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The Effect of Photobiomodulation on Temporomandibular Pain and Functions in Patients With Temporomandibular Disorders: An Updated Systematic Review of the Current Randomized Controlled Trials

Nima Farshidfar[1#], Golnoush Farzinnia[2#], Nazafarin Samiraninezhad[3#], Sahar Assar[4#], Parsa Firoozi[5], Fahimeh Rezazadeh[6*], Neda Hakimiha[7*]

[1]Orthodontic Research Center, School of Dentistry, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Oral and Dental Disease Research Center, School of Dentistry, Shiraz University of Medical Sciences, Shiraz, Iran
[3]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran
[4]Section for Oral Ecology and Caries Control, Department of Dentistry and Oral Health, Aarhus University, Aarhus, Denmark
[5]School of Dentistry, Zanjan University of Medical Sciences, Zanjan, Iran
[6]Oral and Dental Disease Research Center, Department of Oral and Maxillofacial Medicine, School of Dentistry, Shiraz University of Medical Sciences, Shiraz, Iran
[7]Laser Application in Medical Sciences Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

***Correspondence to**
Fahimeh Rezazadeh,
Email: rezazadehf@sums.ac.ir
and Neda Hakimiha,
Email: ned.hakimiha@gmail.com

[#]These authors contributed equally to this work.

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Abstract

Introduction: Temporomandibular disorders (TMDs) are the most prevalent non-dental origin orofacial pain conditions affecting the temporomandibular joints (TMJs) and/or orofacial muscles. Photobiomodulation therapy (PBMT) is a conservative way to improve function and reduce symptoms in TMD patients. This systematic review was conducted to update evidence about the effects of PBMT on pain intensity, TMJ movements, electromyography (EMG) activity, pressure pain threshold (PPT), and TMJ sound in patients with TMDs.

Methods: A systematic literature search was conducted in Web of Science, PubMed/Medline, and Scopus databases using appropriate keywords and specific strategies from January 2000 to September 2022. Data extraction was done based on the inclusion/exclusion criteria.

Results: A total of 40 studies were included. All included studies except one provided information on pain intensity; 27 studies showed a reduction in pain intensity in PBMT groups compared to control groups. Seven out of 15 studies, which reported maximum mouth opening (MMO), showed a greater MMO in PBMT groups than in placebo groups. In addition, the figures for passive maximum mouth opening (PMMO) and active maximum mouth opening (AMMO) in all the studies reporting PMMO and AMMO were higher in PBMT groups. In eight out of ten studies, lateral movement (LM) was greater in PBMT groups. Moreover, in three studies out of four, protrusive movement (PM) was reported to be greater in the PBMT group. Four out of nine studies showed a greater PPT in the PBMT group. Reduced TMJ sounds in the PBMT group were reported in two out of five studies. In addition, in most studies, no difference in EMG activity was detected between the two groups.

Conclusion: This updated systematic review showed the promising effects of PBMT on the alleviation of pain and improvement in MMO. Using the infrared diode laser with a wavelength ranging between 780-980 nm, an energy density of <100 J/ cm^2, and an output power of ≤ 500 mW for at least six sessions of treatment seems to be a promising option for treating mentioned TMDs signs and symptoms based on the previously reported findings.

Keywords: Temporomandibular joint; Temporomandibular joint disorders; Low-level light therapy; Temporomandibular joint disk.

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Introduction

Temporomandibular disorders (TMDs) are the most prevalent non-dental origin orofacial pain conditions influencing the temporomandibular joints (TMJs), orofacial muscles, or both.[1,2] A recent epidemiological review[2] showed that the prevalence of TMDs is higher among people in the 25-45 age range. Moreover, women are more affected, and psychosocial problems cause higher prevalence and greater intensity of TMD symptoms. The significant clinical signs and symptoms of TMDs are muscle/TMJ pain, TMJ sounds, limitation, deviation, or deflection of mandibular movements.[3]

Studies have shown that only a few percent of TMD patients need treatment, and almost half have spontaneous resolution of symptoms.[4] Due to the multifactorial etiology of TMDs, a wide range of multidisciplinary therapies are required for the management of this group of patients.[4,5] Pain and dysfunction in most cases are alleviated by a combination of non-invasive therapies, including pharmacotherapy, acupuncture, physical therapy, occlusal devices, relaxation techniques, cognitive behavior therapy, passive stretching, self-care, and patient education.[6] Muscle relaxants and nonsteroidal anti-inflammatory drugs are among the medications that are recommended initially.[4] Moreover, in chronic cases of TMD, benzodiazepines or antidepressants are among the prescribed medications.[4,6] Surgical approaches are only indicated in patients without any improvement following conservative treatments after at least six months and those with severe disability.[6]

In dentistry, Light Amplification by Stimulated Emission of Radiation (LASER) is regarded as one of the latest treatments successfully used in practice to treat hard and soft tissue diseases in the last few years.[7-9] Low-level laser therapy (LLLT), recently named photobiomodulation therapy (PBMT), which has been indicated to have bio-stimulating and analgesic effects without making a thermal response, is considered a conservative way to improve function and reduce symptoms in TMD patients.[9] It has also been shown that PBMT has an anti-inflammatory effect due to the light absorption in intracellular photo-acceptors and modulation of cell responses.[10,11] PBMT increases the blood microcirculation, vascularization, and proliferation of the fibroblasts cells, ATP production, as well as reducing edema and the level of cyclooxygenase-2 (COX-2) and prostaglandin E2 (PGE2) as a result of increased lymphatic flow.[11,12] In addition, PBMT has no serious reported side effects.[11] The most applicable wavelengths used in PBMT are between 600-1000 nm.[11,13] Despite all the mentioned positive effects, it is critical to clinically evaluate the impact of PBMT on TMDs.[9]

