to the rigid bone–implant interface, which may have

concealed the effect of PBM. Similarly, Mandić et al.[24] also reported no positive impact on self-tapping implants' osseointegration when placed into the low-density bone of the posterior maxilla. In this study, the spot size, irradiance and exposure duration were not reported. These parameters may have influenced the results. Moreover, the distance (10 mm) between the probe and tissues may have caused significant amount of laser energy to be reflected, thereby reducing the effectiveness of LLLT or rendering it ineffective. In contrast, Memarian et al.[25] found that PBM by LLL or LED had a positive influence on dental implant stability 3 weeks post surgery. Although this study is of moderate risk of bias, its finding supports previous in vivo study on rabbit mandible, which used 830 nm wavelength at 20 J/cm² and demonstrated a significant positive effect on new bone formation around dental implants inserted in the rabbit mandible.^[8]

Research using the split-mouth design for PBM is arguable owing to its potential systemic effect.^[37-39] Nonetheless, other studies were also found in the searches that used different individuals as control groups to exclude such systemic effect.^[26-29] Karaca *et al.*^[29] used the same laser parameters previously used by García-Morales *et al.*,^[23] but in different individuals, and reported a positive influence on the healing of the bone surrounding immediately loaded implants and showed a clinically insignificant increase in implant stability. Nevertheless, the results of the later García-Morales *et al.*^[23] may be considered more reliable because of the more appropriate blinding and randomization, rendering it a high-quality study with lower risk of bias.

Gokmenoglu *et al.*^[28] also showed a positive impact of PBM on implant's osseointegration and stability. They reported that in the control group during the evaluation period, the primary stability revealed significant reduction. Conversely, an insignificant decrease in the primary stability was found in the LED group. In other words, PBM using LED may have maintained the primary implant stability. In the same vein, a more recent RCT^[27] concluded that PBM insignificantly improved secondary implant stability – measured by periotest – and significantly improved the bone density after 12 weeks at the middle and apical parts of the implant, as calculated by the cone-beam computed tomography. It is also worth noting that this study used a dose of 8 J/cm² in the contact mode, which is within the recommended therapeutic window of PBM.^[4] In contrast, Torkzaban *et al.*^[26] found that postoperative application of PBM had no significant influence on the stability of dental implants. It is worth noting that they used irradiance of 354.6 mW/cm², but the values recommended for stimulation and healing range from 5 to 50 mW/cm²;^[4] therefore, the insignificant effect may be explained by the biphasic response phenomenon.

The energy dose used in the studies included ranged from 6.2 to 92.1 J/cm², thereby reflecting an absence of uniformity in the ideal dose for PBM. Moreover, the results are heterogeneous, indicating that the effectiveness of PBM on dental implants' stability and osseointegration remains controversial. This may be due to the diversity in the parameters used: energy density, number of applications, wavelength and power. This information is of importance for readers and researchers to be able to appraise the studies' results and the specific treatment applied.

The lack of consensus on the optimal PBM protocol for dental implants osseointegration may be due to different devices and different application protocols used. In addition, the results of this review should be interpreted cautiously owing to the presence of uncontrolled factors in the included studies such as intra- and inter-subject variations; for instance, the thickness and the light absorption characteristics of the intervening tissue affect the dose delivered at the target tissue. Nevertheless, a positive insignificant influence of PBM application on implant stability was reported in four studies,^[25,27-29] which cannot be disregarded and warrants further research that controls for confounding factors to provide a clearer understanding. In addition, substantial efforts are necessary to achieve standardized clinical dosing and delivery protocols for PBM therapy to warrant the maximum efficacy and safety for PBM and allow for more conclusive studies with meta-analysis.

Regarding the impact of PBM on biomarkers and the inflammatory factors, Memarian *et al.*^[25] reported a significant decrease of both prostaglandin-E2 and interleukin-1 β after 2 months. This is a natural phenomenon due to the decline in the inflammatory processes while healing is completed. However, PBM had no impact on the level of these inflammatory markers at different time intervals compared with the control group. Their results are consistent with

those of Gokmenoglu et al.,[28] which indicates that the PBM had no influence on the inflammatory factors. A possible explanation is that the influence of PBM on these factors may be considered effective in real infectious situations such as periimplantitis and not natural healing phenomenon of inflammation, i.e. it has no effect on the cells in homeostasis.^[40] Moreover, Mandić et al.^[24] showed that there was no statistically significant difference in the alkaline-phosphatase (ALP) activity between the test and control groups at all observation points. However, the pattern of ALP activity changes over time was different. In contrast to the control group, where continuous decrease of ALP activity was recorded, in the test group, after the initial decline, an increase was observed in the 4th week. The increase in ALP activity in the laser group might be interpreted as an indication of enhanced osteoblast activity, and thus improved bone neo-formation and mineralization. This biochemical result may suggest a positive influence of PBM on osseointegration.

