FLEX CEUs

Cervicogenic Headaches

Cervicogenic headache: too important to be left un-diagnosed

Abstract

A comparison has been made between the cervicogenic headache criteria in the new IHS classification of headaches (3rd edition- beta version) and The Cervicogenic Headache International Study Group's (GHISG) criteria from 1998. In a more recent version, the CHISG criteria consist of 7 different items. While "core cases" of cervicogenic headache (CEH) usually fulfill all 7 criteria, the IHS classification - 3rd edition beta version- fulfills only 3 criteria. Although the new three beta version represents an improvement from the previous one, it does not quite seem to live up to the expectations for a diagnostic system for routine, clinical use.

Keywords: Cervicogenic headache; Headache classification; Unilaterality of headache; Mechanical precipitation of headache

Status as regards classification of Cervicogenic headache

The present version of cervicogenic headache classification from IHS (3rd edition beta version) [1] is better than the previous one, which mixed- up headache and facial pain. That does not mean that it is flawless. A classification should not only be recognition of disorders, with a minimalist description of some characteristic traits of each disorder. It should also, definitely, serve as a guideline in practical, clinical work, like the IHS criteria do in other disorders in the field, e.g. migraine [1]. That is the main aim of the CHISG criteria [2]. The CHISG and IHS have essentially different approaches to these problems.

Background

A clinician confronted with a headache patient decides to consult a diagnostic guideline. In the IHS system, he will find that the mode of presentation of criteria seems to differ in primary and secondary headaches. In primary headaches, the headache itself is described in detail, whereas in secondary headaches, like CEH, the (putative) underlying pathology is focused. For example at C I, under "Diagnostic criteria": "Headache has developed in temporal relation to the onset of the cervical disorder—". In the actual, clinical situation, this statement will be inutile for all practical purposes. It may concern a situation in the remote future and will accordingly not be very illuminating. One will only rarely be in a position to watch the growth of an underlying pathological process in CEH: such a process presumably develops insidiously slow. C I should probably be removed from the criteria and placed under another heading. C I seems to be some type of writing desk medicine- not a guideline for practical work.

Moreover, in our opinion, headache characteristics (localization, intensity, and duration) should come first, followed by other characteristic traits (precipitation mechanisms, reduction in range of motion etc.) [3].

Clinical symptoms and signs

The same last as in C I is found in point C 2: "Headache has significantly improved or resolved in parallel with improvement in or resolution of the cervical disorder—". The usefulness of this criterion is also limited in the diagnostic situation. One exceptional disorder that may seem to fit both C1 and C2 is: "Tractor drivers´ head- and neck-ache" [4]. This headache comes in connection with tractor-driving during chores and fades away after the chore. This headache does not become chronic—the stimulus is turned on and off. –-

Point C3.comes in another category. It, moreover, seems to contain at least *two c*riteria: I. Reduction, cervical range of motion. And II: Significant worsening of

headache by mechanical influence. These two criteria are not directly akin. It would, therefore, probably be best to have them under different numbers. As for range of motion, the extent of normalcy should be outlined. Otherwise, this point may not be of optimal value. The magnitude of the stimulus, needed during provocations, should be specified, in order to create a useful criterion. Mechanical precipitation of pain attacks can be obtained in two ways: by external pressure or by positioning the neck in unphysiological positions for a prolonged time. This should probably also have been mentioned under C3.

C3 is important, but in our estimation it needs an upgrading. If left like it is, it will leave the clinician with more questions than advices. ––C4 is unproblematic.

Then, under what is termed "Comments" side-locked pain is mentioned. This is a fundamental quality of CEH. It has not been mentioned previously by IHS. IHS has thus been following our footsteps. Does not bilaterality exist in CEH? It probably does, but then the level of pathology in the neck may be ("is"?) different on the two sides. It is then probably a question of "unilaterality on two sides". According to the IHS Committee, side-locked pain should not be regarded as "unique" (together with mechanical precipitation procedures and posterior → anterior movement (probably not radiation!) of the pain). All these features are, in our estimation, major criteria of CEH. (Posterior → anterior movement of pain has previously been *sub judice* as a symptom in CEH. It was investigated in 1989 by Fredriksen [5]. However, in the Vågå study, where it was a *free variable,* it proved to be present almost invariably [3,6]. It has, therefore, more recently been formally recognized as a true CEH criterion (by the CHISG classification committee; TAF & OS: two of the three original members, and by: FA, previous chairman of the group). –- It seems to be a misunderstanding to speak about "unique" criteria. Are the migraine criteria "unique"? Each solitary of them? Of course not. That is not the way headache descriptions are built up. It is the impact of all of them, e.g. pulsating pain, photophobia etc. that viewed together make up the picture of migraine. –Some of the CEH criteria may, nevertheless, be somewhat more specific than the migraine criteria, e.g. unilaterality without sideshift; and pain that starts in the posterior part of the head and then "crawls" to the front.

There exists no gold standard as far as CEH criteria are concerned. Closest to this, probably comes the CHISG diagnostic criteria. These are not even cited in the IHS beta version, so a comparison between them could not be made.

We are highly uncertain as to how the "Comments" should be regarded. Apparently, they are not regarded as criteria, on line with "Diagnostic criteria". If so, they should primarily have been placed there. This leaves us as readers and future potential users with a considerable dilemma.

The grave question is: does the IHS scheme stand the test? Can CEH diagnosis be made on the basis of this scheme? In connection with the CHISG criteria, we proposed two constellations of diagnostic phenomena, as minimum requirement for the diagnosis.: I: "Confirmatory" combination of criteria for CEH diagnosis and II: "Provisional" criteria, both categories containing 4 solitary, obligatory items; two items overlapped [2]. The IHS criteria do not fulfill any of the two combinations: one criterion is lacking for each of them. If what *we* understand by criteria, in the "Comments" [1] were included, the situation would change.

As already mentioned: In connection with the Vågå study [3,6], we introduced an enumeration of diagnostic factors, with a total of 7 or 8 factors, depending upon whether diagnostic blockades are incorporated or not:

I Unilateral head pain, without side shift ¤
II Provocation, unphysiological neck positions *
III Provocation, externally; neck/occipital area *
IV Range of motion, neck; deficit *
V Shoulder pain, diffuse
VI Arm pain, diffuse
VII Pain, starting posteriorly- ending up anteriorly ¤
VIII Diagnostic, anesthetic blockades

* IHS diagnostic criteria (C3); n = 3. ¤ "Criteria", mentioned under" Comments" n = 2; a total of 5 criteria.

Diagnostic blockades are not obligatory in routine work, for which reason they are placed below a line.

Discussion

The Vågå study showed a close-to-complete congruity between the orthodox application of the criteria [2] and the aforementioned enumeration [3,6]. This means that the IHS criteria also can be compared with the enumeration criteria. Also in this comparison, the IHS criteria seem to fail: with three out of seven criteria present. If the criteria from the "Comments" section were added, there would be five out of seven CHISG criteria present. In this situation, a CEH diagnosis could have been made. In the first situation, it could definitely not have been made. –The "enumeration" method is easier to apply than the original "orthodox" method. –- In the Vågå study, there were 41 "core" CEH cases; prevalence: 2.2% [6]. The mean number of criteria was close to 6.0; or: 7.0, if the 7th criterion was included. To use only core cases, is probably the best way to calculate CEH prevalence. If cases of co-morbidity with migraine and tension-type headache were added, the prevalence of CEH in Vågå would be: 4.1%. CEH diagnosis is no left hand work, and the diagnostic accuracy is probably reduced in the latter situation. –This, nevertheless, means that in medical practice, one will with not too long intervals encounter CEH patients [7].

Conclusion

The present IHS criteria version is still probably not a safe basis for diagnosing CEH, although it represents an improvement from the previous IHS version. With the present CHISG criteria, the CEH diagnosis [8] may seem safer than e.g. the migraine diagnosis. It is advocated that the symptoms from the "comments" section of the IHS description are included as criteria to improve the diagnostic accuracy.

