Efficacy of Low-Level Laser Therapy in the Treatment of Temporomandibular Myofascial Pain: A Systematic Review and Meta-Analysis

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Aims: To conduct a systematic review and meta-analysis to determine the efficacy of low-level laser therapy (LLLT) in treating temporomandibular myofascial pain in adults compared to laser placebo. **Methods:** Randomized, placebo-controlled studies were identified by a search on March 2, 2016 and updated on February 9, 2017 in the PubMed, Web of Science, and Cochrane Library databases. Three of the authors assessed the studies for risk of bias. Outcomes included pain reduction on a visual analog scale (VAS) and interincisal opening. **Results:** The initial search strategy yielded 142 unduplicated references assessed independently by three review authors. After evaluation, this number was reduced to eight relevant studies for inclusion in this review. Of these eight studies, four were at unclear risk of bias and four were at high risk. In a meta-analysis, pain intensity was significantly reduced after treatment in the group that received LLLT as compared to laser placebo (an average of 2.2 units on a scale of 0 to 10) (P = .005) and an average of 2.4 units 3 to 4 weeks later (P = .022). Pooled results showed a significant increase in interincisal opening at 1 month after treatment (P = .012), but not when the treatment was completed (P = .079). **Conclusion:** The findings from this systematic review showed that LLLT seems to be effective in reducing pain in patients with temporomandibular myofascial pain with moderate-quality evidence. However, due to the high heterogeneity, small number, and high risk of bias of the included studies, the results are not definitive, and further well-designed studies are needed. *J Oral Facial Pain Headache 2018;32:287–297. doi: 10.11607/ofph.2032*

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Myofascial pain syndrome (MPS) is classified by the International Association for the Study of Pain Subcommittee on Taxonomy as pain in any skeletal muscle or muscle fascia with trigger points. Travell and Simons[1] define a trigger point as ". . . a hyper-irritable spot, usually within a taut band of skeletal muscle or in the muscle fascia which is painful on compression and can give rise to characteristic referred pain, motor dysfunction, and autonomic phenomena." Myofascial pain falls under the classification of Axis I of the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD).[2,3] Although there is no consensus on the etiology of myofascial pain, one possible theory is the "integrated hypothesis," which suggests that multiple muscle fibers with endplates release excessive acetylcholine, resulting in sarcomere shortening and establishing a positive-feedback loop until it is interrupted.[4] The cause is hypothesized to be muscle overload, which could result in repetitive low-level muscle contractions, eccentric muscle contractions, and maximal or submaximal concentric muscle contractions.[5] Several noninvasive and invasive treatment modalities have been used to interrupt this positive-feedback loop and subsequently inactivate trigger points. The treatments include the spray and stretch technique, ultrasonography, manipulative therapy, occlusal splints, pharmacologic-based therapy, transcutaneous electrical stimulation, and low-level laser therapy (LLLT). Invasive treatments mainly include injections of local anesthesia, dry needling, and sterile saline injections.

LLLT refers to Class IIIb lasers with less than 600 mW of power. They do not heat the skin or underlying tissue, and the depth of penetration is determined by wavelength.[6] LLLT is noninvasive, nonthermal, safe, and biostimulative.[7] The exact mechanism of action is unknown, but there are many proposed mechanisms by which LLLT exerts its positive effects in the treatment of myofascial pain and dysfunctions. One mechanism suggests that LLLT improves local microcirculation, resulting in increased oxygen supply to the hypoxic cells related to the trigger point area.[8] A systematic review suggests strong evidence that LLLT may have a positive biologic effect on the soft tissue after injury in two ways: According to cell and animal studies, *(1)* LLLT improves angiogenesis through increased growth factor secretion and formation of collateral vessels in the injured region; and *(2)* LLLT modulates biochemical inflammatory markers and produces local anti-inflammatory effects in cells and soft tissue.[9]

Publications using LLLT to deactivate trigger points in the orofacial region are scarce and provide controversial results. Some studies show positive results of LLLT, while others show no difference between treatment and placebo groups. Therefore, the aim of this systematic review and meta-analysis was to determine the efficacy of LLLT in treating myofascial pain in adults compared to laser placebo.

Materials and Methods

This systematic review and meta-analysis adheres to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[10]

Inclusion and Exclusion Criteria

Only studies that satisfied the following criteria were included in the systematic review:

- Prospective controlled clinical trials conducted in humans
- Studies comparing LLLT to placebo laser
- Diagnosis of myofascial pain based on the RDC/TMD Axis I Group I[3] or on the presence of six MPS criteria[11] (the combination of regional pain, reference pain pattern, palpable taut band, presence of trigger point, motion restriction, and induction of pain with pressure on a trigger point)
- Only articles written in English

Studies comparing LLLT to other treatments were not included. Case reports, literature reviews, editorials, and animal studies were also excluded.

Primary outcomes were changes from baseline to posttreatment in pain intensity measured using a visual analog scale (VAS) and the percentage of responders (patients with at least a 50% reduction in pain on a VAS). A secondary outcome measure was baseline to posttreatment changes in maximum mouth opening (interincisal opening).

