Effectiveness of low-level gallium aluminium arsenide laser therapy for temporomandibular disorder with myofascial pain
A systematic review and meta-analysis

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Abstract

Purpose: Temporomandibular disorder (TMD) causes masticatory muscle pain and mouth opening limitations and affects patients’ ability to eat, practice oral health and perform other activities of daily living. Although the benefits of low-energy lasers in treating TMD have been reported, the results vary greatly depending on the equipment used and the energy output. This study systematically evaluated the efficacy of a low-level gallium aluminium arsenide (GaAlAs) laser treatment for TMD with myofascial pain and maxillary pain.

Methods: We searched the PubMed, EMBASE, Cochrane Library, Web of Science, and ClinicalTrials.gov databases for randomized controlled trials (RCTs) published since database inception to April 5, 2020, that compared low-level laser treatment to sham/placebo treatment or no intervention in patients suffering from TMD with myofascial pain. Three reviewers independently screened the literature, extracted data, and assessed the quality of the included studies according to the risk-of-bias tool recommended by the Cochrane Handbook V.5.1.0 (Cochrane Collaboration, London, UK). Then, a meta-analysis was performed using RevMan 5.3 and Stata 15.1 software.

Results: The data from 8 randomized controlled trials including 181 patients were analyzed. The severity of myofascial TMD pain (measured on a visual analogue scale, VAS) at the end of treatment was significantly different between the control laser therapy and the low-level GaAlAs laser therapy (weighted mean difference [WMD] = −0.76, 95% confidence interval [CI] −1.51 to 0.01, \( P = .046 \)); at 3 to 4 weeks after treatment, there was no significant difference (WMD = 1.24, 95% CI −0.04 to 2.51, \( P = .057 \)). In addition, there was no significant improvement in maximum mouth opening (MMO) at the end of treatment (WMD = −0.03, 95% CI −4.13 to 4.06, \( P = .987 \)) or at 3 to 4 weeks after treatment (WMD = 1.22, 95% CI −2.94 to 5.39, \( P = .565 \)).

Conclusions: The results of this study suggest that there is insufficient evidence to indicate an efficacy of low-level GaAlAs laser therapy in improving TMD pain and maximal oral opening. These results suggest that clinicians should make appropriate recommendations to inform patient decision-making.

Abbreviations: CI = confidence interval, GaAlAs = gallium aluminium arsenide, HE-NE = He-neon laser, LLLT = low-level laser treatment, MMO = maximum mouth opening, Nd:YAG = doped yttrium aluminium garnet laser, RCTs = randomized controlled trials, ROB = risk of bias, TMD = temporomandibular disorder, VAS = visual analogue scale.

Keywords: GaAlAs laser, low-level laser therapy, myofascial pain syndrome, temporomandibular disorder, visual analogue scale, maximum mouth opening
1. Introduction

Temporomandibular disorder (TMD) is a group of common oral and facial signs and symptoms related to the masticatory muscles, temporomandibular joints (TMJs), or related structures. TMD may be accompanied by various symptoms of tenderness or local pain, joint popping, movement disorders and other clinical dysfunction syndromes. Pain and functional limitations, especially in chewing and mouth opening, affect patients’ ability to eat, practice oral hygiene, speak and perform other aspects of daily life. In serious cases, patients may have headache, tinnitus, and other symptoms, which are the main reasons patients seek medical treatment. TMD is a disease with a complex etiology and various treatments. Some scholars believe that TMD may be related to myofascial trigger points. In addition, the extent of mouth opening limitation is positively correlated with the degree of pain; such pain may be caused by the triggering of highly sensitive nODULES or areas in the muscle, resulting in increased local muscle tension and pain and thus affecting the range of joint motion. The treatment goal for myofascial pain is to reduce the activity of the trigger points; examples of available treatments include the use of an occlusal plate, exercise therapy, postural training, psychotherapy, joint loosening, and medication. A large number of studies have shown that the clinical application of low-level laser treatment (LLLT) can effectively treat myofascial pain, improve the movement ability of the TMJ and improve mouth opening. In addition, LLLT has the advantages of being noninvasive, painless, and aseptic.

