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ORIGINAL ARTICLE

Temporomandibular Disorders Treatments and Its Effects on Headaches: Systematic Review and Meta-analysis of Randomized Controlled Trials

Tratamentos das Disfunções Temporomandibulares e seus Efeitos nas Cefaleias: Revisão Sistemática e Metanálise de Ensaios Controlados Randomizados

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Abstract

Objective: temporomandibular Disorders (TMD) are the most common causes of chronic orofacial pain and, along with primary headaches, are considered Chronic Overlapping Pain Conditions (COPCs). The aim of this study is to evaluate TMD treatment effects in individuals with comorbid headaches. **Methods**: a systematic review was conducted over a search in the database up to October 2020. Selected studies were randomized clinical trials with individuals diagnosed with TMD and comorbid headaches compared to a control group after treatments for TMD. All included studies were evaluated for their methodological quality through the Cochrane Collaboration tool for assessing the risk of bias. **Results:** seven studies fulfilled the inclusion criteria and were applied in the review, with a total of 432 participants. Four studies were included in a meta-analysis. There was no significative mean difference in the frequency of headache after TMD treatment, nor for a reduction in pain, after TMD intervention for less than 12 weeks. Although for an individual with a TMD intervention period higher than 12 weeks, there was a significant reduction in pain. **Conclusion**: there is moderate evidence that painful TMD therapies for 12 weeks or higher reduce headache intensity in individuals with painful TMD and headaches. Simultaneous management of TMD and headache must be prioritized for more effective results on both conditions.

Keywords: migraine; pain; temporomandibular joint; tension-type headache; facial pain.

Resumo

Objetivo: as Disfunções Temporomandibulares (DTM) são as causas mais comuns de dor orofacial crônica e, junto com as cefaleias primárias, são consideradas Condições de Dor Sobrepostas Crônicas (CPOCs). O objetivo deste estudo é avaliar os efeitos do tratamento das DTMs em indivíduos com cefaleia comórbida. **Métodos**: foi realizada uma revisão sistemática por meio de uma busca em banco de dados até outubro de 2020. Os estudos selecionados foram ensaios clínicos randomizados com indivíduos diagnosticados com DTM e cefaleia comórbida em comparação com um grupo controle após tratamentos para DTM. Todos os estudos incluídos foram avaliados quanto à sua qualidade metodológica por meio da ferramenta Cochrane Collaboration para avaliar o risco de viés. **Resultados:** sete estudos preencheram os critérios de inclusão e foram incluídos na revisão, totalizando 432 participantes. Quatro estudos foram incluídos em uma meta-análise. Não houve diferença média significativa na frequência de cefaleia após tratamento para DTM, nem para redução da dor, após intervenção para DTM por menos de 12 semanas. Para indivíduos com DTM, o tempo de intervenção maior que 12 semanas resultou em uma redução significativa da dor. **Conclusão**: há evidências moderadas de que terapias para DTM dolorosa por períodos de 12 semanas ou mais reduzem a intensidade da cefaleia em indivíduos com DTM dolorosa e cefaleia. O manejo simultâneo de DTM e cefaleia deve ser priorizado para resultados mais efetivos em ambas as condições.

Palavras-Chave: enxaqueca; dor; articulação temporomandibular; cefaleia do tipo tensional; dor facial.

INTRODUCTION

Temporomandibular disorders (TMD) are the most common causes of chronic orofacial pain[1,2]. TMD is described as dysfunctions associated with the Temporomandibular Joint (TMJ), muscles of mastication, and/or other orofacial regions, characterized by pain in the jaw, ear, and temples, TMJ clicking or noises, limited mouth opening, that can be aggravated by function or parafunction movements of the jaw[3,4,5].

TMD is included in a group of Chronic Overlapping Pain Conditions (COPCs) that share similar physiopathology and are usually comorbid conditions resulting in pain amplification when presented in the same individua[l6,7,8]. The COPCs include TMD, fibromyalgia, irritable bowel syndrome, vulvodynia, chronic fatigue syndrome, endometriosis, chronic tension-type headache, migraine headache, and chronic lower back pain. Among those, has been reported a considered overlapping between TMD and headaches[7,9-14].

Comorbid headaches and TMD can lead to a high disability impact. Studies show higher migraine disability assessment (MIDAS) scores associated with masticatory myalgia[15,16]. The primary headache most associated with TMD is migraine, which alone is considered the second most disabling condition worldwide and is related to occupational, social, and academic incapacity[16]. Because headaches and TMD share pathophysiological mechanisms, they can interact in several

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ways. It is required a precise diagnosis and multidisciplinary approach to the successful management of these conditions.