CONCLUSION

This systematic review found that postoperative application of PBM may have a potential positive clinical influence on dental implants' osseointegration and stability. However, there were limited number of high-quality studies in addition to the diversity in methodologies and laser parameters used. Therefore, PBM protocols need to be standardized and additional RCTs with larger sample size and less intersubject variations should be performed to confirm the effectiveness of PBM on dental implants' osseointegration and stability.

Peer review

This article was peer reviewed by three independent and anonymous reviewers.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Verma SK, Maheshwari S, Singh RK, Chaudhari PK. Laser in dentistry: An innovative tool in modern dental practice. Natl J Maxillofac Surg 2012;3:124-32.
- Sgolastra F, Petrucci A, Severino M, Gatto R, Monaco A. Lasers for the treatment of dentin hypersensitivity: A meta-analysis. J Dent Res 2013;92:492-9.
- Arany PR. Craniofacial wound healing with photobiomodulation therapy: New insights and current challenges. J Dent Res 2016;95:977-84.
- Hamblin MR. Handbook of Low-Level Laser Therapy. Singapore, Pan Stanford Publishing Pte, Ltd.; 2017.

- Carroll JD, Milward MR, Cooper PR, Hadis M, Palin WM. Developments in low level light therapy (LLLT) for dentistry. Dent Mater 2014;30:465-75.
- Chung H, Dai T, Sharma SK, Huang YY, Carroll JD, Hamblin MR. The nuts and bolts of low-level laser (light) therapy. Ann Biomed Eng 2012;40:516-33.
- Blay A, Blay CC, Tunchel S, Gehrke SA, Shibli JA, Groth EB, et al. Effects of a Low-Intensity Laser on Dental Implant Osseointegration: Removal Torque and Resonance Frequency Analysis in Rabbits. J Oral Implantol 2016;42:316-20.
- Massotti FP, Gomes FV, Mayer L, de Oliveira MG, Baraldi CE, Ponzoni D, *et al.* Histomorphometric assessment of the influence of low-level laser therapy on peri-implant tissue healing in the rabbit mandible. Photomed Laser Surg 2015;33:123-8.
- Mayer L, Gomes FV, Carlsson L, Gerhardt-Oliveira M. Histologic and resonance frequency analysis of peri-implant bone healing after low-level laser therapy: An *In vivo* study. Int J Oral Maxillofac Implants 2015;30:1028-35.
- Mayer L, Gomes FV, de Oliveira MG, de Moraes JF, Carlsson L. Peri-implant osseointegration after low-level laser therapy: Micro-computed tomography and resonance frequency analysis in an animal model. Lasers Med Sci 2016;31:1789-95.
- Kim YD, Kim SS, Hwang DS, Kim SG, Kwon YH, Shin SH, et al. Effect of low-level laser treatment after installation of dental titanium implant-immunohistochemical study of RANKL, RANK, OPG: An experimental study in rats. Lasers Surg Med 2007;39:441-50.
- 12. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. Int J Surg 2010;8:336-41.
- Higgins JP, Green S. Cochrane Handbook for Systematic Reviews of Interventions. Chichester: Wiley-Blackwell; 2009.
- CvfcSterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, *et al.* ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions. BMJ 2016;355:i4919.
- Sleem SS, Zayet MK, El-Ghareeb TI, Saleh HA. Evaluation of the bio-stimulatory effect of platelet rich fibrin augmented by diode LASER compared to platelet rich fibrin alone on dental implant replacing posterior mandibular teeth. Randomised Clinical Trial: Split Mouth Study. Open Access Maced J Med Sci 2019;7:869-75.
- Flieger R, Gedrange T, Grzech-Leśniak K, Dominiak M, Matys J. Low-level laser therapy with a 635 nm diode laser affects orthodontic mini-implants stability: A randomized clinical split-mouth trial. J Clin Med 2019;9:1-11.
- Marañón-Vásquez GA, Lagravère MO, Borsatto MC, de Souza SS, Watanabe PC, Matsumoto MA, *et al.* Effect of photobiomodulation on the stability and displacement of orthodontic mini-implants submitted to immediate and delayed loading: A clinical study. Lasers Med Sci 2019;34:1705-15.
- Arakeeb MA, Zaky AA, Harhash TA, Salem WS, El-Mofty M. Effect of combined application of growth factors and diode laser bio-stimulation on the osseointegration of dental implants. Open Access Maced J Med Sci 2019;7:2520-7.
- Abohabib AM, Fayed MM, Labib AH. Effects of low-intensity laser therapy on the stability of orthodontic mini-implants: A randomised controlled clinical trial. J Orthod 2018;45:149-56.
- Mikhail FF, El-Din M, Ibrahim T, Zekry K, Nemat A, Nasry S. Effect of laser therapy on the osseointegration of immediately loaded dental implants in patients under vitamin C, Omega-3 and calcium therapy. Open Access Maced J Med Sci 2018;6:1468-74.
- Awad SM, Mounir RM, Dine E, Salah M, Nasry SA. Effect of laser irradiation on bony implant sites in diabetic patients: A preliminary study. Res J Pharm Biol Chem Sci 2017;8:1484-95.
- 22. Yanaguizawa MS, Suzuki SS, Martinez EF, Suzuki H, Pelegrin MC, Garcez AS. Effects of low-level laser therapy in orthodontic patients on immediate inflammatory response after mini-implants insertion: A preliminary report. Photomed Laser Surg 2017;35:57-63.