Reviewing the literature, we found that different types of lasers, such as the He-neon (HE-NE) laser, gallium aluminium arsenide (GaAlAs) laser, and doped yttrium aluminium garnet (Nd:YAG) laser, have different therapeutic effects. These differences may be related to inconsistencies among laser types in wavelength band and energy conversion efficiency. The GaAlAs laser is an electric injection semiconductor or laser diode laser with high energy conversion efficiency, good beam quality, weight, lightness, and other advantages. GaAlAs lasers have short wavelengths (780–850 nm) of near-infrared light, which achieve greater penetration than other wavelengths and stimulate tissue cells to produce the desired biological effects. Light particles cause biochemical reactions in tissue, improve tissue blood supply and accelerate the excretion of metabolites. They also increase the excitability of nerve endings and raise the pain threshold. Most studies of semiconductor GaAlAs low-energy lasers suggest that they have good therapeutic effects on acute and chronic pain. Due to its advantages of sterile and noninvasive application, it has been proposed that GaAlAs laser therapy be widely used for oral-facial pain to increase the pain threshold and improve the range of oral opening.

2. Material and methods

2.1. Database search and retrieval strategies

The PubMed, EMBASE, Cochrane Library, Web of Science, and ClinicalTrials.gov databases were searched for articles published from database inception to April 5, 2020. The searches were limited to randomized clinical trials and studies published in English.

The search strategy was as follows:

1. In step 1, the following medical subject headings (MeSHs) were used in the search: myofascial pain syndrome, temporomandibular disease, and random control.
2. In step 2, the texts were searched for these terms.
3. In step 3, the following search method was applied: MeSH 1 OR text words 1 AND MeSH 2 OR text words 2 AND MeSH 3 OR text words 3.
4. An example of our PubMed search strategy is provided in Annex 1, http://links.lww.com/MD/G512.

2.2. Inclusion and exclusion criteria

2.2.1. The inclusion criteria were as follows:

1. RCTs;
2. Studies published in English;
3. Studies in which low-level GaAlAs laser treatment was included as an intervention;
4. Studies in which the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) axis 1 was used.

2.2.2. The exclusion criteria were as follows:

1. Studies with designs other than RCTs;
2. Studies that included other types of lasers;
3. Studies that included individuals with fibromyalgia, injury, osteoarthritis, or other diseases;
4. Studies involving animal experiments, conference summaries, reviews, and case reports;
5. Studies in which the experiment was not completed or the full text could not be obtained;
6. RCTs that did not provide complete data.

2.3. Interventions and outcomes

The only study intervention included in the meta-analysis was low-level GaAlAs laser therapy, and the control group could include groups receiving other interventions, sham or placebo or no intervention. The primary outcome index was the degree of pain, reported on a visual analogue scale (VAS), and the secondary outcome index was the maximum mouth opening (MMO) distance of the mandibular joint.

2.4. Data analysis

The extracted data included the following: basic information on the study, for example, the research topic and the first author; the baseline characteristics of the subjects and the intervention...
measures that they underwent; the key elements of the risk-of-bias (ROB) assessment; and the outcome indicators and outcome measures of interest.

Review Manager 5.3 and Stata 15.1 were used for analysis. The mean, standard deviation, and 95% confidence interval (CI) of the continuous variables were calculated. \( I^2 < 50\% \) was interpreted as indicating no substantial heterogeneity. In the absence of substantial heterogeneity, a fixed-effects model was used; otherwise, a random-effects model was used. To explore the heterogeneity among studies, sensitivity analysis was conducted, mainly to assess the factors that were most likely to have an impact. Furthermore, a funnel plot was used to inspect the data for publication bias.

3. Data extraction and quality evaluation

Two independent examiners (Zheng, Liu) read the full texts of the articles, screened the articles according to the inclusion and exclusion criteria, and extracted the data, and the first author examined their results. Then, the quality of each RCT was evaluated. Any disagreements between the 2 examiners were resolved through consultation with the third researcher (Zhu). The ROB tool recommended in the Cochrane Handbook (version 5.1.0, Cochrane Collaboration, London, England) was used to evaluate the quality of the RCTs. This tool addresses 6 aspects: random sequence generation, allocation concealment, blinding method for participants and outcome evaluators, incomplete outcomes, selective reporting, and the timing of outcomes.