AIM

Some therapies can be indicated for primary headaches and they can also be effective for myofascial TMD and vice versa[17]. Therefore, this systematic review aims to verify if TMD treatment effect individuals with comorbid headaches and TMD.

SEARCH METHODS

Protocol and Registration

It is a systematic review synthesizing temporomandibular disorder treatments and their effects on headaches. This study was registered at PROSPERO (International Prospective Register of Systemic Reviews, http://www.crd.york.ac.uk/prospero; CRD42020212530). The review was performed according to a prospective protocol using PRISMA (Preferred reporting items for systematic reviews and meta-analyses).

Eligibility criteria

For selection criteria, randomized clinical trials with people diagnosed with TMD and headaches compared to a control group after treatments for TMD were included.
P: People diagnosed with TMD and headache.
I: Treatments for TMD: use of occlusal splint/ occlusal device, orofacial/TMD physical therapy, counseling, education, and control of parafunctional habits.
C: Control group (participants with TMD and headache but did not perform interventions for TMD or performed one intervention that was also used in the experimental group along with others).
O: Reduction in frequency and intensity of headaches and improved quality of life.
S: Randomized clinical trials.

Information sources and search strategy

The search was conducted in the following electronic databases: MEDLINE (PubMed), Embase (Elsevier), Web of Science, and Cochrane Library. The databases were searched using the following terms: “Temporomandibular Joint Disorders", "migraine disorders", " Tension-Type Headache”, and “Headache” and their synonyms up to October 2020. Searches were limited to humans, regardless of the language published. The reference lists of all selected studies were checked as well as the grey literature.

Study Selection

Two investigators (JNZ and MC) independently examined the titles and abstracts of all articles identified by the searches, obtained the full text of all potentially relevant studies, and determined which studies met the inclusion criteria. A third review author (TC) resolved any disagreements in the selection of included studies. The screening process was conducted at Rayyan (rayyan.qcri.org). When we were unable to reject a title or abstract, we obtained the full text of the article for further evaluation.

Two investigators (JNZ and MC) independently evaluated the articles included for full text, selecting those that meet all the eligibility criteria. A third reviewer (TC) assessed cases of conflict.

Data extraction

Two investigators (JNZ and MC) independently extracted data on participants, interventions, and outcomes, as described above in the selection criteria section using a standardized form.
The data extraction form was composed of the author, year, country, age, number of individuals in the population and control group, outcomes pre-specified in this protocol, and the characteristics of each study included.

Quality assessment

All included studies were evaluated for their methodological quality through the Cochrane Collaboration tool for assessing the risk of bias (RoB 2). The risk of bias analysis consists of analyzing the information from the biased studies resulting from the randomization process; Bias due to deviations from the intended intervention; Bias due to lack of outcome data; Bias in outcome measurement and Bias in outcome selection.

