Effectiveness of Low-Level Laser Therapy in Temporomandibular Disorders: A Systematic Review and Meta-Analysis

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Aim: *To assess the scientific evidence on the efficacy of low-level laser therapy (LLLT) in the treatment of temporomandibular disorders (TMD).* ***Methods:*** *The databases of PubMed, Science Direct, Cochrane Clinical Trials Register, and PEDro were manually and electronically searched up to February 2010. Two independent reviewers screened, extracted, and assessed the quality of the publications. A meta-analysis was performed to quantify the pooled effect of LLLT on pain and function in patients with chronic TMD.* ***Results:*** *The literature search identified 323 papers without overlap between selected databases, but after the two-phase study selection, only six randomized clinical trials (RCT) were included in the systematic review. The primary outcome of interest was the change in pain from baseline to endpoint. The pooled effect of LLLT on pain, measured through a visual analog scale with a mean difference of 7.77 mm (95% confidence interval [CI]: –2.49 to 18.02), was not statistically significant from placebo. Change from baseline to endpoint of secondary outcomes was 4.04 mm (95% CI 3.06 to 5.02) for mandibular maximum vertical opening; 1.64 mm (95% CI 0.10 to 3.17) for right lateral excursion and 1.90 mm (95% CI: –4.08 to 7.88) for left lateral excursion.* ***Conclusion:*** *Currently, there is no evidence to support the effectiveness of LLLT in the treatment of TMD.* J OROFAC PAIN 2011;25:298–307

Key words: laser, meta-analysis, systematic review, temporomandibular disorders, temporomandibular joint

In the last 30 years, many nonsurgical therapies have been suggested for the treatment of temporomandibular disorders (TMD), including physical therapy, pharmacologic therapy, occlusal splints, occlusal adjustment, acupuncture, and low-level laser therapy (LLLT).[1–7] The main objective of all these treatment modalities is to reduce symptom intensity, thereby improving the function of the masticatory system and adjacent structures.[1]

Among nonsurgical treatments, LLLT has increased in interest in the last few years, probably due to its ease of use in combination with reports of positive effects on pain alleviation.[8] LLLT is a nonthermal type of light, which causes internal changes in cells and tissues, leading to different types of metabolic activations.[9] These include stimulation of the cellular respiratory chain[10] and increase in vascularization and fibroblast formation,[11,12] which have been suggested to play an important role in the analgesic effect of LLLT. Despite the fact that there is no universally accepted theory to explain the mechanism of either "laser analgesia" or "laser biostimulation,"[8] LLLT can be expected to promote some anti-inflammatory effect and pain relief in painful and dysfunctional joints and muscles.

The most clinically used LLLT include the helium-neon laser (632 nm He-Ne) and infrared laser, as diode-gallium-arsenide (904 nm Ga-As) or gallium-aluminium-arsenide (830 nm Ga-Al-As). The

mechanism of pain relief via mid-laser therapy is not clearly understood and several theories have been suggested. One theory considers the analgesic effect to be a consequence of the reduction of levels of prostaglandin E_2 (PGE_2), which is one of the most important proinflammatory mediators. This theory is based on in vivo and in vitro findings of a reduction of PGE_2 both in cultures of ligament cells and in the joint capsule of animals after laser exposure. The PGE_2 reduction probably derives from the inhibition made by laser radiation of cyclooxygenase-2 (COX-2), the enzyme involved in the synthesis of PGE_2.[13–15] Another theory takes into account the effect of laser therapy on neuronal cells: The effect involves the possible selective inhibition of nociceptive signals[16] and the microcirculation regulation; this action could interrupt the origin and development of pain and thus could provide analgesic effects.[17,18] The magnitude of the laser effect seems to depend on the wavelength and dosage of the laser light.[11] It has been reported that reduction of PGE_2 could be observed within a range of dose between 0.4 and 19 J and within a range of power density between 5 and 21.2 mW/cm^2.[19]