Search Methods for Identification of Studies

Three electronic databases were searched by one author (R.E.) using the following strategies:

- MEDLINE via PubMed (searched on March 2, 2016; updated on February 9, 2017) search was limited to English language and Humans: ("Trigger Points"[Mesh] OR "Myofascial Pain Syndromes"[Mesh] OR myofascial OR trigger point*) AND (temporomandibular OR temporo-mandibular OR TMD OR TMJ OR masseter OR temporalis OR muscle* mastication OR jaw OR facial OR orofacial) AND (laser OR needling OR lidocaine OR procaine OR mepivacaine OR sodium chloride OR bupivacaine OR local anesthetic OR wet needling).
- The Web of Science (searched on March 2, 2016; updated on February 9, 2017) search strategy used was: TOPIC (myofascial OR trigger point*) AND (temporomandibular OR temporo-mandibular OR TMD OR TMJ OR masseter OR temporalis OR muscle* mastication OR jaw OR facial OR orofacial) AND (laser OR needling OR lidocaine OR procaine OR mepivacaine OR sodium chloride OR bupivacaine OR local anesthetic OR wet needling) AND TOPIC: random.
- The Cochrane Library (searched on March 2, 2016; updated on February 9, 2017) search strategy used was: (myofascial OR trigger point*) AND (temporomandibular OR temporo-mandibular OR TMD OR TMJ OR masseter OR temporalis OR muscle* mastication OR jaw OR facial OR orofacial) AND (laser OR needling OR lidocaine OR procaine OR mepivacaine OR sodium chloride OR bupivacaine OR local anesthetic OR wet needling).

Data Collection and Assessment of Risk of Bias

Three authors (F.M., J.J., M.S.) independently screened titles and abstracts of the search results to assess inclusion and exclusion criteria. In the event of disagreement among the three review authors, a fourth author (R.E) made the final decision regarding inclusion or exclusion. Authors recorded the reasons for exclusion for each reference.

The three reviewers individually scanned all the reference sections of the reviews, systematic reviews, and included articles for additional relevant articles. They also independently extracted the data from the

full-text articles meeting the inclusion criteria. Data extraction included the number of participants and their demographics, inclusion/exclusion criteria, interventions, and outcome data[11–18] (Table 1). The assessment of risk of bias in the included studies was undertaken independently by the three authors as part of the data extraction process described above and in accordance with the approach described in the Cochrane Handbook.[19]

Statistical Analyses

Only prospective controlled trials comparing laser treatment to laser placebo and using similar outcomes were pooled into a paired meta-analysis. Treatment effects for continuous variables (change from baseline to posttreatment in VAS pain and interincisal opening) were expressed as standardized difference in means (SDM)—which standardizes measurements on a uniform scale—with 95% confidence intervals (CI). Statistical heterogeneity was tested with Cochran Q test[20] and the I^2 statistic.[21] If there was heterogeneity (Q test P value < .10), estimates of effect were combined with a random-effects model; otherwise, the fixed-effects model was used. All analyses were performed using Comprehensive Meta-Analysis version 3 software (Biostat). Quality of evidence assessment and summary of the findings were conducted using the software GRADE (Grader) following the Cochrane Collaboration and GRADE Working Group guidelines.[19]

Results

The initial search strategy yielded 167 references, and 8 additional references were found by cross-referencing. After removing duplicates, the number of references was reduced to 142. This number was further reduced to 20 based on abstracts and titles. The main reasons for exclusion were: review or systematic review (n = 11); measurement of different outcomes (n = 3); different population (adolescents) (n = 1); protocol of a study (n = 1); no placebo group (n = 3); pilot study (n = 1); open-label study (n = 2); uncontrolled trials (n = 2); different conditions (n = 42); and different interventions (n = 56). The remaining 20 manuscripts identified as relevant were analyzed for inclusion independently by the three review authors. Eight manuscripts were included after this analysis; reasons for exclusion were: intervention was dry needling (n = 5) or lidocaine (n = 1); different conditions (n = 4); orofacial pain was not of myofascial origin or mix of patients of myogenic and arthrogenic origin (n = 1); not in the orofacial region (n = 1; upper trapezius); and conference abstract lacking length and details (n = 1). Due to the heterogeneity of outcomes, only six studies could be included in the meta-analyses. The PRISMA flowchart[10] shows a summary of the results (Fig 1).

Included Studies

Eight studies were eligible for qualitative analysis[11–18] (Table 1). Studies included were single or double-blinded prospective controlled trials using LLLT as the intervention compared to an inactive or sham laser (placebo). However, one study was not clearly indicated as randomized.[13] The number of participants in the eight studies ranged from 16[16] to 60,[11] and the ages of the patients ranged from 16[13] to 62 years old.[11] Most of the studies had both male and female patient participation, with females being the predominant group.[13,15,16,18] Two studies had only female participants,[12,17] and two more did not report gender.[11,14]

Five studies used the RDC/TMD criteria for Axis I, Group I (Ia and Ib; subjects suffering from myofascial pain with or without limited mouth opening) as the inclusion criteria[12–15,17,18] (Table 1). One study[11] included patients diagnosed with the presence of all six myofascial pain criteria.[11] One study included only patients with myofascial pain who did not have any other TMD symptoms.[16] Finally, one study included only patients who were female, Caucasian, and more than 20 years of age with the presence of active myofascial trigger points.[17] The exclusion criteria varied widely within each study (Table 1). Laser characteristics (ie, laser type, wavelength, laser energy density, and pulse/continuous mode) and the application time and frequency of sessions are presented in Table 2.

Risk of Bias

The risk of bias data are summarized in Table 3.

Random sequence generation bias was classified as low risk of bias in one study[18] (which used computer software to assign random groups) and high risk in one study[13] (which did not state if the subjects were randomized). Six studies[11,12,14–17] were classified as unclear risk of bias because the authors reported the patients were randomized but did not provide details on the method of randomization.

Allocation concealment was classified as unclear risk in seven studies[11–13,15–18] due to no specific reporting of allocation concealment. One study[14] had high risk of bias since the study was not blinded and the authors did not report the allocation concealment.