Data synthesis and analysis

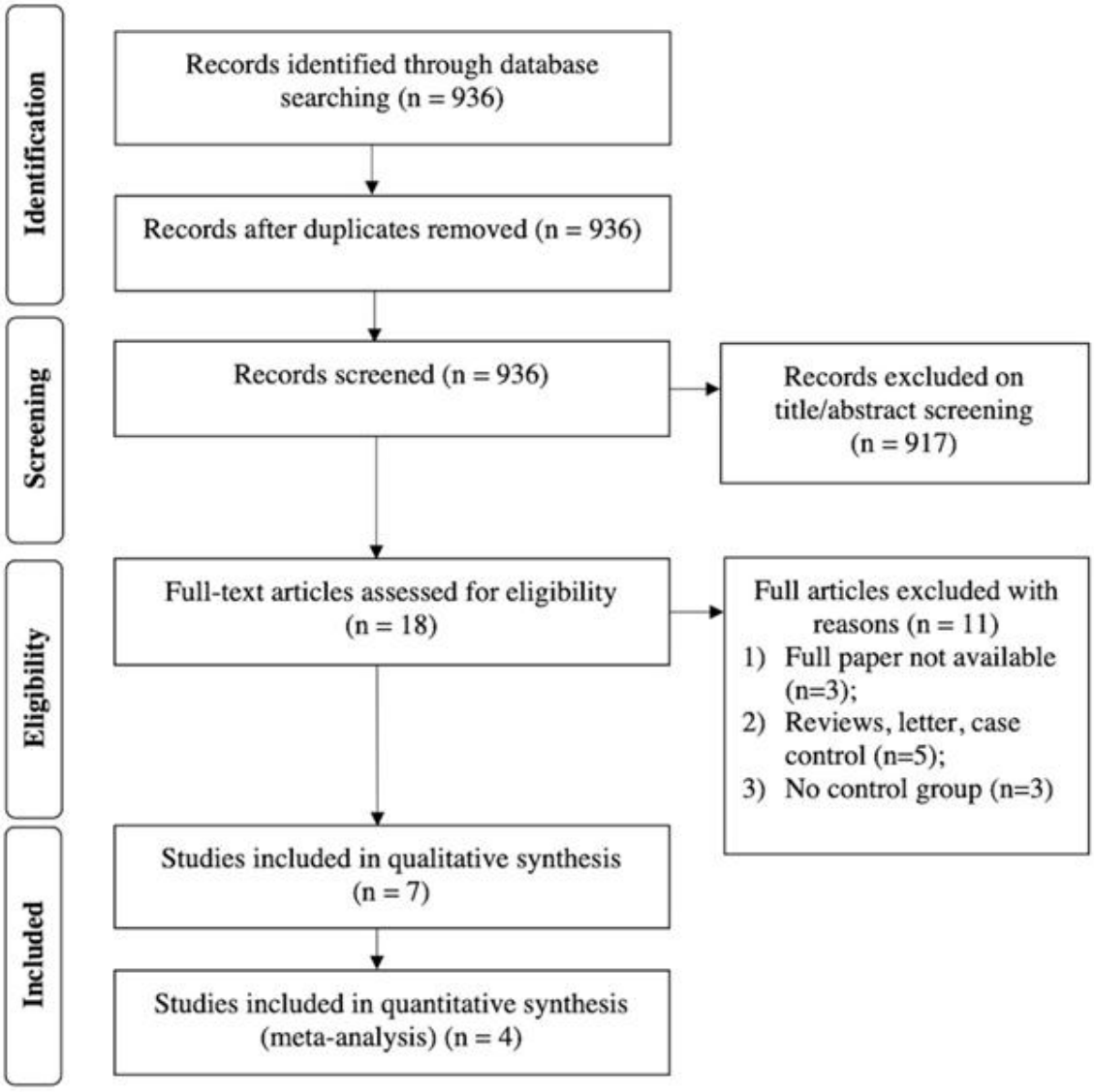
We used mean difference for continuous variables, with 95% confidence intervals using the RevMan 5.4 software.
Cochran's Q-statistic and I^2 tests were used to test for heterogeneity between the included studies. If the I^2 value is greater than 30% or the p-value of the Q-test is less than 0.05, indicating maximal heterogeneity among the included studies, a random-effects model was used. Aggregate data extracted from included studies were used for quantitative synthesis.

RESULTS

Study selection

The initial result from the database search strategy identified 936 potentially relevant articles. Of those, none were duplicated. After titles and abstracts screening, 917 articles were excluded because they did not meet the inclusion criteria. The full-text assessment was performed on 18 articles, and 11 were excluded. The reasons they were excluded were, three articles were not available in full version, five presented another study design, and three did not fulfill the inclusion criteria. For the qualitative synthesis were included a total of even studies, and for quantitative analysis, only four were used. The complete study selection process is presented as a flow chart in Figure 1.

Figure 1. Flow diagram of literature search and selection criteria according to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA).



Study characteristics and results of individual studies

In the end, seven studies fulfilled the inclusion criteria and were applied in the review, with a total of 432 participants. The studies were published between years 1985 and 2019. All studies were randomized clinical trials and evaluated the efficacy of interventions for the treatment of TMD in a population with comorbid headaches, which included migraine, tension-type headaches, muscle contraction headaches, and headaches attributed to TMD. Of these, three studies evaluated if the use of a stabilization appliance reduced the symptoms of headaches[18-20]. One of the studies[21] combined the stabilization appliance with usual care to reduce the symptoms of migraine and tension-type headaches. Garrigós-Pedrón et al (2018)[22] analyzed if physiotherapy in the orofacial region and counseling could contribute to reducing chronic migraine. The study of Costa et al (2015)[23] used counseling oral habits and the use of a stabilization splint for headaches attributed to TMD, and Gonçalves et al (2013)[24] approaches were the use of propranolol and stabilization splint for migraine. The characteristics of the included studies are summarized in Table 1.

Table 1. Summary of descriptive characteristics of included articles.