Several systematic reviews and meta-analyses have analyzed the effect of laser therapy in musculoskeletal disorders, but only one[19] partially focused on TMD; it considered the effective dosage and power density, related to specific anatomical factors, in order to assess the reduction of symptoms. Despite the important calculation of the location-specific doses, only three studies focused on TMD and reported the use of only two wavelengths (904 nm and 830 nm). Considering these methodological issues, the efficacy of LLLT in the treatment of TMD, supported by this systematic review, is doubtful. Furthermore, many questions about the effective improvement of temporomandibular joint (TMJ) function still persist. For these reasons, there was a need to conduct a systematic review that addresses all of these shortcomings, and the aim of this study was to assess the scientific evidence on the efficacy of LLLT in the treatment of TMD.

Materials and Methods

Search Strategy

The following electronic databases were searched up to February 2010: PubMed, Science Direct, Cochrane Clinical Trials Register, and PEDro. Screening was performed independently by two reviewers (FS and AP). Disagreement regarding inclusion was resolved by discussion. The search strategy in PubMed, Science Direct, and Cochrane Clinical Trials Register databases involved the terms: *"temporomandibular disorder" OR "temporomandibular disorders" OR "temporomandibular joint disorder" OR "temporomandibular joint disorders" OR "tmj disorder" OR "tmj disorders" OR "tm disorder" OR "tm disorders" OR "temporomandibular joint pain" OR "temporomandibular pain" OR "tm pain" OR "tmj pain" OR "myofascial pain" OR "temporomandibular osteoarthritis" OR "craniomandibular disorder" OR "craniomandibular disorders" AND "low level laser therapy" OR "low intensity laser therapy" OR "low energy laser therapy" OR "LLLT" OR "LILT" OR "LELT" OR "infrared laser" OR "IR laser" OR "diode laser" OR "gallium-aluminium-arsenide laser" OR "GaAlAs laser" OR "gallium-arsenide laser" OR "GaAs laser" OR "helium-neon laser" OR "HeNe laser"*. In the PEDro database, the terms were crossed without Boolean (*OR, AND*) operators. To avoid inappropriate exclusion, noun, adjective, singular, and plural forms of all keywords were used. No language restriction was applied. A manual screening was performed in the following journals between 1990 and February 2010: *Journal of Oral Rehabilitation*, *Journal of Orofacial and Maxillo facial Surgery, Journal of Cranio-Maxillofacial Surgery, Journal of the American Dental Association*, *Cranio*, *Lasers in Medical Science, Journal of Orofacial Pain,* and *Physical Therapy*. Finally, the references of all selected full-text articles and related reviews were screened for publications that were missed by the electronic search engines.

Inclusion and Exclusion Criteria

The study selection process was performed in two phases. In the first, the studies were analyzed according to the following inclusion criteria (A):

- Randomized, controlled clinical trials (RCTs) including placebo control group (A.1)
- Implementation of LLLT for chronic myogenous or arthrogenous temporomandibular pain (A.2)
- Studies involving adult human subjects (age > 18 years) (A.3)

Only studies that fulfilled all of the inclusion criteria were admitted to the second phase, which consisted of the analysis of the preselected studies according to the following exclusion criteria (B):

- LLLT conducted in association with other treatments or after surgical intervention on TMJ or in an invasive way (intramuscular or intra-articular way), or focused on trigger points (B.1)

- Studies involving patients with systemic diseases (ie, rheumatoid arthritis, fibromyalgia, etc) or pain not related to TMD (ie, toothache, neuralgia, psychological disturbances) (B.2)
- Absence of complete data from baseline to the end of the follow-up (B.3)
- No definition of inclusion or exclusion criteria (B.4)
- No assessment of temporomandibular chronic pain by scale or score (B.5)

Authors' Contact Process

After the selection phase A, if a study met the B.3 or the B.4 exclusion criteria, the corresponding author was contacted, via email, in order to retrieve missing data or to obtain better information. If the author did not satisfy the request, did not respond, or did not have the requested data, the study was excluded from the systematic review.