Magnetic resonance imaging of craniovertebral structures: clinical significance in cervicogenic headaches

Abstract This paper aims to investigate the relevance of morphological changes in the main stabilizing structures of the craniocervical junction in persons with cervicogenic headache (CEH). A case control study of 46 consecutive persons with CEH, 22 consecutive with headache attributed to whiplash associated headache (WLaH) and 19 consecutive persons with migraine. The criteria of the Cervicogenic Headache International Study Group (CHISG) were used for diagnosing CEH; otherwise the criteria of the International Classification of Headache Disorders (ICHD II) were applied. All participants had a clinical interview, and physical and neurological examination. Proton weighted magnetic resonance imaging (MRI) of the craniovertebral junction, and the alar and transverse ligaments were evaluated and blinded to clinical information. The MRI of the craniovertebral and the cervical junctions, the alar and transverse ligaments disclosed no significant differences between those with CEH, WLaH and or migraine. The site of CEH pain was not correlated with the site of signal intensity changes of the alar and transverse ligaments. In fact, very few had moderate or severe signal intensity changes in their ligaments. MRI shows no specific changes of cervical discs or craniovertebral ligaments in CEH.

Keywords Cervicogenic headache · Alar ligaments · Transverse ligaments · Craniovertebral junction · Cervical junction · MRI

Introduction

Cervicogenic headache (CEH) is a symptomatic headache characterized by chronic unilateral headache possibly secondary to dysfunction of the cervical spine [1–3]. CEH is often worsen by neck movement, sustained awkward head position, external pressure of the upper cervical or occipital region on the symptomatic side [1, 2]. Anaesthetic blockades of cervical structures or related nerves can temporarily abolish pain in CEH patients, which may suggest that the pain could be attributed to a neck disorder or structural lesion [1, 2, 4]. Clinical and/or imaging evidence of neck disorder or lesion can be accepted as a valid cause of headache. However, there is an agreement that degenerative changes in the cervical spine do not necessarily correlate with pain [1, 5]. Nevertheless, the research is striven to identify causative changes in the cervical spine, which may be attributed to CEH. The craniovertebral junction is stabilized by joint capsules, tectorial membrane, transverse and alar ligaments. Those anatomic structures are innervated by C2 root [6]. Convergence of the nociceptive afferents of the trigeminal and upper three cervical spinal nerves onto the second-order neurons in the trigemino-cervical nucleus in the upper cervical spinal cord referrers the pain from the cervical spine to the head [7, 8].

The pain in CEH may originate from various anatomic structures in the cervical spine. A German study suggests that lower cervical disc prolapse may cause CEH [9]. It is conceivable that injury to the ligamentous structures can trigger CEH. High-resolution proton density-weighted magnetic resonance imaging (MRI) can visualize structural changes of ligaments and membranes in the upper cervical spine, and it is possible to grade the severity of these structural changes [10–12]. The diagnostic value of such changes is still controversial and their relevance in CEH is unknown. The aim of our study was to examine the frequency of structural changes in the alar and transverse ligaments in persons with CEH, whiplash associated headache (WLaH) and migraine.

Materials and methods

Study sample

The case–control study included patients referred to a general neurological outpatient clinic (Dept. of Neurology, Innlandet Hospital, Norway). A total of 118 participants were eligible for the study, but 31 refrained from participation. Of the 87 participants, 46 had CEH, 22 had WLaH, and 19 had migraine. The participants were interviewed and examined by a neurological resident (HK). CEH was classified according to the criteria of the Cervicogenic Headache International Study Group (CHISG) requiring at least three criteria to be fulfilled, not including a Greater Occipital Nerve (GON) blockade, i.e. criterias 1a, 1a1, 1a2, 1b, 1c and/or III (Table 1), [13]. Otherwise, the criteria of the International Classification of Headache Disorders (ICHD II) were applied [1]. WhipLash was defined by an acceleration/deceleration trauma that caused flexion/extension distortion of the neck followed by pain/stiffness. Three persons (two with CEH and one with migraine) refrained from MRI due to claustrophobia and two persons with CEH were excluded due to reduced image quality, ending up with 82 participants.

Magnetic resonance imaging protocol and evaluation

We examined the craniovertebral junction in three orthogonal planes (Siemens Symphony, Erlangen, Germany). The persons were scanned in supine position using both the neck coil and the attachable anterior element from the head coil. Images were obtained using a fast spin-echo (SE) T2 and proton-density-weighted sequences.

MR protocol

We did a T2-weighted series covering the whole cervical spine. Repetition time (TR) and echo time (TE) were TR/TE 3,360/103, slice thickness 3 mm without gap, number of excitation (nex) 3, matrix 276 × 512 mm and field of view (FoV) 280 × 280 mm. We did proton-weighted series of the craniovertebral junction with 1.5 mm slice thickness without gap covering the alar and the transverse ligaments in three orthogonal planes. Axial series (12 images) covered from the base of the dens upward, TR/TE 2,660/15, matrix 276 × 512, nex 5, FoV 200 × 165 mm. Coronal series (13 images) covered from anterior atlantal arch backward, TR/TE 2,870/15, matrix 271 × 512, nex 5, FoV 200 × 200 mm. Sagittal series (20 images) covering the entire length of both alar ligaments, TR/TE 2,150/15, matrix 211 × 512, nex 3, FoV 200 × 150 mm.

Table 1 The diagnostic criteria of cervicogenic headache by the Cervicogenic Headache International Study Group

Major criteria	I. Symptoms and signs of neck involvement
	Ia. Precipitation of head pain, similar to the usually occurring one
	Ia (1) by neck movement and/or sustained, awkward head positioning, and/or
	Ia (2) by external pressure over the upper cervical or occipital region on the symptomatic side
	Ib. Restriction of the range of motion (ROM) in the neck
	Ic. Ipsilateral neck, shoulder or arm pain of a rather vague, non-radicular nature, or—occasionally—arm pain of a radicular nature
	II. Confirmatory evidence by diagnostic anaesthetic blockades
	III. Unilaterality of the head pain, without side shift
Head pain characteristics	IV. Moderate–severe, non-throbbing pain, usually starting in the neck. Episodes of varying duration, or fluctuating, continuous pain
Other characteristics of some importance	V. Only marginal effect or lack of effect of indometacin. Only marginal effect or lack of effect of ergotamine and sumatriptan. Female sex. Not infrequent occurrence of head or indirect neck trauma by history, usually of more than only medium severity
Other features of lesser importance	VI. Various attack-related phenomena, only occasionally present, and/or moderately expressed when present: (a) nausea, (b) phono- and photophobia, (c) dizziness, (d) ipsilateral "blurred vision", (e) difficulties swallowing, (f) ipsilateral oedema, mostly in the periocular area

It is obligatory that one or more of the phenomena Ia–Ic are present

Table 2 Demographic data

	Cervicogenic headache $N = 46$	Whiplash associated headache $N = 22$	Migraine $N = 19$
Women (*n*)	36	13	17
Men (*n*)	10	9	2
Age mean (SD)	43.2 (9.2)	41.5 (7.1)	42.3 (11.2)
Age range (year)	27–61	27–57	21–58
Age at onset mean years (SD)	31.3 (11.9)	33.4 (9.8)	19.9 (8.1)
Headache duration mean (SD)	12.4 (10.4)	8.6 (7.1)	22.1 (11.6)

The classification of the alar and transverse ligament lesions is based on the ratio between any high-signal part and the total cross-sectional area of the ligament. The alar and the transverse ligaments were graded according to the following criteria: grade 0—ligament with low signal throughout the entire cross-section; grade 1—ligaments with high signal in <1/3 or less of cross-section; grade 2—high signal in 1/3–2/3 of cross-section and grade 3—high signal in >2/3 or more of cross-section. Both sides of the alar and transverse ligaments were visualized in all participants [10–12, 14].

MRI evaluation

All MR images were evaluated by an experienced consultant in Neuroradiology (JK), who was blinded to clinical information.

Statistical analysis

The statistical analysis was performed using SPSS Base System for Windows 15.0 for all four MRI gradings and dichotomized groups (Grade 0–1 and Grade 2–3). We used the χ^2-test with 5% level of significance.

Ethical issues

The Regional Committees for Medical Research Ethics and the Norwegian Social Science Data Services approved the project. The participants that received GON blockade were informed about the procedure and side effects. All participation was based on informed consent.

