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# Non-invasive therapies for management of temporomandibular disorders: a systematic review

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## ABSTRACT

**Introduction:** As a multifactorial disease, temporomandibular disorders (TMD) require a complex therapeutic approach, being noninvasive therapies the first option for most patients. The aim of this study was to perform a systematic review to analyze the most common non-invasive therapies used for TMD management.

**Methods:** The review was done by searching electronic databases to identify controlled clinical trials related to pharmacologic and non-invasive treatments. Of all potential articles found, 35 were included in this review.

**Results:** Low-level laser therapy (LLLT), occlusal splints (OS) and oral exercises/behavior education (OE/BE) were the most common therapies used. LLLT showed significant results in pain and movement improvement in most studies. OS was usually combined to other therapies and resulted in improvement of pain. OE/BE showed significant results when combined with ultrasound, LLLT, and manual therapy.

**Conclusions:** Non-invasive treatments can provide pain relief and should be prescribed before surgical procedures. LLLT was the therapy with the higher number of studies showing positive results. Based in heterogeneity of treatment protocols, diagnostic and outcomes criteria used, new well-designed randomized controlled trials (RCT) are necessary.

***Keywords:*** *Temporomandibular disorder; temporomandibular joint; myofascial pain; treatment; temporomandibular dysfunction; pharmacologic*

Temporomandibular disorders (TMD) are the most common chronic orofacial pain conditions. TMD include several clinical disabilities affecting the temporomandibular joint (TMJ) and masticatory muscles. Mainly characterized by pain, movement limitation, and TMJ sounds, TMD are usually associated with headache, cervical dysfunction, and other related signs and symptoms[1-5]. Pain is the most debilitating symptom, interfering with daily activities, quality of sleep, and psychological aspects as anxiety, stress, and depression[6].

As multifactorial disorders, TMDs require a multidisciplinary approach. Usually, first treatment options are noninvasive treatments, including occlusal splint (OS), photobiomodulation (PBM), manual therapy (MT), electrotherapy, acupuncture, oral exercises and behavioral education therapies (OE/BE), as well as pharmacological therapy[7-13]. The primary goal of noninvasive therapies is pain relief, avoiding acute pain to become a chronic condition, which leads to changes of pain perception and delay of treatment responses[4,6,10,14,15].

### *Occlusal splint (OS)*

Among management possibilities, OS is the most frequently recommended. OS is a removable appliance that covers all the occlusal and incisal surfaces of teeth in the upper or lower jaw[6,10,11]. Although the mode of action of OS is not fully clear, studies show that it promotes bilateral balancing and protects teeth


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from wear caused by bruxism[6,10,16]. There are many types of OS with different indications and functions[1,13,17]. The most used are the stabilization splints, also known as Michigan splints. Usually made with hard acrylic, the splint is designed to provide a temporary and ideal occlusion leading to neuromuscular balance and decreasing muscle tension[1,13,17,18].

### *Low-level laser therapy (LLLT) – Photobiomodulation Therapy*

LLLT is the application of light within the red and near infra-red wavelength range of 600-1000 nm. It is a non-ablative and non-thermal light[4,7,8,19], which has been widely used due its low cost, easy application, and short treatment time[3]. There is evidence that LLLT modulates the inflammatory process, reduces pain and edema, and increases blood circulation and extensibility of the nervous system[4]. In addition, no side effect is reported when correctly administered[20]. The clinical efficacy of TMD is controversial due to the difference in parameters, dosimetry, and assessment criteria used by studies, besides the clinical variability of TMD patients. For TMD symptoms, the commonly used wavelength is in the infrared spectrum from 780 nm to 904 nm[3-7].

### *Therapeutic ultrasound (US)*

US is the application of mechanical vibrations, known as sound energy, at increasing frequencies above 16 Hz generated by a piezoelectric effect using a frequency between 1.0 and 3.0 MHz. It is useful in fresh injuries with acute inflammation[21,22]. The right dosimetry ensures an optimal outcome with minimum risk of adverse effects[21]. Another useful application of ultrasound is in the administration of anti-inflammatory ointments with a hand-held transducer. The energy forces the diffusion of medications through the skin to target underneath soft tissues. This method is called phonophoresis[21].

### *Transcutaneous electrical nerve stimulation (TENS)*

Among therapies for TMD, TENS has been proposed as a safe and noninvasive therapy with low-voltage electrical pulses. Using electrodes on the skin over the painful area, TENS can modulate the control system of endogenous pain promoting pain relief and reduction of muscular activity[6,22,23]. There are two theories explaining its action on pain modulation. One theory suggests that the rhythmic contractions of muscles caused by TENS increase blood and lymph circulation, resulting in the decrease of interstitial swelling and improvement of the circulation of noxious tissue metabolites, leading to muscle relaxation[22,24]. The other theory is based on gate control, which preconizes that the electrical stimulus travels faster in afferent fibers of large diameters closing the pain gates of the spinal cord[24].