Blinding is possible with LLLT by inactivation of the laser by using very low power or no power or by having a second laser applicator identical to the laser but with no energy output. Only one study reported on how blinding was achieved, and this study was identified as low risk of bias.[11] Six studies reported that blinding was done but did not explain how this was achieved, and so were determined as unclear risk of bias.[12,13,15–18]

Table 1 Summary of Eligible Studies

Study	Year of publication, country, study type	Interventions and sample size	Inclusion criteria
Ahrari et al[12]	2014, Iran, RCT	N = 20 LLLT 3.4 J/cm^2: n = 10 Placebo LLLT: n = 10	Subjects suffering from myofascial pain with/without limited mouth opening (RDC/TMD Axis I, Groups Ia and Ib)
Carrasco et al[11]	2009, Brazil, RCT	N = 60 LLLT 25 J/cm^2: n = 10 60 J/cm^2: n = 10 105 J/cm^2: n = 10 Placebo LLLT 25 J/cm^2: n = 10 60 J/cm^2: n = 10 105 J/cm^2: n = 10	Presence of all six MPS criteria[a]
Cetiner et al[13]	2006, Turkey, prospective controlled study	N = 39 LLLT: n = 24 Placebo LLLT: n = 15	Patients with myogenic orofacial pain and limited mouth opening (RDC/TMD Axis I, Groups Ia and Ib); chewing difficulties or having tender points; and pain in the myofascial area during either compression or jaw movements
Demirkol et al[14]	2015, Turkey, RCT	N = 30 LLLT: n = 10 Placebo laser: n = 10 OS: n = 10	Patients with MPS according to the RDC/TMD; combination of regional pain, reference pain pattern, presence of trigger points, and induction of pain with pressure on a trigger point, as described by Carrasco et al[11]
de Moraes Maia et al[15]	2014, Brazil, RCT	N = 21 LLLT: n = 12 Placebo: n = 9	Patients reporting pain in the facial region at a minimum intensity of 5 on a 0–10-cm VAS with a duration of at least 3 mo; Diagnosis of myofascial pain according to the RDC/TMD (Axis I, Groups Ia and Ib)
Shirani et al[16]	2009, Iran, RCT	N = 16 LLLT 6.2 J/cm^2 : n = 8 Placebo 1 J/cm^2: n = 8	Myofascial pain with no other TMD; unilateral pain in masticatory muscles for up to 1 mo
Uemoto et al[17]	2013, Brazil, RCT	N = 21 LLLT 4 J/cm^2: n = 7 Placebo LLLT: n = 7 Dry needling: n = 7	Female and Caucasian; more than 20 years of age; Presence of active TrPs in both masseter muscles, previously identified by manual palpation
Venezian et al[18]	2010, Brazil, RCT	N = 48 LLLT 25 J/cm^2: n = 12 60 J/cm^2: n = 12 Placebo group 25 J/cm^2: n = 12 60 J/cm^2: n = 12	Patients under Axis I, Groups Ia and Ib of RDC/TMD Patients were instructed to avoid using any analgesic and/or anti-inflammatory medication during the applications and evaluations

RCT = randomized controlled trial; MPS = myofascial pain syndrome; TrP = trigger points; OS = occlusal splint; RDC/TMD = Research Diagnostic Criteria for Temporomandibular Disorders; RPD = removable partial denture. [a]Six criteria for myofascial pain = the combination of regional pain, reference pain pattern, palpable taut band, presence of trigger point, motion restriction, and induction of pain with pressure on a trigger point.

One study was considered to have a high risk of bias because the authors did not report any effort to blind the patients, investigators, personnel, or statistician for randomization.[14]

The authors identified a total of six studies as low risk of bias for incomplete outcome data due to no dropouts of their participants.[11,12,14,16–18] One study[13] was assessed at unclear risk because it did not report the number of drop-outs, and one study[15] was determined to have high risk of bias because there was an imbalance in the numbers of dropouts (14% in the laser group and 25% in the placebo group) and reasons for the dropouts were not provided. Furthermore, due to the overall small number of participants in that study, the percentage of dropouts, particularly in the placebo group (3/12 = 25%), could affect the quality of the study.

Six studies were classified as low risk of bias for selective reporting since the pre-specified outcomes were reported.[11–14,16,18] The remaining two studies[15,17] were determined as unclear risk of bias; one study investigated the effect of LLLT on masticatory performance and pain intensity in patients with myofascial pain, but the authors did not provide quantitative values (mean and standard deviation [SD]) and instead only showed graphs[15]; the authors finally provided the data when requested and the data were included in this review. The other study also lacked quantitative values, but its authors did not provide data when requested.[17] One study reported mean values without SDs.[18]

