Physical Therapy Intervention in Management of Patient with Cervicogenic Headache: Systematic

Abdallah Megahead Ibrahim Badr; Supervisors: prof.Dr.Wael S. Shendy,

Faculty of Physical Therapy; Prof.Dr. Eman S. Fayez. Faculty of Physical Therapy, Cairo University; Master Thesis P.T., Physical Therapy for Neuromuscular Disorder and its surgery, 2022.

ABSTRACT

Background: Cervicogenic headache (CEH) is a form of headache generated by cervical spine disorder. Certain symptoms and characteristics separate CEH from other types of headaches. It often develops or worsens in response to neck movement and is frequently accompanied by a reduced range of motion of cervical spine. Physical therapy is the major initial treatment for CEH. CGH can be treated with a variety of different physical therapy techniques such as exercises, manipulation and mobilization. **Objectives:** The purposes of this study were to systematically review the randomized controlled trials which investigated the efficacy of several physical therapy treatments on CGH. **Study Design:** Systematic review of RCT. **Methods:** comprehensive search was conducted up to July 8, 2020 , on the following databases: Physiotherapy Evidence Database (PEDro), Medline, Embase, CENTRAL through The Cochrane Library, AMED and Google Scholar. **Intervention:** Physical therapy intervention performed by the physical therapists on adult patients (> 18 years) diagnosed with CCH. **Outcomes Measures:** Headache pain intensity, headache frequency and headache duration. **Results:** Only twelve studies, including 946 patients that met inclusion criteria, The interventions used were as follows: cervical and upper thoracic manipulation, cervical mobilization, and ischemic compression of cervical muscular trigger points, studies showed that Cervical mobilization has been demonstrated to be useful in in lowering pain but ineffective in reducing headache frequency, SMT decreased headache frequency but did not significantly reduce pain intensity. While trigger point compression in the sternomastoid muscle was not effective for pain and symptom reduction. **Conclusion:** manual therapy techniques provide significant but small and short-term effects for pain intensity, frequency, and disability but not on the duration of CGH.

INTRODUCTION

Headaches are a major health concern because they are one of the most common symptoms in the world. **(1,2).** It is one of the most debilitating illnesses, leading to a decrease in both quality of life and productivity at work **(3)**. Between the many forms of headache disorders, Cervicogenic headaches are distinct from other types of headaches **(5,6)**.

Cervicogenic headache is a type of headache that is lateralized and does not throb and is produced by a source of nociception in the cervical spine. CEH can be distinguished from other types of headaches by the presence of particular symptoms and characteristics. It frequently begins or worsens following movement of the neck and is typically accompanied by a decreased range of motion (ROM) in the neck. Pain that is diffused throughout the ipsilateral shoulder and arm can be an associated characteristic **(10)**. It is thought to be a referred pain that originates owing to irritation of tissues in the cervical region that are largely innervated by nerves in the upper cervical region (spinal nerves C1, C2, and C3). Any structure that is supplied with sensory information by the C1–C3 spinal nerves has the potential to be a source of cervicogenic headache **(11,12)**. The convergence of upper cervical nerves (C1-3) and the trigemino-cervical complex in the upper cervical spinal cord is thought to be the root cause of cervicogenic headaches. However, CGH is frequently documented in middle-to-lower cervical spine problems, which cannot be explained by this approach. Because of its complex etiology, Management of CGH is still challenging. The treatment of benign chronic and recurrent headaches can involve a wide variety of therapeutic techniques, including medication, cognitive therapy, relaxation therapy, biofeedback, physical therapy, and many more. People who suffer from headaches frequently seek treatment from physical therapists, massage therapists, and chiropractors **(4)**.

Treatment demands a multimodal approach, including pharmacological and non-pharmacological interventions. Common treatments include 1) Exercise and physical therapy, 2) various types of percutaneous procedures, such as anesthetic blocks and pulsed radiofrequency therapy, and 3) operation. Early diagnosis and management are critical to reducing the risk of treatment desensitization **(10,13)**.

Physical therapy is the primary initial treatment for cervicogenic headaches, several predictors of positive outcomes after physiotherapy treatment of CGH have been identified such as relief of headache with certain neck movements and reduce headaches and disability. Therefore, the aim of the current systematic review was to assess the efficacy of physical therapy interventions for the management of patients diagnosed with CCH.

MATERIALS AND METHODS

This systematic review follows the revised PRISMA 2020 declaration **(Page et al., 2021)** as well as the guidelines outlined in the Cochrane Handbook for Systematic Reviews of Interventions. The population, intervention, comparison, outcome, and study design (PICOS) question were then chosen as follows: population: adult with cervicogenic headache; intervention: Physical therapy intervention; control: any form of placebo intervention or any other kind active intervention.; outcome: (Headache (pain) intensity, Headache frequency, and Headache duration); and study design: randomized controlled trials.

2.1 Search strategy and study selection

A comprehensive search of electronic database was conducted from

commencement to July 8, 2020, on the following databases:

1) PEDro (physiotherapy evidence-based database)

2) Medline (NLM) through the PubMed

3) Embase

4) AMED through the EBSCO

5) CENTRAL through The Cochrane Library

6) Google Scholar

The search approach incorporated phrases that referred to the population that was investigated, the intervention that was the primary focus of the study, the intervention that served as the control, and the outcome that was analyzed. The following combinations of search phrases were used:

- Population: adult AND (cervicogenic headache)
- Intervention: physiotherapy OR physical therapy OR exercises OR training OR manual therapy OR mobilization
- Comparison: sham OR placebo OR control
- Outcome: pain intensity OR frequency OR duration

Table (1): The search strategy according to the focused PICOS question is presented.

Database	Search syntax
PEDro	('Abstract & Title: Physical therapy intervention management for treating patients with cervicogenic headache,' 'Therapy: stretching, mobilization, manipulation, massage', 'Problem: pain', 'Body Part: head or neck', 'Subdiscipline: musculoskeletal', 'Topic: chronic pain', 'Method: clinical trial')
PubMed	("Homo sapiens" OR "Human" OR "Humans" [Mesh Terms] OR "Humans" OR "Man (Taxonomy)" OR "Man, Modern") AND ("Cervicogenic Headache" OR "Post-Traumatic Headache" [Mesh Terms] OR "Post-Traumatic Headache") AND ("Group Physiotherapy" OR "Neurological Physiotherapy" OR "Neurophysiotherapy" OR "Physical Therapy Modalities" [Mesh Terms] OR "Physical Therapy Modalities" OR "Physical Therapy Techniques" OR "Physiotherapy (Techniques)") AND ("Therapeutics" [Mesh Terms] OR "Therapeutics" OR "Therapy" OR "Treatment") AND ("Habilitation" OR "Rehabilitation" [Mesh Terms] OR "Rehabilitation") AND ("Analgesic Overuse Headache" OR "Analgesic Rebound Headache" OR "Headache Disorders, Secondary" [Mesh Terms] OR "Headache Disorders, Secondary" OR "Medication Overuse Headache" OR "Secondary Headache Disorders") AND ("Ache" OR "Pain" [Mesh Terms] OR "Pain" OR "Pain, Burning" OR "Pain, Crushing" OR "Pain, Migratory" OR "Pain, Radiating" OR "Pain, Splitting" OR "Suffering, Physical") AND ("Bilateral Headache" OR "Cephalalgia" OR "Cephalgia" OR "Cephalodynia" OR "Cranial Pain" OR "Generalized Headache" OR "Head Pain" OR "Headache" [Mesh Terms] OR "Headache" OR "Hemicrania" OR "Ocular Headache" OR "Orthostatic

Study selection:

For the selection of study, the inclusion criteria were derived from the research question: "Does physical therapy intervention affect patients with cervicogenic headache?"