### *Manual therapy (MT)*

MT has been increasingly used due to the positive outcomes in some musculoskeletal and hypomobility conditions[25,26]. In masticatory muscles, MT promotes muscular relaxation, stimulates joint proprioception, relieves pain, and improves mandibular movements[26]. The literature reports that MT is an important method that promotes the release of opioid and non-opioid substances and inhibitory neurotransmitters that act in the central nervous system. Moreover, some studies suggest that MT can decrease the EMG activity in masticatory muscles[26-28].

### *Oral exercises and behavioral education (OE/BE)*

Self-management (SM) or self-care includes cognitive behavioral therapies as education about negative habits and counseling, relaxation techniques, and home exercises[6]. There is poor evidence of its effectiveness due to the differences on prescription[12,29]. Benefits of exercises include decrease in pain due to the release of endogenous non-opioid and opioid substances by stretching and strengthening masticatory muscles, increasing mobility, and tissue regeneration[4-6,12,29]. Stretching and relaxation exercises are first recommended when pain is present, helping patients to overcome the fear of moving the TMJ[6,29]. However, most studies compare these exercises with other therapies, which makes it difficult to evaluate the real effectiveness of this therapy alone[25,29-31]. While some studies indicate therapeutic exercises and BE as an essential part of treatment, others show the difficulties to define one program, since there is no established and tested gold standard for SM programs yet. In fact, previous studies present inconsistent results of therapeutic exercises and SM programs[5,6,32].

### *Acupuncture*

This millenary Chinese therapeutic method consists of placing needles into the skin for pain management. The technique uses specific acupoints and painful points. A variation of traditional acupuncture that has been widely used is dry needling, which applies needles with vigorous stimulation at trigger points[33-35]. Although several explanations are proposed, the mode of action is not fully clear. It is accepted that the needle penetration causes a micro-inflammation process improving blood circulation and neurotransmitters release, such as serotonin, encephalin, and endorphin, which prevent the propagation of painful stimuli[36-38]. In addition, acupuncture promotes muscle relaxation, reestablishing body and mind balance, with recent studies showing benefits in anxiety, depression, and insomnia[6,36,37]. For TMD patients, acupuncture is suggested as an adjunctive and important method with positive effects such as decreased muscle tension and pain[35].

### Pharmacological treatments

Pharmacological treatment is a common approach for orofacial pain as a monotherapy or associated with other therapies and surgical interventions. Used alone, it is considered a palliative therapy[39,40]. The most commonly used drugs to decrease pain and inflammatory process in joints and/or muscles are myorelaxants, non-steroidal anti-inflammatory drugs (NSAIDs), analgesics, tricyclic antidepressants (TCAs), benzodiazepines, and corticosteroids[9,39,41]. A wide range of pharmacotherapeutic agents is available; however, there is a lack of scientific evidence and no conclusive result for any of these drugs for the TMD population[6,10,39,42].

Many clinical trials were performed with controversial results. Therefore, the main question of our review was: "Are non-invasive therapies effective to decrease pain and improve movements in TMD patients?".

## METHODS

### Search strategy and inclusion criteria

The bibliographical search was performed between January and August 2019. PubMed, Embase, and Scielo databases were used in two independent searches to identify relevant randomized clinical trials (RCTs) using non-invasive therapies in TMD patients, performed in the last 12 years. The first search used the keywords "*temporomandibular disorder*" *OR* "*temporomandibular joint*" *AND* "*myofascial pain*" *AND* "*treatment*". The second used the search terms "*temporomandibular dysfunction*" *AND* "*pharmacologic*". In addition, a hand search in the reference lists of included articles was done to identify other relevant studies and review articles.

### Data collection and analysis

Two reviewers independently identified titles and abstracts resulting from the search strategy for potentially eligible studies. Duplicate items were removed as well as studies with surgical intervention, invasive therapies, and rheumatic and neurologic diseases. Afterwards, a full text reading was performed for final eligibility.

### Data extraction

The data and results of each included study were extracted using a standard form. All data were cross-checked by a second reviewer. Any lack of agreement was resolved by discussion. The data analysis was based on the type of intervention and outcomes. The primary outcome of interest for this review was pain and the secondary outcome was range of motion (ROM).