Exclusion criteria	Participant gender and age	Summary of risk of bias
Patients diagnosed as RDC/TMD Axis I Group II and/or Group III; who received analgesic or antidepressant medicine or underwent any other form of treatment for TMD	20 F/0 M Mean age 35.5 y (age range not reported)	Unclear
Patients who had systemic, infectious, inflammatory, tumoral, cardiopulmonary, and psychiatric diseases that posed a conflict to the clinical picture; TMD disc derangement; multiple active or latent TrPs; regularly taking medicines such as analgesics, anti-inflammatory, and/or psychotropic medication; use of an occlusal splint or other treatment for pain control	Not reported	Unclear
Patients who had disc displacements (with/without reduction), arthralgia, and osteoarthrosis according to RDC/TMD; patients regularly taking medicines such as analgesics and anti-anxiety drugs; missing molar teeth	35 F/4 M Mean age 31.7 y (range 16–62)	Unclear
Patients with systemic diseases such as diabetes mellitus, epilepsy, heart disease, and pacemakers; intra-capsular disorders such as degenerative joint disease, rheumatoid arthritis, and psychiatric diseases; TMD with multiple active or latent TrPs; disc displacement; ongoing treatment for TMD	Not reported	High
Patients missing more than two posterior teeth (excluding third molars); presence of full denture or RPD; presence of gross malocclusion (overbite and overjet greater than 6 mm, unilateral or anterior crossbite, or discrepancy of centric relation to maximum intercuspation greater than 5 mm); undergoing orthodontic treatment, medical treatment, or on medication for pain (all patients were instructed not to take nonsteroidal anti-inflammatory drugs or other analgesics during treatment and follow-up)	19 F/2 M Mean age: 27.76 ± 14.44 y for F group (M mean age not reported)	High
Patients with psychiatric disorders, epilepsy, heart diseases, or pregnant; and those with pacemakers, tumors, intracapsular disorders (degenerative joint disease, rheumatoid arthritis, and disc displacement)	12 F/4 M Mean age 23.8 y (range 16–37 y)	Unclear
Patients using pain killers, muscle relaxants, and/or anti-inflammatory medication and benzodiazepines; pregnancy; receiving treatment for TMD	21 F Mean age not reported (range 20–52 y)	High
Patients using chronic analgesic, anti-inflammatory, or psychotropic medication; use of an occlusal splint or had previously had any other kind of TMD	43 F/5 M Mean age 41.58 y (range 18–60 y)	Unclear

Other potential sources of bias identified four studies at low risk of bias with balanced groups at baseline, no reported funding by companies, and no reported co-interventions.[12,14,16,18] One study had a high risk of bias due to exercise co-intervention.[17] Three of the studies were at unclear risk of bias because they either had unbalanced groups at baseline or no demographic information was presented.[11,13,15]

Overall, four of the studies[11,12,16,18] were considered at unclear risk of bias, while the remaining four studies[13–15,17] were considered at high risk. There were no studies in this review that showed an overall low risk of bias (Table 3).

Effects of Interventions

The primary outcome measure reviewed was the change in pain intensity levels on a VAS (Table 4). The secondary outcome was maximum interincisal opening.

Change in Pain Intensity from Baseline. Six studies reported mean and SD of pain intensity at baseline and end of treatment.[11,13–16,18] Statistically significant heterogeneity was found (Q $P < .001$; $I^2 = 80\%$). LLLT provided significantly better reduction in pain intensity from baseline compared to laser placebo (random-effects model: SDM = –1.241; 95% CI = –1.999 to –0.483; $P = .001$) (Fig 2). Similar results were found for 3 to 4 weeks after treatment, with statistical heterogeneity (Q $P < .001$; $I^2 = 91\%$) and a

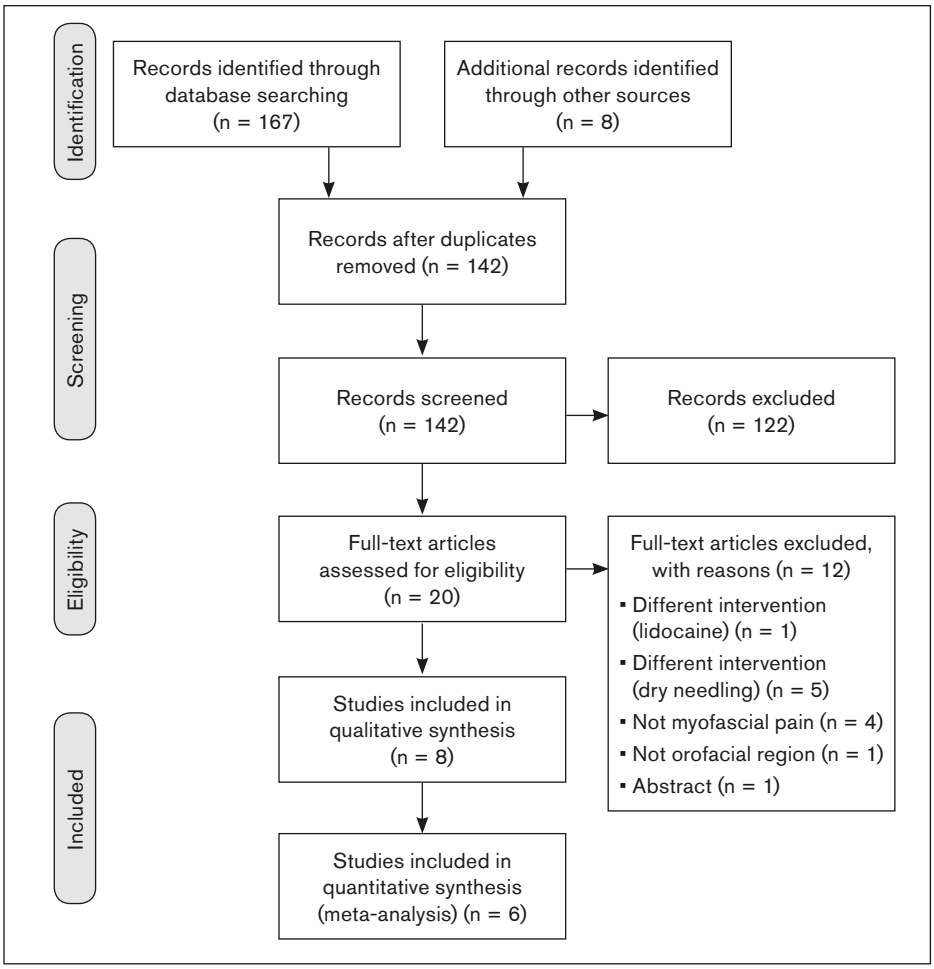


Fig 1 PRISMA flow diagram.[10]