Results

Table 2 shows demographic data of the participants. Signal intensity changes in the alar and transverse ligaments were found in 43% ($n = 18$) of persons with CEH, in 41% ($n = 9$) in persons with WLaH and in 50% ($N = 9$) of the persons with migraine. The results were dichotomized in two groups between none to mild (grade 0–1) and moderate to severe (grade 2–3) signal intensity changes. Table 3 shows that moderate to severe signal intensity changes in any of the transverse or alar ligaments (graded 2–3) were equally distributed on the right and left side and there were no statistical significant differences between the CEH, WLaH or migraine groups. Only 16% had moderate or severe signal changes. Mild signal intensity changes (grade 1) were found in 21, 32, and 44% of the subjects with CEH, WLaH and migraine, respectively. We disclosed no statistical significant changes regarding side of the change or between the CEH, WLaH and migraine groups dichotomizing the groups into none and mild to severe signal intensity changes (graded 0 and 1–3).

Table 4 shows disc degeneration. Moderate or severe degeneration of the craniovertebral and cervical discs was rare and only found in the C4/5, C5/6 and C6/7. Changes were seen in all three diagnostic groups, although there were no significant differences among the groups.

Signal intensity changes in the transverse and alar ligaments in relation to the location of the CEH are shown in Table 5. The statistical analyses showed no significant correlation between the site of signal intensity change and site of CEH. Dichotomizing the results in none and mild to severe signal intensity changes did not change the outcome of the analyses.

Discussion

We found no significant difference in MRI signal intensity changes in the alar and transverse ligaments or any difference in disc degenerative between subjects with CEH, WLaH and migraine. However, the pain in CEH may originate from various other structures in the cervical spine and cervical ligaments not identified with this MRI protocol which focused on certain structures [15]. But still all pathological changes in the cervical spine with sensory connection to the spinal tract of the trigeminal nerve might potentially be the pain generating structures which has to be focused on [7]. The alar ligament system is involved during cervical extension, lateral flexion, and ipsilateral rotation; nevertheless we found no correlation between side

Table 3 Signal intensity changes in any of the transverse or alar ligaments (details for grading is described in "Materials and methods" section)

	CEH $N = 42\%$ (n)	WLaH $N = 22\%$ (n)	Migraine $N = 18\%$ (n)	p value
Right alar ligament				
Grade 0–1	86 (36)	86 (19)	89 (16)	n.s.
Grade 2–3	14 (6)	14 (3)	11 (2)	
Left alar ligament				
Grade 0–1	86 (36)	95 (21)	89 (16)	n.s.
Grade 2–3	14 (6)	5 (1)	11 (2)	
Both sides alar ligament				
Grade 0–1	83 (35)	86 (19)	89 (16)	n.s.
Grade 2–3	17 (7)	14 (3)	11(2)	
Right transverse ligament				
Grade 0–1	90 (38)	95 (21)	100 (18)	n.s.
Grade 2–3	10 (4)	5 (1)	0 (0)	
Left transverse ligament				
Grade 0–1	88 (37)	95 (21)	89 (16)	n.s.
Grade 2–3	12 (5)	5 (1)	11 (2)	
Both sides transverse ligament				
Grade 0–1	88 (37)	91 (20)	89 (16)	n.s.
Grade 2–3	12 (5)	9 (2)	11 (2)	

n.s. denotes non-significant

Table 4 Signal intensity changes in the craniovertebral and cervical junction (details for grading is described in "Materials and methods" section)

	CEH $N = 42\%$ (n)	WLaH $N = 22\%$ (n)	Migraine $N = 18\%$ (n)	p value
C2/3				
Grade 0–1	100 (42)	100 (22)	100 (18)	n.s.
Grade 2–3	0 (0)	0 (0)	0 (0)	
C3/4				
Grade 0–1	100 (42)	100 (22)	100 (18)	n.s.
Grade 2–3	0 (0)	0 (0)	0 (0)	
C4/5				
Grade 0–1	88 (37)	91 (20)	89 (16)	n.s.
Grade 2–3	12 (5)	9 (2)	11 (2)	
C5/6				
Grade 0–1	69 (29)	91 (20)	83 (15)	n.s.
Grade 2–3	31 (13)	9 (2)	17 (3)	
C6/7				
Grade 0–1	95 (40)	100 (22)	100 (18)	n.s.
Grade 2–3	5 (2)	0 (0)	0 (0)	
C7/TH1				
Grade 0–1	100 (42)	100 (22)	100 (18)	n.s.
Grade 2–3	0 (0)	0 (0)	0 (0)	
Change any junctions				
Grade 0–1	70 (29)	86 (19)	84 (15)	n.s.
Grade 2–3	30 (13)	14 (3)	16 (3)	

n.s. denotes non-significant

location of pathological signal intensity (higher signal intensity) in the ligaments and the side location of the CEH [16, 17]. The transverse ligaments are strained at various movements of the head, still high-signal intensity (graded 2–3) in those ligaments was rare in all three diagnostic groups. A cross-sectional study applying conventional

Table 5 Signal intensity changes in the transverse and alar ligaments in relation to location of the cervicogenic headache (CEH)

	Grade of structural changes on MRI		*p* values
	0–1	2–3	
Right-sided CEH $n = 19$	*N* (%)	*N* (%)	
Right alar ligament	17 (89)	2 (11)	n.s.
Left alar ligament	17 (89)	2 (11)	
Right transverse ligament	15 (80)	4 (20)	n.s.
Left transverse ligament	14 (74)	5 (26)	
Left-sided CEH $n = 23$			
Right alar ligament	19 (83)	4 (17)	n.s.
Left alar ligament	19 (83)	4 (17)	
Right transverse ligament	23 (100)	0	n.s.
Left transverse ligament	23 (100)	0	

n.s. denotes non-significant

cervical MRI found no significant difference between patients with CEH and control subjects [18]. More specifically designed MRI protocols and evaluation grading scales were introduced focusing on the structural assessment of craniovertebral ligaments and craniovertebral junctions in persons with whiplash associated disorders [12, 14, 19, 20]. High grade changes were far more frequently observed in cases with a previous whiplash trauma than in a control group using a high-resolution proton density-weighted MRI in three orthogonal planes [10, 11].

There are at least four case control studies that used similar MRI methodology as our present study—two of those studies suggests injury of craniocervical structures, while two recent studies failed to reproduce those findings. A new improved MRI protocol showing the ligaments and membranes in the craniovertebral junction was developed 10 years ago [14]. Further, they studied and classified structural changes in the alar ligaments in the late stage of whiplash injuries by the use of a new MRI protocol [10]. Almost half of whiplash associated disorder (WAD) subjects had structural changes in the alar ligaments, while no grade 2 or 3 lesion was found in the control group. Authors suggest that whiplash trauma might cause permanent damage to the alar ligaments, shown by high-resolution proton density-weighted MRI but the reliability of this classification had to be improved. A similar study has been performed by the same group focusing on MRI changes of the tectorial and posterior atlanto-occipital membranes [11]. A study on the radiologic spectrum of craniocervical distraction injuries used fat suppressed T2 weighted images a method that might be more sensitive to demonstrate increased signal intensity in the atlantoaxial and atlanto-occipital joints, craniocervical ligaments, prevertebral soft tissue and spinal cord than conventional MRI, however, we used a specific MRI protocol developed with special emphasis on imaging the ligaments [14, 21]. Those studies triggered lively discussion between neurologists and radiologists and there was a need of similar studies from other groups that could confirm diagnostic value of those MRI techniques. Myran et al. [20] compared subjects with WAD, chronic non-traumatic neck pain and subjects without neck pain or previous neck trauma. Alar ligament changes grade 0 to 3 were seen in all three groups. Areas of high-signal intensity (grade 2–3) were found in at least one alar ligament in 49% of the patients in the whiplash associated disorder grade I–II group, in 33% of the chronic neck pain group and in 40% of the control group. The diagnostic value and the clinical relevance of magnetic resonance detectable areas of high intensity in the alar ligaments are questionable. Another study examined ligaments and membranes in the craniocervical junction with MRI in patients with WAD and compared them with healthy control subjects [22]. High-signal intensity of the alar and transverse ligaments was quite common and was reported at an average of about 50% both among patients and control subjects. The incidence of abnormalities of the tectorial and posterior atlanto-occipital membranes was low in both groups. No statistically significant difference between control subjects and patients with WAD was revealed for any of the structures assessed.

Our study failed to show differences or specific changes of cervical discs or craniovertebral ligaments in any studied group. However, our primary focus was somehow different compared with other similar studies. CEH is a defined headache syndrome, while WLaH or WAD could be defined by different symptoms and only one thing in common—neck trauma in the past. Unilaterality of symptoms in CEH allowed us to look for MRI changes at corresponding side.