- P: Adults (>18 years of age) with cervicogenic headache diagnosed according to International Headache Society's (IHS) 2018 criteria **(20)** or the Cervicogenic Headache International Study Group **(21)**
- I: Physical therapy intervention
- C: Short- and long-term effects of different interventions compared to active or placebo/sham comparison
- O: headache pain intensity, duration, and frequency

2.2 Exclusion criteria

The studies were excluded if they were:

- Unpublished studies
- Irrelevant diagnosis of the outcome:
  - o Neck pain
  - o Migraine headache
  - o Tension-type headache
- Studies didn't get the minimum score on the PEDro scale for quality assessment.
- Quasi-randomized studies (e.g., treatment allocation by date of birth, hospital record number, or alternation).
- Comorbid conditions (e.g., fracture in the region, cancer, neurological disease)

Data Extraction

After removing duplicates, and manually double-checked. Each citation's titles and abstracts were evaluated based on the following criteria:

1) Study design: clinical trials with concurrent comparator groups
2) Study participants should have cervicogenic headache
3) Participants in the research should be older than 18 years old
4) The primary outcome should be pain or disability in the studies
5) The primary intervention should be manual physiotherapy.

After meeting all criteria, the study's text was assessed for eligibility. The criteria for inclusion and exclusion shall be adhered to very strictly throughout the selection process.

Data from all eligible studies were extracted and placed into a table with predetermined column headers to satisfy

the aims of the study. The table of extracted data contains the following items:

The trial's author, publication date, and trial's country

- Type, length, and frequency of intervention(s), as well as the number of intervention group participants
- The type(s) of control intervention(s) used and the total number of people in the control group
- Outcome measure(s)
- Timepoint(s) of measurement(s)

Critical appraisal of included studies:

Each study was critically appraised utilizing the Modified McMaster Critical Appraisal Tool for Quantitative Studies (CASP). CASP tool offers a standardized approach for evaluating the rigor of RCTs. The studies were evaluated using the Physiotherapy Evidence Database scale, which assesses the internal validity of an RCT. Those with a PEDro score of 7 or higher out of 10 were regarded to be of "excellent quality," while those with a score of 5 or 6 were thought to be of "moderate quality," and those with a score of 4 or less were considered to be of "poor quality.".

Methodological quality appraisal:

All of the papers that were selected were analyzed using a set of methodological criteria focusing on clinical trial quality (Table 3). These criteria are focus on well-established intervention research principles. These criteria independently cover four different primary categories: (1) the participants in the study, (2) the interventions, (3) effect measurement, and (4) the presentation and analysis of the data. Consequently, there are a total of 16 elements throughout the four categories, and the possible score spans from 0 to 100, with higher values indicating studies with stronger methodologies. The study is considered to have an excellent methodological quality if it has a score that is equal to or greater than 50 points.

Level of Evidence

We utilized the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system in order to evaluate the overall quality of the evidence based on the methodological quality of the trials that were included in the study. The following outlined the standards for the evidence's quality: 1) high quality: the results of subsequent research are not likely to shake our faith in the reliability of the estimate of the effect; (2) moderate quality: more research is likely to have a significant impact on our confidence in the estimate of effect and could change the estimate. (3) low quality; new research is likely to have a major impact on our confidence in the estimate of effect, and it is likely to affect both the estimate and the probability that the effect existed. (4) low quality standard, there is substantial uncertainty in the estimate.

RESULTS:

Study selection

The search of the literature showed up 12 RCTs, including 946 patients that met our inclusion criteria (Table 2). Four researches used cervical spinal manipulation (SMT) [35–38]. Two researches compared manipulation versus mobilization [16,39]. Four studies compared mobilization versus sham treatment or traditional treatment [40–43]. The last two studies applied ischemic compression versus a control untreated group or sham therapy [26,44]. Three studies were concerned with the dose-response evaluation of SMT [36–38]. The rationale for excluding ten studies after full article revision is shown in table 3