Recently, a few systematic reviews with or without meta-analysis have been conducted to demonstrate the effect of PBMT on TMDs.[14,15] A meta-analysis in 2014 showed the limited efficacy of PBMT in reducing pain.[15] In contrast, another meta-analysis in 2018 indicated that PBMT could effectively relieve pain in TMD patients.[14] However, both of these studies[14,15] showed that PBMT could significantly improve function in TMD patients. Moreover, a recent meta-analysis in 2022,[16] manifested beneficial effects of PBMT on mandibular movements, especially on the extent of mouth opening. However, in this study,[16] the effect of PBMT on masticatory function was indefinite. Other systematic reviews in recent years have also considered PBMT as an effective approach for the treatment of temporomandibular myofascial pain.[17-19] Nevertheless, previous results are not definite due to the lack of enough included studies,[15,17,19] a limited number of involved subjects in randomized controlled trials (RCTs),[18] and assessed parameters.[15,18]

Considering the lately published RCTs, this systematic review was conducted to update data evidence and reevaluate the effects of PBMT on pain intensity, maximum mouth opening (MMO), lateral movements (LM), protrusive movement (PM), pressure pain threshold (PPT), electromyography (EMG) activity, and TMJ sounds in patients with TMDs.

Materials and Methods

Protocol Development

This systematic review was conducted in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[20,21]

Eligibility Criteria

Table 1 depicts the eligibility criteria regarding participants, intervention, comparison, outcomes, and study design (PICOS). All prospective published or unpublished RCTs involving patients with a diagnosis of TMD in which PBMT was compared to a placebo or sham photobiomodulation (PBM) intervention were considered for inclusion. No age or gender limitations were applied to the inclusion criteria. Studies without any placebo/sham groups or studies that involved patients with systemic diseases or those experiencing pain unrelated to TMD were excluded from our review. Articles in languages other than Persian or English were also excluded from our review.

Information Sources and Search Strategy

We searched PubMed/Medline, Scopus, and Web of Science electronic databases from January 2000 to September 2022. We also reviewed the reference list of the relevant studies as a complementary search.

We searched the databases, as mentioned earlier using the following combination of free-text terms:

(“temporomandibular disorder” OR “TMD” OR “temporomandibular joint disorder” OR “temporomandibular joint dysfunction” OR “TMJ

Table 1. Eligibility criteria for the present systematic review.

Domain	Inclusion Criteria	Exclusion Criteria
Participants	- Patients with a diagnosis of TMD	- Patients with systemic diseases or pain unrelated to TMD
Intervention	- Local application of PBM on TMJ area and its related muscles	- Local or systemic application of other treatment modalities rather than PBM - Simultaneous application of PBMT and other treatment modalities
Comparison	- Placebo or sham PMB intervention	- No placebo or sham PBM intervention
Outcome	- Qualitative or quantitative data regarding the pain intensity, TMJ movements, EMG activity, PPT, and TMJ sounds.	-
Study Design	- RCTs	- In-vitro studies, ex-vivo studies, in-vivo studies, case reports/series, letters to the editor, short communications, non-comparative studies, narrative reviews, and systematic reviews with or without meta-analysis

disorder" OR "temporomandibular joint pain" OR "temporomandibular pain" OR "TMJ pain" OR "temporomandibular osteoarthritis" OR "myofascial pain syndrome" OR "MPDS" OR "craniomandibular disorder" OR "mandibular dysfunction") AND ("laser" OR "laser therapy" OR "photobiomodulation" OR "photobiomodulation therapy" OR "low-level laser therapy" OR "LLLT" OR "low-intensity laser therapy" OR "LILT" OR "low energy laser therapy" OR "LELT" OR "infrared laser" OR "IR laser" OR "diode laser")

Study Selection, Data Collection, and Measurements

Five authors (N.F, G.F, N.S, S.A, and P.F) independently screened the titles and abstracts and excluded the articles that did not meet the inclusion criteria. Afterward, the same authors reviewed the full texts and extracted the data independently. Another two authors (F.R and N.H) resolved the disagreements. The following data were extracted for each study: Study ID, treatment-related information, and relevant clinical outcome.

The primary outcome was any change in pain intensity based on the visual analog scale (VAS). The secondary outcomes included any changes in TMJ functions, including TMJ movements, EMG activity, PPT, and TMJ sounds. All parameters were measured between placebo and PBMT groups from the baseline to the last treatment session and after the follow-up session.

TMJ movements were evaluated in terms of passive maximum mouth opening (PMMO), active maximum mouth opening (AMMO), PM, and LM expressed in millimeters.

Quality Assessment

Five authors (N.F, G.F, N.S, S.A, and P.F) independently conducted the quality assessment of the included studies and the data extraction process via the modified Jadad scale,[22,23] and conflicts between authors were settled. From a maximum of eight points, papers with four or more points were regarded as "high quality," whereas studies achieving below four scores were regarded as "low quality."

Results

Characteristics of the Studies

Overall, the primary search strategy generated 1544 articles. After removing the duplicate papers, 1057 articles remained to evaluate titles and abstracts. After the removal of 951 articles, a total of 106 articles were assessed for eligibility. Sixty-six articles were excluded due to inconsistencies with our exclusion criteria. Finally, 40 articles were eligible for data extraction (Figure 1). A summary of the included studies is presented in Table 2.[1,24-62] The sample size of the included studies ranged from 14 to 202.

Age and Gender Distribution

A total of 1927 patients were included in the data synthesis. Within the studies that reported the participants' age, the overall age ranged between 8 to 76 years. Eight studies[3,9,15,16,19,30,33,35] did not report the participants' age. The overall male/female ratio of the participants was 1:4.02.