Structural alterations of the alar ligaments and upper articular joints are frequent in asymptomatic patients [19]. Focussing on only one particular structural change in the cervical spine might not be a suitable diagnostic method to detect possible pathological finding in patients with CEH.

Future investigations might have to focus more on the heterogenic origin of CEH and alternative operational tests in addition to the MRI.

Conclusion

Morphological MRI changes in craniovertebral ligaments showed similar frequency in patients with CEH compared to those with WLaH and/or migraine. According to our data, such changes have no established value for the diagnosis or work up of CEH.

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Conflict of interest None.

Effect of natural apophyseal glides on cervicogenic headache: A randomized controlled trial

Abstract

Background: Headache is that the most prevailing pain disorder, affecting sixty six percent of the worldwide population. Cervicogenic headache may be a common condition inflicting significant disability.

Purpose: To determine the efficacy of Mulligan Natural apophyseal glides (NAGs) on pain intensity level, functional ability and cervical range of motion in subjects with cervicogenic headache.

Methods: Thirty patients with clinicaldiagnosis of cervicogenic headache were assigned randomly into two groups: Group (A) patients received conventional physical therapy program 3 sessions per week for 4 weeks. Group (B) patients received conventional physical therapy program in addition to Mulligan, natural apophyseal glides (NAGs) 3 sessions per week for 4 weeks. Pain intensity level, neck functional disability level, and cervical range of motion were measured pre and post intervention period.

Results: Patients of bothgroups showed statistical significant improvement in all the measured variables after treatment program. Between groups difference the natural apophyseal glides group (B) showed a statistical significant improvement in pain intensity level, neck functional disability level than in group (A) but there was no statistical significant difference between both groups in cervical range of motion (p value<0.05).

Conclusions: Mulligan (natural apophyseal glides) had an effect on decreasing pain intensity level, improving functional abilityand cervical range of motion in patients with cervicogenic headache.

Keywords: Cervicogenic Headache, Natural Apophyseal Glides

Introduction

Physiotherapists commonly come across patients complaining of headache in their clinical practice [1]. Headache can be classified as primary or secondary. Primary headache originates from a vascular or muscular source such as tension-type headache. Secondary headache is related to other structures with cervicogenic headache (CGH) being the most common type that is related to cervical spine dysfunction [2,3].

The International Headache Society (IHS) defined cervicogenic headache as "pain caused by neck source and perceived in one or more parts of the head and/or face" [4]. It accounts for 15% to 20% of cases of chronic and recurrent headache [4,5]. CGH may originate from different structures of the cervical spine including the zygapophyseal joints (occiput-C3) [6,7]. This type of headache has been found to be four times more common in subjects with musculoskeletal symptoms [8]. Also, individuals with neck pain are more frequently exposed to headache than those with symptoms in other areas [9].

Subjects with chronic cervicogenic headache have considerable limitation of daily function, restriction of social participation, and emotional distress with profound impact on quality of life [10,11]. Major signs and symptoms of CGH include unilateral head pain without side-shift, with neck pain and limitation of neck movement [12]. Muscle dysfunction is an important feature of CGH. Various studies have shown significant hypomobility of craniocervical joints and impaired overall mobility of

cervical spine [5,6]. Moreover, muscle tightness especially of the upper trapezius and sternocleidomastoid muscles with impaired strength and neuromotor contract of the cervical flexors(superficial and deep) are frequently encountered in subjects with CGH [13].

However, diagnosis of cervicogenic headache is difficult because up to 70% of subjects with frequent intermittent headache report accompanying neck pain [14]. It is therefore logical that subjects who experience headaches may receive unwarranted treatment to the neck unless an accurate, exact assessment is made [15].

Different therapeutic approaches have been proposed for treatment of headaches; with physical therapy, pharmacological drugs, and cognitive therapies the most commonly used [9]. Several studies reported that manual therapy of the cervical spine can decrease pain intensity, frequency, and duration in addition to reducing in neck pain and disability [16]. Jull et al. [17] reported that neck exercises are effective in the management of cervicogenic headache.

Mulligan Natural apophyseal glides (NAGs) are oscillatory mobilizations which can be applied to the facet joints and graded according to the tolerance of the patient. They are used to increase spinal movement and decrease the pain associated with it [18]. Mulligan Techniques have mechanical and neurological effects, resulting in a sympatheoexcitatory effect which may be instrumental in producing an analgesic response[19]. NAGs mobilization technique produces a fast and long-term effect in pain reduction and improvement of range of motion with functional activities in subjects with pain and stiffness of the neck [20]. Although the Mulligan technique is frequently used in clinical practice, there is limited evidence about its effect, in the treatment of CGH.

Therefore, the purpose of this study was to determine the efficacy of natural apophyseal glides (NAGs) on pain intensity, functionalabilityand cervical range of motion in subjects with cervicogenic headache.

Material and methods

Design of the study

Pretest-Posttest randomized controlled experimental design was used in this study.

Subjects

Thirty patients (10 males and 20 females) with cervicogenic headache were selected from the outpatient clinic of the faculty of physical therapy, Cairo University. They assigned randomly using a random sequence generator to one of the two study groups. Subjects were recruited using publically distributed posters, online social media, and by verbal invitation. Subjects participated in the current study after approval of ethical committee of faculty of physical therapy, Cairo University with number (P.T.REC /012/001815) and all subjects provided written informed consent.

Subjects whose age ranged from 20 to 40 and BMI ranged from18.5–24.9 kg/m^2. were selected. The study procedureswere explained. **Group(A)** control group included 15 CGH patients, with a mean age of (26.64±2.23) years (6 male and 9 female), received the conventional physical therapy program (hot packs, isometric neck flexor strengthening exercises, chin in exercises for deep neck flexor muscles and stretching exercise for upper trapezius and sternocleidomastoid muscles) 3 session per week for 4 weeks. **Group(B)** experimental group included 15CGH patients, with a mean age of(25.86±3.62) years(4 male and 11female) received Mulligan **NAGs** technique in addition to the conventional physical therapy program 3 session per week for 4 weeks.

Inclusion criteria

All participants were referred from physicians. They were diagnosed with CGH matching CGH diagnostic criteria established by international headache society, had unilateral headache without side shift, headache with neck stiffness and or pain, headache frequency of at least once per week over a period of 3 months.

Exclusive criteria

If they had headache not of cervical origin, headache with any associated symptoms like dizziness or visual disturbance, history of any surgeryaround cervical region, sever trauma, disc prolapse, spinal stenosis, specified bilateral headache, pregnancy, as well as frequent migraine.

Sample-size determination

For sample size estimation of the study, 80% power, 0.05 type one error (2 tailed) and effect size of 0.90;15 subjects were recruited in each group and total number recruited was 30. G*power 3.1 software (Universities, Dusseldorf, Germany) was used for calculation.

Instrumentation

1)Numerical Pain Rating Scale (NPRS)

The NPRS is a valid and reliable scale to measure pain intensity [21]. (NPRS; 0–10) is utilized to assess pain intensity level, where 0 indicates no pain and 10 indicates maximum pain. Measurement results of NPRS for all participants showed average pain rating [22].

2)Neck disability index (NDI)

Neck Disability Index **(NDI)** is considered a reliable and valid measurement for the disability accompanying neck pain. The Arabic version of NDI was used in the current study to investigate pain intensity level in Arabic speaking patients suffering from **CGH** [14]. The Arabic version of NDI has two factors with ten items structure and has proven to be a reliable, valid, and responsive tool [23].

3) Myrin goniometer (OB)

Myrin goniometer was utilized to measure cervical range of

motion **(ROM)**. This measurement tool consists of a compass needle affected by the earth's magnetic field and an inclination needle affected by gravity. The compass needle measures motion on the horizontal plane, and the inclination needle measures motion on the vertical plane. Thus, it has proven to be reliable and valid for neck ROM measurement [24].

All measures were assessed by an assessor blinded to group allocation before intervention and reassessed in similar way following 4-weeks intervention had been completed.

Procedures

The current study consisted of three Stages: Pre-test measurements, Intervention period and Post-test measurements:

Pre-test measurements

Pain intensity level measurement

The patient was asked to place mark at his/her level of pain at sheet of NPRS.

Neck functional disability level measurement

The neck functional disability level was measured by the neck disability index (NDI) pre and post treatment. In this study we used the Arabic version of the NDI.