Assessment of Methodological Quality of Reviewed Studies

As recommended by Armijo-Olivo et al,[20] the methodological quality of the articles was assessed by using a list of 10 criteria developed by the University of Sydney (Australia) for the PEDro database,[21] that appears to be a more useful tool, among the available scales, to assess the methodological quality of physical therapy trials.[20] The assessment was made by two assessors (AM and RG) who were blinded to the trial results. No specific cut-off limit for method scores was used to exclude studies.

Power Density and Dosage Evaluation

The scientific evidence on actual outcomes of the effectiveness of LLLT in the treatment of TMD as derived from the existing literature in peer-reviewed gnathologic journals, according to Cochrane Collaboration's principles,[22] was analyzed as suggested in the protocol developed by Bjordal et al.[19] In particular, power density and dose were calculated according to the following formulas:

- Power density for GaAs 904 nm pulse lasers (mW/cm2) = (peak power pulse × pulse duration × pulses frequency)/spot size on skin
- Power density for lasers with continuous output (mW/cm2) = mean power/spot size on skin
- Dose (J) = mean power × treatment time per session

The optimal range of dose was considered to be from 0.5 to 15 J for infrared 780 nm, 820 nm, 830 nm, and 1,060 nm; from 0.2 to 1.4 J for infrared 904 nm; and from 6 to 30 J for HeNe 632.8 nm. The optimal range of power density was reported to be from 15 to 105 mW/cm^2 for infrared 820 nm, 830 nm, and 1,060 nm; from 6 to 42 mW/cm^2 for infrared 904 nm; and 30 to 210 mW/cm^2 for HeNe 632.8 nm.[19]

Outcome Measures

The primary outcome of interest was the change of pain intensity evaluated through visual analog scale (VAS) scores, expressed in millimeters, between baseline and end of the follow-up (baseline-end), between the laser and placebo groups. The second main outcome of interest was the change in TMJ function between baseline and end of the follow-up between the laser and placebo groups. TMJ function was assessed in terms of maximum vertical opening (MVO), protrusion excursion (PE), and right and left lateral excursion (RLE and LLE, respectively), expressed in millimeters.

Statistical Analysis

A decision to perform a meta-analysis was made if there were sufficient similarities between studies in types of participants, interventions, and outcomes. Pooled effect sizes were based on the results of pain intensity (VAS), as well as the amount of MVO, PE, RLE, and LLE in millimeters. Revman 5.0 Software was used to summarize the effects (ie, pooled weighted mean differences [WMD]) and to construct the forest plots for all comparisons. A random effect model (DerSimonian and Laird model) on the assumption of the presence of interstudy variability to provide a more conservative estimate of the true effect, with corresponding Z-statistics, *P* values, and 95% CI, was calculated. Also, a test for heterogeneity was performed. For this test, the I^2-statistic describes the proportion of total variation due to heterogeneity, where 0% indicates no heterogeneity and 100% indicates maximal heterogeneity among studies included in the meta-analysis. The forest plots for each meta-analysis present the raw data (means, standard deviation [SD], and sample sizes) for each arm per included study, point estimates and CI for the chosen effect measure (as blocks and lines, respectively), heterogeneity statistic (I^2), the total number of participants per group, the overall average effect (WMD and Z-statistics) in the random effect model, and percent weight given to each study.

Table 1 Abstracts Retrieved by Electronic, Manual, and Reference Searching

Search method	No. of abstracts without overlap
PubMed	43
Science Direct	194
Cochrane Controlled Clinical Trials Register	25
PEDro	59
Manual search	1
Reference review articles	1
Reference selected articles	0
Total	323