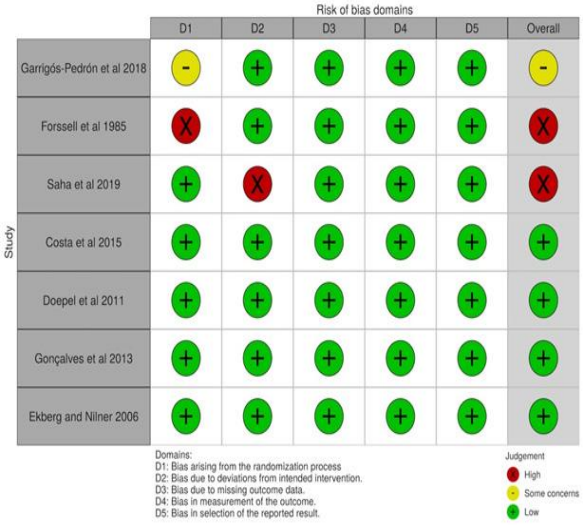
Author (year)	Country	Headache type	Patients	Intervention	Control	N total	N Treatment	N placebo
Costa et al (2015)	Brazil	Headache attributed to TMD	Adults (men and woman) with masticatory myofascial pain according to RDC/TMD and headache, meeting ICHD-2 criteria for headache attributed to TMD	Counseling for habits and behavioral changes and SS	Counseling for habits and behavioral changes	41	24	17
Doepel et al (2011)	Sweden and Finland	Headache	Adult patients (men and woman) with headache complain and myofascial pain	SS	Prefabricated appliance	65	32	32
Eckberg; Nilner (2006)	Sweden	Tension-type headache	Adult patients (men and woman) with temporomandibular disorders (TMD) of myogenous origin and chronic or episodic tension-type headache, according to ICHD	SS	Control appliance (non occlusal splint)	60	30	30
Forssell et al (1985)	Finland	Migraine, Combination headache and Muscle contraction						
headache	Adults (men and women) with migraine, combination headache or muscle contraction headache and symptoms of TMD	Occlusal adjustment and/or SS	Placebo group received mock adjustment of their dental occlusion	96	48	43		
Garrigós-Pedrón et al (2018)	Spain	Chronic Migraine	Adults (men and woman with 18 to 65 years) with chronic migraine and TMD	Combined manual therapy and both therapeutic and home exercises for cervical and orofacial region.	Combined manual therapy and both therapeutic and home exercises for cervical region.	45	23	22
Gonçalves et al (2013)	Brazil	Migraine	Adult woman with migraine with or without aura, according to ICHD-2 criteria, and myofascial TMD	Propanolol + SS (Group 1) / Placebo + SS (Group 2)/ Propanolol + Non occlusal Splint (Group 3)	Placebo + Non occlusal Splint (Group 4)	81	22 (Group 1)/ 23 (Group 2)/ 23 (Group 3)	21 (Group 4)
Saha et al (2019)	Germany	Migraine and tension-type headache	Adult patients (men and woman) with migraine and/or tension-type headache and comorbid TMD	SS (day/night) and usual care	Usual care alone	44	26	18

TMD: Temporomandibular Disorder; ICHD: International Classification of Headache Disorders; RDC/TMD: Research Diagnostic Criteria/Temporomandibular Disorders; SS: Stabilization Splint.

Risk of bias in individual studies

The analysis for risk of bias was performed using the Cochrane Collaboration tool for assessing the risk of bias (RoB 2) and is presented in Figure 2.

Figure 2. Analysis for Risk of Bias of the included studies.



Domain 1 is to access the bias from the randomization process. The study by Garrigós-Pedrón et al 2018 did not specify if the randomization was concealed, being classified in this domain as some concern. The study by Forssell et al 1985 was considered a high risk of bias because it did not specify if the randomization process was concealed and the baseline data differenced from the intervention group suggesting a problem with the randomization process. The studies of Saha et al 2019, Costa et al 2015, Doepel et al 2011, Gonçalves et al 2013, and Ekberg and Nilner 2006, were considered low risk of bias because they presented a detailed randomization process.

Domain 2 is to access the bias of deviation from the intended intervention. The study by Saha et al 2019 was considered a high risk of bias because the participants and delivering intervention people who were aware of the intervention were not blinded. The other studies Garrigós-Pedrón et al 2018, Costa et al 2015, Forssell et al 1985, Doepel et al 2011, Gonçalves et al 2013, and Ekberg and Nilner 2006, were considered low-risk of bias in this domain because they maintained the blinding. Domain 3 accesses the bias of missing outcome data, Domain 4 accesses the bias of measurement of outcomes, and Domain 5 accesses the bias of selection of the reported result. All of these domains in the seven studies included were classified as low risk of bias.