The ROB assessment was performed for a total of 8\( ^{10,29,31–36} \) studies. Five\( ^{29,31–36} \) of the 8 studies described suitable random sequence generation methods, and 2\( ^{32,33} \) studies reported low-risk allocation concealment methods. Seven studies\( ^{29,31–36} \) reported a low-risk blinding approach (Fig. 2).

4. Results

4.1. Search results

A total of 85 articles were retrieved from the PubMed, EMBASE, Web of Science, Cochrane Library, and ClinicalTrials.gov databases. After screening the articles according to the inclusion and exclusion criteria, 8 studies involving a total of 181 patients were considered eligible. For a flow chart and the results of the literature retrieval process, see Figure 1.

4.2. Basic characteristics of the included studies and the results of the ROB assessment

The ROB assessment was performed for a total of 8\( ^{10,29,31–36} \) studies. Five\( ^{29,31–36} \) of the 8 studies described suitable random sequence generation methods, and 2\( ^{32,33} \) studies reported low-risk allocation concealment methods. Seven studies\( ^{29,31–36} \) reported a low-risk blinding approach (Fig. 2).

The basic characteristics of the studies that were assessed included the sample size, the numbers of men and women, the average age of the population, the intervention (independent variable), the outcomes (dependent variables), and the assessment time. All 8 studies were RCTs published between 2009 and 2020. The total number of patients in each study ranged from 9 to 60, and 25 (13.8%) of the total 181 subjects were male. (Two studies\( ^{33,35} \) did not report the number of subjects of each sex.)

The main anatomical sites assessed in the 6 studies reporting the primary outcome were also included. The laser treatment parameters of each study are shown in Table 2.

4.3. Statistical results

4.3.1. Degree of pain (VAS score). All 8 studies were included in this analysis because all used VAS score to evaluate the degree of pain reduction after treatment. We initially adopted a fixed-effects model. The results (\( Q = 63.4, I^2 = 89.3\% \), \( Z = 11.18, P = .00 \)) suggested substantial heterogeneity; therefore, we selected a random-effects model for analysis (\( t = 4.68, Q = 63.4, I^2 = 89\% \), \( Z = 11.65, P = .00 \)). The difference was significant, but there was still nonnegligible heterogeneity. We conducted a sensitivity analysis of the 8 articles to determine the sources of the heterogeneity and found that the studies by Khalighi (2016) et al\( ^{32} \) and Çetiner (2006) et al\( ^{36} \) were the main contributors (Fig. 3). Ultimately, we analyzed the data from the remaining 6\( ^{10,29,31,33,34} \) articles with a fixed-effects model, which yielded \( I^2 = 19\% \), \( Z = 2.00 \), and \( P = .046 \) and indicated a significant difference in VAS score between the interventions at the end of the treatment (Fig. 4).

Six\( ^{29,34–36} \) studies in this meta-analysis included measurements taken 3 to 4 weeks after treatment. A fixed-effects model (\( Q = 45.08, I^2 = 89\% \), \( Z = 6.05, P = .00 \)) suggested substantial heterogeneity; thus, we then employed a random-effects model for analysis (\( t = 6.95, Q = 45.08, I^2 = 89\% \), \( Z = 0.66, P = .51 \)), but nonnegligible heterogeneity persisted. Heterogeneity assessments were needed. Based on the sensitivity analysis of the six articles, we found that the studies by Ferreira (2013) et al\( ^{34} \) and Çetiner (2006) et al\( ^{36} \) were the main sources of heterogeneity. The 4\( ^{29,33} \) remaining studies were analyzed using a fixed-effects model; the results (\( I^2 = 0 \), \( Z = 1.90 \) and \( P = .057 \)) revealed no significant difference in VAS score between the interventions 3 to 4 weeks after treatment.