Cervical ROM measurement

The cervical ROM by Myrin goniometer in all directions (flexion, extension, side bending and rotation) was measured. The patient was seated in erect and comfortable position while his/her feet were placed flat on the floor. Knee kept in right angle. The strap was fixed around the head with the instrument at the side. The inclination needle was set at zero. The head was bent forward (neck flexion), and backward (neck extension). The instrument was placed at the front or the back. The inclination needle was reset again at zero, the neck was bent to right side (right lateral flexion) and was bent to the left side (left lateral flexion), The patient sat on low stool with his/her head erect. The straps were fixed round the head and over the vertex. The compass needle was set at zero. The patient was asked to rotate his/ her neck to the right side (right rotation), and to the left side (left rotation). The mean of 3 repetitions was calculated for each type of movement and used for the analysis.

Intervention

Group (A)

Participants of this group received conventional physical therapy program three sessions per week for four weeks. This program included 4 components;1) hot packs application prior to exercise. An electric hot pack for cervical region 10 x16 inches. It was done from sitting position for 20 minutes on cervical region with head resting on a pillow [13].

2)passive stretching for upper trapeziusby contra lateral side bending, the patient placed in sitting position and the head-neck region was passively bent on right side (to stretch left side) to the restrictive barrier and asked the patient not to move the shoulder [13], and passive stretching sternocleidomastoid the patient placed in sitting position , slowly brought patient's head from the neutral position into a position of contralateral side flexion,ipsilateral rotation, , and slight extension [25]. Stretching exercises 6-15 seconds for 3 times repetition.

3)Isometric neck flexion exerciseswere performed from sitting position, low back support was provided with hold for 6 seconds, and then relax for 6 seconds. These procedures were repeated 15 times (**Figure 1**).

Figure 1. Isometric neck flexor ex.

4) and chin in exercises (for deep neck flexor muscles)were performed from supine lying position, in these exercises, a roll of towel was placed which wasplaced suboccipitally to monitor the subtle flattening of the cervical lordosis that occurswith the contraction of the longus colli muscle. The patient asked to carefully nod his head as he was saying "yes" while not restoring to retraction, while not strictly involvement of superficial flexors, and without fast, jerky cervical flexion movement and hold for thirty seconds and recurrent 3 times [26].

Group (B)

Participants of this group received conventional physical therapy programin addition to NAGs technique. The patient was seated on low chair in erect and comfortable position. The therapist stood facing the patient in step stance posture stabilizing patient's shoulder/ trunk. Painless oscillatory mid to end-range mobilization was applied in the plane of the facet joints (upward direction). It was applied between C4–C5 and C5–C6.

The therapist's middle phalanx of left little finger was

placed under the Spinous process of the superior vertebra of the mobilized segment. The other fingers on that hand were wrapped around the occiput, stabilizing the head. The lateral border of the thenar eminence of right hand partially covered the little finger of the therapist left hand. The therapist took up slack in the soft tissue to come into contact with the vertebrae to be moved. It was applied with 2 hertz in 3 sets, whereas glides were rhythmical. Mobilizations were repeated 6 times. The program was performed for three sessions per week for four weeks (**Figure 2**).

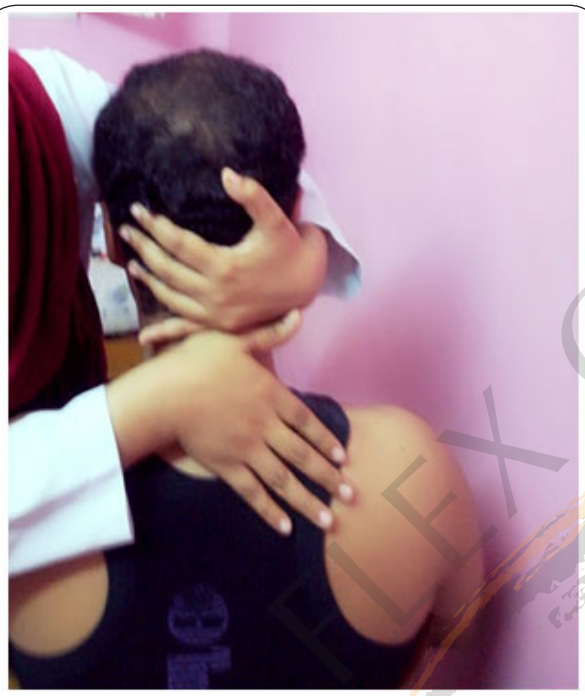

Figure 2. Mulligan NAGs technique.

Both groups were treated under the same conditions and each subject was treated individually to avoid influencing one another.

Post-test measurements

Pain intensity level, Neck functional disability level, and cervical ROM measurements were conducted twice pretest measurements and after the intervention period to determine its effect.

Data analysis and statistical design

All statistical analysis was carried out by using the SPSS computer program, version 20. Data were expressed as mean ± standard deviation (SD). Descriptive data and t-test were used for comparison of the mean age, height, weight and body mass index (BMI). Mean changes within groups (pre and post-study) were analyzed using Paired T-test while mean changes between groups (pre and post-study) were analyzed using unpaired T-test to test hypothesis between groups. The level of significance was set at $p<0.05$.

Results

This study was conducted todetermine the efficacy of natural apophyseal glides (NAGs) on pain intensity, functional ability and cervical range of motion in subjects with cervicogenic headache. Thirty subjects were assigned randomly into two equal groups.

Group (A)

Fifteen CGH patients received conventional physical therapy program. The data in (**Table 1**) represented their mean age (26.64±2.23) years, weight (66.9±8.3) kg, height (165.8±5.23) cm and BMI (24.8±2.18) kg/m2.

Group (B)

Fifteen CGH patients r received conventional physical therapy in addition to NAGstechnique The data in (**Table 1**) represented their mean age (25.86±3.62) years, weight (67±6.22) kg, height (163.8±4.5) cm and BMI (24.3±1.96) kg/m2. There was no significant difference between two groups in their mean age, weight, height and BMI.

Table 1. General Characteristics of the Subjects in both groups.

Items	Age (Year)	Weight (kg)	Height (cm)	BMI (kg/m^2)
Group A mean ±SD	26.64 ±2.23	66.9 ±8.3	165.8 ±5.23	24.8 ±2.18
Group B mean ±SD	25.86 ±3.62	67±6.22	163.8 ±4.5	24.3 ±1.96
t-value	0.546	- 0.025	1.121	0.605
P-value	0.589	0.980	0.272	0.550
P<0.05	NS	NS	NS	NS

Pre study means values within both groups

As shown in **Table 2**, There were no significant differences between two groups pre-study in pain intensity level, NDI and neck ROM where P-values were greater than 0.05.

Post study means values within both groups

As shown in **Table 3**, There were no significant differences between two groups post-study in neck ROM where P-values were greater than 0.05.

Comparison between pre and post study for group A

As shown in **Table 4**, for group A, there were significant differences in pain intensity level, NDI and neck ROM between pre and post-study, where P-value were less than (0.05).

Comparison between pre and post study for group B

As shown in **Table 5**, for group B, there were significant differences in pain intensity level, NDI and neck ROM between pre and post-study, where P-value were less than (0.05).

Discussion

In the twenty-first century, headachesare very common and

Table 2. Pre-study mean values of measured variables for both groups.

Pre-study		Group A Mean ±SD	Group B Mean ±SD	t-value	P-value
Pain intensity level		6.70 ±2.45	5.80 ±1.75	-0.905	0.373
Neck disability index		14.6 ±5.57	14.86 ±4.37	0.146	0.885
Neck ROM	flexion LT	35.33 ±4.76	36.53 ±4.6	0.7	0.490
	extension	36.66 ±3.95	37.06 ±3.86	0.28	0.781
	Rt lateral flexion	34.53 ±5.96	37.73 ±4.19	1.69	0.1
	Lt lateral flexion	37.33 ±4.04	35.46 ±7.8	0.822	0.418
	Rt Rotation	51.73 ±8.37	51.13 ±7.18	0.211	0.835
	Lt Rotation	53.66 ±10.2	49.26 ±9.7	1.207	0.238

Table 3. Post-study mean values of measured variables for both groups.