Synthesis of results

The most frequently therapy used was the SS, applied in six studies, two of them, only SS[19,20], and 4, SS combined with other therapy[18,21,23,24]. There was one study21 that applied the SS therapy on a day and night routine, removing the appliance only for eating and brushing teeth, all other studies used the splint only overnight.

All seven studies included showed an improvement in the frequency of headaches after the intervention when comparing the treatment group to the baseline. Difference between groups ($p<0.05$) was only found in Forssell's 1985 study for participants that presented muscle contraction headache and combination headache and were submitted to occlusal adjustment or splint therapy compared to control.

In the pain intensity analysis, six studies[19-24] presented a significant difference in pain reduction between baseline and treatment groups after the intervention. In 4 of them[20-23] the p-value reached <0.001. Between group analysis, three studies reached significance[18,19,22].

The results of the qualitative analysis from included studies are summarized in Table 2 concerning the frequency and intensity of headaches, showing the intervention results compared to the baseline and the difference between intervention groups and controls.

A meta-analysis was conducted over four of the selected studies (Figures 3, 4, and 5). For a better interpretation of the results, the studies were clustered into three different comparison groups.

1) Frequency of headache (days of headache/month): Two included studies21,24 evaluated the frequency of headache through reported headaches days per month. There was a total of 87 participants, of which 48 received the intervention and 39 were in the control group. After the quantitative analyses, it could not be observed any significative mean difference between groups MD: -1.06 (IC 95%, -3.30, 1.19) p=0.35), I^2 = 39%.

2) Headache intensity with intervention period <12 weeks (VAS): For this analysis, three studies could be compared20,21,23. The intensity of the headache was measured by a visual analogic scale of 0 to 10, 0 with no pain, and ten (10) being the worst pain experienced by the participant. A total of 130 participants received treatment for less than 12 weeks. After quantitative analyses it could not be observed any significative mean difference between groups MD: -0.26 (IC 95%, -0.95, 0.42) p=0.45), I^2 = 0%.

3) Headache intensity intervention period >12 weeks (VAS): Four studies were included in this analysis[20,21,23,24]. The intensity of the headache was measured by a visual analogic scale of 0 to 10, 0 with no 10, 0 with no pain, and ten (10) being the worst pain experienced by the participant. It evaluated the difference in pain intensity after an intervention period greater than 12 weeks, in 96 individuals, compared to 78 in the control group, a total of 174 participants. After quantitative analyses, it could be observed a significative mean difference between groups favorable for intervention group MD: -1,72 (IC = 95%, -2,61, -0,83) p = (0.0001), I^2 = 23%.

Table 2. Results of qualitative analysis of included studies.

	Difference from baseline (baseline x intervention group)			Difference between groups (intervention x control group)				
Author (year)	Frequency of headache	Intensity of headache	Intent to treat	Frequency of headache	Intensity of headache	Intent to treat	Time (post-treatment)	Follow up
Costa et al (2015)	Reduced frequency of headache at Follow up **	VAS (0-10) - Post-treatment: -3.1 **; Follow up: - 4 **	NR	Frequency of headache did not differ between groups	VAS Scale (0-10) - Post-treatment: -1; Follow up: - 0.6	NR	8 weeks	20 weeks
Doepel et al (2011)	The frequency of headache decreased compared to baseline at all follow-ups*	VAS (0-10) - Follow up 2: -3.2**	At post-treatment was 58% of all patients reported a 30% reduction in intensity of headache and 43% reported a 50% reduction. At follow up 2 48% reported a 30% reduction and 43% reported 50% reduction	The frequency of headache was not statistically different at baseline or at follow-ups, between groups	VAS (0-10) - Follow up 2: 0.8	NR	10 weeks	Follow up 1: 24; Follow up 2: 48 weeks
Eckberg; Nilner (2006)	Post-treatment: reduction on patients reporting headache once a week* and daily*; Follow up 1: reduction on patients reporting headache once a week*; Follow up 2: reduction on patients reporting headache once a week*	Reported improvement of headache*	NR	Reported reduction of headache but did not differ between groups	Post-treatment: headache improvement*; Follow up 1: headache improvement **; Follow up 2: headache improvement *	NR	10 weeks	Follow up 1: 24 weeks; Follow up 2: 28 weeks
Forssell et al (1985)	60% reduced frequency of headache	35% reduced intensity of headache	NR	Muscle contraction headache and combination headache had a reduction in stable occlusion sub-group compared to control *	There was a reduction on intensity in intervention group compared to control*	NR	8 weeks	24 weeks
Garrigós-Pedrón et al (2018)	NR	VAS (0-10) - Post-treatment: -1.67 **; Follow up 1: -2.25 **; Follow up 2: -3.50 **	NR	NR	VAS (0-10) - Post-treatment -0.021; Follow up 1: -0.57/ Follow up 2: -2.28 **	NR	3 weeks	Follow-up 1: 6 weeks; Follow-up 2: 12 weeks
Gonçalves et al (2013)	Days of headache/month - Post-treatment: - 5.4*	VAS (0-10) - Post-treatment: -3.5*	Reduction of frequency of headache at follow up *	Days of headache/month - Post-treatment: - 1.9	VAS (0-10) - Post-treatment: -2.8	NR	12 weeks	24 weeks
Saha et al (2019)	Days of headache/month - Post-treatment: - 2; Follow up: -2.8	VAS (0-10) - Post-treatment: -0.36 **; Follow up: -1.03 **	NR	Days of headache/month - Post-treatment: -0.5	VAS (0-10) - Post-treatment: -1.21	NR	12 weeks	24 weeks