PBM Irradiation Parameters

Wavelength

The type of light source was different among the studies. Thirty-six studies used diode lasers[1,24-27,29-37,39-42,44-46,48-53,55-60,63,64] with different wavelengths, including 635 nm,[56] 640 nm,[52,57] 660 nm,[33,65] 780 nm,[25,26,30,32,37,38,48,50,53,59] 795 nm,[40] 808 nm,[42,45,54,58] 810 nm,[1,41,44,49,51,60] 820 nm,[39,46,62] 830 nm,[27,34,36] 875 nm,[52,57] 890 nm,[33] 904 nm,[24,29] 905 nm,[52,57] 910 nm,[35] 940 nm,[55] and 980 nm.[31] Moreover, some other studies used a neodymium-doped yttrium aluminum garnet (Nd: YAG, 1064 nm) laser,[43,49] a helium-neon (HeNe, 632 nm) laser,[28,47,61] and also a combination of a diode laser (905 nm) with an LED (640 and 875 nm).[52,57]

Mode of Irradiation

The irradiation mode in the majority of the studies was continuous. Only ten studies[24,31,35,41,44,45,49, 52,57,58] reported using pulsed laser irradiation. Different frequencies or pulse repetition rates of 15000 Hz,[58] 1500 Hz,[41,44,45] 1000 Hz,[24,52,57] 80 Hz,[31] and 10 Hz[49] were used in these studies.

Energy/Energy Density

Among the studies, laser energy density ranged from 0.9 J/cm² to 300 J/cm². Energy density in twenty studies[24,25,28,29,33,36,40,41,43,44,46,47,49-51,56,58-60,62] was reported

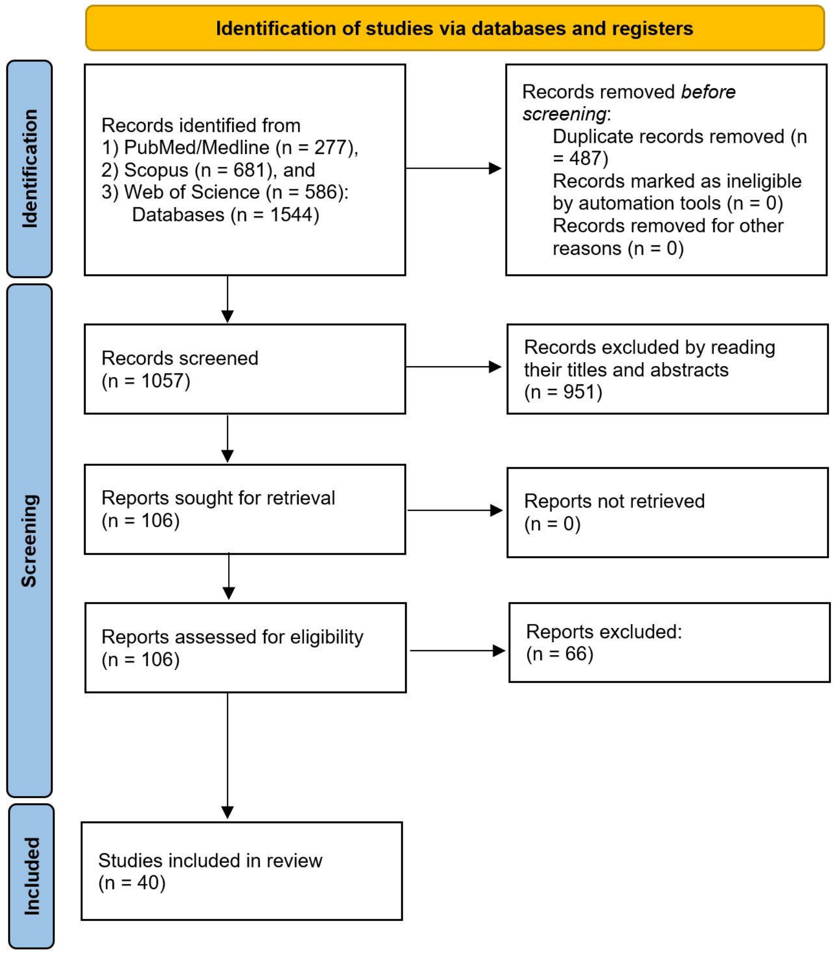

Figure 1. PRISMA 2020 Flowchart

below 10 J/cm² in 13 studies[1,26,27,32,34,37-39,42,48,53,54,57] were between 19 to 100 J/cm², and in five studies[30,32,38,39,55] was over 100 J/cm². Moreover, laser energy in eight studies[27,29,31,39,41,42,44,52] was reported below 10 J, and in three studies[39,45,58] was over 10 J.

Power/Power Density

Among the studies, laser power density varied from 0.38 mW/cm² to 2500 mW/cm². Also, laser power ranged from 0.9 mW to 500 mW, but in most studies, it was reported to be from 10 mW to 100 mW. Moreover, in eleven studies,[1,27,35,39,43,45,46,49,56,58,62] power was over 100 mW. Three studies did not disclose laser power.[31,47,55]

Time of Irradiation

The time of laser treatment in the studies ranged from 9 seconds to 15 minutes in each treatment session.

Number of Treatment Session(s), Treatment Frequency, and Follow-up Sessions

An overall range of 1 to 20 treatment sessions was given to patients, and the number of treatment session(s) per week ranged from 1 to 7 days. Moreover, the frequency of follow-up sessions varied from one day to 12 months after the last treatment session.

Site of PBMT Application

The TMJ and/or the afflicted muscles were the main laser application points in all RCTs. In 14 RCTs, laser treatment was particularly applied on the TMJ.[25,26,28-30,35,36,43,45,49,58,61,64,65] In addition, 15 RCTs[32-34,37,40-43,46-48,52,55,57,66] focused on the application of laser on muscles (temporalis, masseter, and pterygoid muscles) only. Regardless of whether they were the points of most significant discomfort, laser application was made at pre-determined sites in most investigations.