Table 2 Characteristics of Laser Intervention

Study	Laser type (manufacturer)	Wavelength (nm)	Laser energy density (J/cm^2)	Power density (mW)	Pulsed (HZ) or continuous mode	Application time	Frequency and no. of sessions
Ahrari et al[12]	Diode laser (Mustang 2000+)	810	3.4	50	1,500	120 s	3× wk for 4 wk
Carrasco et al[11]	GaAlAS (Twin Laser, MM Optics)	780	25, 60, and 105	50, 60, and 70	Continuous mode	NR	2× wk for 4 wk
Cetiner et al[13]	GaAlAs diode laser (BTL 2000, Medictinedic)	830	7	NR	NR	162 s	10 sessions daily for 2 wk, excluding weekends
Demirkol et al[14]	Nd:YAG laser (Fidelis Plus III, Fotona)	1,064	8	250	Continuous mode	20 s	5× wk, total of 10 sessions
de Moraes Maia et al[15]	GaAlAs (PhotonLase III, DMC Equipmentos)	808	70	100	Continuous mode	19 s	2× wk for 1 mo, total of 8 sessions
Shirani et al[16]	In-Ga-Al-P: (AZOR-2K) GaAs: (AZOR-2K)	In-Ga-Al-P: 660 GaAs: 890	In-Ga-Al-P: 6.2 GaAs: 1	In-Ga-Al-P: 17.3 GaAs: 9.8	In-Ga-Al-P: 0 GaAs: 1,500	In-Ga-Al-P: 6 min GaAs: 10 min	2× wk for 3 wk
Uemoto et al[17]	Infrared laser (Model Three Light, Clean Line brand)	795	4 (right side), 8 (left side)	80	NR	NR	4 sessions each 48 to 72 h
Venezian et al[18]	GaAlAs (Twin Laser, MM Optics)	780	Group 1: 25 Group 2: 25; placebo Group 3: 60 Group 4: 60; placebo	50 or 60	Continuous mode	Group 1: 20 s Group 2: Placebo Group 3: 40 s Group 4: Placebo	2× wk, total of 8 sessions

Table 3 Summary of Risk of Bias for Eligible Studies

Study	Random sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective reporting	Other potential bias	Overall bias
Ahrari et al[12]	?	?	?	–	–	–	?
Carrasco et al[11]	?	?	–	–	–	?	?
Cetiner et al[13]	+	?	?	?	–	?	+
Demirkol et al[14]	?	+	+	–	–	–	+
de Moraes Maia et al[15]	?	?	?	+	?	?	+
Shirani et al[16]	?	?	?	–	–	–	?
Uemoto et al[17]	?	?	?	–	?	+	+
Venezian et al[18]	–	?	?	–	–	–	?

– = low risk; ? = unclear risk; + = high risk.

Table 4 Primary Outcome (Pain on a 0- to 10-cm Visual Analog Scale [VAS]) Reported in Included Studies

	Laser group			Placebo group			
Study	Baseline	Pain at end of Tx Pain 3–4 wk after Tx	Sample size	Baseline	Pain at end of Tx Pain 3–4 wk after Tx	Sample size (n)	Comparison
Ahrari et al[12]	Missing SD	Missing SD	10	Missing SD	Missing SD	10	–
Carrasco et al[11]	7.67 ± 1.13	6.40 ± 2.32 5.67 ± 2.99	30	7.86 ± 1.26	6.80 ± 1.74 5.40 ± 3.06	30	No difference
Cetiner et al[13]	7.56 ± 1.46	2.25 ± 2.05 0.82 ± 1.33	24	6.57 ± 1.91	5.60 ± 1.76 5.19 ± 2.01	15	Favors LLLT
Demirkol et al[14]	6.60 ± 1.506	2.00 ± 2.309 2.00 ± 2.309	10	7.40 ± 2.459	6.60 ± 2.319 6.60 ± 2.319	10	Favors LLLT
de Moraes Maia et al[15]	8.0 ± 1.414	2.0 ± 2.242 3.08 ± 2.713	12	6.4 ± 1.333	2.5 ± 2.398 4.9 ± 2.713	9	Favors LLLT
Shirani et al[16]		Change from baseline: –5.38 ± 2.615	8		Change from baseline: –1.25 ± 1.488	8	Favors LLLT
Uemoto et al[17]	Data shown only in graph	Data shown only in graph		ND	ND		
Venezian et al[18]	6.75 ± 3.37	3.66 ± 2.30 3.50 ± 2.15	12	5.41 ± 2.71	4.33 ± 2.02 5.00 ± 2.79	12	Favors LLLT

SD = standard deviation; Tx = treatment; ND = no data.

significant decrease of pain from baseline with laser therapy (random-effects model: SDM = –1.045; 95% CI = –2.611 to –0.199; P = .022) (Figs 2 and 3).

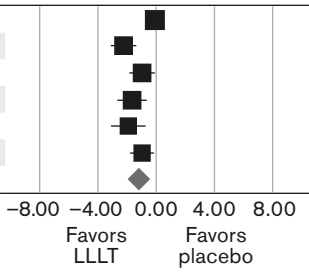
Difference in Posttreatment Pain Intensity. Posttreatment pain intensity was significantly lower (an average of 2.2 units on a VAS of 0 to 10) in the laser group compared to the placebo group (P = .005). This improvement was 2.4 units (on a VAS of 0 to 10) for 3 to 4 weeks after the last session (P = .020) (Figs 4 and 5).