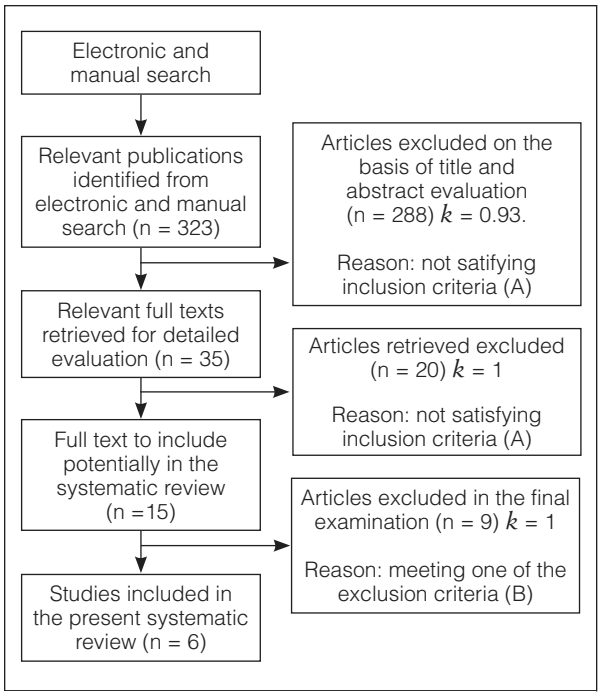


Fig 1 QUORUM flowchart of the search strategy.

Table 2 Full-Text Articles Excluded According to the Inclusion/Exclusion Criteria

Authors	Reasons for exclusion
Carvalho et al[23] (2010)	Controlled clinical trial (A.1)
Gül and Onal[24] (2009)	TMD diagnosis not included (A.2)
Kuan[25] (2009)	Review (A.1)
Fikácková et al[26] (2007)	Controlled clinical trial (A.1)
Dundar et al[27] (2007)	TMD diagnosis not included (A.2)
Núñez et al[28] (2006)	Controlled clinical trial (A.1)
Kato et al[29] (2006)	Controlled clinical trial (A.1)
Cetiner et al[30] (2006)	Controlled clinical trial (A.1)
De Medeiros et al[31] (2005)	Clinical trial (A.1)
Kogawa et al[32] (2005)	Absence of placebo (A.1)
Ilbuldu et al[33] (2004)	TMD diagnosis not included (A.2)
Hakgüder et al[34] (2003)	TMD diagnosis not included (A.2)
Hong[35] (2002)	Review (A.1)
Fargas-Babjak[36] (2001)	Review (A.1)
Criscuolo[37] (2001)	Review (A.1)
Pinheiro et al[38] (1997)	Clinical trial (A.1)
Simunovic[39] (1996)	Controlled clinical trial (A.1)
Hansson[40] (1989)	Clinical trial (A.1)
Bezuur et al[41] (1988)	Clinical trial (A.1)
Waylonis et al[42] (1988)	Clinical trial (A.1)
Katsoulis et al[43] (2010)	Laser treatment with acupuncture (B.1)
Carrasco et al[44] (2009)	Laser treatment on trigger points (B.1)
Shirani et al[45] (2009)	Missing data (B.3)
Mazzetto et al[46] (2007)	Laser treatment with acupuncture (B.1)
Ceylan et al[47] (2004)	Laser and medical treatment (B.1)
Tullberg et al[48] (2003)	Missing data (B.3)
Bertolucci and Gray[49] (1995)	Missing exclusion criteria (B.4)
Bertolucci and Gray[50] (1995)	Missing exclusion criteria (B.4)
Gray et al[51] (1994)	Missing exclusion criteria (B.4)

Results

Study Selection

The electronic and manual literature search identified 323 abstracts without overlap, which are described in Table 1 and entered into a QUORUM flowchart (Fig 1) to illustrate the path for selecting the final trials. Two hundred eighty-eight articles were excluded on the basis of title and abstract evaluation for not satisfying the inclusion criteria (inter-reviewer agreement, k = 0.93). The relevant full-text articles of the remaining 35 publications[23–57] were thoroughly evaluated. A total of 20 papers[23–42] had to be excluded during this stage of selection (inter-reviewer agreement, k = 1): 16 trials for not fulfilling the inclusion criteria spelled out in A.1 and 4 studies for not fulfilling inclusion criteria for A.2. Of the remaining 15 publications, a total of 9 full-text articles[43–51] had to be excluded because of meeting one or more of the