4.3.2. MMO. A total of 5 studies measured MMO at the end of treatment, among which those of de Godoy (2014) et al\( ^{29,35} \) and Borges (2018) et al\( ^{31} \) were excluded because of the different measurement methods used. There was high heterogeneity (\( \chi^2 = 10.15 \) [d.f. = 2], \( P = .006 \), \( I^2 = 80.3\% \), \( z = 4.83 \), and \( P = .000 \)) among the remaining 3 studies in the meta-analysis. Through sensitivity analysis, we identified the study by Khalighi (2016) et al\( ^{32} \) as the source of heterogeneity. The remaining 3\( ^{29,36} \) studies were analyzed, and the results revealed no significant difference in MMO between the groups (\( \chi^2 = 0.52 \) [d.f. = 1], \( P = .469 \), \( I^2 = 0.0\% \), \( z = 0.02 \), and \( P = .987 \) ) (Fig. 5).

Additionally, 2\( ^{29,36} \) studies measured MMO 3 to 4 weeks after treatment; both studies yielded \( P > .05 \), indicating no significant difference between the groups (\( \chi^2 = 0.79 \) [d.f. = 1], \( P = .373 \), \( I^2 = 0.0\% \), \( z = 0.58 \), and \( P = .565 \)). The results are shown in Figure 6.

4.3.3. Descriptive analysis. Because different measurement tools and evaluation methods were used among the studies, a meta-analysis of the pooled outcome data could not be carried out. Instead, we performed a descriptive analysis; the results are as follows:

4.3.3.1. Degree of pain. The studies by Khalighi (2016) et al\( ^{32} \) and others showed that the intensity of pain decreased significantly after GaAlAs laser treatment (\( P < .05 \)). Ferreira (2013) et al\( ^{34} \) found that the intensity of pain decreased significantly faster and to a lower level (\( P \leq .002 \)) in the intervention group than in the control group. Çetiner (2006) et al\( ^{36} \) also reported that the intensity of pain decreased significantly after treatment (\( P < .001 \)), but they found no significant difference between the interventions at the 1-month follow-up.
4.3.3.2. MMO. de Godoy (2015) et al\textsuperscript{[33]} applied GaAlAs LLLT, drugs, and a combination of the two treatments as interventions. The results showed no change in MMO from the beginning to the end of treatment for any intervention ($P > .1$). Borges et al\textsuperscript{[31]} evaluated the mobility of the temporomandibular joint by computer biophotogrammetry and found that the opening of only the left side significantly improved after GaAlAs laser treatment ($P < .05$). Khalighi (2016) et al\textsuperscript{[32]} found significant improvement in MMO after GaAlAs laser treatment ($P < .05$).

4.3.4. Publication bias assessment. A funnel plot was generated to investigate whether there was publication bias among the studies in this meta-analysis; a funnel chart with left-right symmetry suggests no publication bias. The resulting funnel plot was symmetrical, suggesting the absence of publication bias among the included studies (Fig. 7).

5. Discussion
This systematic review included a meta-analysis of 8\textsuperscript{[10,29,31–36]} studies (with 6 employing sham interventions\textsuperscript{[10,29,31–36]} and 2 employing other interventions [piroxicam\textsuperscript{[29]} and naproxen\textsuperscript{[29]}] as the comparison interventions), and the GaAlAs laser showed good efficacy in treating myogenic TMD pain at the end of treatment. We found evidence of moderate quality compared to the control group: 1. The GaAlAs laser decreased the severity of
pain at the end of treatment but did not maintain it. The GaAlAs laser was not shown to be effective in improving MMO either at the end of treatment or 3 to 4 weeks later. The quality of the RCT designs and reports included in our study ranged from low to high, with high ROB detected for random sequence generation, blinding methods, complete outcome indicators, among others.

**Table 1**

| Study                  | Sex     | age                          | Interventions and sample size | Control and sample size | Primary outcome | Therapeutic site | Assessment time                           |
|------------------------|---------|------------------------------|------------------------------|-------------------------|----------------|------------------|-------------------------------------------|
| Carrasco et al, 2009   | —       | —                           | 25 J/cm² n = 10              | 25 J/cm² n = 10         | VAS            | Ma               | Before; immediately after 8th application; 30 days after the last application |
| Ferreira et al, 2013   | 40 F/0 M| 34.17 ± 8.83 (20–40)         | n = 20                       | n = 20                  | VAS            | Ma               | Before; After the first mo               |
| de Godoy et al, 2014   | —       | (14–23)                      | n = 5                        | n = 4                   | VAS            | Ma               | Before; after LLLT                         |
| Khalighi et al, 2016   | 30 F/10 M| 36 ± 12.34                   | n = 20                       | n = 20                  | VAS            | Ma, Te           | Before; each session                     |
| De Carli et al, 2013   | 29 F/3 M| 32.4 (18–58)                 | n = 11                       | n = 10                  | VAS            | Ma               | Before; after LLLT at 30 days follow-up   |
| Borges et al, 2018     | 40 F/4 M| 31.9 ± 12.9 (15–59)          | n = 11                       | n = 11                  | VAS            | JC               | Before; post-intervention                |
| Çetiner et al, 2006    | 35 F/4 M| 31.7 (16–62)                 | n = 24                       | n = 15                  | VAS            | JC, Ma           | Before, just after, 1 mo after            |
| Khavi et al, 2020      | 11 F/4 M| —                           | n = 5                        | n = 5                   | VAS            | Ma, Te           | Before; each session                     |