Assessment Methods

All of the included studies provided information on pain intensity except one.[48] Fifteen RCTs evaluated MMO,[1,25,34,36,38,40,41,44,46,50-52,54,57,61] two evaluated AMMO and PMMO,[35,60] ten evaluated LM,[1,24,25,34,36,38,46,54,60,61] four evaluated PM,[1,25,38,46] nine evaluated PPT,[25,39,40,42,46,50,52,53,60,64] five evaluated EMG activity,[37,39,40,48,52] and five evaluated sounds of TMJ.[24,31,34,44,51]

Twenty-seven studies out of 39 showed a reduction in pain intensity in the PBMT groups in comparison with the control groups.[1,24,26,29-31,33-38,40-43,45-47,49,52,55-58,60,61] Among

Table 2. Characteristics of the Included Studies

Study	Total No. of Patients	F/M	Laser	Placebo	Age (Range)	Laser Type	Wavelength (nm)	Energy (J)/ Energy Density (J/cm²)	Power (mW)/ Power density (mW/ cm²)	Mode of Irradiation	Application Site	Treatment time/ number of total sessions/ number of sessions per week	Evaluations	Main Parameters Evaluation	Overall Outcome	Modified Jadad Score
Kulekcioglu et al [24]	35	28/7	20	15	37.0 ± 12.3 (20-59)	Diode (GaAs)	904	NR/3	17/NR	Pulse (1000 Hz)	TMJ and muscles (tender point)	180s/15/ NR	Before, immediately after, and one month after treatment	VAS, AMMO, PMMO LM, TMJ sounds	VAS: PBMT< Placebo AMMO, PMMO, LM: PBMT > Placebo TMJ sounds: PBMT = Placebo	5
de Abreu Venancio et al [25]	30	25/5	15	15	L:34.9 P:37.6 (13-63)	Diode (GaAlAs)	780	NR/6.3	30/NR	CW	TMJ	10s/6/2	Before the 1st, 3rd, and 5th treatment sessions, and at the follow-up appointments after 15, 30, and 60 days after the last application	VAS, MMO, LM, PM, PPT	All parameters: PBMT = Placebo	2
Mazzetto et [26]	48	NR	24	24	NR	Diode (GaAlAs)	780	NR/89.7	70/NR	CW	TMJ	10s/8/2	Before the treatment, after the 4th and 8th sessions, and one month after the last application	VAS	PBMT < Placebo	6
Da Cunha et al [27]	40	39/1	20	20	L:40.15 P:46.6 (20-68)	Diode (GaAlAs)	830	4/100	500/NR	CW	TMJ and muscles	20s/4/1	Before the treatment and after the last session	VAS	PBMT = Placebo	4
Emshoff et al [28]	52	42/10	26	26	L:44.1 ± 16.6 P:41.8 ± 11.2 (18-58)	HeNe	632.8	NR/1.5	30/NR	NR	TMJ	2min/20/2-3	Before the treatment, and on the 2nd, 4th, and 8th weeks after the first session	VAS	PBMT = Placebo	8
Frare et al [29]	18	18/0	10	8	27 ± 7 (18-45)	Diode (GaAs)	904	6/6	15/0.38	CW	TMJ	16s/8/2	Before the treatment and after all sessions	VAS	PBMT < Placebo	5
Carrasco et al [30]	14	NR	7	7	NR	Diode (GaAlAs)	780	NR/105	70/NR	CW	TMJ	60s/8/2	Before the treatment, after the 8th session, and one month after the last application	VAS	PBMT < Placebo	5
Lassemi et al[31]	48	24/24	26	22	L:8.6 ± 8.37 P:33 ± 9	Diode (GaAs)	980	Muscle: 1.5/ NR TMJ: 2/NR	NR/NR	Pulse (80 Hz)	TMJ and trigger points of adjacent muscles	60s/2/2	Before the treatment, and after the 2nd session, and four days, six months, 12 months after the last application	VAS, TMJ sounds	All parameters: PBMT < Placebo	4

Table 2. Continued.

Study	Total No. of Patients	F/M	Laser	Placebo	Age (Range)	Laser Type	Wavelength (nm)	Energy (J)/ Energy Density (J/cm²)	Power (mW)/ Power density (mW/ cm²)	Mode of Irradiation	Application Site	Treatment time/ number of total sessions/ number of sessions per week	Evaluations	Main Parameters Evaluation	Overall Outcome	Modified Jadad Score
Carrasco et al[32]	60	NR	G1:10 G2:10 G3:10	G1′:10 G2′:10 G3′:10	NR	Diode (GaAlAs)	780	G1:NR/25 G2:NR/60 G3:NR/105	G1:50/NR G2:60/NR G3:70/NR	NR	Muscles (anterior masseter and anterior temporalis)	60s/8/2	Before treatment, after the 4th and 8th sessions, and 15 days and one month after the last application	VAS	PBMT = Placebo	6
Shirani et al[33]	16	12/4	8	8	23.8	Diode G1:In-Ga-Al-P G2:GaAs	G1:660 G2:890	G1:NR/6.2 G2:NR/1	G1:17.3/17.3 G2:9.8/9.8	CW	Muscles (medial and lateral pterygoid)	G1:6min/6/2 G2:10min/6/2	Before and immediately after the treatment, one week after, and on the day of complete pain relief.	VAS	PBMT < Placebo	7
de Santana et al[34]	50	NR	25	25	NR	Diode (GaAlAs)	830	NR/80	40/NR	NR	Muscles	16s/1/ NR	Before the treatment and after the first week	VAS, MMO, LM TMJ sounds	VAS, TMJ sounds: PBMT < Placebo MMO, LM: PBMT > Placebo	4
Marini et al[35]	69*	L:28/11 P:22/8	39	30	L:41.93 ± 11.51 P:36.23 ± 11.30 (15-50)	Diode (GaAs)	910	NR/NR	400/NR	Pulse G1:220 kHz G2: 18 kHz G3: 16 kHz	TMJ	20 kHz for 10 min, 18 kHz for 5 min, 16 kHz for 5 min/10/5	Before the treatment, after the 2nd, 5th, 10th, and 15th and 30th session	VAS	PBMT < Placebo	6
Mazzetto et al[36]	40	NR	20	20	NR	Diode GaAlAs	830	NR/5	40/NR	CW	TMJ	10s/8/2	Before, immediately after the treatment, and seven days and 30 days after the treatment	VAS, LM, MMO	VAS: PBMT < Placebo LM, MMO: PBMT > Placebo	6
Venezian et al[37]	48	43/5	G1:12 G2:12	G1′:12 G2′:12	41.58 (18-60)	Diode GaAlAs	780	G1:NR/25 G2:NR/60	G1:50/NR G2:60/NR	CW	Muscles (temporalis and masseter)	G1:20s/8/2 G2:40s/8/2	Before the treatment, immediately after the treatment, and 30 days after treatment for VAS	VAS, EMG	VAS: PBMT < Placebo EMG: PBMT = Placebo	5
da Silva et al[38]	45	30/15	G1:15 G2:15	15	39.7 (25-53)	Diode GaAlAs	780	G1:NR/52.5 G2:NR/105	70/NR	CW	TMJ and muscles (masseter and anterior temporalis)	G1:30s/10/2 G2:60s/10/2	Before the treatment, and after the 1st, 5th, and 10th sessions and 32 days after the last application	VAS, MMO, LM, PM	VAS: PBMT < Placebo MMO, LM, PM: PBMT > Placebo	5

Table 2. Continued.