Figure 1: PRISMA flowchart of inclusion

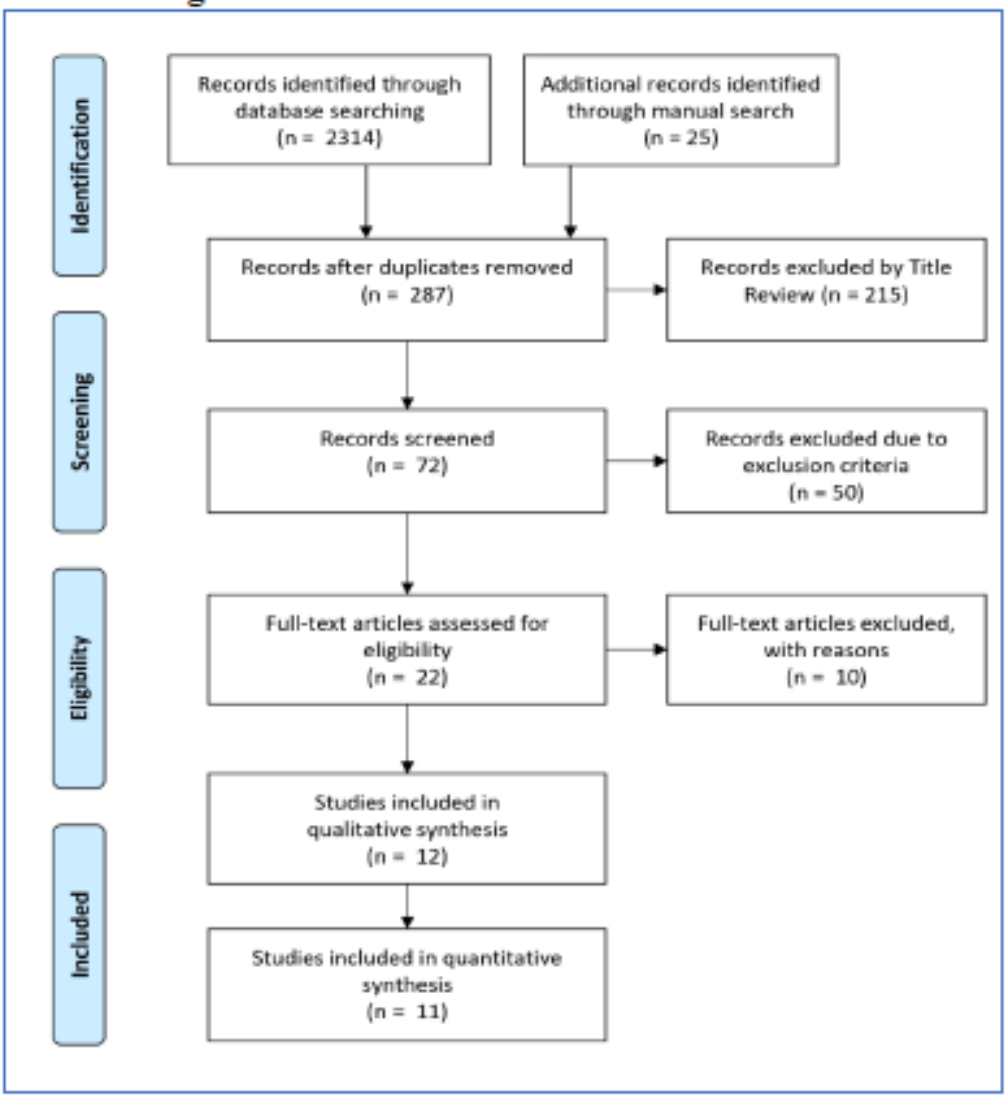


Table (2): List of the included studies

Author, year, country	Diagnostic Criteria	Intervention	Comparator	Outcome measures	Measurement time
Jull et al. (2002); Australia [35]	Sjaastad (1998)	Manipulation, 6 wks, 8-12 sessions	Low-load exercise	Frequency, Intensity, Duration	After one week and 12 months
Haas et al. (2004); USA [36]	IHS	Manipulation, 1, 3, or 4 times/week (n=8 for each)	Dose	Intensity, Frequency, Disability	After 4 and 12 weeks
Hall et al. (2007); Australia [40]	IHS	Mobilization (Self-SNAG), (n=16)	Sham treatment (n=16)	Severity index	After 4 weeks and 12 months
Haas et al. (2010); USA [37]	IHS	Manipulation, 8 or 16 sessions, total 80 participants	Light massage	Intensity, Disability, Frequency	After 12 and 24 weeks
Youssef & Shanb (2013); Egypt [41]	CHISG	Mobilization, 6 wks, 12 sessions (n=18)	Massage (n=18)	Intensity, Frequency, Duration, Disability	After 1 week
Bodes-Pardo et al. (2013); Spain [26]	CHISG	Ischemic compression, 3 sessions in 3 days (n=10)	Simulated therapy (n=10)	Intensity, Frequency, Duration	After 1 week
Dunning et al. (2016); USA [39]	CHISG	Manipulation, 4 wks, 8-12 sessions (n=58)	Mobilization (n=52)	Intensity, Disability, Frequency, Duration	After 1 week, 1 month, 3 months
Jafari et al. (2017); Iran [44]	IHS	Ischemic compression, 4 sessions in 8 days (n=9)	No therapy (n=10)	Frequency, Intensity, Duration	After 2 weeks
Malo-Urriés et al. (2017); Spain [43]	CHISG	Upper cervical translatoric spinal Mobilization (n=41)	No treatment (n=41)	Intensity (secondary)	Immediate
Haas et al. (2018); USA [38]	IHS	Manipulation 6 weeks, 1, 2, or 3 sessions (n=64, each)	Light massage (n=64)	Frequency, Intensity, Disability (HIT-6)	After 12 and 24 weeks
Khalil et al. (2019); Egypt [42]	CHISG	Mulligan upper cervical traction, 9 sessions/other day + TT (n=15)	Traditional Treatment (TT) (n=15)	Intensity, Frequency, Duration,	After 1 week, and 3 months
Lerner-Lentz et al. (2020); USA [16]	Not clear	Mobilization (n=24)	Manipulation (n=21)	Disability, Intensity, QoL (HIT-6)	After 48 hours, 4 weeks

IHS: International Headache Society, CHISG: Cervicogenic Headache International Study Group

Table (3): Rationale for excluded full-text articles

Article	Rationale for exclusion
Borusiak et al. [45]	Restriction of participation for children and adolescents
von Piekartz et al. [46]	Combined diagnosis and treatment for temporomandibular disorders
Huber et al. [47]	Combined diagnosis of dysfunction of cervical and shoulder girdle muscles
Shin and Lee [48]	The disorder was neck pain and not CGH, as the title indicates
Khan et al. [49]	Treatment was comparing two techniques of mobilization
Yang and Kang [50]	The main outcome was cervical muscle fatigue and tone
Chaibi et al. [51]	Very small sample size (n=4 per group)
Uthaikhup et al. [52]	Restriction of participation for an older age group 50–75 years
Mohamed et al. [53]	Outcome measures beyond the study specified outcomes
Togha et al. [54]	Double reporting of data in a previous study, historical control without indication

Outcome assessments

1. Headache intensity, which was measured using the visual analog scale (VAS) [35,38,41,43,44] or numerical pain rating scale (NPRS) [26,42].
2. Headache frequency defined as the number of headache days per week [35,39,42], two weeks [44], or four weeks [26,37,41]
3. Headache duration defined as the mean number of headache hours per day or week [35,41,44]
4. Headache severity index (0-100) measured by a headache questionnaire [40].

5-Headache intensity and disability measured by the modified Von Korff pain scale [36,37]

6-Neck pain and disability, which were assessed using the Northwick Park Neck Pain Questionnaire [16,39].

7-Flexion rotation test (FRT).

8-Analgesic use.

9-General health status.

Three studies compared the effects of SMT versus an alternate intervention, either low-load exercise [35] or massage [37,38]. Jull et al. [35]conducted by 25 experienced physiotherapists with unblinded treatment and blinded outcome measures [35]. The study participants were diagnosed according to the CHISG [21]. The participants were randomized to receive either SMT following the regimen described by Maitland et al. [23], exercise, or a combination of both. A control group did not receive any treatment. The treatment extended over six weeks and

included a minimum of 8 and a maximum of 12 treatment sessions. The primary endpoint was a change in headache frequency from baseline to immediately after treatment (during week 7) and 12 months after the intervention, while headache intensity, duration, and neck pain were secondary endpoints. All interventions significantly reduced headache frequency and intensity and neck pain immediately after treatment compared with the control group. The corresponding effect sizes were 0.71, 0.62, and 0.53, respectively. These differences were maintained at 12 months. Headache duration was the exception where the combined program only was effective at seven weeks and 12 months. Therefore, SMT was as effective as low-load exercise up to a one-year follow-up. Also, medication intake comparing baseline with 12-month follow-up was reduced by 93% to 100% in the intervention groups compared to an increase by 33% in control ($p=0.015$ for all). Jull et al. [35] scored a 6/10 on the PEDro scale and 71 on methodological quality assessment. There were insufficient data available to calculate effect sizes at the 12-month follow-up.

Haas et al. [36] conducted a pilot study including 24 participants to test dose-response to the number of chiropractic treatments for pain relief. Three experienced chiropractors treated patients for three weeks Follow-up time points were 4 and 12 weeks after randomization conducted by mailed questionnaire. There was no control group in this study. Diagnosis of CGH was according to the International Headache Society (IHS) The primary outcome was self-reported CGH pain intensity measured by the Modified Von Korff (MVK) scale. The secondary outcomes were CGH-related disability measured by MVK Disability Scale and headache frequency. The authors considered a 20% to 25% difference from baseline score to be clinically important. The authors reported significant differences between participants receiving one treatment per week and those receiving either 3 or 4 treatments per week at four weeks and 12-week follow-up in CGH pain intensity. There was also a considerable reduction in frequency, neck pain, and associated disability. At 4- and 12-week follow-up, pain intensity was reduced by 21%, 49%, 58% and 5%, 44%, and 38% in the SMT 1, 3, and 4 times per week groups. At 4- and 12-week follow-up, headache disability was reduced 44%, 50%, 76% and 20%, 52%, 55% in the SMT 1, 3, and 4 times per week groups. Neck pain was reduced by 31%, 50%, 55% and 30%, 54%, 38%, respectively. The results showed substantial improvement compared with baseline for the higher dose groups but without statistical significance. There was a tendency toward favoring SMT three or four times a week for SMT once a week.