Sensitivity Analysis #1. Venezian et al[18] provided results for 48 patients (12 received therapy at 25 J/cm^2, 12 received 60 J/cm^2, and 24 received placebo laser). Pooled results were similar using left- or right-side data and using results at the two different powers (25 J/cm^2 and 60 J/cm^2). Results for 60J/cm^2 power[18] are shown in Figs 2 and 3.

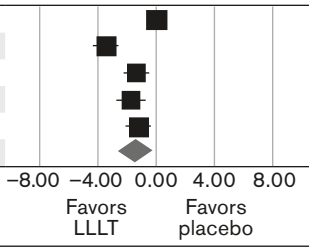
Sensitivity Analysis #2. Carrasco et al[11] did not use the RDC/TMD classification of Axis I Group I to diagnose patients, so a sensitivity meta-analysis was conducted without this study. LLLT provided significantly better reduction in pain intensity from baseline compared to laser placebo when measured at the end of treatment (SDM = –1.511; 95% CI = –2.069 to –0.952; P < .001) and at 3 to 4 weeks after the final session (SDM = –1.826; 95% CI = –2.801 to –0.851; P < .001).

Interincisal Opening. In one study,[12] maximum mouth opening increased in the laser group by 7.6 mm just after the treatment and by 9.1 mm after 1 month, compared to 2.0 mm after treatment and –0.6 mm after 1 month in the placebo group. In a second study,[13] interincisal opening increased in the laser group by 5.7 mm just after treatment and 7 mm after 1 month, compared to 2.8 mm after treatment and at 1 month in the placebo group. A meta-analysis including these two studies showed no statistically significant heterogeneity (I^2 = 0%). LLLT provided a nonsignificant increase in interincisal opening just after treatment compared to placebo (SDM = 0.472; 95% CI = –0.055 to 0.999; P = .079) and a significant increase in opening at 1 month after treatment (SDM = 0.686; 95% CI = 0.151 to 1.220; P = .012) (Figs 6 and 7).

Statistics						
Study	Time point	SDM	95% CI (lower)	95% (upper)	*P* value	SDM and 95% CI
Carrasco et al[11]	End of treatment	−0.102	−0.609	0.404	.692	
Cetiner et al[13]	End of treatment	−2.231	−3.044	−1.418	.000	
De Moraes Maia et al[15]	End of treatment	−0.909	−1.816	−0.003	.049	
Demirkol et al[14]	End of treatment	−1.642	−2.656	−0.629	.001	
Shirani et al[16]	End of treatment	−1.939	−3.127	−0.751	.001	
Venezian et al[18]	End of treatment	−0.929	−1.771	−0.086	.031	
Overall		−1.241	−1.999	−0.483	.001	

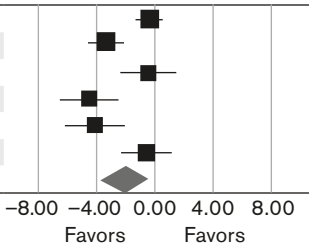


Statistics						
Study	Time point	SDM	95% CI (lower)	95% (upper)	*P* value	SDM and 95% CI
Carrasco et al[11]	3–4 wk	0.152	−0.355	0.659	.556	
Cetiner et al[13]	3–4 wk	−3.306	−4.283	−2.329	.000	
De Moraes Maia et al[15]	3–4 wk	−1.261	−2.205	−0.316	.009	
Demirkol et al[14]	3–4 wk	−1.642	−2.656	−0.629	.001	
Venezian et al[18]	3–4 wk	−1.140	−2.003	−0.278	.010	
Overall		−1.405	−2.611	−0.199	.022	

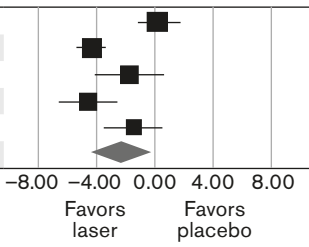


Figs 2 (top) and 3 (bottom) Change in pain rated on a visual analog scale (VAS) from baseline. Overall pooled results show a statistically significant decrease in pain intensity from baseline in the laser group compared to the laser placebo group immediately after the final session (Fig 2; *P* = .001) and 3 to 4 weeks after the end of the treatment (Fig 3; *P* = .022). SDM = standardized difference in means; CI = confidence interval.

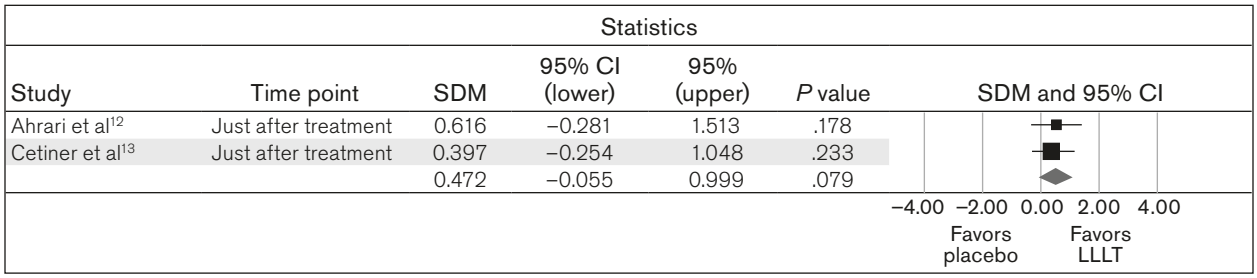
Statistics						
Study	Time point	DM	95% CI (lower)	95% (upper)	*P* value	DM and 95% CI
Carrasco et al[11]	End of treatment	−0.400	−1.438	0.638	.450	
Cetiner et al[13]	End of treament	−3.350	−4.605	−2.095	.000	
De Moraes Maia et al[15]	End of treatment	−0.500	−2.496	1.496	.623	
Demirkol et al[14]	End of treatment	−4.600	−6.628	−2.572	.000	
Shirani et al[16]	End of treatment	−4.125	−6.210	−2.040	.000	
Venezian et al[18]	End of treatment	−0.670	−2.402	1.062	.448	
Overall		−2.211	−3.755	−0.666	.005	