Post-study		Group A Mean ±SD	Group B Mean ±SD	t-value	P-value
Pain intensity level		2.80 ±1.22	1.83 ±1.39	0.984	0.032
Neck disability index		4.93 ±2.57	3.26 ±2.01	2.47	0.043
Neck ROM	flexion LT	42.86 ±1.84	43.66 ±1.49	-1.34	0.203
	extension	42.46 ±2.13	43.26 ±1.48	-1.19	0.243
	Rt lateral flexion	40.8 ±6.27	43.73 ±1.57	-1.75	0.09
	Lt lateral flexion	42.2 ±3.6	42.86 ±5.23	-0.406	0.688
	Rt Rotation	57.8 ±3.48	57.93 ±4.11	-0.096	0.924
	Lt Rotation	59.86 ±1.3	59.13 ±1.24	2.19	0.243

cause substantial pain and disability [27]. Cervicogenic headache is a secondary headache, which means "head pain with a cervical source". Prevalence rates for CGH within the general population varied from 0.4% to 2.5% and in some researches up to 4.1% [25]. Cervicogenic headache associated with ahigh burden of suffering and considerable socio-economic cost [27]. Although the Mulligan technique is frequently used in clinical practice, there is limited evidence about its effect, in the treatment of CGH. So, the purpose of this study was to investigate the efficacy of Mulligan (NAGs) on cervicogenic headache regarding reduction of pain intensity level, increasing cervical range of motion and improving in functional ability.

Our results revealed that there were significant differences in pain intensity level, NDI and neck ROM between pre and post-study for both groups. Also, the result revealed that there were statistical significant differences between both groups in favour to NAGs group post-study in pain intensity level, NDI. While there were no significant differences between two groups post-study in neck ROM.

The results indicated that NAGs group showed a significant decrease in pain intensity level and significant improvement in functional ability than the other group.

Mulligan techniques have both mechanical and neurological effects, Exelby L. [28], argued that the zygoapophyseal joints guide the spine and so improving their glide by applying NAGs and SNAGs will increase the range of spinal movement. Also, they may cause hypoalgesic effects by many mechanisms, a) Local mechanical disturbance which may modify the chemical environment, altering the concentration of inflammatory mediators. b) Movement may also trigger segmental inhibitory mechanisms. c) Activate the descending pain inhibitory systems, mediated supraspinally that involves serotonin and noradrenalin receptors in the spinal cord. d) Sympathetic nervous system and motor system excitation [29].

In the available literature, there is limited researches that studied the effect of NAGS on CGH. A few studies support the current findings.

Gautam R et al. [30] conducted a comparative study between Maitland and Mulligan Mobilization in improving neck pain range of motion (ROM) and disability. This study validated that Mulligan mobilization was more effective in reducing neck pain, disability and improving ROM. Kumar D [19], investigated the effectiveness of Mulligan NAGS in neck pain and stiffness. It was concluded that NAGs is a beneficial mobilization technique for providing faster and prolonged effect in reducing pain and improving range of motions with functional activities

The finding of this study come in agreement with Ali et al. [31] who investigated the efficiency of sustained natural apophyseal glides SNAGs with and without isometric exercise training in nonspecific neck pain. They found that when

Table 4. Pre-study post-study mean values of measured variables for group A.

Group A		Pre-study Mean ±SD	Post-study Mean ±SD	% of change	t-value	P-value
Pain intensity level		6.70 ±2.45	2.80 ±1.22	58.2 %	-10.2	0.000*
Neck disability index		14.6 ±5.57	4.93 ±2.57	66.23 %	-7.4	0.000*
Neck ROM	flexion LT	35.33 ±4.76	42.86 ±1.84	21.31 %	6.45	0.000*
	extension	36.66 ±3.95	42.46 ±2.13	15.82 %	9.37	0.000*
	Rt lateral flexion	34.53 ±5.96	40.8 ±6.27	18.15 %	4.21	0.001*
	Lt lateral flexion	37.33 ±4.04	42.2 ±3.6	13 %	6.44	0.000*
	Rt Rotation	51.73 ±8.37	57.8 ±3.48	11.73 %	3.07	0.008*
	Lt Rotation	53.66 ±10.2	59.86 ±1.3	11.55 %	2.36	0.033*

Table 5. Pre-study post-study mean values of measured variables for group B.

Group B		Pre-study Mean ±SD	Post-study Mean ±SD	% of change	t-value	P-value
Pain intensity level		5.80 ±1.75	1.83 ±1.39	68.96 %	-13.4	0.000*
Neck disability index		14.86 ±4.37	3.26 ±2.01	71.33 %	-9.92	0.000*
Neck ROM	**flexion** LT	36.53 ±4.6	43.66 ±1.49	19.5 %	5.07	0.000*
	Extension	37.06 ±3.86	43.26 ±1.48	16.72 %	6.8	0.000*
	Rt lateral flexion	37.73 ±4.19	43.73 ±1.57	15.9 %	4.58	0.000*
	Lt lateral flexion	35.46 ±7.8	42.86 ±5.23	20.68 %	5.44	0.000*
	Rt Rotation	51.13 ±7.18	57.93 ±4.11	11.73 %	4.92	0.000*
	Lt Rotation	49.26 ±9.7	59.13 ±1.24	20 %	3.91	0.002*

they applied sustained natural apophyseal glides techniques with isometric exercise on patients having nonspecific neck pain, there was significant decrease in pain and significant improvement in functional ability when compared to those who were treated with sustained natural apophyseal glides techniques alone.

Our results were supported by Shahzada Iftikhar Hussain et al. [32], who concluded that Mulligan natural apophyseal glide mobilization technique NAGs for treatment of nonspecific neck pain has been confirmed to be more helpful than Grade I & II Maitland mobilization in reducing pain, and restoration of function by progressing NPRS and NDI scores in patients having nonspecific neck pain.

Another agreement with Eui-Ju Shin1 and Byoung-Hee Lee [33], who concluded that application of the SNAGs technique to middle-aged women with CGH is considered effective in decreasing the duration time of headache, and neck pain, as well as in development of neck function.

Also, our finding is consistent with Miller et al. [34], who stated in their systematic review regarding manual therapy and exercises for neck pain that combined mobilization and exercise had greater effect in reducing pain and improving functional abilitythan exercise only.

The results of the current study come in agreement with Barton&Halyes [35] who concluded that maximal neck flexor muscle strength was decreased by 50% in patients with unilateral neck pain and headache compared with normal subjects. Other study has also pointed that strength of neck flexor muscle was significantly reduced in patients with cervicogenic headache [36] So, strengthening exercises for neck flexor help in managing the headache. Similarly,Rbiul Islam et al. [13] found that a reduction in cervical muscle strength was associated with cervicogenic headache, and deep flexors training was effective for the treatment of cervicogenic headache because improvement in muscle strength (isometric exercises) was a main cause f reducing pain and improvingfunctional ability.

Also,JariYlinen et al. [37] investigated the effect of neck exercises on cervicogenic headache and reported that both stretching and strengthening exercises reduce neck pain and disability.

Shannon M Petersen [3] attributed the increasing mobility and decreasing pain intensity in patients of cervicogenic headache to the application of neck manual therapy for (strengthening, stretching and mobilization exercises).

Our conclusion come in consistence with the work of Jull et al. [17] who examined the effectiveness of manual therapy and low load exercise program for individuals with cervicogenic headache. They reported that both manual therapy and specific exercise were effective in reducing headache frequency and intensity.

Also, our results can be explained by the work ofGema Bodes-Pardo et al. [25] who suggested that sternocleidomastoid muscle may be particularly a common source of myofascial CGH. So, stretching of this muscle is a main cause of improvement and treatment of CGH.

This study was limited by small sample size and un availability of Arabic version of Headache Disability Index.

Conclusion

Mulligan NAGs technique could be effective on decreasing pain intensity level, improving functional abilityand cervical range of motion in patients with cervicogenic headache.

Further studies would be worth while because CGH affecting sixtysix percent of the world wide population, Subjects with chronic cervicogenic headache have considerable limitation of daily function, restriction of social participation, and emotional distress with profound impact on qualityof life. future studies can consider a large sample size, pain threshold, Assessing electrophysiological parameters.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Authors' contributions	GIM	WSS
Research concept and design	--	--
Collection and/or assembly of data	✓	✓
Data analysis and interpretation	✓	✓
Writing the article	✓	✓
Critical revision of the article	--	--
Final approval of article	✓	✓
Statistical analysis	✓	--

Upper cervical and upper thoracic manipulation versus mobilization and exercise in patients with cervicogenic headache: a multi-center randomized clinical trial

Abstract

Background: Although commonly utilized interventions, no studies have directly compared the effectiveness of cervical and thoracic manipulation to mobilization and exercise in individuals with cervicogenic headache (CH). The purpose of this study was to compare the effects of manipulation to mobilization and exercise in individuals with CH.