Study	Total No. of Patients	F/M	Laser	Placebo	Age (Range)	Laser Type	Wavelength (nm)	Energy (J)/ Energy Density (J/cm²)	Power (mW)/ Power density (mW/cm²)	Mode of Irradiation	Application Site	Treatment time/ number of total sessions/ number of sessions per week	Evaluations	Main Parameters Evaluation	Overall Outcome	Modified Jadad Score
Sattayut et al[39]	30	30/0	G1:10 G2:10	10	35 ± 9 (20-50)	Diode GaAlAs	820	G1:4/21.4 G2:20/107	G1:60/NR G2:300/NR	NR	TMJ and muscles	NR/3/1	Before the treatment, and after the 1, 3, 5, and 8 days after treatment	VAS, PPT, EMG	PPT and EMG: G1: PBMT = Placebo G2: PBMT > Placebo VAS: G1: PBMT = Placebo G2: PBMT > Placebo	7
Uemoto et al[40]	21*	21/0	7	7	(20-52)	Diode	795	NR/4 and 8	80/NR	NR	Muscles (masseter)	NR/4/NR	Before the treatment and after the last session	VAS, MMO, PPT, EMG	VAS: PBMT < Placebo (4, 8 J/cm²) MMO and EMG: PBMT = Placebo (4, 8 J/cm²) PPT: PBMT > Placebo (4 J/cm²) PBMT = Placebo (8 J/cm²)	5
Ahrari et al[41]	20	20/0	10	10	35.5	Diode GaAlAs	810	6/3.4	50/NR	Pulse (1500 Hz)	Muscles (masseter, temporalis, and medial pterygoid)	120s/12/3	Before the treatment, after the 6th and last sessions, and one month after the last application	VAS, MMO	VAS: PBMT < Placebo MMO: PBMT > Placebo	6
de Moraes Maia et al[42]	21	19/2	12	9	27.76 ± 10.44	Diode GaAlAs	808	1.9/70	100/NR	CW	Muscles (Masseter and anterior temporalis	19s/8/2	Before the treatment, after the last session, and 30 days after the last application	VAS, PPT	VAS: PBMT < Placebo PPT: PBMT > Placebo	5
Demirkol et al[43]	30*	NR	10	10	NR	Nd:YAG	1064	NR/8	250/NR	CW	Muscles (Masseter)	20s/10/5	Before the treatment, after the last session, and three weeks after the last application	VAS	PBMT < Placebo	4
Madani et al[44]	20	NR	10	10	NR	Diode GaAlAs	810	6/3.4	50/NR	Pulse (1500Hz)	TMJ and muscles (Masseter, temporalis and medial pterygoid)	120s/12/3	Before the treatment, after the 6th and 12th sessions, and one month after the last session	VAS, MMO, and TMJ sounds	All parameters: PBMT = Placebo	6
Fornaini et al[45]	24	19/5	12	12	(17-64)	Diode GaAlAs	808	14.4/NR	250/NR	Pulse (1500Hz)	TMJ	15min/14/7	Before the treatment and one and two weeks after the last session	VAS	PBMT < Placebo	5

Table 2. Continued.