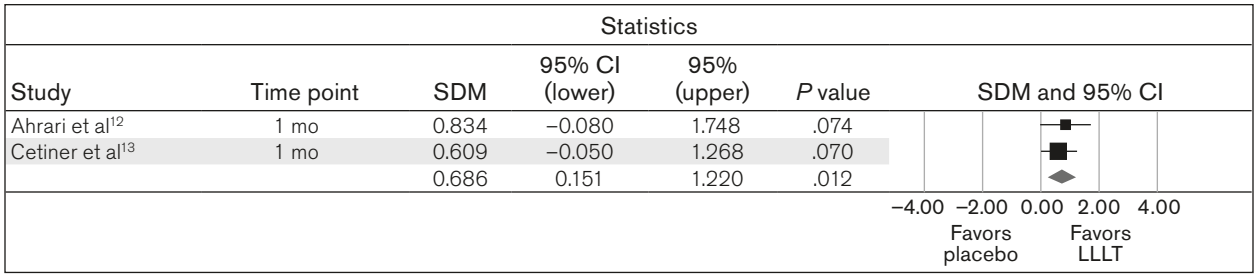


Statistics						
Study	Time point	DM	95% CI (lower)	95% (upper)	*P* value	DM and 95% CI
Carrasco et al[11]	3–4 wk	0.270	−1.261	1.801	.730	
Cetiner et al[13]	3–4 wk	−4.370	−5.416	−3.324	.000	
De Moraes Maia et al[15]	3–4 wk	−1.820	−4.165	0.525	.128	
Demirkol et al[14]	3–4 wk	−4.600	−6.628	−2.572	.000	
Venezian et al[18]	3–4 wk	−1.500	−3.493	0.493	.140	
Overall		−2.425	−4.474	−0.376	.020	



Figs 4 (top) and 5 (bottom) Differences in mean VAS pain. Pooled results show a significantly lower VAS pain in the laser group compared to the placebo group immediately after the final session (Fig 4; *P* = .005) and 3 to 4 weeks after the end of treatment (Fig 5; *P* = .020). DM = difference in means; CI = confidence interval.





Figs 6 (top) and 7 (bottom) Interincisal opening. Overall pooled results show a nonsignificant increase in interincisal opening from baseline just after treatment (Fig 6; $P = .079$) and a significant increase from baseline 1 month after the end of treatment (Fig 7; $P = .012$) in the laser group compared to the placebo group. SDM = standardized difference in means; CI = confidence interval.

Table 5 Summary of the Evidence and Quality of the Findings (GRADE)[19]: LLLT Compared to Laser Placebo for Treatment of Myofascial Pain

Outcomes	No. of Participants (studies)	Quality of the evidence (GRADE)	Anticipated absolute effects (Risk difference with laser placebo (95% CI))
Pain intensity at end of treatment (VAS)	176 (6 studies)	⊕⊕⊕⊖ MODERATE[a] due to risk of bias	The mean change in pain intensity in the LLLT group was 1.241 standard deviations lower than the placebo group (1.999 to 0.483 lower)
Pain intensity 3–4 weeks after treatment (VAS)	160 (5 studies)	⊕⊕⊕⊖ MODERATE[a] due to risk of bias	The mean change in pain intensity in the LLLT group was 1.405 standard deviations lower than the placebo group (2.611 to 0.199 lower)
Interincisal opening at end of treatment (mm)	59 (2 studies)	⊕⊕⊖⊖ LOW[a,b] due to risk of bias, imprecision	The mean change in interincisal opening in the LLLT group was 0.472 standard deviations higher than the placebo group (0.055 lower to 0.999 higher)
Interincisal opening 3–4 weeks after treatment (mm)	59 (2 studies)	⊕⊕⊖⊖ LOW[a,b] due to risk of bias, imprecision	The mean change in interincisal opening in the LLLT group was 0.686 standard deviations higher than the placebo group (0.151 to 1.220 higher)

CI = confidence interval; VAS = visual analog scale.
GRADE Working Group grades of evidence:
High quality = further research is very unlikely to change the level of confidence in the estimate of effect; moderate quality = further research is likely to have an important impact on the level of confidence in the estimate of effect and may change the estimate; low quality = further research is very likely to have an important impact on the level of confidence in the estimate of effect and is likely to change the estimate; very low quality = review authors are very uncertain about the estimate. [a]All included studies assessed at unclear risk of bias. [b]Small number of studies (n = 2) with small number of patients.

Quality of the Evidence

Only trials reporting similar outcomes were pooled into meta-analyses. Due to unclear or high risk of bias, the small sample sizes in each meta-analysis, and the small number of studies pooled into each meta-analysis, the quality of the evidence was moderate for the primary outcome (change in VAS pain intensity) in five studies. The quality of the evidence was low for interincisal opening, with only two studies reporting this outcome (Table 5).