Table 3 Characteristics of the Included Studies

Study	No. of subjects	Treatment design	Age range/ mean age	Sex	Type of TMD	Criteria for diagnosis
Carrasco et al[52] (2008)	14	7 patients GaAlAs (test) 7 patients placebo (control)	– –	– –	TMD of muscular and articular origin	Anamnesis Muscle palpation TMJ palpation TMJ auscultation Radiographs
Conti[53] (1997)	20	10 patients GaAlAs (test) 10 patients placebo (control)	– 39.8 years	2 M 18 F	TMD of muscular and articular origin	Anamnesis Muscle palpation TMJ palpation TMJ auscultation
Da Cunha et al[54] (2008)	40	20 patients GaAlAs (test) 20 patients placebo (control)	20–68 years 43.3 years	1 M 39 F	TMD of muscular origin	Anamnesis Muscle palpation TMJ palpation TMJ auscultation
De Abreu Venancio et al[55] (2005)	30	15 patients GaAlAs (test) 15 patients placebo (control)	– 36.2 years	5 M 25 F	TMD of articular origin	Anamnesis Muscle palpation TMJ palpation TMJ auscultation Radiographs
Emshoff et al[56] (2008)	52	26 patients HeNe (test) 26 patients placebo (control)	18–58 years 42.9 years	10 M 44 F	TMD of muscular and articular origin	–
Kulekcioglu et al[57] (2003)	35	20 patients GaAs (test) 15 patients placebo (control)	20–59 years 38.1 years	7 M 28 F	TMD of muscular and articular origin	Muscle palpation TMJ palpation TMJ auscultation MRI

MRI = magnetic resonance imaging; GaAlAs = gallium-aluminium-arsenide laser; HeNe = helium-neon laser; GaAs = gallium-arsenide laser.

exclusion criteria (inter-reviewer agreement, $k = 1$): 4 studies were excluded for not meeting the exclusion criteria spelled out in B.1, 3 for the exclusion criteria in B.4, and 2 for the exclusion criteria in B.3. The explanations for excluding these articles are given in Table 2. Finally, a total of 6 studies[52–57] fulfilled the required selection criteria and were included in the present systematic review. A list of the included trials and their treatment characteristics is summarized in Table 3.

Dose Assessment

The results of the dose assessment revealed that only one study[54] used doses inside the dose range suggested by Bjordal et al.[19] The remaining five trials,[52,53,55–57] which included 151 patients, did not reach the suggested dose range. In only two trials[52,53] was it possible to calculate the power density, and results were outside the suggested range (Table 4).

Quality Assessment

Quality assessment for two trials[54,55] satisfied 7 out of 10 possible criteria on the PEDro scale, while three trials[52,53,57] satisfied 6 out of all 10 criteria on the PEDro scale. For one trial,[56] the score differed from that given by the PEDro database: method scores revealed that the trial satisfied all 10 criteria, while, according to the PEDro scores, one criterion was not satisfied (inter-reviewer agreement, $k = 1.0$). The most frequently missing item of the scale was "concealed allocation to groups." The results of the quality assessment are summarized in Table 5.

Meta-Analysis

Primary Outcome. All trials provided data on pain intensity as evaluated on VAS. Two trials[52,53] reported a nonsignificant difference in pain reduction between pre- and posttreatment, while in the remaining four trials,[54–57] the difference was statistically significant. According to VAS scores, pain intensity decreased in both active and placebo groups, but all trials showed no statistically significant difference between laser and placebo groups. Use of a random effects model revealed weighted mean differences (WMD) in change of pain on a 100-mm VAS to be 7.77 mm (95% CI: –2.49 to 18.02) (Table 6); the WMD for the means of VAS differences baseline–end between treated and placebo groups was found to be not statistically significant (test of overall effect