Study	Total No. of Patients	F/M	Laser	Placebo	Age (Range)	Laser Type	Wavelength (nm)	Energy (J)/ Energy Density (J/cm²)	Power (mW)/ Power density (mW/ cm²)	Mode of Irradiation	Application Site	Treatment time/ number of total sessions/ number of sessions per week	Evaluations	Main Parameters Evaluation	Overall Outcome	Modified Jadad Score
Sancakli et al[46]	30	21/9	G1:10 G2:10	10	39.2 ± 2.8	Diode GaAs	820	NR/3	300/NR	CW	Muscles (Masseter and temporalis)	10s/12/3	Before the treatment and after the last session	VAS, MMO, LM, PM, PPT	VAS: PBMT < Placebo MMO, LM, PM PPT: PBMT > Placebo	7
Ghanjal et al[47]	142*	120/22	71	71	L:35.3 ± 2.4 P:34.2 ± 4.5 (10-61)	He-Ne	632.8	NR/2.5	NR/NR	NR	Muscles	15min/12/3	Before the treatment and after the last session	VAS	PBMT < Placebo	7
de Godoy et al[48]	16	NR	9	7	(14-23)	Diode GaAlAs	780	NR/25	50/1.25	CW	Muscles (Masseter and anterior temporalis)	20s/12/2	Before the treatment and after the last session	EMG	PBMT = Placebo	6
Demirkol et al[49]	46	23/23	G1:15 G2:16	G′: 15	G1:36.6 ± 14.7 G2:40.1 ± 14.6 G′:37.7 ± 13.8 (13-65)	G1:Nd: YAG G2:Diode laser	G1:1064 G2:810	NR/8	250/NR	Pulse (10 Hz)	TMJ	20s (Nd:YAG), 9s (Diode)/10/5	Before, immediately after, and one month after the treatment	VAS	PBMT < Placebo	4
Magri et al[50]	61*	91/0	31	30	L: 38.45 ± 12.56 P: 38.67 ± 11.18	Diode GaAlAs	780	Muscles: NR/5 TMJ: NR/7.5	Muscles: 20/ NR TMJ: 30/NR	CW	TMJ and Muscles (Masseter and Anterior temporalis)	10s/8/2	Before the treatment and after each session, and 30 days after the last application	VAS, PPT	All parameters: PBMT = Placebo	7
Shobha et al[51]	40	NR	20	20	L:30.85 ± 6.31 P:27.55 ± 4.58 (18-40)	Diode GaAlAs	810	NR/6	100/NR	CW	TMJ and Muscles	60s/8/2	Before and one month after the treatment	VAS, MMO, and TMJ sound	All parameters: PBMT = Placebo	7
Herpich et al[52]	60	60/0	G1:15 G2:15 G3:15	15	(18-40)	G1: Super-pulsed diode laser G2: Infrared LED G3: Red LED	G1:905 G2:640 G3:875	G1:2.62/NR G2:5.24/NR G3:7.86/NR	G1:0.9/NR G2:15/NR G3:17.5/NR	Pulse (1000 Hz)	Muscles (Temporalis and Masseter)	G1:20s/1/1 G2:40s/1/1 G3:60s/1/1	Before the treatment, and 1 and 2 days after treatment	VAS, MMO, PPT, EMG	VAS: PBMT < Placebo Other parameters: PBMT = Placebo	8
Rodrigues et al[53]	78*	78/0	30	29	31.94 ± 9.57 (18-60)	Diode GaAlAs	780	Muscles: NR/30 TMJ: NR/75	50, 60, and 70/NR	CW	TMJ and Muscles (Masseter and Anterior temporalis)	Muscles: 20s/8/2 TMJ: 50s/8/2	Before the treatment, after the last session, and 30 days after the last application	VAS	PBMT = Placebo	7
De Oliveira Chami et al[54]	18	13/5	10	8	(18-60)	Diode GaAlAs	808	NR/80	100/NR	CW	Pain points during palpation	22s/2/2	Before and after each treatment session, and 7 and 30 days after the first application	VAS, MMO, LM	MMO: PBMT > Placebo VAS, LM: PBMT = Placebo	6
Nadershah et al[55]	202	110/92	108	94	33.3 ± 10.7	Diode -	940	NR/300	NR/2500	CW	Muscles (Masseter and Temporalis)	120s/NR/NR	Before the treatment, and 2, 4, 6, 8, and 10 days after treatment	VAS	PBMT < Placebo	4

Table 2. Continued.

Study	Total No. of Patients	F/M	Laser	Placebo	Age (Range)	Laser Type	Wavelength (nm)	Energy (J)/ Energy Density (J/cm²)	Power (mW)/ Power density (mW/ cm²)	Mode of Irradiation	Application Site	Treatment time/ number of total sessions/ number of sessions per week	Evaluations	Main Parameters Evaluation	Overall Outcome	Modified Jadad Score
Monteiro et al[56]	42	32/10	22	20	27.4 ± 9.71	Diode	635	NR/8	200/400	CW	Sensitive points	20s/4/1	Before and one month after the treatment	VAS	PBMT < Placebo	7
Herpich et al[57]	30	30/0	15	15	L:25.44 ± 5.76 P:26.55 ± 4.6	Super-pulsed diode Infrared LED red LED	Super-pulsed diode: 905 Infrared LED: 640 red LED: 875	NR/99.67	Super-pulsed diode: 0.9/ NR Infrared LED: 15/NR red LED: 17.5/NR	Pulse (1000 Hz)	Pterygoid muscles	NR/6/2	Before and immediately after the treatment, 1 and 2 days after the first session	VAS, MMO	VAS: PBMT < Placebo MMO: PBMT = Placebo	8
Madani et al[1]	30*	23/7	15	15	38 ± 15.3 L:32 ± 12.9 P:35 ± 3.4 (15-71)	Diode GaAlAs	810	NR/21	200/NR	CW	TMJ and Muscles (sensitive points)	30s/10/2	Before the treatment, after the 5th and 10th sessions, and one month after the last application	VAS, MMO, LM, PM	VAS: PBMT < Placebo LM, PM: PBMT > Placebo MMO: PBMT = Placebo	7
Del Vecchio et al[58]	90	78/12	30	30	42.55 ± 14.84 (18-73)	Diode GaAlAs	808	40/8	250/NR	Pulse (15000 Hz)	TMJ	8min/7/7	Before the treatment, and after the last session	VAS	PBMT < Placebo	8
Magri et al[59]	41	41/0	20	21	31.7 ± 5.2 (18-49)	Diode GaAlAs	780	G1:NR/5 G2:NR/7.5	G1:20/NR G2:30/NR	CW	TMJ and Muscles (Masseter and Anterior Temporalis)	10s/8/NR	Before the treatment, after the last session, and six months and one year after the last application	VAS, MMO	VAS: PBMT > Placebo MMO: PBMT = Placeb	7
Aisaiti et al[60]	100	76/24	50	50	(18-60)	Diode GaAlAs	810	NR/6	100/NR	CW	TMJ and Muscles (Masseter)	TMJ:30s/7/7 Masseter:60s/7/7	Before the treatment, and one day and one week after the treatment	VAS, AMMO, PMMO, LM, PPT	VAS: PBMT < Placebo Other variables: PBMT > Placebo	8
Desai et al[61]	60	38/22	30	30	38.4 (25-54)	HeNe	632.8	NR/NR	30/NR	CW	TMJ	2min/20/2-3	Before, 2,4 and 8 weeks after the treatment	VAS, MMO, LM	VAS: PBMT < Placebo Other variables: PBMT > Placebo	5
Yamaner et al[62]	62*	NR	18	13	31.51 ± 10.32 (18-60)	Diode GaAlAs	820	NR/3	300/NR	CW	TMJ	10s/6/3	Before the treatment, after the last session, and 3 and 6 months after the last application	VAS, PPT	VAS: PBMT = Placebo PPT: PBMT > Placebo	7