VAS: Visual Analog Scale; *: p<0.05; **: p<0.001; NR: Not reported.

Figure 3. Forest plot for overall mean differences of intervention groups against control groups in regards of frequency of headache. Graphs generated with Review Manager 5.4 (RevMan 5.4, The Nordic Cochrane Centre, Copenhagen, Denmark)

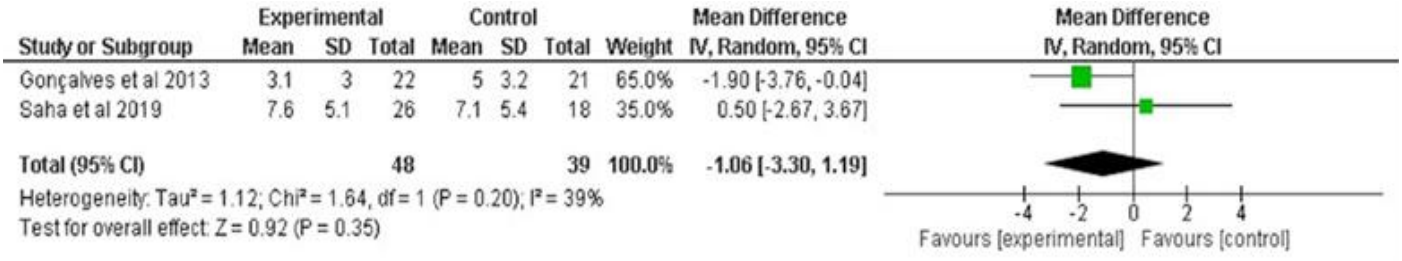


Figure 4. Forest plot for overall mean differences of intervention groups against control groups in regards of headache intensity, when intervention period was less than 12 weeks. Graphs generated with Review Manager 5.4 (RevMan 5.4, The Nordic Cochrane Centre, Copenhagen, Denmark)

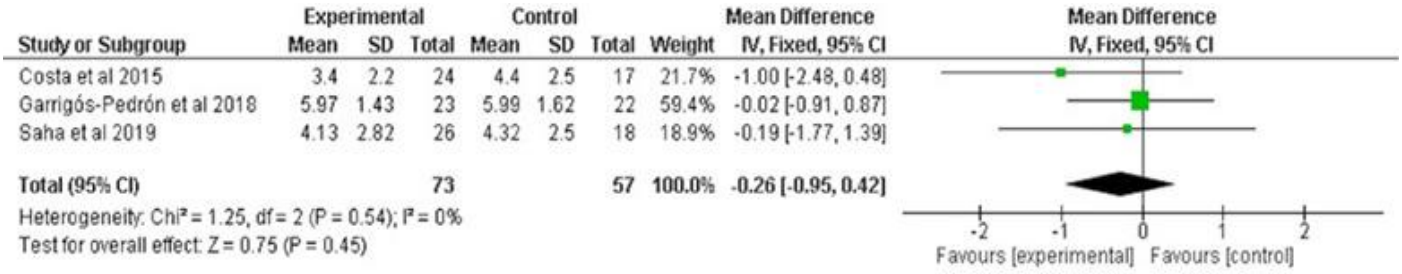
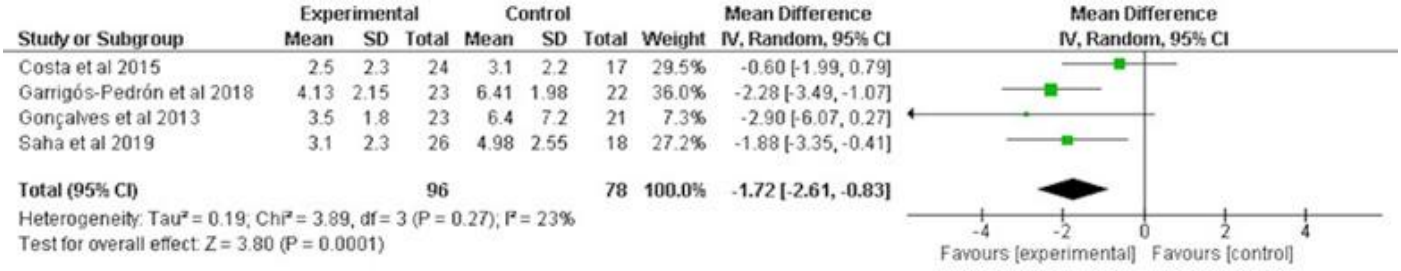