Table 4 Technical Features of Laser Used in the Included Trials

Author	Laser type	Laser model (manufacturer)	Treatment time/ No. of total sessions/ No. of sessions/wk	Laser continuous output (maximum pulse)	Power density (mW/cm^2)	Dose (J)
Carrasco et al[52]	GaAlAs 780 nm	GaAlAs Twin (MM Optics)	60 s/8/3	70 mW	3,500	4.2
Conti[53]	GaAlAs 830 nm	Ga-Al-As low level laser (OMNILASE)	40 s/3/1	100 mW	38,887	4
Da Cuhna et al[54]	GaAlAs 830 nm	Ga-Al-As low level laser (Biolux laser)	20 s/4/1	500 mW	–	10
De Abreu Venancio et al[55]	GaAlAs 780 nm	GaAlAs Twin (MM Optics)	10 s/6/2	30 mW	–	0.3
Emshoff et al[56]	HeNe 632.8 nm	Model 2000 (Helbo Medizintechnik)	120 s/20/2–3	30 mW	–	3.6
Kulekcioglu et al[57]	GaAs 904 nm	Roland Serie CE Infrared-27 (Elettronica Pagani)	180 s/15/–	17 mW (1,000 Hz)	–	3

The studies that used dose or power density out of the suggested range are marked in italics.

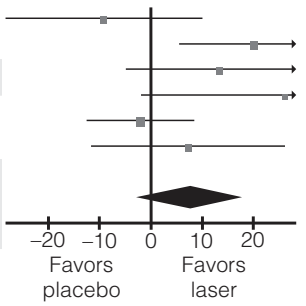
Table 5 Quality Assessment of the Included Studies According to PEDro Scale

Author	Randomization performed	Concealed allocation to groups	Baseline similarity	Patient blinded	Therapist blinded	Observer blinded	Withdrawals/ dropouts < 15%	Intention to treat analysis	Between groups†	Mean and variability data	Total score
Carrasco et al[52]	1	0	1	1	1	0	0	1	1	0	6
Conti[53]	1	0	1	1	0	1	1	1	0	0	6
Da Cuhna et al[54]	1	0	1	1	1	0	0	1	1	1	7
De Abreu Venancio et al[55]	1	0	1	1	1	0	0	1	1	1	7
Emshoff et al[56]	1	1	1	1	1	1	1	1	1	1 (0*)	10 (9*)
Kulekcioglu et al[57]	1	0	1	1	0	1	0	0	1	1	6

*Indicates method score by PEDro reviewers where disagreement with this study's assessment existed. †Difference tested statistically.

Table 6 Forest Plot of the Pooled Weighted Mean Differences for Pain Intensity (VAS in mm)

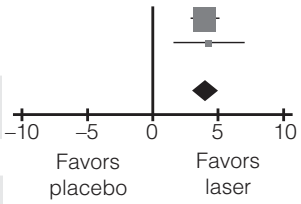
Study or subgroup	Active laser			Placebo			Weight	Mean difference IV, random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Carrasco et al[52]	–0.5	8.8	7	8.8	24	7	15.3%	–9.30 [–28.24, 9.634]
Conti[53]	31	21.92	10	11	7.7	10	19.6%	20.00 [5.60, 34.40]
Da Cunha et al[54]	32.5	29.1	20	19.2	29.3	20	16.0%	13.30 [–4.80, 31.40]
De Abreu Venancio et al[55]	66.7	46.66	15	40.6	28.99	15	9.5%	26.10 [–1.70, 53.90]
Emshoff et al[56]	25.9	18.38	26	27.9	19.7	26	24.1%	–2.00 [–12.36, 8.36]
Kulekcioglu et al[57]	37.3	27.1	20	30	28.5	15	15.5%	7.30 [–11.38, 25.98]
Total			98			93	100%	7.77 [–2.49, 18.02]



Heterogeneity: $Tau^2 = 85.74$; $\chi^2 = 11.08$, df = 5 ($P = .05$); $I^2 = 55\%$.
Test for overall effect: Z = 1.48 ($P = .14$).

Table 7 Forest Plot of the Pooled Weighted Mean Differences for MVO (VAS in mm)

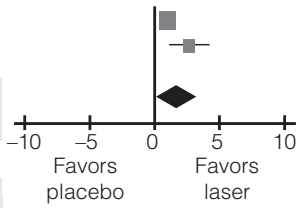
Study or subgroup	Active laser Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean difference IV, random, 95% CI
De Abreu Venancio et al[55]	2.6	1.83	15	–1.4	0.98	15	86.6%	4.00 [2.95, 5.05]
Kulekcioglu et al[57]	7.7	5.44	20	3.4	2.4	15	13.4%	4.30 [1.62, 6.98]
Total			35			30	100%	4.04 [3.06, 5.02]



Heterogeneity: Tau² = 0.00; χ^2 = 0.04, df = 1 (*P* = .84); I² = 0%.
Test for overall effect: Z = 8.10 (*P* = .00001).