- García-Morales JM, Tortamano-Neto P, Todescan FF, de Andrade JC Jr., Marotti J, Zezell DM. Stability of dental implants after irradiation with an 830-nm low-level laser: A double-blind randomized clinical study. Lasers Med Sci 2012;27:703-11.
- 24. Mandić B, Lazić Z, Marković A, Mandić B, Mandić M, Djinić A, et al. Influence of postoperative low-level laser therapy on the osseointegration of self-tapping implants in the posterior maxilla: A 6-week split-mouth clinical study. Vojnosanit Pregl 2015;72:233-40.
- 25. Memarian J, Ketabi M, Amini S. The effect of low-level laser 810 nm and light-emitting diode photobiomodulation (626 nm) on the stability of the implant and inflammatory markers interleukin-1 beta and prostaglandin E2, around implants. Dent Res J 2018;15:283-8.
- Torkzaban P, Kasraei S, Torabi S, Farhadian M. Low-level laser therapy with 940 nm diode laser on stability of dental implants: A randomized controlled clinical trial. Lasers Med Sci 2018;33:287-93.
- Matys J, Świder K, Grzech-Leśniak K, Dominiak M, Romeo U. Photobiomodulation by a 635nm diode laser on peri-implant bone: Primary and secondary stability and bone density analysis-a randomized clinical trial. Biomed Res Int 2019;2019:1-8.
- Gokmenoglu C, Ozmeric N, Erguder I, Elgun S. The effect of light-emitting diode photobiomodulation on implant stability and biochemical markers in peri-implant crevicular fluid. Photomed Laser Surg 2014;32:138-45.
- Karaca IR, Ergun G, Ozturk DN. Is Low-level laser therapy and gaseous ozone application effective on osseointegration of immediately loaded implants? Niger J Clin Pract 2018;21:703-10.
- Raghavendra SJ, Dhinakarsamy V. Osseointegration. J Pharm Bioallied Sci 2015;7:S226-9.
- 31. Bengtson AL, Bengtson NG, Bengtson CR, Mendes FM, Pinheiro SR. Histological and radiographic evaluation of the muscle tissue of rats after implantation of bone morphogenic protein (rhBMP-2) in a scaffold of inorganic bone and after stimulation with low-power laser light. Indian J Dent Res 2010;21:420-4.
- 32. Khadra M, Kasem N, Lyngstadaas SP, Haanaes HR, Mustafa K. Laser therapy accelerates initial attachment and subsequent behaviour of human oral fibroblasts cultured on titanium implant material. A scanning electron microscope and histomorphometric analysis. Clin Oral Implants Res 2005;16:168-75.
- Tang E, Arany P. Photobiomodulation and implants: Implications for dentistry. J Periodontal Implant Sci 2013;43:262-8.
- 34. Jakse N, Payer M, Tangl S, Berghold A, Kirmeier R, Lorenzoni M. Influence of low-level laser treatment on bone regeneration and osseointegration of dental implants following sinus augmentation. An experimental study on sheep. Clin Oral Implants Res 2007;18:517-24.
- Dörtbudak O, Haas R, Mailath-Pokorny G. Effect of low-power laser irradiation on bony implant sites. Clin Oral Implants Res 2002;13:288-92.
- Bashardoust Tajali S, Macdermid JC, Houghton P, Grewal R. Effects of low power laser irradiation on bone healing in animals: A meta-analysis. J Orthop Surg Res 2010;5:1-11.
- Hopkins JT, McLoda TA, Seegmiller JG, David Baxter G. Low-level laser therapy facilitates superficial wound healing in humans: A triple-blind, sham-controlled study. J Athletic Training 2004;39:223.
- Byrnes KR, Waynant RW, Ilev IK, Wu X, Barna L, Smith K, et al. Light promotes regeneration and functional recovery and alters the immune response after spinal cord injury. Lasers Surg Med 2005;36:171-85.
- Weber JB. Effect of three different protocols of low-level laser therapy on thyroid hormone production after dental implant placement in an experimental rabbit model. Photomed Laser Surg 2014;32:11-8.
- 40. Yaghobee S, Khorsand A, Rasouli Ghohroudi AA, Sanjari K, Kadkhodazadeh M. Assessment of interleukin-1beta and interleukin-6 in the crevicular fluid around healthy implants, implants with peri-implantitis, and healthy teeth: A cross-sectional study. J Korean Assoc Oral Maxillofac Surg 2014;40:220-4.