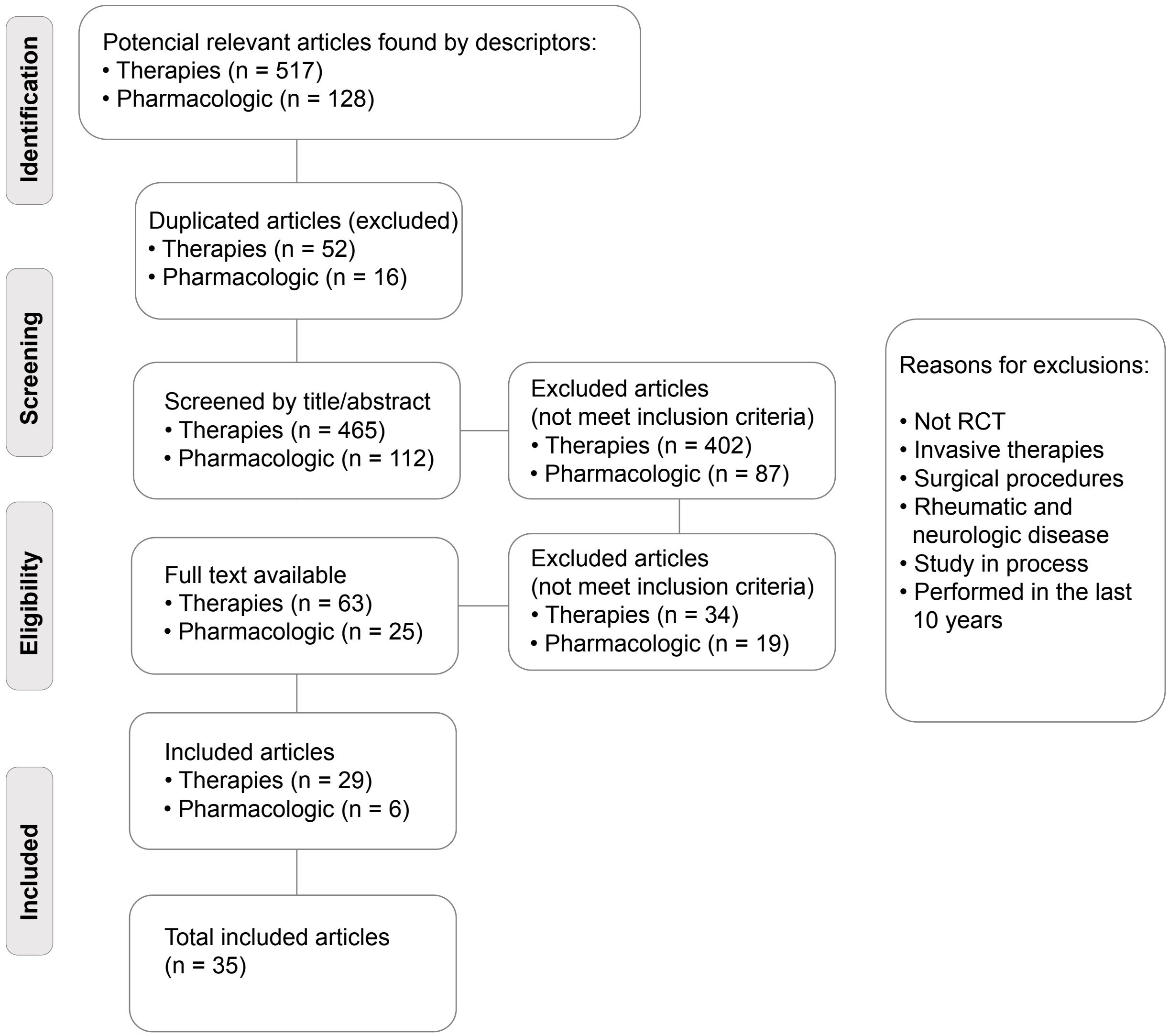
### Methodological quality assessment

The Cochrane risk of bias tool[43] was used to assess the methodological quality of the studies according to the following domains: random sequence generation, allocation concealment, blinding, incomplete data, selective reporting and other potential sources of bias.

## RESULTS

### Literature search

The initial search found 517 articles about therapies and 128 articles about pharmacological treatments, resulting in 645 articles. Of these, 557 were excluded due to duplications, invasive therapies or surgical procedures, reviews, and case reports. A total of 82 articles were selected for full text reading (63 about therapies and 25 about pharmacological treatment) and finally 35 articles were included in this systematic review (Figure 1).




### *Study characteristics and interventions*

The main characteristics of the 35 included studies are described in Chart 1a and Chart 1b. The sample sizes ranged between 12 and 104 individuals with TMD symptoms, including men and women allocated in the same comparison group, except three studies that included only women[4,44,45].

Of all the included studies, 13 (37%) used OS[1,10,16,36,46-54], 12 (34%), OE/BE[1,5,16,25,27,31,47,48,50-52,54], 12 (34%), LLLT[2,5,15,20,24,44,55,57-60], 7 (20%), MT[5,25,27,47,52,54,61], 4 (11%), acupuncture[33,36,46,62], 3 (9%), NSAIDs[10,44,53], 3 (9%), TENS[22,24,54], 2 (6%), US[22,31], one (3%) benzodiazepine[58], one (3%) TCAs and Gabapentin[59], and one (3%), melatonin[45].