Haas et al. [37] used a factorial design to allocate 80 participants (n=20/group) to two dose levels (8 or 16 treatment sessions) and two levels of intervention: SMT or a minimal light massage (LM). The SMT groups received high velocity, low amplitude spinal manipulation of the cervical and upper thoracic (transitional region) spine. The treatment and outcome measures were unblinded. Follow-up was done via mailed questionnaires at 12 and 24 weeks. Diagnosis of CGH was according to the International Headache Society (IHS) in 1998 [41]. The primary outcome was self-reported CGH pain intensity measured by MVK [40]. MVK disability, headache frequency, and medication intake were secondary outcomes. At 24 weeks, mean neck pain and mean neck disability were reduced 28% and 52% in the SMT group treated once a week, 47% and 52% in the SMT group treated twice a week, 29 and 45% in the light massage (LM) group treated once a week, and 18 and 20% in the LM group treated twice a week. However, there were clinically important main effects of dose on the MVK pain scale. Generally, the

impact on disability was of lesser magnitude. Treatment improved over-the-counter medication usage at 12 weeks but was only sustained at 24 weeks for SMT patients. The manipulation had statistically significant decreases in neck disability, CGH frequency, and analgesic use. There were no statistically significant decreases between the manipulation and placebo groups regarding CGH pain intensity, neck pain, and CGH disability. Haas et al. [37] scored a 7/10 on the PEDro scale.

In a larger and more recent study, Haas et al. [38] studied the dose-response and efficacy of SMT in 256 patients diagnosed with CGH as defined by the ISH [56]. They randomized the participants to 4 dose levels over six weeks. One control group received only light massage during all sessions. High velocity, low amplitude thrust manipulation in the cervical and upper thoracic regions were applied for 1, 2, or 3 sessions over the six weeks in the remaining three groups, respectively. The primary outcome was headache frequency in the four weeks before the 12 and 24-week follow-up. Secondary outcomes included headache intensity, medication intake, Headache Impact Test (HIT-6) for headache disability [57], and quality of life. Global improvement was evaluated on a 9-point ordinal scale. Haas et al. [4] scored an 8/10 on the PEDro scale. The methodological score was 80. Headache frequency was reduced in all groups. The greatest benefit of SMT was shown in those receiving 18 sessions with an adjusted mean difference of -3.3 and -2.9, compared to the control group, respectively. However, there were no clinically important differences in pain intensity in all groups, while all the 3 SMT groups showed greater improvement in CGH-related disability. The two higher SMT dose groups (12 and 18 visits) had a clinically important and statistically significant advantage in the perceived change of pain and global improvement. . This relationship was sustained to one year following the start of care.

Six studies compared mobilization with light massage [41], no treatment [43], traditional treatment [42], sham treatment [40], or manipulation [16,39]. Youssef & Shanb [41] compared cervical mobilizations with massage therapy in 38 subjects selected based on CHISG criteria [21]. They randomly allocated the patients to receive mobilization (n = 20) or massage therapy (n = 18).). All patients received 12 treatment sessions over six weeks, the actual intervention was combined exercise and mobilization. Two subjects were dropped from the mobilization group because they preferred medication. The outcomes were assessed one week after the end of treatment, including pain intensity, frequency and duration of headache attacks, and Neck Disability Index (NDI). Headache pain intensity, frequency, and duration of headache attacks were significantly reduced after intervention in both groups. Also, functional activity and active neck range of motion were significantly increased in both groups. The authors found that mobilization was more effective at reducing pain intensity, frequency, and duration than massage. Both groups had improvements for the outcome of disability, and there was not a significant difference between the groups for this outcome measure.

Malo-Urriés et al. [43] tested the immediate effect of upper cervical translatoric spinal mobilization (UC-TSM) on cervical mobility and pressure pain threshold. Headache intensity rated on a visual analog scale (VAS) was a secondary outcome. They included a convenience sample of 82 volunteers randomly divided into two equal groups. The control group received no treatment. In the UC-TSM group, headache Intensity was reduced from 1.31±2.25 to 0.72±1.19 with a moderate effect size (d=0.57) immediately after treatment. Headache intensity was significantly lower in the UC-TSM group ($p = 0.039$) after intervention with a larger between-group effect size (d = 1.26).

Khalil et al. [42] performed an RCT to compare Mulligan upper cervical manual traction (MUCMT) vs. traditional treatment (TT). They included 30 patients 30–55 years old with CGH according to CHISG diagnostic criteria. They evaluated headache intensity (NRS), frequency, and duration one week and three months after treatment. All patients underwent a home exercise program twice a day up to the follow-up assessment. In both groups, there was a significant decrease in headache intensity, frequency, and duration. Hall et al. [40] examined the efficacy of the C1-C2 self-SNAG compared to a placebo intervention in a double-blind study. The study involved 32 participants diagnosed according to the HIS criteria [56]. The primary outcome was Flexion-Rotation Test (FRT) measured using a modified cervical range of motion (CROM) device immediately after treatment. Patients in the experimental group were subjected to mobilization with a C1-C2 cervical self-SNAG strap. The placebo involved a sham mobilization at C1-C2 using the same cervical self-SNAG strap. An assessor, blind to group allocation, then remeasured the FRT. Subjects were then asked to perform two repetitions of the exercise they had been shown, twice daily for the following 12 months. Each subject was given two copies of a headache questionnaire to assess severity with a composite score (0-100) of intensity, frequency, and duration. The benefit of treatment was evaluated on a VAS score. The assessment was performed after four weeks and 12 months. The authors reported a significant difference between the C1-C2 self-SNAG and placebo group at four weeks ($p < 0.001$) and 12 months post-intervention ($p< 0.001$). Hall et al. [40] scored a 7/10 on the PEDro scale.

Dunning et al. [39] was the first included study that compared the efficacy of manipulation with mobilization techniques. Diagnosis of CGH was according to the revised diagnostic criteria developed by CHISG. participants were randomized into a manipulation intervention group or a combined mobilization and exercise group. The treatments and exercise program lasted four weeks, and participants received six to eight sessions of manipulation or mobilization. The assessment was done 1-week, 1-month, and 3- months after treatment using Neck Pain Medical Screening Questionnaire. The primary outcome was headache intensity measured by NPRS (0–10). The secondary outcomes were NDI (0–50), headache frequency and duration, and medication intake in the last week. Improvement was assessed using a 15-point question Global Rating of Change (GRC). This study indicated that manipulation was more effective at reducing CGH intensity and disability at one week, four weeks, and three months ($p < 0.001$ for all). Additionally, the manipulation group experienced significantly reduced duration and frequency of headaches and perceived greater improvement ($p < 0.001$ for all). These findings suggest that the high-velocity, low-amplitude manipulation was more effective at treating CGH than the slow rhythmic mobilization techniques used as an intervention.

A more recent similar study [16] examined the effects of mobilization versus manipulation and exercise on disability and pain. Mobilization targeted the articular pillar or lamina body C2 and C3 as well as the lateral mass of C1. The other group was subjected to thrust high velocity, low amplitude manipulation directed to C1 and C2 levels. The primary outcome was CGH-related disability. Secondary outcomes were pain intensity measured by an 11-point NPRS, Headache Impact Test (HIT-6), the impact of headaches on quality of life, social functioning, cognitive functioning, and psychological distress using a six-item self-report questionnaire. The authors did not find a significant difference between groups in NDI, NPRS, and HIT. However,

both groups improved over time for all outcomes.