Discussion

Main Findings of Meta-Analyses

This systematic review included eight prospective clinical trials[11–18]; four[11,12,16,18] were assessed at unclear risk of bias and the remaining four[13–15,17] at high risk. Pain intensity measured with a VAS was reduced significantly in the group that received LLLT compared to laser placebo at the end of treatment (SDM = −1.241; $P = .001$) and after 3 to 4 weeks

(SDM = –1.045; P = .022). The average pain in the laser group was more than 1 standard deviation lower than the placebo group. According to Cohen's rule of thumb, an SDM value or effect size bigger than 0.6 is a large effect size. Improvement in the laser group after treatment was on average 2.2 units better on a 0 to 10 VAS (P = .005) and 2.4 units better than placebo at 3 to 4 weeks (P = .020). According to Kelly,[22] the minimum clinically significant difference on a VAS is 1.2 cm (95% CI = 0.9 cm to 1.5 cm), so the improvements of 2.2 and 2.4 units on a scale of 0 to 10 shown in this review may be clinically significant.

Agreements and Disagreements with Other Studies or Reviews

The results agree with a literature review in 2013 by Herranz-Aparicio et al[23] who found a level B recommendation strength (moderate evidence) in favor of using LLLT in the treatment of TMD due to insufficient sample size and/or lack of homogeneity among the studied populations or the laser application parameters. Clinical heterogeneity in the studied populations was minimized by including only diagnosed temporomandibular myofascial pain patients. The results partially agree with Chen et al,[24] who also found a significant increase in terms of maximum active vertical opening. These authors also found an increase in maximum passive vertical opening, protrusion excursion, and right lateral excursion in the treatment of TMD patients with laser. Doeuk et al[25] reported: "Five studies dealt with the treatment of myofascial pain, four of which showed that LLLT was beneficial. The other, with a Jadad score of 5, found no significant difference between LLLT group and the control group." Although the inclusion criteria in this review are more strict than those of Doeuk et al,[25] who included cervical myofascial pain and other interventions (occlusal splints) as a comparison group, the results are similar. The results also agree with Shukla and Muthusekhar,[26] who showed that LLLT seems to be effective in reducing pain in TMD. The authors concluded that LLLT may be a treatment option for patients with an interest in a noninvasive, complementary therapy.[26]

The results of this systematic review are in disagreement with those of Chen et al,[24] who concluded that LLLT was not more effective than placebo in reducing chronic TMD pain. However, the inclusion/exclusion criteria differed between Chen et al and the present study, as Chen et al included patients with TMD of muscular and articular origin. Petrucci et al[27] concluded that there is no evidence to support the use of LLLT for the treatment of TMD; however, their inclusion criteria included both myogenous and arthrogenous temporomandibular pain. The results also disagree with a systematic review by Melis et al,[7] which included myogenous and arthrogenous TMD. Although the results were inconclusive, the authors pointed out that LLLT is probably more effective for the treatment of TMD than for muscle disorders. In summary, the present results disagree with systematic reviews that included both myogenous and arthrogenous temporomandibular pain.

Heterogeneity Factors in This Review

This study attempted to minimize heterogeneity by including only studies with patients diagnosed with myofascial pain with or without limited mouth opening (RDC/TMD Axis I, Groups Ia and Ib) or patients diagnosed with the presence of all six criteria of MPS.[11] Studies with patients diagnosed with the RDC/TMD Axis I Group II (disc displacement with or without reduction) or Group III (arthralgia, osteoarthritis, or osteoarthrosis) were excluded from this review. Although there was clinical heterogeneity in terms of type of LLLT (Nd:YAG laser, GaAlAs, GaAS, Ca-Al-P), they were all Class IIIb lasers. There was also clinical heterogeneity in terms of wavelength, laser energy density, power density, pulsed or continuous, application time, and frequency and number of sessions. Meta-analyses for the primary outcome, the change in VAS pain, showed statistically significant heterogeneity at the end of treatment and at 3 to 4 weeks after treatment; therefore, random-effects models were used in this review.

Analysis of the Influence of Risk of Bias on the Results: Quality of the Evidence

The overall quality of the evidence (according to the GRADE system) was moderate due to the risk of bias (which was overall unclear or high in all studies) for the effect of laser therapy on the primary outcome. According to the GRADE classification, moderate quality means further research "is likely to have an important impact on the level of confidence in the estimate of effect and may change the estimate."[19] The quality of the evidence was low for the secondary outcome interincisal opening due to unclear/high risk of bias, small number of studies (n = 2), and small sample sizes. Low quality means further research "is very likely to have an important impact on the level of confidence in the estimate of effect and is likely to change the estimate."[19]

Implications for Research and Clinical Practice

With this systematic review of the available studies involving myogenous TMD-related pain, it is clear that there is a need for a standardized definition of TMD, such as the evidence-based DC/TMD protocol.[28] Another need for standardization in these studies involves the measurement of pain on palpation of specific muscles.

The importance of blinding is essential to the integrity of any study. Carrasco et al[11] have shown the best

strategy is to blind both the subjects and investigators by utilizing two identical probes (one active and one that emits no radiation). What is missing in most of the included trials was a blinding check; ie, asking the patients to which intervention group they were assigned (if a majority of the patients can guess the group that they were assigned to, the blinding technique does not work as expected). Future studies should incorporate appropriate blinding techniques.[11] Finally, Petrucci et al[27] have expressed the need to also standardize the various aspects of laser utilization, specifically, the time of laser application, number of treatment sessions, energy settings, power density and dose, and definition of laser tip placement. As stated by Mazzetto et al,[29] "An unsatisfactory outcome can be due to very low or high dose, incorrect diagnosis, small number of sessions, inadequate energy density, among others."

Conclusions

The findings from this systematic review and meta-analysis have shown moderate-quality evidence that LLLT seems to be effective in reducing pain in patients with temporomandibular myofascial discomfort. However, due to the high heterogeneity, small number of studies, and high risk of bias of the included studies, the results are not definitive, and further well-designed studies are needed.

Acknowledgments

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