Table 8 Forest Plot of the Pooled Weighted Mean Differences for RLE (VAS in mm)

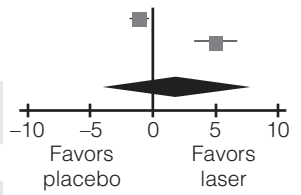
Study or subgroup	Active laser Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean difference IV, random, 95% CI
De Abreu Venancio et al[55]	1.1	0.77	15	0.1	0.07	15	60.1%	1.00 [0.61, 1.39]
Kulekcioglu et al[57]	4.3	3.04	20	1.7	1.2	15	39.9%	2.60 [1.14, 4.06]
Total			35			30	100%	1.64 [0.10, 3.17]



Heterogeneity: Tau² = 0.98; χ^2 = 4.28, df = 1 (*P* = .04); I² = 77%.
Test for overall effect: Z = 2.09 (*P* = .04).

Table 9 Forest Plot of the Pooled Weighted Mean Differences for LLE (VAS in mm)

Study or subgroup	Active laser Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean difference IV, random, 95% CI
De Abreu Venancio et al[55]	0.8	0.56	15	1.9	1.34	15	50.8%	–1.10 [–1.83, –0.37]
Kulekcioglu et al[57]	5.4	3.81	20	0.4	0.28	15	49.2%	5.00 [3.32, 6.68]
Total			35			30	100%	1.90 [–4.08, 7.88]



Heterogeneity: Tau² = 18.17; χ^2 = 42.69, df = 1 (*P* = .00001); I² = 98%.
Test for overall effect: Z = 0.62 (*P* = .53).

P > .05), and moderate but significant heterogeneity was present among the studies (I^2 = 55%, *P* =.05). In view of the small sample of studies included in the meta-analysis, it was not appropriate to perform a meta-regression for heterogeneity analysis.

Secondary Outcome. Only three[53,55,57] of the six included studies analyzed TMJ function in terms of MVO, PE, RLE, and LLE. One study[53] did not report data on posttreatment and did not analyze the significance level between groups, while one study[57] did not consider PE. Only one trial[57] reported a larger increase in MVO, RLE, and LLE between LLLT and placebo groups. The MVO, RLE, and LLE reported by two studies[55,57] were pooled by using a random effects model: the WMD for the means of MVO differences in baseline–end between LLLT and placebo groups was 4.04 mm (95% CI: 3.06 to 5.02) (Table 7) and those for RLE and LLE were 1.64 mm (95% CI: 0.10 to 3.17) and 1.90 mm (95% CI: –4.08 to 7.88), respectively (Tables 8 and 9). However, only

WMD for MVO was statistically significant with no heterogeneity (test of overall effect: $P < .00001$, $I^2 = 0.0\%$). Pooled WMD for RLE was statistically significant (test of overall effect: $P < .05$) with high heterogeneity ($I^2 = 77\%$) and WMD for LLE was not statistically significant with high heterogeneity between the two studies (test of overall effect: $P > .05$, $I^2 = 98\%$). As previously stated, no meta-regression was performed because of the small number of studies included in the meta-analysis.

Side Effects and Adverse Reactions

All RCTs included in the present systematic review did not declare the occurrence of side effects or adverse reactions related to laser exposure or during the follow-up period.

Discussion

This systematic review indicated that LLLT was not better than placebo in reducing chronic TMD pain, which is in agreement with the results reported in previous studies.[51,53,58] On the other hand, the results of this systematic review partly contrasts those reached by another systematic review[19] reporting that LLLT, within a suggested dose range, significantly reduced pain and improved the health status in chronic knee, temporomandibular, or zygapophyseal joint disorders. However, the authors called for caution in the interpretation of their results because of heterogeneity in patient samples, treatment procedures, and trial design.