Lastly, two small studies applied ischemic compression versus no treatment or sham treatment [26,44]. Jafari et al. [44] investigated the effect of ischemic compression on the clinical outcomes of CGH and elastic behavior of myofascial trigger point activity (MTrP) in the sternocleidomastoid (SCM) muscle, using ultrasound imaging. The study included 19 female subjects according to ICHD-3 criteria [7]. The outcome measures were headache intensity, duration, and frequency assessed two weeks before and two weeks after treatment. The treatment group (n=9) received four sessions of ischemic compression within eight days, while the control group (n=10) received no treatment. The subjects who received ischemic compression intervention had lesser intensity, frequency, and shorter duration in their headaches than those of the control group ($p < 0.05$). Jafari et al. [44] scored a 5/10 on the PEDro scale.

The other study [26] investigated the effect of manual therapy on sternocleidomastoid active trigger points (TrPs). They included 20 patients aged 18-60 years. They used a clinical questionnaire to assess headache frequency in days/month, headache duration as hours/day, and headache intensity assessed with an 11-point numerical pain rating scale (NPRS). Trigger point therapy in the form of pressure release over the sternocleidomastoid muscle TrP. The process was repeated three times in each session. The control group received a simulation of the same TrP therapy treatment. Patients receiving trigger point manual therapy experienced greater decreases in headache and neck pain intensity than those receiving the simulated therapy with a large between-group effect size (SMD, 2.25). There was no reporting of headache frequency and duration.

Effects of interventions

Manipulative/mobilization therapy

Ten studies included in this review [16,35–43] assessed the effect of manipulation or mobilization interventions. Jull et al.[35] and Haas et al. [37,38] concluded that manipulative therapy was significantly effective compared to exercise or massage in reducing the frequency of headache attacks. However, SMT effectively reduced pain intensity in the studies of Jull et al. and two pilot studies, while Haas et al. [38] did not find this effect in their large study. Haas et al. [37] found a favorable outcome for the higher dose of SMT.

Mobilization was more effective than light massage [41] or sham treatment [40] in two studies to reduce CGH manifestations. Also, a single session of UC-TSM resulted in an immediate significant decrease in headache intensity [43]. However, in another study [42], MUCMT was no better than traditional treatment in decreasing headache intensity, frequency, and duration. The last two studies, Dunning et al. [39] found that manipulation was more effective than mobilization, while Lerner-Lentz et al. [16] reported comparable results of the two techniques.

Therapeutic exercise

Jull et al. [35] was the only RCT investigating the effects of exercise as the sole treatment of CGH. The exercise-only group displayed statistically significant improvements ($p< 0.001$) at seven weeks compared to the control group for headache frequency, headache intensity, and neck pain, but not headache duration.

Combination treatment of manipulation and exercise therapy

Jull et al. [35] was the only RCT that studied the effects of combined therapy of manipulation and exercise. At 7-week follow-up, the combined treatment achieved significant improvements in all outcome measures compared to the control group that persisted at the 12-month follow-up period.

Ischemic Compression

Jafari et al. [44] found that ischemic compression intervention was associated

with lesser intensity, frequency, and shorter duration in their headaches than the control group. Another small study (n=20) [26] confirmed the superiority of trigger point manual therapy compared to sham treatment (light pressure) in relieving headache and neck pain intensity.

Risk of bias

Methodological weaknesses were found in all studies. The main problem found in 10 studies is lacking blinding of the participants and practitioners during the study procedure. Nevertheless, this type of blinding cannot be accomplished owing to the nature of physiotherapy interventions used in these studies. Therefore, this weakness can be considered "non-applicable" rather than a risk of bias. Only one study was described as a double-blind [40].

Table (4):Critical appraisal of the included studies according to CASP

	Jull et al. [35]	Haas et al. [36]	Hall et al. [40]	Haas et al. [37]	Youssef & Shanb [41]	Bodes-Pardo et al. [26]	Dunning et al.[39]	Jafari et al. [44]	Malo-Urriés et al. [43]	Haas et al. [38]	Khalil et al. [42]	Lerner-Lentz et al. [16]
Clearly focused research question	y	y	y	y	y	y	y	y	y	y	y	y
Randomization and Concealment	y	y	y	y	y	y	y	n	y	y	y	y
All participants analyzed	y	y	y	y	y	y	y	CT	y	y	y	y
Participants blinded	n	n	y	n	n	y	n	n	n	n	n	n
Investigators blinded	n	n	y	n	n	n	n	n	n	n	n	n
Assessors blinded	y	y	y	y	CT	y	n	n	y	y	y	y
Similar groups at baseline	y	CT	y	CT	y	y	y	y	y	y	y	y
Treatment equality	y	y	y	y	y	y	y	y	CT	y	y	y
Comprehensive reporting	y	y	n	y	y	n	y	y	y	y	y	y
Estimate precision (CI)	n	n	y	y	n	y	y	y	n	y	n	y
Benefit/harms balance	y	y	y	y	CT	n	y	CT	CT	y	CT	y
Validity	y	n	CT	y	y	y	y	n	y	y	y	y
Generalizability	y	y	CT	y	y	y	y	CT	n	y	y	y

The risk of bias assessment (PEDro) of each trial is summarized in table (7). The assessment using the PEDro scale (scored out of 10) revealed a mean score of 6.7 (SD = 1.5). Eight studies were considered 'high quality' [16,26,37–40,42,43]. four studies were considered 'moderate quality' [35,36]

Table (5): Quality scores of included studies using the PEDro scale

	Jull et al. [35]	Haas et al. [36]	Hall et al. [40]	Haas et al. [37]	Youssef & Shanb [41]	Bodes-Pardo et al. [26]	Dunning et al. [39]	Jafari et al. [44]	Malo-Urriés et al. [43]	Haas et al. [38]	Khalil et al. [42]	Lerner-Lentz et al. [16]
Random allocation of subjects	1	1	1	1	1	1	1	1	1	1	1	1
Allocation concealment	1	1	0	1	1	1	1	0	1	1	1	1
Similar groups at baseline	1	0	1	1	1	1	1	0	1	1	1	1
Subjects blinded	0	0	1	0	0	1	0	0	0	0	0	0
Therapists administering treatment blinded	0	0	0	0	0	0	0	0	0	0	0	0
Assessors blinded	1	1	1	1	0	1	1	0	1	1	1	1
One key outcome obtained from 85% of subjects initially allocated to groups	1	1	1	1	1	1	1	1	1	1	1	1
Intention to treat used for analysis of one key outcome	0	1	1	1	0	0	1	0	1	1	1	1
Between-group statistics for one key outcome reported	1	1	1	1	1	1	1	1	1	1	1	1
Point measures and measures of variability for one key outcome	0	0	1	1	0	1	1	1	1	1	1	1
Score	6	6	8	8	5	8	8	5	8	8	8	8

Methodological considerations

All of the RCTs, with the exception of one, were thought to have at least good methodological quality, which is defined as a score of 50 or higher (Table 8). The study of Haas et al. [38] eceived an impressive 80 out of a possible 100 points.