Abbreviations: F, female; M, male; L, laser; P, placebo; PBMT, photobiomodulation therapy; G, Group; GaAs, gallium arsenate; GaAlAs, gallium aluminum arsenate; HeNe, helium-neon; In-Ga–Al–P, indium gallium aluminum phosphor; VAS, visual analogue scale; MMO, maximum mouth opening; AMMO, active maximum mouth opening; PMMO, passive maximum mouth opening; LM, lateral movement; PM, protrusive movement; PPT, pain pressure threshold; EMG, electromyography; d, day; m; month; w, week; y, year; s, seconds; NR, not reported; CW, continuous wavelength

* Means that the article had more sample groups; however, we merely considered the number of patients in the laser and placebo groups. Additionally, > or < means statistically significant, whereas = means not statistically significant.

the RCTs that reported MMO, seven studies[34,36,38,41,46,54,61] showed a greater MMO in the PBMT groups compared to the placebo groups; while others showed no difference. Also, AMMO and PMMO were reported to be greater in the PBMT groups.[24,60] In eight studies,[1,24,34,36,38,46,60,61] LM was greater in the PBMT groups, whereas only two studies[25,54] reported no difference. In three studies,[1,38,46] the PBMT groups demonstrated a higher PM level, and one study[25] showed no difference. Among the studies that reported PPT, four RCTs[42,46,60,64] showed a greater amount in the PBMT groups, and three [25,50,52] showed no difference between the PBMT and placebo groups. In one study[40] which compared two different energy densities of 8 J/cm^2 and 4 J/cm^2, a greater PPT was shown in the PBMT group with 4 J/cm^2 energy density; however, in another study[39], with two different types of PBMT dosimetry (20 J-107 J/cm^2-300 mW versus 4 J-21.4 J/cm^2-60 mW), PPT was greater in the PBMT group with a higher dose. Out of five RCTs that reported EMG, four studies[37,40,48,52] showed no difference between the PBMT and placebo groups. Only one study [39] reported a greater EMG in the PBMT groups with higher energy and power parameters (20 J-107 J/cm^2-300 mW versus 4 J-21.4 J/cm^2-60 mW). Three studies[24,44,51] reported no difference in TMJ sounds between the PBMT and placebo groups, while two studies[31,34] showed fewer TMJ sounds in the PBMT groups than the placebo groups.

Quality Assessment and Overall Outcome

Table 2 summarizes the quality assessment using the modified Jadad scale. Of 40 studies, 39 (97.5%) were highly methodological, with an overall low quality, while only one showed high quality.[25] Out of 40 included RCTs, 33 studies showed improving effects of PBMT on the evaluated outcomes.

Discussion

The current systematic review updated evidence concerning the efficacy of PBMT in alleviating TMD signs and symptoms, including pain intensity, MMO, LM, PM, EMG activity, PPT, and TMJ sounds.

The literature review demonstrated a higher incidence of TMD in women than men.[67,68] It might be connected to behavioral, hormonal, social, and psychological variations.[69] Moreover, differences in pain sensitivity thresholds[70] and health-seeking behaviors[71] between the genders have been proposed.

Infra-red diode lasers were the most used light sources among the included studies. The wavelengths of 820, 810, 808, and 780 nm[1,25,26,30,32,37-39,41,42,44-46,48-51,53,54,58-60,62] were the most prevalent studied wavelengths among the reviewed articles. In TMD photobiomodulation, we need a light source with efficient penetration depth to reach the TMJ structure; hence, red light cannot be efficient.[72] It has been shown that 808 nm light penetrates as much as 54% deeper than 980 nm in bovine tissues.[73] LED application as a light source for PBMT was reported in two studies.[52,57] These studies used a 905 nm diode laser with wavelengths of 640 and 875 nm LEDs. Nowadays, the number of research comparing non-coherent light sources such as LEDs with a laser is increasing to find a better substitute for a laser in PBMT. This is because LED technology provides several advantages, including irradiation of a large area at once, easier use, and notably much lower cost.[74]

The continuous mode of irradiation was utilized in the majority of the retrieved studies. Among the diode lasers, just the range of 904-905 nm (GaAs) can emit super pulse mode, while other diodes create a 'pulse' by chopping the beam or turning the laser on and off at regular intervals.[75] In a rat model, Joensen et al[76] concluded that 904 nm super pulsed PBM penetrated the skin barrier 2-3 times more readily than 810 nm continuous wave PBM. None of the included studies compared the effects of continuous and pulsed mode on TMD patients, but this might be an interesting area for future research. There was also a wide range of energy densities among the investigations. Still, those around 10 Jcm^{-2} were the most common, particularly in more recent ones.[18,77] Energy density, also called dose, is an essential parameter in PBMT that was less discussed in similar previous studies.[14,19] According to the biphasic dose-response or Arndt-Schulz curve in PBMT, an insufficient dose does not affect the target cells, while a high dose may induce inhibitory effects on cell responses.[13] The reason might be that PBMT leads to the production of reactive oxygen species (ROS), which serve as a stimulation factor in lower doses while inducing inhibition and destruction effects in higher doses on target cells.[13] However, some studies have recently argued that several parameters, such as wavelengths, tissue types, and redox states, can determine this optical dose for PBMT.[13] In this research, we found that both low and high doses of PBMT were effective in TMD sign and symptom relief, indicating the need to consider other factors—such as wavelength, power density, and target depth—when defining an effective PBMT protocol. This study's most prevalent output power ranged between 10-100 mW. However, power density is another crucial factor reported in only five studies out of all included studies.[29,33,48,55,56] In PBMT, it is essential to calibrate the device using a power meter in addition to using the manufacturer's stated settings for power measurement because this parameter frequently decreases with time. However, several research studies overlooked this aspect, which compromised the validity of the findings and/or the effectiveness of patient therapies.[78]

The number of PBMT sessions and frequency of treatment per week varied among the studies. The most prevalent protocol included eight treatment sessions (2-3 sessions/week). There is no consensus on the optimal number of sessions or their intervals[79]; however, it has been reported that multiple sessions of PBMT are associated with a faster and higher reduction in proinflammatory mediators.[80] These multiple sessions can be facilitated by using home-use lasers or LEDs.[79,80]

The irradiation point(s) in the included studies were muscles and/ or TMJ. PBMT was applied on the trigger points and/or adjacent masticatory muscles to exert its beneficial effect.[1,24,31-34,37-44,46-53,55,57,59,60] In a recently published study, Furquim et al[81] compared the effectiveness of 780 nm diode laser PBM on pain points in patients with chronic pain-related TMD with pre-established points in an RCT. They found that PBMT on pain points was more effective than irradiation of pre-established points, which suggests individualizing the PBM protocol.