The LLLT provided a statistically significant mean gain of 4.04 mm in MVO. This positive effect of laser therapy on mouth opening could be due to the anti-inflammatory changes and to the alteration of pain muscle inhibition, secondary to the alteration of firing of hyperactive sensory receptors of the joint capsule, as suggested by Bertolucci and Grey.[50] However, this result must be interpreted with caution, as the WMD was obtained from only two studies.

This systematic review has several strengths. It was performed on the basis of the Cochrane Collaboration's principle[22] and was designed to be rigorous in the search strategy and in the selection of the included studies. The quality of the six RCTs included in the systematic review was analyzed according to the PEDro scale for physical therapy trials. According to this evaluation, each included study had internal and external validity. Furthermore, the study selection as well as the quality assessment were performed by two different authors, with good inter-reviewer agreement. This approach led to the exclusion of a large number of studies addressing the treatment of TMD with LLLT that had been retrieved with an extensive literature search performed with an adequate and wide search strategy. The reduction of the systematic review to studies having well-defined qualitative standards allowed for the drawing of meaningful conclusions. Another strength of the review was the inclusion of a meta-analysis that allowed a better estimate of the true "effect size" by increasing the number of subjects pooled in the statistical analysis.

However, the study also has some shortcomings that need to be considered in interpreting the results and that are due to the inherent methodological limitations of the analyzed studies, like the high degree of heterogeneity between the pooled studies, the small sample sizes of the included studies, the lack of definition of the used dose and power density in several studies, and the lack of two important qualitative parameters, ie, "blinding" and "concealed allocation to groups." Since the small number of included studies made it difficult to perform sensitivity or subgroup analysis, the influence of these methodological issues on meta-analysis results could not be analyzed.

The high degree of heterogeneity between the pooled studies concerned the treatment time per session, the number of laser therapy sessions, and the variation in laser dose and power density. These are important laser therapy parameters, as they influence the applied energy dose; for instance, the treatment time (between 10 and 180 seconds per session), the number of treatment sessions (between 3 and 20), and the number of sessions per week.

As far as sample size, only one of the six involved studies enrolled a sufficient number of patients.[56] Indeed, a power analysis revealed that the number of patients required should have been 21 (with a power of 90% and a type I error of 5%). This may have contributed to not finding significant differences between LLLT and placebo. However, it must be kept in mind that the larger the number of subjects necessary to show that the difference between an experimental intervention and placebo is statistically significant, the smaller the effect size is.

This systematic review also tried to assess the doses and power densities applied in the different studies and compare them to the values suggested by Bjordal et al.[19] Only one study[54] applied a dose that corresponded to the suggested one. Unfortunately, the power density could not be calculated for four studies.[54–57] This is a serious problem, as it cannot be excluded that the lack of LLLT efficacy could have been due to the inadequacy of the energy doses used.

Clinical Implications

The results of this meta-analysis do not support an evidence-based use of laser therapy in TMD chronic pain; furthermore, the finding that LLLT was not superior to placebo in TMD treatment seems to indicate that placebo is involved in the LLLT effect. Therefore, at the present time, LLLT seems unlikely to be a predictable and reliable TMD treatment modality.

Implications for Future Research

Future research must clarify the unclear issues of laser therapy in TMD treatment, in particular, time of laser application, number of treatment sessions, energy settings, power density and dose, and definition of laser tip placement. Furthermore, future RCTs should include appropriate power analysis, proper allocation concealment analysis, adequate randomization method, and double-blind design. In addition, the effect of LLLT should be assessed not only for pain intensity reduction and TMJ mobility improvement but in a more comprehensive manner, ie, assessing six core outcome domains (pain, physical functioning, emotional functioning, participant ratings of global improvement, symptoms and adverse events, and participant disposition) as recommended by the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT).[59,60]

Conclusions

The results of this systematic review and meta-analysis indicated that there is no evidence to support the use of LLLT in the treatment of TMD.

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