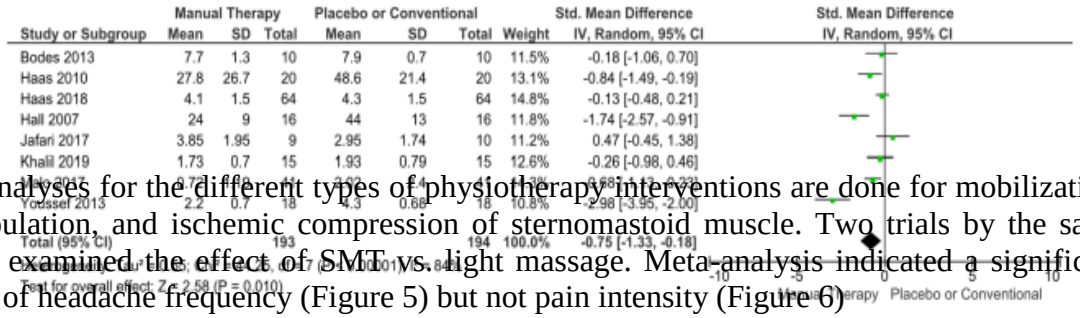
Table (6): Methodological quality assessment of included studies

	Jull et al. [35]	Haas et al. [36]	Hall et al. [40]	Haas et al. [37]	Youssef & Shanb [41]	Bodes-Pardo et al. [26]	Dunning et al.[39]	Jafari et al. [44]	Malo-Urriés et al. [43]	Haas et al. [38]	Khalil et al. [42]	Lerner-Lentz et al. [16]
1. Study population (30 points)												
a) Inclusion and exclusion criteria	2	2	2	2	2	2	2	2	2	2	2	2
b) Comparable baseline characteristics	3	3	4	4	4	4	3	4	4	4	4	4
c) Randomization procedure	4	4	4	4	4	4	4	2	4	4	4	4
d) Description of dropouts	2	3	3	3	3	2	2	0	2	2	0	2
e) Small Loss to follow-up	4	4	4	4	4	4	4	4	6	4	4	4
f) Adequate Sample size	4	1	1	2	1	2	6	1	4	6	2	2
2. Interventions (30 points)												
g) Description of interventions	10	10	5	10	10	10	10	5	7	10	10	10
h) Pragmatic study	2	2	2	2	2	0	2	2	0	2	2	5
i) Co-interventions avoided	2	5	5	5	0	5	2	5	5	5	2	5
j) Placebo control group	5	0	5	5	5	5	0	5	5	5	5	0

	Jull et al. [35]	Haas et al. [36]	Hall et al. [40]	Haas et al. [37]	Youssef & Shanb [41]	Bodes-Pardo et al. [26]	Dunning et al.[39]	Jafari et al. [44]	Malo-Urriés et al. [43]	Haas et al. [38]	Khalil et al. [42]	Lerner-Lentz et al. [16]
k) Experience of therapists	2	5	2	5	0	5	5	0	5	5	5	2
3. Measurement of effect (30 points)												
l) Blinding	0	0	3	0	0	3	0	0	3	0	0	0
m) Outcome measures assessed	8	6	6	8	8	3	4	6	3	8	8	6
n) Blinded outcomes	8	6	6	8	8	3	4	6	3	8	8	6
o) Follow up	5	3	5	4	3	3	3	2	0	5	3	3
4. Presentation and analysis (10 points)												
p) Intention-to-treat analysis	5	5	2	5	2	5	5	2	5	5	4	5
q) Correct presentation	5	5	5	5	5	5	4	4	5	5	5	5
Total SCORE	**71**	**64**	**64**	**76**	**61**	**65**	**60**	**50**	**63**	**80**	**66**	**65**

Quantitative Analysis

Eight trials that compared the efficacy of manual treatments utilized by physiotherapists to that of a control group or to usual care were combined in meta-analyses (Figure 2-4). The combined mean effect for pain reduction (8 trials, 387 participants) was statistically significant. The combined mean effect for reduced frequency (6 trials, 273 participants) was statistically significant. The combined mean effect for the reduced duration (4 trials, 105 participants) was not statistically significant. The combined mean effect for pain reduction, reduced frequency, and duration is shown in Table 7.



Sub-analyses for the different types of physiotherapy interventions are done for mobilization, manipulation, and ischemic compression of sternomastoid muscle. Two trials by the same group examined the effect of SMT vs. light massage. Meta-analysis indicated a significant effect of headache frequency (Figure 5) but not pain intensity (Figure 6)

Figure 2: Meta-analysis showing the reduction in cervicogenic headache intensity with manual physiotherapy, CI: confidence interval

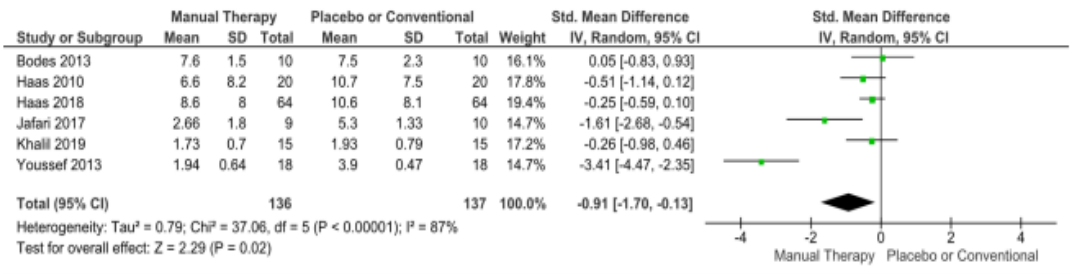


Figure 3: Meta-analysis showing the reduction in cervicogenic headache frequency with manual physiotherapy, CI: confidence interval

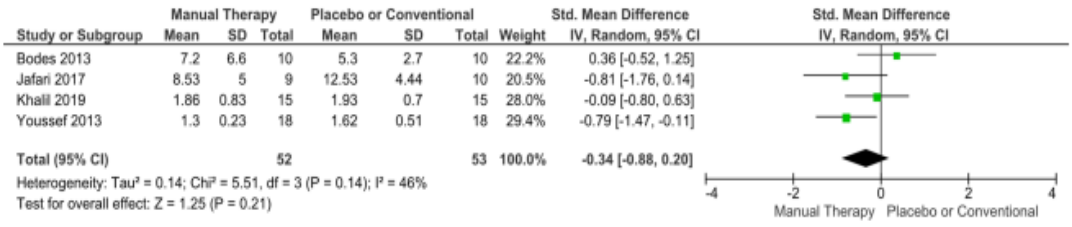


Figure 4: Meta-analysis showing the reduction in cervicogenic headache duration with manual physiotherapy, CI: confidence interval

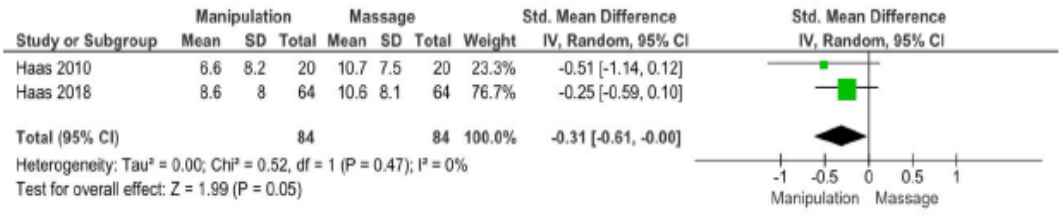


Figure 5: Meta-analysis showing the reduction in cervicogenic headache frequency with SMT, CI: confidence interval

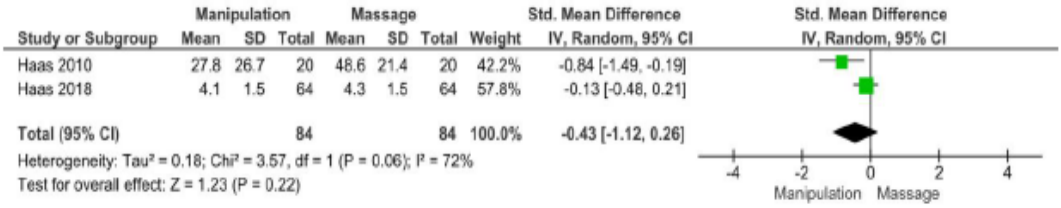


Figure 6: Meta-analysis showing the effect of SMT on cervicogenic headache pain intensity, CI: confidence interval

The same group was interested in determining the dose-response of SMT in reducing CGH pain intensity and CGH-related disability (184 participants). Meta-analysis indicated no significant effect of SMT dose on pain intensity (Figure 7) and CGH-related disability (Figure 8).