Fourteen studies (40%) did not use control or placebo groups for comparison with the test therapy. The comparison of techniques using 2 or more groups was done in 30 (86%) studies[2,5,10,24,33,44,45,54-59,61-63].

Risk of bias is shown in Chart 2. A total of 29 (82%) studies presented low risk[1,2,5,10,15,16,20,24,25,27,31,33,36,45-48,50,51,54-59,61-64] and three (9%) presented high risk[44,49,61]. Other three (9%) studies showed an unclear risk of bias due to insufficient information in at least one domain[22,52,53].

Chart 1a: Main characteristics of the included studies – Therapies

| Study | Diagnostic Criteria | Outcomes | Groups | Location of application and type of exercises | Effects |
|---|---|---|---|---|---|
| Ismail et al., 2007 | RDC/TMD<br>VAS | Pain<br>Mouth opening | Occlusal splint<br>MT + OE + Occlusal splints | Muscles | Pain: significant decrease intragroup and no difference between the groups.<br>Function: significant decrease intragroup and no difference between the groups. |
| Carrasco et al., 2008 | VAS<br>Palpation<br>Colorimetric Method | Pain<br>Mouth opening | LLLT (780nm)<br>LLLT Placebo | Joint (5 points) | Pain: significant reduction in the LLLT group<br>Function: No significant difference |
| Cuccia et al., 2009 | VAS<br>Calibrated caliper | Pain<br>Mouth opening | Osteopathic manual therapy (OMT)<br>Conventional conservative therapy (CCT) | Cervical and masticatory muscles | Pain: Significant difference intragroup in both groups. No significant difference between groups.<br>Function: Significant difference intragroup in the OMT group. No significant difference between groups. |
| Felício et al., 2009 | RDCTMD<br>Helkimo's Indexes<br>ProTMDMulti protocol<br>Orofacial Myofunctional Evaluation (OMES Protocol). | Pain<br>Mandibular range of motion<br>Function | Orofacial myofunctional therapy<br>Occlusal splint<br>Control TMD<br>Control | Masticatory muscles<br>Tongue | Pain: Significant reduction in the exercise group (intergroup)<br>Function: Significant difference in the exercise group (intergroup) |
| Fernández-Carnero et al., 2010 | RDC/TMD<br>VAS<br>Algometer | Pain<br>Mouth opening | Acupuncture<br>Sham Acupuncture | Muscular pain points | Pain: significant difference<br>Function: significant difference |
| Mazzeto et al., 2010 | VAS<br>Millimeter ruler | Pain<br>Mouth opening | LLLT (830 nm)<br>LLLT Placebo | Joint (4 points) | Pain: significant difference<br>Function: significant difference |
| Kalamir et al., 2011 | RDC/TMD<br>Rating scale – 0-10 | Pain<br>Mouth opening | Manual therapy (IMT)<br>OE + BE (ESC) | Intra oral masticatory muscles | Pain: significant reduction IMT group (intergroup)<br>Function: no significant between groups |
| Vicente-Barrero et al., 2012 | VAS<br>Millimeter ruler<br>pressure algometer | Pain<br>Mouth opening | Acupuncture<br>Occlusal splints | Acupoints | Pain: significant reduction myofascial pain in both groups. No significant reductions in subjective pain and pain on pressure points in occlusal splints.<br>Function: significant improvements in the Acupuncture group. No significant difference between groups. |

Continue...

Chart 1a: Continuation.