Ma = Masseter, Te = temporalis, MP = medial pterygoid, LP = lateral pterygoid, JC = joint capsule, Pr = preauricular region, VAS = visual analogue scale, MMO = maximum mouth opening, LLLT = low-level laser treatment.
Regarding the design and reporting, allocation concealment was the most common source of ROB, as only 2\cite{32,29} reports performed allocation concealment.

The meta-analysis of the GaAlAs laser and control groups showed that pain relief was achieved only at the end of treatment. This finding is consistent with the results of most LLLT studies on TMD myofascial pain relief, in which LLLT was found to reduce pain at the myofascial trigger point\cite{32,29,37}. Studies of these interventions have shown that a low-energy laser exerts pressure and chemical action on the tissue, improves the microcirculation of the trigger area, increases metabolism, and thus breaks the vicious cycle of pain-spasmodic pain\cite{10,28,38}. In addition, compared with the control treatment, the GaAlAs laser treatment did not significantly affect MMO with or without pain, which may be related to overall muscle and joint function\cite{42}. Overall, the GaAlAs laser reduced pain compared to the control group at the end of treatment but did not show a performance advantage at the short-term follow-up. The influence of GaAlAs laser therapy on MMO is also not promising.

Of the studies reviewed here, 6 included a sham surgery group, and some reported partial improvement in symptoms in the sham treatment group. This improvement may have been detected because during treatment in the sham treatment group, the laser probe was vertically and gently pressed on the trigger point, producing a mild pressure stretch at the trigger point, and had a certain comforting psychological effect on the patients\cite{31,39}. In the studies employing a drug group as the comparison group, two different results were reported. Khalighi et al (2016)\cite{32} proposed that GaAlAs laser treatment performed better than drug treatment for pain and MMO at follow-up.

| Study                  | Laser type | Wavelength, nm | Laser energy density, J/cm² | Power density, mw | Pulsed, Hz, or continuous mode | Application time | Frequency and no. of sessions |
|------------------------|------------|----------------|----------------------------|------------------|-------------------------------|------------------|-------------------------------|
| Carrasco et al, 2009\cite{35} | GaAlAs diode laser | 780 | 25 | 50 | Continuous | — | Twice a wk, for 4 wk |
| Ferreira et al, 2013\cite{34} | GaAlAs diode laser | 780 | 112.5 | 50 | Continuous | 90 s | Once a wk for 3 mo |
| de Godoy et al, 2014\cite{33} | GaAlAs diode laser | 780 | 33.5 | 50 | Continuous | 20 s | twice a wk, for 6 wk |
| Khalighi et al, 2016\cite{32} | GaAlAs diode laser | 810 | — | 500 | Continuous | 60 s | 12 Sessions |
| De Carli et al, 2013\cite{29} | GaAlAs diode laser | 808 | 100 | 100 | Continuous | 28 s | Twice a wk, total of 10 sessions |
| Borges et al, 2018\cite{31} | GaAlAs diode laser | 830 | 8 | 30 | Continuous | 32s | 3 × wk/10 sessions |
| Çetiner et al, 2006\cite{36} | GaAlAs diode laser | 830 | 7 | — | — | 162 s | 10 Sessions daily for 2 wks |
| Khiavi et al, 2020\cite{10} | GaAlAs diode laser | 940 | 2.5 | 200 | — | 10 s | 3 Days a wk for a total of 10 sessions |

GaAlAs = gallium aluminium arsenide.