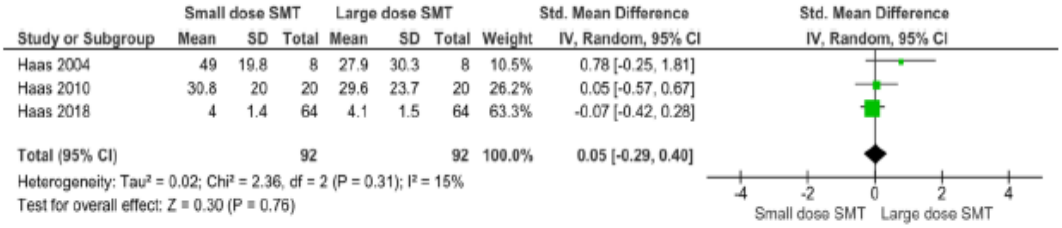


Figure 7: Meta-analysis showing the effect of dose of SMT on cervicogenic headache pain intensity, CI: confidence interval

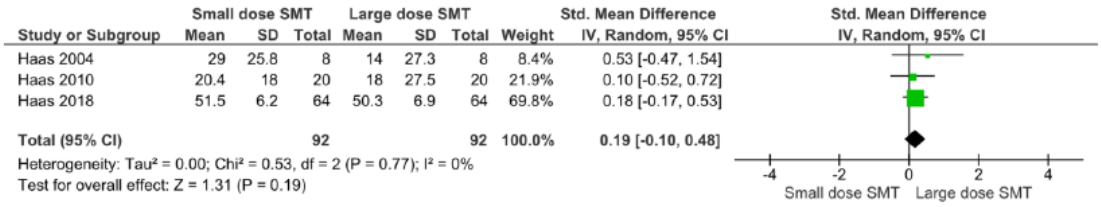


Figure 8 Meta-analysis showing the effect of dose of SMT on CGH-related disability, CI: confidence interval

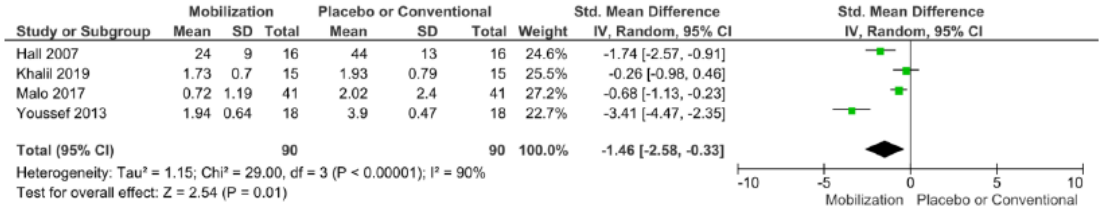


Figure 9: Meta-analysis showing the effect of spinal mobilization on cervicogenic headache pain intensity, CI: confidence interval

Figure 10: Meta-analysis showing the effect of spinal mobilization on cervicogenic headache frequency, CI: confidence interval

Four trials (180 participants) investigated the effect of spinal mobilization vs. traditional treatment or no therapy on pain intensity. Meta-analysis indicated a significant effect on CGH pain intensity (Figure 9). Two trials (66 participants) investigated the effect of spinal mobilization vs. traditional treatment or no therapy on headache frequency. Meta-analysis indicated no significant effect on frequency (Figure 10).

Two trials (155 participants) compared the effect of spinal mobilization vs. manipulation. Meta-analysis indicated no significant effect on CGH pain intensity (Figure 10) or neck disability (Figure 12).

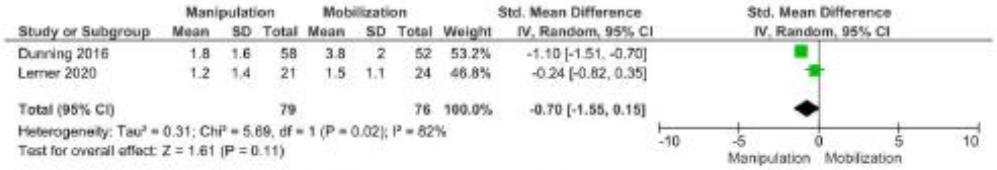


Figure 11: Meta-analysis showing the effect of spinal mobilization and manipulation on cervicogenic headache pain intensity, CI: confidence interval

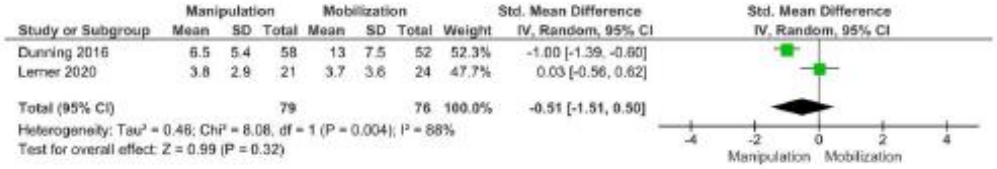


Figure 12: Meta-analysis showing the effect of spinal mobilization and manipulation on neck disability, CI: confidence interval

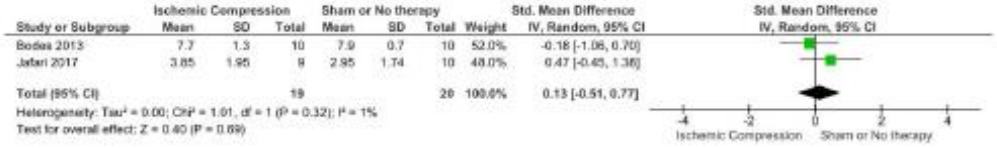


Figure 13: Meta-analysis showing the effect of ischemic compression on CGH pain intensity, CI: confidence interval

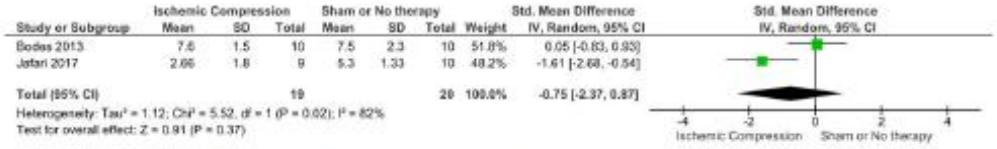


Figure 14: Meta-analysis showing the effect of ischemic compression on headache frequency, CI: confidence interval

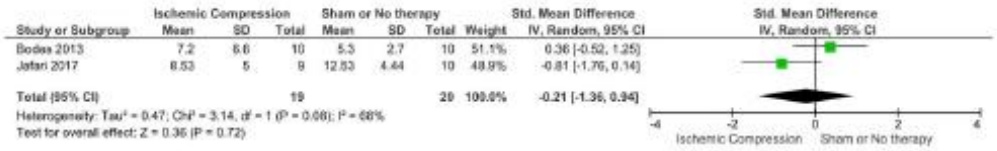


Figure 15: Meta-analysis showing the effect of ischemic compression on headache duration, CI: confidence interval

Two trials (39 participants) investigated the effect of trigger point therapy with ischemic compression of the sternomastoid muscle vs. no or simulated therapy. Meta-analysis indicated no significant effect on pain intensity, frequency, or duration (Figures 12-15). In most analyses, heterogeneity was a major observation. It is an indication of the inconsistency of the results of different studies. Table 8 shows a summary of the findings of meta-analyses.