| Study | Diagnostic Criteria | Outcomes | Groups | Location of application and type of exercises | Effects |
|---|---|---|---|---|---|
| Itoh et al., 2012 | Palpation<br>VAS<br>Millimeter ruler | Pain<br>Mouth opening | Acupuncture<br>Sham Acupuncture | Masticatory and cervical muscles | Pain: significant reduction in both groups<br>Function: no significant difference |
| Niemela et al., 2012 | VAS<br>Clinical examination | Pain<br>Mouth opening | Occlusal splints<br>OE/BE | Muscles | Pain: no significant difference between groups<br>Function: no significant difference in between groups |
| Katyayan et al., 2014 | RDC/TMD. VAS | Pain<br>Mouth opening | Occlusal splints<br>OE/BE | Muscles | Pain: no significant difference between groups<br>Function: no significant difference in between groups |
| Grillo et al., 2015 | RDC/TMD<br>VAS<br>Millimeter ruler<br>digital algometer<br>Pulsology and tongue observation | Pain<br>Mouth opening | Acupuncture<br>Occlusal splints | Acupoints<br>Flat occlusal splint | Pain: significant reduction in both groups<br>Function: significant increase in both groups |
| Michelotti et al., 2012 | RDC/TMD. VAS | Pain<br>Mouth opening | Occlusal splints<br>Behavioral education (BE) | Muscles | Pain: significant reduction in the BE group<br>Function: no significant difference |
| Qvintus et al., 2015 | RDC/TMD. VAS | Pain<br>Mouth opening | Occlusal splints<br>Control – OE +BE | Muscles | Pain: no significant difference between groups.<br>Function: no significant difference between groups |
| Ucar et al.,2014 | RDC/TMD<br>VAS<br>Millimeter ruler | Pain<br>Mouth opening | US + OE<br>Control -OE | Muscles | Pain: significant reduction in both groups<br>Function: significant reduction in both groups |
| Salmos-Brito et al., 2013 | RDC/TMD<br>VAS<br>Millimeter ruler | Pain<br>Mouth opening | LLLT (830 nm) | Joint (5 points) | Pain: no significant difference<br>Function: significant increase in the acute group |
| Tuncer et al., 2013 | VAS<br>Millimeter ruler | Pain<br>Mouth opening | OE/BE (HPT)<br>Manual therapy + OE/BE (MT+HPT) | Muscles | Pain: significant decrease in the MT + HPT<br>Function: significant improvement MT + HPT |
| Ahari et al., 2014 | RDC/TMD<br>VAS<br>Millimeter ruler | Pain<br>Mouth opening | LLLT (810 nm)<br>Placebo | Muscular (pain) | Pain: significant decrease<br>Function: significant improvement |

Continue...

Chart 1a: Continuation.

| Study | Diagnostic Criteria | Outcomes | Groups | Location of application and type of exercises | Effects |
|---|---|---|---|---|---|
| Sancakli et al., 2015 | RDC/TMD<br>VAS<br>Algometer | Pain<br>Mouth opening | LLLT (820 nm) – pain points<br>LLLT (820 nm) – pre-established points | Masseter and temporalis.<br>3 points on the temporalis muscle. | Pain: significant reduction in both groups<br>Function: significant reduction in both groups |
| Pereira et al., 2014 | RDC/TMD<br>Numerical rating scale | Pain<br>Mouth opening | LLLT (660 nm)<br>LLLT (795 nm) | Muscles and joint | Pain: significant reduction in the infrared group (180 days)<br>Function: significant increase in the infrared group (180 days) |
| Rai et al., 2016 | RDC/TMD<br>VAS | Pain<br>Mouth opening | Control<br>US<br>Tens | Muscles | Pain: significant decrease US<br>Function: no significant improvement |
| Machado et al.,2016 | RDC/TMD | Pain palpation<br>Mouth opening | LLLT (780 nm) + OE (GI)<br>Orofacial myofunctional therapy (GII)<br>LLLT placebo + OE (GIII)<br>LLLT (780 nm) (GIV)<br>LLLT Placebo | 5 points TMJ and painful muscles | Pain: significant reduction in the Combined, GII and GI groups<br>Function: significant increase in the Combined, GII and GI groups |
| Grootel et al., 2017 | RDC/TMD<br>VAS | Pain<br>Mouth opening | Occlusal splints<br>OE | Muscles | Pain: no significant difference<br>Function: no significant difference |
| Seifi et al., 2017 | VAS<br>Millimeter ruler | Pain<br>Mouth opening | TENS<br>LLLT (810 nm)<br>Sham TENS<br>Sham LLLT | Muscles | Pain: significant reduction on experimental groups.<br>Function: significant improvement in the mouth opening on experimental groups. |
| Ferreira et al., 2016 | RDC/TMD<br>VAS<br>Algometer<br>Electromyography (EMG) | Pain<br>Mouth opening | TENS<br>TENS Placebo | Masticatory muscles | Pain: significant decrease<br>Function: no significant difference |

Continue...

Chart 1a: Continuation.