Figure 3. Meta-analysis.
De Carli (2012) et al\textsuperscript{[29]} reported that the effect of GaAlAs laser therapy was similar to that of drug therapy at the end of treatment but that the drug performance was more stable during follow-up. These differing findings may be related to the studies differences in trial design and the pharmacological action of the drug.\textsuperscript{[29]}

Figure 4. Forest plot of VAS score after treatment.

Figure 5. Forest plot of MMO immediately after treatment.

Figure 6. Forest plot of MMO 3 to 4 weeks after treatment.
Most of the patients in the study had chronic pain. The causes of chronic pain are complex and can be related to muscles, joints, gender, mood, etc. In this study, we found that the proportion of women participating in the study was higher than that of men, which may have been because women are more sensitive to pain or more susceptible to psychological effects. However, the results of this systematic review are inconsistent with those of Munguia (2018) et al, who concluded that LLLT is more effective than a placebo in relieving chronic TMD pain at 3 to 4 weeks after treatment. Munguia (2018) et al used various types of lasers and different inclusion and exclusion criteria for the sham treatment group, which might explain the inconsistent results between the studies.

TMD pain is a common source of facial pain and can be divided into two categories: muscle-derived TMD and arthrogenic TMD. The triggering factors of muscle-derived TMD pain mainly exist in the masseter muscle, temporal muscle and pterygoid muscle. In the included studies, an intervention at the dominant trigger point was reported, and 7 masseter muscles, 6 temporalis muscles, 3 medial pterygoids (MPs), 3 lateral pterygoids (LPs), and 3 joint capsules (JCs) were used to intervene in the dominant trigger point. We found that the GaAlAs laser was effective in the treatment of muscle-derived TMD after the completion of treatment. In addition, De Carli (2012) et al showed that the effect of piroxicam was consistent with that of the GaAlAs laser during treatment but better than that of the GaAlAs laser after 30 days of follow-up. Although analgesics are a major component of the treatment of TMD-related pain and are of great benefit to patients, further evidence regarding their safety and side effects is needed.

Heterogeneity was observed in our analysis. The GaAlAs laser is a class IIIb laser with clinical heterogeneity in terms of treatment parameters. These parameters include laser energy density, power density, pulse or continuity, application time, frequency, and number of treatments. The meta-analysis of the main results showed that VAS pain changes at the end of treatment presented statistical heterogeneity. The sensitivity analysis showed that the studies of Decali et al (2014) and Khalighi et al. (2016) were the main sources of heterogeneity. The different results of Decali et al (2014) may have been due to the small number of participants and the use of a left-right intrathematic design, which was inconsistent with the methods of the other studies. The Khalighi et al (2016) study was identified as a low-quality study based on the ROB tool. A fixed effect model was used to analyze the data. As the observational indicators were consistent, a descriptive analysis of the 2 studies was conducted.

There was ROB in the included studies, which was reflected mainly in allocation concealment. In this meta-analysis, although study heterogeneity in posttreatment pain was detected ($I^2 = 19\%$), the $I^2$ value was $<25\%$; as this is suggestive of only weak heterogeneity, we considered it unlikely to have substantially influenced the results.

In summary, this study extracted data from previous studies on the application of the GaAlAs laser for TMD treatment. The operation parameters of the GaAlAs laser, included the wavelength range, are largely fixed. Although the sample included in this study was small, we completed this study in strict accordance with the PRISMA statement and strictly controlled the data included in the analysis. Therefore, the results of this study regarding the GaAlAs laser can help guide the treatment of TMD.

6. Conclusions

In this review, the meta-analysis of the included studies showed that GaAlAs laser therapy is superior to control treatment in reducing pain at the end of treatment. However, there is only moderate evidence. Furthermore, GaAlAs laser therapy is not advantageous in terms of outcome stability or MMO. To this end, there are insufficient data and high-quality evidence to draw strong conclusions about GaAlAs laser treatment of TMD myofascial pain, especially with respect to MMO, and data from large samples are lacking. Therefore, clinicians need to consider the value orientation of this intervention before applying it to patients. Given the individual differences and the complexity of the disease, more evidence is needed for future clinical research and practice.

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