Figure 5. Forest plot for overall mean differences of intervention groups against control groups in regards of headache intensity, when intervention period was more than 12 weeks. Graphs generated with Review Manager 5.4 (RevMan 5.4, The Nordic Cochrane Centre, Copenhagen, Denmark)



Quality of evidence

According to the GRADE approach (Table 3), a descriptive quality of evidence and strength of the systematic review was done, the outcomes Intensity of Headache (VAS) intervention for less than 12 weeks and more than 12 weeks and Frequency of headache (days of headache) was overall judged as moderate quality evidence. We downgraded the body of evidence -1 for the risk of bias. This moderate evidence is due to the presence of risk of bias in primary studies. The study by Saha et al (2019) did not present information on the blinding of participants and professionals, which is a key point in RCTs since it is one of the factors that most reduce potential bias, and Garrigós-Pedrón et al (2018) did not specify if the randomization was concealed.

Table 3. Quality of evidence and strength of the systematic review, GRADE approach

Temporomandibular Disorder treatments and its effect on Headache Reduction compared to control				
Patient or population: Population with Headache and Temporomandibular Disorder. **Intervention**: Temporomandibular Disorder treatments and its effect Headache. **Comparison**: Control.				
Outcomes	**№ of participants (studies) Follow up**	**Certainty of the evidence (GRADE**	**Relative effect (95% CI)**	**Anticipated absolute effects** **Risk difference with TMD treatments and its effect on Headache Reduction**
Intensity of Headache (VAS) >12 weeks	174 (4 RCTs)	⊕⊕⊕◯ MODERATE[a]	-	MD 1.72 lower (2.61 lower to 0.83 lower)
Intensity of Headache (VAS) <12 weeks	130 (3 RCTs)	⊕⊕⊕◯ MODERATE[a]	-	MD 0.26 lower (0.95 lower to 0.42 higher)
Frequency of headache (days of headache)	87 (2 RCTs)	⊕⊕⊕◯ MODERATE[a]	-	MD 1.06 lower (3.3 lower to 1.19 higher)
***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effec**t of the intervention (and its 95% CI). **CI:** Confidence interval; **MD**: Mean difference; **TMD**: Temporomandibular Disorder				

DISCUSSION

This is the first review to evaluate the effect of TMD treatment on a population with TMD and comorbid headaches. It has been reported in the literature several studies[10,11,25-35] indicate the high prevalence of comorbid primary headache and TMD and how this relation is bidirectional, where the presence of TMD increases the prevalence of headache and vice versa[36].

Therefore, the two main characteristics evaluated in this review were the influence of TMD treatment on the frequency and intensity of reported headaches. The results showed a significant frequency reduction of headaches when the intervention group was compared to the baseline, but only one had significative difference between groups18. These results could be justified by various methodological differences such as headache type, different classification or evaluation methods, and type of group control used (standard intervention or placebo). In the quantitative analysis, there was no significant mean difference in TMD treatment on the frequency of headaches.

The second characteristic analyzed was the intensity of the headache which shows more promising results. In a meta-analysis comparison for interventions applied for less than 12 weeks, it could not reach a significative mean difference for pain intensity reduction. Although when comparing studies where intervention was applied for more than 12 weeks, it had a significative mean difference, favoring the experimental group, that is, TMD treatment can be effective in reducing headache intensity, in a population presenting painful TMD and comorbid headache.