Methods: One hundred and ten participants ($n = 110$) with CH were randomized to receive both cervical and thoracic manipulation ($n = 58$) or mobilization and exercise ($n = 52$). The primary outcome was headache intensity as measured by the Numeric Pain Rating Scale (NPRS). Secondary outcomes included headache frequency, headache duration, disability as measured by the Neck Disability Index (NDI), medication intake, and the Global Rating of Change (GRC). The treatment period was 4 weeks with follow-up assessment at 1 week, 4 weeks, and 3 months after initial treatment session. The primary aim was examined with a 2-way mixed-model analysis of variance (ANOVA), with treatment group (manipulation versus mobilization and exercise) as the between subjects variable and time (baseline, 1 week, 4 weeks and 3 months) as the within subjects variable.

Results: The 2X4 ANOVA demonstrated that individuals with CH who received both cervical and thoracic manipulation experienced significantly greater reductions in headache intensity ($p < 0.001$) and disability ($p < 0.001$) than those who received mobilization and exercise at a 3-month follow-up. Individuals in the upper cervical and upper thoracic manipulation group also experienced less frequent headaches and shorter duration of headaches at each follow-up period ($p < 0.001$ for all). Additionally, patient perceived improvement was significantly greater at 1 and 4-week follow-up periods in favor of the manipulation group ($p < 0.001$).

Conclusions: Six to eight sessions of upper cervical and upper thoracic manipulation were shown to be more effective than mobilization and exercise in patients with CH, and the effects were maintained at 3 months.

Trial registration: NCT01580280 April 16, 2012.

Keywords: Cervicogenic headache, Spinal manipulation, Mobilization, High velocity low amplitude thrust

Background

The International Classification of Headache Disorders defines cervicogenic headache (CH) as, "headache caused by a disorder of the cervical spine and its component bony, disc, and/or soft tissue elements, usually but not invariably accompanied by neck pain." [1] (p.760) The prevalence of CH has been reported to be between 0.4 and 20 % of the headache population [2, 3], and as high as 53 % in patients with headache after whiplash injury [4]. The dominant features of CH usually include: unilaterality of head pain without side-shift, elicitation of pain with external pressure over the ipsilateral upper neck, limited cervical range of motion, and the triggering of attacks by various awkward or sustained neck movements [4, 5].

Individuals with CH are frequently treated with spinal manipulative therapy including both mobilization and manipulation [6]. Spinal mobilization consists of slow, rhythmical, oscillating techniques whereas manipulation consists of high-velocity low-amplitude thrust techniques. [7] In a recent systematic review, Bronfort and colleagues reported that spinal manipulative therapy (both mobilization and manipulation) were effective in the management of adults with CH [8]. However, they did not report if manipulation resulted in superior outcomes compared to mobilization for the management of this population.

Several studies have investigated the effect of spinal manipulation in the management of CH [9–13]. Haas et al. [10] investigated the effectiveness of cervical manipulation in subjects with CH. Jull et al. [11] demonstrated treatment efficacy for manipulative therapy and/or exercise in the management of CH. However the manipulative therapy group included manipulation and mobilization therefore it cannot be determined if the beneficial effect was a result of the manipulation, mobilization or the combination.

A few studies have examined the benefits of manipulation versus mobilization for the management of mechanical neck pain with or without exercise [14–16]. However, no studies have directly compared the effects of manipulation versus mobilization and exercise in patients with CH. Considering the purported risks of manipulation [17], it is essential to determine if manipulation results in improved outcomes compared to mobilization for the management of patients with CH. Therefore, the purpose of this randomized clinical trial was to compare the effects of manipulation versus mobilization and exercise in patients with CH. We hypothesized that patients receiving manipulation over a 4-week treatment period would experience greater reductions in headache intensity, headache frequency, headache duration, disability, and medication intake at a 3-month follow-up than patients receiving cervical and thoracic mobilization combined with exercise.

Methods

Participants

In this multi-center randomized clinical trial, consecutive patients with CH presenting to 1 of 8 outpatient physical therapy clinics from a variety of geographical locations (Arizona, Georgia, New York, Ohio, Pennsylvania, South Carolina) were recruited over a 29-month period (from April 2012 to August 2014). For patients to be eligible, they had to present with a diagnosis of CH according to the revised diagnostic criteria [5] developed by the Cervicogenic Headache International Study Group (CHISG) [5, 18, 19]. CH was classified according to the "major criteria" (not including confirmatory evidence by diagnostic anesthetic blockades) and "head pain characteristics" of the CHISG. Therefore, in order to be included in the study, patients had to exhibit all of the following criteria: (1) unilaterality of the head pain without sideshift, starting in the upper posterior neck or occipital region, eventually spreading to the oculofrontotemporal area on the symptomatic side, (2) pain triggered by neck movement and/or sustained awkward positions, (3) reduced range of motion in the cervical spine [20] (i.e., less than or equal to 32 ° of right or left passive rotation on the Flexion-Rotation Test [21–23], (4) pain elicited by external pressure over at least one of the upper cervical joints (C0-3), and (5) moderate to severe, non-throbbing and non-lancinating pain. In addition, participants had to have a headache frequency of at least 1 per week for a minimum of 3 months, a minimum headache intensity pain score of two points (0–10 on the NPRS scale), a minimum disability score of 20 % or greater (i.e., 10 points or greater on the 0–50 NDI scale), and be between 18 and 65 years of age.

Patients were excluded if they exhibited other primary headaches (i.e., migraine, TTH), suffered from bilateral headaches, or exhibited any red flags (i.e., tumor, fracture, metabolic diseases, rheumatoid arthritis, osteoporosis, resting blood pressure greater than 140/90 mmHg, prolonged history of steroid use, etc.), presented with two or more positive neurologic signs consistent with nerve root compression (muscle weakness involving a major muscle group of the upper extremity, diminished upper extremity deep tendon reflex, or diminished or absent sensation to pinprick in any upper extremity dermatome), presented with a diagnosis of cervical spinal stenosis, exhibited bilateral upper extremity symptoms, had evidence of central nervous system involvement (hyperreflexia, sensory disturbances in the hand, intrinsic muscle wasting of the hands, unsteadiness during walking, nystagmus, loss of visual acuity, impaired sensation of the face, altered taste, the presence of pathological reflexes), had a history of whiplash injury within the previous 6 weeks, had prior surgery to the head or neck, had received treatment for head or neck

pain from any practitioner within the previous month, had received physical therapy or chiropractic treatment for head or neck pain within the previous 3 months, or had pending legal action regarding their head or neck pain.

The most recent literature suggests that pre-manipulative cervical artery testing is unable to identify those individuals at risk of vascular complications from cervical manipulation [24, 25], and any symptoms detected during pre-manipulative testing may be unrelated to changes in blood flow in the vertebral artery [26, 27]. Hence, pre-manipulative cervical artery testing was not performed in this study; however, screening questions for cervical artery disease had to be negative [24, 28, 29]. This study was approved by the Institutional Review Board at Long Island University, Brooklyn, NY. The study was registered at www.clinicaltrials.gov with trial identifier NCT01580280. All patients were informed that they would receive either manipulation or mobilization and exercise and then provided informed consent before their enrollment in the study.

Treating therapists

Twelve physical therapists (mean age 36.6 years, SD 5.62) participated in the delivery of treatment for patients in this study. They had an average of 10.3 (SD 5.66, range 3–20 years) years of clinical experience, and all had completed a 60 h post-graduate certification program that included practical training in manual techniques including the use of cervical and thoracic manipulation. To ensure all examination, outcome assessments, and treatment procedures were standardized, all participating physical therapists were required to study a manual of standard operating procedures and participate in a 4 h training session with the principal investigator.

Examination procedures

All patients provided demographic information, completed the Neck Pain Medical Screening Questionnaire, and completed a number of self-report measures, followed by a standardized history and physical examination at baseline. Self-report measures included headache intensity as measured by the NPRS (0–10), the NDI (0–50), headache frequency (number of days with headache in the last week), headache duration (total hours of headache in the last week), and medication intake (number of times the patient had taken narcotic or over-the-counter pain medication in the past week).

The standardized physical examination was not limited to, but included measurements of C1-2 (atlanto-axial joint) passive right and left rotation ROM using the Flexion-Rotation Test (FRT). The inter-rater reliability for the FRT has been found to be excellent (ICC: 0.93; 95 % CI: 0.87, 0.96) [30].