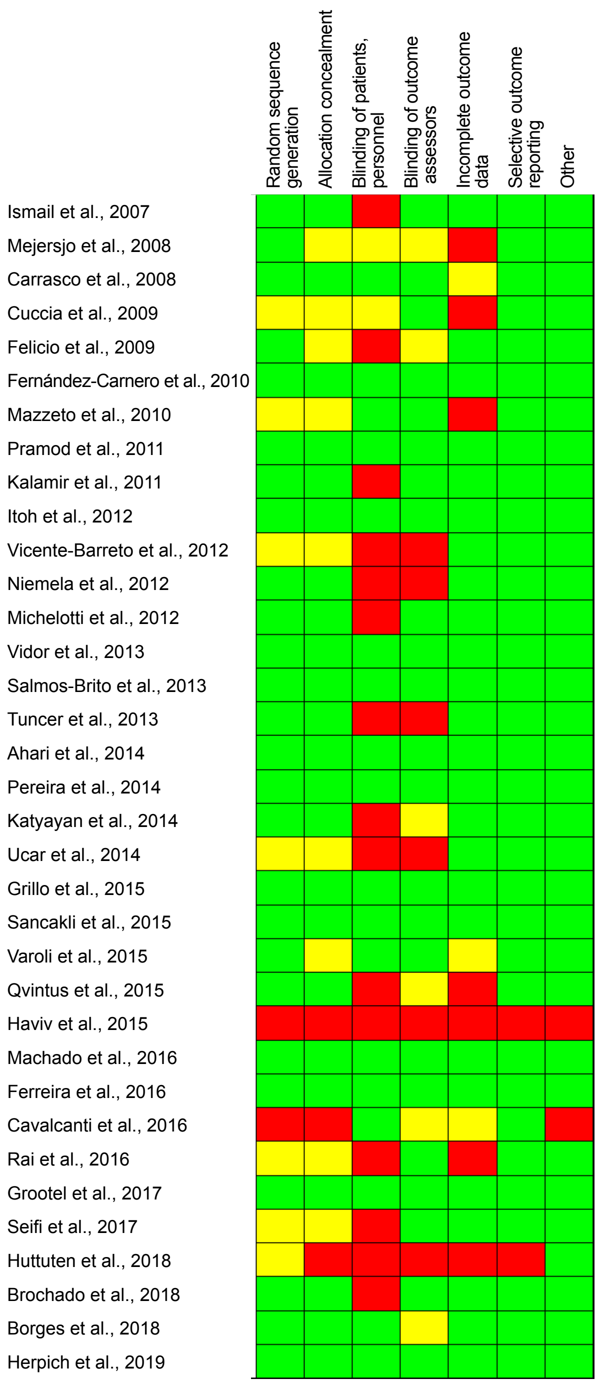
| Study | Diagnostic Criteria | Outcomes | Groups | Location of application and type of exercises | Effects |
|---|---|---|---|---|---|
| Huttunen, et al., 2018 | RDC /TMD (axis I and II)<br>VAS<br>Helkimo´s Index | VAS<br>Psychosocial effects | Splint<br>Control group | | Pain: No significant difference |
| Brochado et al., 2018 | RDC/TMD<br>VAS<br>Beck inventory | Pain<br>Range of motion<br>Psychosocial effects | Manual Therapy<br>LLLT (810 nm)<br>Manual therapy + LLLT | Joint (5 points)<br>Muscles | Pain: No significant difference between groups<br>Function: No significant difference between groups |
| Borges et al., 2018 | VAS<br>Fonseca questionnaire<br>Computerized biophotogrammetry | Pain<br>Mobility | LLLT (830 nm) – 8 J/cm²<br>LLLT (830 nm) – 60 J/cm²<br>LLLT (830nm) – 105 J/cm²<br>Control | Joint (4 points) | Pain: No significant difference between groups<br>Function: Significant improvement in the 8 J/cm2 MMO |
| Herpich et al., 2019 | RDC/TMD<br>VAS<br>Digital Caliper<br>Patient-Specific Functional Scale | Pain<br>Mouth opening | Intraoral Laser (905 nm) + red LED<br>(670 nm) + infrared LED (875 nm)<br>Sham group | Intraoral | Pain: Significant difference in the treatment group after 48hs and 6 sessions<br>Function: No significant difference between groups |

Continue...

Chart 1b: Main characteristics of the included studies – Therapies.

| Study | Diagnostic Criteria | Outcomes | Groups | Effects |
|---|---|---|---|---|
| Mejersjo et al, 2008 | VAS<br>Helkimo index | Pain | NSAID Occlusal splints | Pain: No significance between groups<br>Significant reduction intragroup |
| Pramod et al, 2011 | RDC/TMD<br>VAS<br>Millimeter ruler | Pain<br>Tenderness<br>Mouth opening | Benzodiazepine<br>Placebo | Pain: no significant reduction intergroup<br>Function: significant increase intergroup |
| Vidor et al, 2013 | RDC/TMD<br>VAS | Pain<br>Sleep quality | Melatonin<br>Placebo | Pain: significant reduction in the melatonin group |
| Varoli et al, 2015 | RDC/TMD<br>VAS | Pain | NSAID + Occlusal splints<br>Occlusal splints<br>Panacea + Occlusal splints | Pain: significant reduction in all groups. No significant reduction between the groups. |
| Haviv et al, 2015 | Verbal pain Scale (VPS)<br>RDC/TMD | Pain | TCAs<br>GBP | Pain: significant reduction in both groups. In pain spread, GBP had significant better results. |
| Cavalcanti et al, 2016 | Palpation<br>Fonseca questionnaire | Pain | LLLT (780 nm)<br>Myorelaxing drug +anti-inflammatory drug + OE + hot packs<br>Placebo light | Pain: significant reduction in experimental groups |

Chart 2: Risk of bias




### *Outcomes*

To assess the presence of TMD, as well as the type of disorder and diagnosis of myofascial pain, 24 (68%) studies applied the standardized evaluation protocol, the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD)[1,2,5,10,15,16,20,22,27,31,45-49,50,54,56,58,61,62,64], three (9%) used the Helkimo index[49,53,54], and two (6%) applied the Fonseca questionnaire[44,63]. The remaining 8 (23%) studies adopted non-standard evaluation protocols, using clinical evaluation to include patients with signs and symptoms of TMD[24,25,33,36,51,52,55,57].