Pain intensity measured by the VAS was the most frequently reported outcome among the included studies. The efficacy of PBMT as a non-invasive pain reduction approach has been shown in several studies.[82-85] The analgesic effect of PBMT might be a result of its positive impact on the reduction of muscle spasms,[86] a decrease of inflammation by attenuating the levels of PGE2[87] and inhibiting COX-2,[88] an increase in nociceptive threshold,[83] enhancing the peripheral endogenous opioid production,[89] and suppression of nerve conduction in myelinated Aδ and unmyelinated C fibers.[90] One of the unique advantages of the PBMT analgesic effect is that no development of tolerance or adaptation to the PBMT has been reported so far.[91]

Among the included studies, different energy densities resulted in different PPT results.[39,40] For instance, Uemoto et al[40] showed that lower energy density (790 nm, 80 mW, 4 J/cm^2) resulted in greater PPT compared to the higher energy density (790 nm, 80 mW, 8 J/cm^2). In contrast, Sattayut and Bradley[39] showed that 820 nm mediated PBMT with higher energy density (300 mW, 107 J/cm^2) increased PPT in the laser group compared to the lower energy density (60 mW, 21.4 J/cm^2). These contradictory results might be due to other factors, such as different wavelengths or output powers.

The included studies evaluated Jaw movements through MMO, AMMO, PMMO, LM, and PM outcomes. It has been shown that jaw movement limitations are attributed to muscle (extracapsular) and TMJ (intracapsular) disorders.[92] Our findings confirm that PBMT significantly improved jaw movements in most of the studies; however, in a few studies, PBMT failed to affect the laser groups positively compared to the control groups. This finding confirms the results of the previous systematic reviews on this topic.[16] Reduction in pain, muscle spasms, and inflammation induced by PBMT might be the reason for improvements in jaw movements. However, the initial restriction rate in jaw movements, different PBMT protocols, and the origin (extracapsular or intracapsular) of this limitation might be the reasons for controversy among various studies.

Among the included studies, only one out of five reported a significant improvement in EMG recorded from the masseter and anterior temporalis muscles in the PBMT group (820 nm, 107 J/cm^2) compared to the control group.[39] This finding should be evaluated in further well-designed RCTs.

Our results also revealed the contrary effects of PBMT on TMJ sounds. Only two out of five studies with 980 nm[31] and 830 nm[31,34] light sources showed a reduction in click sounds in the PBMT groups compared to the control groups. At the same time, no remarkable differences were detected in the other three articles.[24,44,51] This inconsistency among the studies might result from heterogeneity in PBMT protocols and patient populations.

This review faced considerable hindrances, including high heterogeneity among the patients' populations with no exact definition of their TMD type and PBMT protocols. Using different wavelengths, powers, energy densities, and several treatment sessions were noticed among the retrieved studies. Accordingly, the quantitative synthesis of the results was not feasible. In addition, although the terms quality, validity, and bias have been used interchangeably in the systematic reviews, we have to distinguish between quality and bias based on the study conducted by Furuya-Kanamori et al.[93] Nevertheless, a Cochrane study has shown a positive correlation between risk of bias (ROB) overall risks and Jadad Scale scores (Kendall's Tau = 0.491, $P < 0.0005$). In this review, the quality of the included studies was evaluated, and the risk of bias assessment was not undertaken; nonetheless, based on the abovementioned Cochrane study, we can rely on the results of the modified Jadad Scale scores. Moreover, Google Scholar and other grey literature databases were not searched for this systematic review.

Included RCTs in the current systematic review did not provide detailed data on the category of TMD patients, which is one of the critical drawbacks of these studies. Moreover, the irradiation protocol for TMJ or muscle was not different in each related study. Therefore, we can just suggest the irradiation protocols for TMJ and muscle points in patients with TMD based on the beneficial results of the included articles.

The authors of this study suggest evaluating the efficacy of PBMT in sufficient sample sizes of TMD patients with a defined category of TMD to offer a specified PBMT protocol based on the type of TMD. Moreover, a comparison of different PBMT protocols and spontaneous use of PBMT with other treatment interferences such as medications or exploring its effect in laser acupuncture technique should be considered in future studies.

Conclusion

This updated systematic review showed the promising effects of PBMT on reducing the signs and symptoms of TMDs. Alleviation of pain and improvement in MMO were the most prevalent reported outcomes. Heterogeneity in PBMT protocols makes it challenging to define a standard protocol for treatment; however, using the infrared diode laser with a wavelength range between 780-980 nm, an energy density of < 100 J/ cm^2, and output power of ≤ 500 mW for at least six sessions of treatment seems to be promising parametric options for the management of pain and mandibular movements associated with TMDs based on the previously reported findings. Since various parameters play a crucial role in defining a specific PBMT protocol for treating TMD, the current findings open new doors for future studies to design a standard protocol in this regard.

Authors' Contribution

Conceptualization: Nima Farshidfar, Golnoush Farzinnia, Nazafarin Samiraninezhad Fahimeh Rezazadeh.
Investigation: Nima Farshidfar, Golnoush Farzinnia, Nazafarin Samiraninezhad, Sahar Assar.
Supervision: Nima Farshidfar, Fahimeh Rezazadeh, Neda Hakimiha.
Writing–original draft: Nima Farshidfar, Golnoush Farzinnia, Nazafarin Samiraninezhad, Sahar Assar, Parsa Firoozi, Neda Hakimiha.
Writing–review & editing: Fahimeh Rezazadeh, Neda Hakimiha.

Competing Interests

None.

Ethical Approval

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