Table (7): Meta-analyses results of different types of manual therapy

Type of Manual Therapy	Manifestation	Mean Effect	95% CI	p-value	Tau^2	I^2
All therapies	Pain	-0.75	[-1.33, -0.18]	0.01	0.55	84%
	Frequency	-0.91	[-1.70, -0.13]	0.02	0.79	87%
	Duration	-0.34	[-0.88, 0.20]	0.21	0.14	46%
Mobilization	Pain	-1.46	[-2.58, -0.33]	0.01	1.15	90%
	Frequency	-1.81	[-4.90, 1.28]	0.25	4.76	96%
Manipulation	Pain	-0.43	[-1.12, 0.26]	0.22	0.18	72%
	Frequency	-0.31	[-0.61, -0.00]	0.05	0.00	0%
Ischemic compression	Pain	0.13	[-0.51, 0.77]	0.69	0.00	1%
	Frequency	-0.75	[-2.37, 0.87]	0.37	1.12	82%
	Duration	-0.21	[-1.36, 0.94]	0.72	0.47	68%

CI: Confidence interval, Tau^2: reflect the variance of the true effect sizes (heterogeneity), I^2: percentage of variation across studies due to heterogeneity

DISCUSSION

Cervicogenic headache has been included in the International Classification of Headache Disorders as a secondary headache arising from musculoskeletal disorders in the cervical spine but not necessarily accompanied by neck pain [59]. Structures such as the upper cervical synovial joints, upper cervical muscles, and C2–C3 intervertebral disc have been raised as possible origins of CGH [60]. Some findings suggest the involvement of the neck structures in CGH; for example, a reduction in upper cervical rotation [62] reduced cervical flexion/extension or painful upper cervical joints as assessed by manual palpation [63]. Given the problem of relapses at the neck, conservative treatment has focused on the neck structures. Hence, the objective of this systematic review was to assess the effectiveness of various conservative manual physical therapy interventions for the management of CGH. The interventions assessed included cervical and upper thoracic manipulation, cervical mobilization, and ischemic compression of cervical muscular trigger points. This systematic review and meta-analysis demonstrated that manual physiotherapy provides significant, small short-term effects for pain intensity, frequency, and disability but not pain duration among individuals suffering from CGH. However, high heterogeneity reduces the applicability of the evidence. The lack of a high-quality evidence approach creates some uncertainly in these results. Cervical mobilization has been demonstrated to be useful in in lowering pain but ineffective in reducing headache frequency. On the contrary, SMT decreased headache frequency but did not significantly reduce pain intensity. According to the IHS guidelines for controlled trials, headache frequency is considered the most important primary measure in efficacy studies for headache [65]. Trigger point compression in the sternomastoid muscle was not effective for pain and symptom reduction.

Our findings generally agree with previous contemporary systematic reviews regarding the efficacy of manual therapies for CGH. Only two RCTs were included in one review in 2005. The two trials reported a positive effect of SMT on headache intensity, headache duration, and medication intake. However, SMT did not reduce headache frequency significantly [68]. Subsequently, in a review of 6 RCTs, Racicki et al. found that exercise intervention demonstrated significant improvement of pain intensity and frequency of symptoms after seven weeks. Combined exercise and manipulative therapy achieved significant pain reduction and improvement in symptoms frequency that persisted at the 12-month-follow up period.

Luedtke et al. performed a systematic review to assess the efficacy of physiotherapy approaches in three types of headaches. Eight studies involved patients with CGH. Meta-analyses indicated a reduction of CGH pain intensity, frequency, and duration. However, pain reduction and CGH frequency decrease do not achieve clinically significant effect sizes. Small sample sizes, improper classification of headaches, and other methodological flaws diminish the reliability of these results. Garcia et al. reported that 7 of 10 included trials had a significant impact of mobilization or manipulation in improving headache pain and frequency compared to control subjects. However, like the current study, the authors found it difficult to generalize the findings due to the studies' heterogeneity. In another review, Coelho et al found that manipulation was equally as effective as conservative treatment in reducing pain, disability, and headache frequency in individuals with CGH. Most recently, Fernandez included 7 trials investigating the effectiveness of SMT exclusively for CGH. They demonstrated a significant small effect favoring SMT over

other manual therapies for pain intensity in the short term. However, there was a non-significant difference between groups in the mid- and long-term.

The current review suggests that SMT can be utilized to reduce headache frequency, and on the other hand, cervical mobilization can reduce pain intensity. A recently published evidence-based guideline for the non-pharmacological management of headaches associated with neck pain recommends using SMT, spinal mobilization, or craniocervical scapula exercises for CGH management [72]. But this guideline did not recommend combining these therapeutic modalities. Actually, a large reliable study [35] not included in the quantitative analysis in the current review utilized a combination of manipulation and mobilization in their RCT, although they described their intervention as manipulation. Another study [16] found both techniques to be equally effective for pain reduction. Dunning et al. [39] provided evidence that the care of patients with CGH should include some type of cervical manipulation Despite the fact that cervical manipulation is frequently advised to be avoided due to the danger of major adverse outcomes[73]. A systematic review determined that both mobilization and manipulation are useful for treating patients with CGH, but was unable to identify whether strategy was better [74]. In addition, clinical guidelines revealed that manipulation, mobilization, and exercise were useful for the management of patients diagnosed with CGH; however, the guidelines did not make any suggestions regarding the superiority of each treatment modality [75]. A significant issue is that clinical diagnostic criteria for CGH have not been shown to be valid, Probably, there is no gold standard when it comes to CEH diagnosis criteria. However, CHISG criteria are superior for CEH diagnosis [5]. The results of this study suggest that manual physical therapy, including SMT and spinal mobilization, could significantly reduce the symptoms of CGH as pain intensity and headache frequency [35,39]. These results need to be viewed cautiously because of the methodological discrepancies in the studies and the small sample size in most of them. Also, the large heterogeneity of the included studies is another factor decreasing the generalizability of the findings. As a result, the clinical impact of the findings is level B (good) based on the current evidence base.

CONCLUSIONS:

Manual therapy techniques provide significant but small and short-term effects for pain intensity, frequency, and disability but not the duration of CGH. Spinal manipulative therapy can be utilized to reduce headache frequency, and on the other hand, cervical mobilization can reduce pain intensity. Manipulation and mobilization need to be investigated in well-designed large studies. A Combination of manipulation and mobilization could be effective for reducing pain intensity and headache frequency. Trigger point compression in the sternomastoid muscle was not effective for pain and symptom reduction.