All studies evaluated the outcomes at baseline and after the treatment protocol[61], with number of sessions varying from 1 week to 1 year. Pain levels were assessed as the primary outcome in all studies using Visual Analogic Scale (VAS) in 29 (83%) studies[1,2,10,15,16,22,24,25,31,33,36,45-59,61-64] or an algometer to evaluate the pressure pain threshold in 5 (14%) studies[2,36,46,58,62]; one study (3%) used the Verbal Pain Scale[59]. The results of an intragroup analysis demonstrated that 27 (77%)[5,10,20,22,24,25,27,31,33,36,44,45,46,47,50,52-63] of the studies presented reduction in pain and 22 (62%)[2,5,10,15,20,24,25,31,36,44-47,52-54,56,57,59,60,62,64], improvement in function. Among them, LLLT (34%)[2,515,20,24,44,55-58,63,64], OE/BE (28%)[5,16,21,25,27,47,48,50,51,54], and OS (31%)[1,10,16,36,46-51,53,54] were the most used. When analyzing the differences between treatments at the end of the protocols (intergroup analysis), 20 (57%) of the studies showed no significant difference in the levels of pain[1,2,10,15,16,24,31,33,36,44,46-49,51-53,59,63,64].

In terms of secondary outcome measures, changes in mouth opening were evaluated in 29 (82%) studies. A millimeter ruler was used in 10 (29%) studies[15,24,25,31,33,36,46,56,57,63] and a caliper in 4 (11%)[1,27,52,58]. The remaining 6 (17%) studies did not describe the secondary outcome[10,44,45,49,53,60]. Significant improvement in mouth opening was described only in 13 (37%) studies using LLLT (17%)[15,20,24,56,57,64], acupuncture (6%)[36,62], MT (6%)[25,52], TENS (3%)[24], OMT (3%)[54], and benzodiazepine (3%)[59]. The combination of MT and OE/BE (9%)[5,25,54] or LLLT and OE (3%)[5] had significantly better results than the therapies alone or placebo.

## DISCUSSION

Non-invasive therapies have been recommended as first choice treatment for TMD arousing the interest of many authors who attempted to find a gold standard treatment protocol[6,7]. Despite the wide use of these therapies in clinical practice, the efficacy of most of them in TMD is still controversial, probably due to the variety of parameters and protocols[7,60,65]. Our results demonstrated that non-invasive therapies presented a low positive response, found in only 43% of the studies. Among them, OS, OE/BE and LLLT were the most commonly used. LLLT was the treatment with the highest rate of improved TMD symptoms. The absence of a placebo or a control group was noteworthy. The included RCTs had good methodological quality with low risk of bias.

The correct diagnostic of TMD is complex but essential to decide treatment strategies and follow the patients. The diagnosis is usually based on validated questionnaires and clinical tests[4,7]. The RDC/TMD is one of the most used instruments which classified the types and subtypes of TMD (axis I) and information related to psychosocial aspects (axis II) of patients[6,8]. Our review showed that 24 (68%)[1,2,5,10,15,16,20,22,27,31,45-49,50,54,56,58,61,62,64] studies used a gold standard method (RDC/TMD-axis I) to diagnose TMD, which ensures a good analysis of the effects of therapies. Only few studies applied other validated index, such as Helkimo's[49,53,54] and Fonseca[44,64], to assess the severity of TMD symptoms, but these questionnaires present some limitations and are not able to provide sufficient information to classify TMD dysfunction[44,53,54]. Besides that, our results showed only one study[63] that considered the psychosocial aspects and their influence on primary and secondary outcomes. TMD treatment has been considered a challenge because of its multifactorial origin, including a complex interaction among physical, behavioral, social, and psychological factors[49,52,60]. Based on these aspects, the analysis of the impact of treatment strategies based on the perspective of quality of life has been currently suggested. Therefore, new clinical trials involving TDM treatment should include Axis II of RDC and other questionnaires of anxiety and/or quality of life.