Although painful TMD and headaches are frequently found in the same individual, their etiologies are different. Each condition has its initiating and perpetuating factors that may contribute to each other but vary according to headache type, TMD diagnosis, and individual characteristics. There are two common headaches that painful TMD may contribute to initiating the headache attack. One is migraine, where some patients report painful TMD as a trigger for the headache attack[37], the other is a secondary headache, classified as a headache attributed to TMD, according to ICHD-3, where the initiating factor is associated with TMD complaints and jaw motion[37-39]. Because TMD is not a common trigger for migraine, the majority of patients may not report a reduction in headache frequency only with TMD treatments[40]. Although when we evaluate the effect of TMD therapies on individuals with secondary headaches attributed to TMD, its treatment tends to reduce the frequency of headaches[42,43]. It is important to remind that TTH diagnosis is frequently overlapped with this type of headache, and if so, painful TMD treatment benefits may be limited[39,40].

Furthermore, many other factors could influence the frequency of headaches. Poor sleep quality, smells, long periods without food, alcohol, some types of foods, stressful situations, lack of physical activity, and many others could begin an attack[40]. All these factors should be controlled, according to each patient trigger and correct headache diagnosis, to have more efficiency

in its frequency reduction[40,44].

Another important relation between primary headaches and painful TMD is that they are considered Comorbid Overlapping Pain Conditions (COPCs)[7,45]. This bidirectional relationship can be explained by some hypotheses: that they share the same nociceptive system, the trigeminal nerve, and it can occur a conversion of nociceptive information[17,36,46], they share central pathways involved in pain modulation[41,46-48], they have common genetic influence[49,50] and, both can involve craniofacial allodynia[36,47,49-51]. Therefore, the presence of painful TMD and headache in the same individual may intensify pain perception, and both conditions should be treated simultaneously, to have more favorable treatment results and pain control[52].

The central sensitization mechanism that TMD and primary headaches share changes the pain modulation pathways in the central nervous system, which can be evaluated by quantitative sensory testing and conditioned pain modulation test, presented as hyperalgesia and allodynia by the individual[53-56]. The involvement of the central sensitization mechanism can justify significative pain reduction only after 12 weeks of therapy found in this study once there is a need for medium to long-term therapies to obtain neuroplasticity, reduction of central sensitization, and then reestablish pain mechanism pathways[57,58].

As painful TMD is a multifactorial condition, its treatment involves control of biological, psychological, social, and environmental factors, and an isolated therapy may not be sufficient for pain control[53]. Most of this review included studies that applied single therapy for TMD and focused only on its peripheral action, such as SS, habit control, and physical therapy[54]. These interventions present partial therapeutic results, whereas it is known central sensitization is frequent in patients with comorbid pain conditions, and Central Nervous System (CNS) dysfunction therapies must also be approached[7,45].

Conti et al (2016) describe some management modalities that can be indicated for primary headaches and are also effective for myofascial TMD and vice versa. Some examples are integrated education and self-care programs, psychological therapy, relaxation techniques, therapeutic massage, physical therapy, tricyclic antidepressants, muscle relaxants, and beta-blockers[17,46,60]. In addition, it must be paid attention to environmental and social factors[59]. All therapies should be indicated according to individual peculiarities and applied simultaneously, aiming for better results, as it is known that many factors can converge and contribute to the same dysfunction[7,61]. If pain pattern and a main cause of pain maintenance, such as descending modulation pathways or calcium channels dysfunction, conversion of neurons, peripheral sensitization, or psychological interference, are known, it contributes to and facilitates the differential diagnosis and identification of primary headaches phenotypes, allowing a more effective therapy choice[17,51,61].

This review has many strengths. There was a rigorous literature search strategy, including only randomized controlled trials, screening for eligibility, assessment of the risk of bias, and evaluation of the quality of evidence and strength of quantitative analysis. Although, it is also worth mentioning that there are some methodological limitations. The study's inclusion criteria did not follow a specific type of headache or classification criteria. Besides, different TMD interventions were compared, and many studies did not have a placebo group to be used as a control; then, some of the control groups included also received an intervention, which may have affected the results for comparison.

This review highlights that there is moderate evidence for painful TMD therapies in reducing headache intensity in individuals with painful TMD and comorbid headaches. Painful TMD and primary headaches must be treated together and, if possible, with therapies that are effective for both conditions, using the least amount of interventions to control pain intensity and frequency. More criteria for randomized controlled trials

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