Pain is well known as the main symptom of TMD leading the patients to incapacity and a poor quality of life.[7] Corroborating with these, our review showed that all analyzed studies evaluated pain as the primary outcome. VAS was the most common strategy to evaluate the levels of pain in 29 (83%) studies[1,2,10,15,16,22,24,25,31,33,36,45-53,55-59,61-64.] Another important outcome observed in the studies analyzed was mouth opening[2,5,10,15,20,24,25,31,36,44-47,52-54,56,57,59,60,62,64]. This is an important aspect to be addressed because it can interfere with patient's daily activities such as chewing, oral hygiene, smiling and others.

Interestingly, results were observed regarding the effect of different non-invasive therapies especially evaluating pain (main outcome). Analyzing intragroup data, all therapies demonstrated positive effect to relieve pain comparing the baseline with the end of the treatment. However, the intergroup analysis (comparison among groups) does not demonstrate the same positive results. Only 15 (43%) of the 35 studies presented significant difference between groups. The LLLT presented better results in most of the studies evaluating pain (17%)[5,20,55-58] and range of movement (17%)[2,15,20,56,57,59].

The interest on LLLT is increasing, since its application is easy with no reported side effects[4]. Different parameters, such as number of sessions, sites of application, and dosimetry have been described, which indicate that this is a controversial therapy[3]. Some authors believe that 8 sessions with applications twice a week promote positive effects[52,57]. However, other authors[2,5,15,56] propose 12 sessions. In addition, two authors applied the therapy using 3[20] or 4 sessions[24] during only one week, although they found inconsistent results. LLLT application points also varied among studies, being the most common the jaw, masseter, temporalis, and pterygoid muscles (intraorally)[2,56]. Better results in pain and mobility were described using pre-established muscular points (masseter, temporalis, and pterygoid) or trigger points[2] rather than the joint points. In addition, the infrared laser provides better results in the long term (180 days) compared with red laser. However, short-term effects did not show statistical difference between red and infrared wavelengths[20]. One recent study[64], compared different protocols of LLLT (830 nm) showing that 8J/cm$^2$ is more effective to improve mouth opening than 60 J/cm$^2$ or 105 J/cm$^2$. However, all protocols of LLLT promoted pain relief.

The OS is widely recommended[49] and is one of the most used treatments in the RCTs included in the present review. However, the analysis of our results showed that its benefits in improving TMD symptoms are controversial[6,49] especially because OS had been used in combination with other therapies. Among the 12 studies that used OS[1,10,16,36,46-51,53,54], only 4 (33%) used as an individual treatment option and showed reduction in pain[36,46,49,54]. The other studies compared the effects of OS with acupuncture[36,46], Manual therapy[55] and/or NSAIDs[10,53] and showed improvement in pain in all different treatment groups. These results indicated that all of these treatments reduced pain and can be applied alone or in combination as good choice for TMD patients.

Another non-invasive therapy commonly used in our review was OE/BE. Like OS, OE/BE had been used in clinical trials mostly in combination with other therapies. In general, among the 10 studies included, 6 (60%) showed positive results with decrease of TMD symptoms[5,25,27,50,52,54]. It is difficult to compare the results among studies due to the differences in exercise protocols, time of duration of the treatment that varied from 10[1,48,51] to 45 min[47] and from 2 to 3 times/day[1,31,48,51] to 2 times/week[25,47]. Two studies used a very well-designed protocol called oral myofunctional therapy which combined BE instruction, oral, respiratory and cervical exercises with thermotherapy and self-massage. Both evidenced positive results in improvement of pain and masticatory function in OE/BE group[5,54].

Pharmacological treatment is frequently recommended for orofacial pain[42]; however, we found only 6 (18%) RTCs using pharmacological treatments for TMD. Most of the existing literature evaluating pharmacologic treatments are observational clinical studies instead of RCTs[40,59]. The selected studies evaluated the effects of benzodiazepine (16%)[59], anti-inflammatory (33%)[10,53], myorelaxant drugs (16%)[44], melatonin (16%)[45], and TCA and gabapentin (16%)[60]. Positive improvements were found only with melatonin[45]. Besides that, significant results for pain spread were found using gabapentin[60]. These results indicated that more clinical trials studies are necessary to evaluate the impact of pharmacological treatment in TMD patients.

## CONCLUSION

TMD is a complex musculoskeletal disorder with several clinical, psychological, and behavioral components, leading to a difficult standardization of protocols and treatment evaluation. In this review, non-invasive therapies were the first choice for TMD patients and all of them improve, at least partially, TMD signs and symptoms. Therefore, noninvasive treatments can provide pain relief and should be prescribed before surgical procedures. LLLT, OS, OE/BE were the most commonly used therapies. LLLT was the therapy with the higher number of studies showing positive results compared to placebo, control, or other therapies. In general, important heterogeneity in treatment protocols, diagnostic and outcomes criteria was observed indicating the necessity of new well-designed randomized controlled trials.

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