Outcome measures

The primary outcome measure used in this study was the patient's headache intensity as measured by the NPRS. Patients were asked to indicate the average intensity of headache pain over the past week using an 11-point scale ranging from 0 ("no pain") to 10 ("worst pain imaginable") at baseline, 1-week, 1-month, and 3-months following the initial treatment session [31]. The NPRS is a reliable and valid instrument to assess pain intensity [32–34]. Although no data exists in patients with CH, the MCID for the NPRS has been shown to be 1.3 in patients with mechanical neck pain [32] and 1.74 in patients with a variety of chronic pain conditions [34]. Therefore, we chose to only include patients with an NPRS score of 2 points (20 %) or greater.

Secondary outcome measures included the NDI, the Global Rating of Change (GRC), headache frequency, headache duration, and medication intake. The NDI is the most widely used instrument for assessing self-rated disability in patients with neck pain [35–37]. The NDI is a self-report questionnaire with 10-items rated from 0 (no disability) to five (complete disability) [38]. The numeric responses for each item are summed for a total score ranging between 0 and 50; however, some evaluators have chosen to multiply the raw score by two, and then report the NDI on a 0–100 % scale [36, 39]. Higher scores represent increased levels of disability. The NDI has been found to possess excellent test-retest reliability, strong construct validity, strong internal consistency and good responsiveness in assessing disability in patients with mechanical neck pain [36], cervical radiculopathy [33, 40], whiplash associated disorder [38, 41, 42], and mixed non-specific neck pain [43, 44]. Although no studies have examined the psychometric properties of the NDI in patients with CH, we chose to only include patients with an NDI score of ten points (20 %) or greater, because this cut-off score captures the MCID for the NDI, which has been reported to approximate four, eight, and nine points (0–50) in patients with mixed non-specific neck pain [44], mechanical neck pain [45], and cervical radiculopathy [33], respectively. Headache frequency was measured as the number of days with headache in the last week, ranging from 0 to 7 days. Headache duration was measured as the total hours of headache in the last week, with six possible ranges: (1) 0–5 h, (2) 6–10 h, (3) 11–15 h, (4) 16–20 h, (5) 21–25 h, or (6) 26 or more hours. Medication intake was measured as the number of times the patient had taken prescription or over-the-counter analgesic or anti-inflammatory medication in the past week for their headaches, with five options: (1) not at all, (2) once a

week, (3) once every couple of days, (4) once or twice a day, or (5) three or more times a day.

Patients returned for 1-week, 4-weeks, and 3-months follow-ups where the aforementioned outcome measures were again collected. In addition, at the 1-week, 4-weeks and 3-months follow-ups, patients completed a 15-point GRC question based on a scale described by Jaeschke et al. [46] to rate their own perception of improved function. The scale ranges from -7 (a very great deal worse) to zero (about the same) to +7 (a very great deal better). Intermittent descriptors of worsening or improving are assigned values from -1 to -6 and +1 to +6, respectively. The MCID for the GRC has not been specifically reported but scores of +4 and +5 have typically been indicative of moderate changes in patient status [46]. However, it should be noted that recently Schmitt and Abbott reported that the GRC might not correlate with changes in function in a population with hip and ankle injuries [47]. All outcome measures were collected by an assessor blind to group assignment.

On the initial visit patients completed all outcome measures then received the first treatment session. Patients completed 6–8 treatment sessions of either manipulation or mobilization combined with exercise over 4 weeks. Additionally, subjects were asked if they had experienced any "major" adverse events [48, 49] (stroke or permanent neurological deficits) at each follow-up period.

Randomization

Following the baseline examination, patients were randomly assigned to receive either manipulation or mobilization and exercise. Concealed allocation was performed by using a computer-generated randomized table of numbers created by an individual not involved with recruiting patients prior to the beginning of the study. Individual, sequentially numbered index cards with the random assignment were prepared for each of 8 data collection sites. The index cards were folded and placed in sealed opaque envelopes. Blinded to the baseline examination, the treating therapist opened the envelope and proceeded with treatment according to the group assignment. Patients were instructed not to discuss the particular treatment procedure received with the examining therapist. The examining therapist remained blind to the patient's treatment group assignment at all times; however, based on the nature of the interventions it was not possible to blind patients or treating therapists.

Manipulation group

Manipulations targeting the right and left C1-2 articulations and bilateral T1-2 articulations were performed on at least one of the 6–8 treatment sessions (Figs. 1 and 2). On other treatment sessions, therapists either repeated the C1-2 and/or T1-2 manipulations or targeted other spinal articulations (i.e., C0-1, C2-3, C3-7, T2-9, ribs 1–9) using manipulation. The selection of the spinal segments to target was left to the discretion of the treating therapist and it was based on the combination of patient reports and manual examination. For both the upper cervical and upper thoracic manipulations, if no popping or cracking sound was heard on the first attempt, the therapist repositioned the patient and performed a second manipulation. A maximum of 2 attempts were performed on each patient similar to other

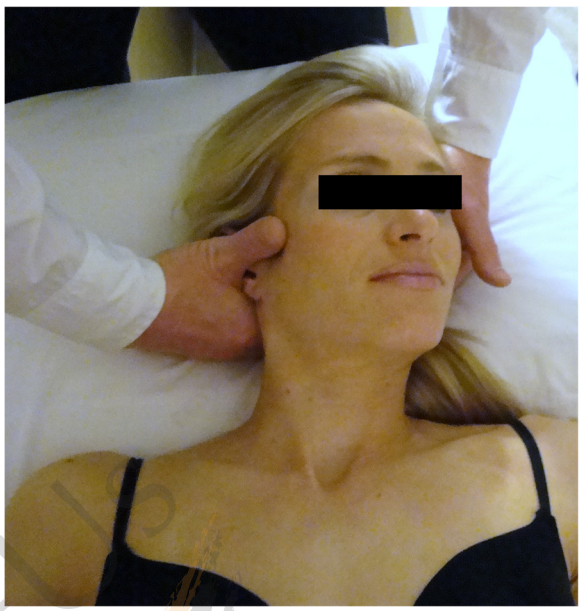

Fig. 1 High-velocity low-amplitude thrust manipulation directed to the right C1-2 articulation. The subject provided consent for her image to be used

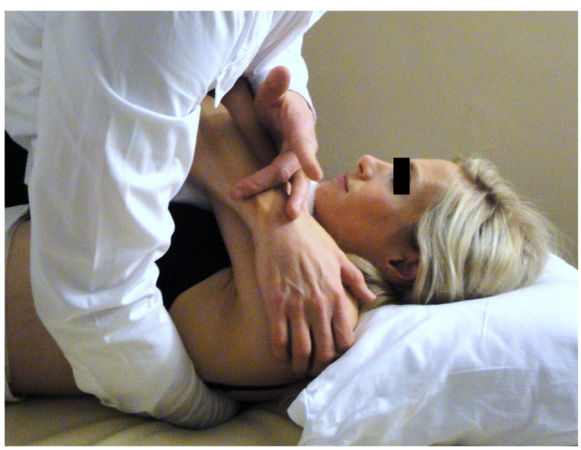

Fig. 2 High-velocity low-amplitude thrust manipulation directed bilaterally to the upper thoracic (T1-2) spine. The subject provided consent for her image to be used

studies [14, 50–53]. The clinicians were instructed that the manipulations are likely to be accompanied by multiple audible popping sounds [54–58]. Patients were encouraged to maintain usual activity within the limits of pain; however, mobilization and the prescription of exercises, or any use of other modalities, were not provided to this group.

The manipulation targeting C1-2 was performed with the patient in supine. For this technique, the patient's left posterior arch of the atlas was contacted with the lateral aspect of the proximal phalanx of the therapist's left second finger using a "cradle hold". To localize the forces to the left C1-2 articulation, the patient was positioned using extension, a posterior-anterior (PA) shift, ipsilateral side-bend and contralateral side-shift. While maintaining this position, the therapist performed a single high-velocity, low-amplitude thrust manipulation to the left atlanto-axial joint using right rotation in an arc toward the underside eye and translation toward the table (Fig. 1). This was repeated using the same procedure but directed to the right C1-2 articulation.

The manipulation targeting T1-2 was performed with the patient in supine. For this technique, the patient held her/his arms and forearms across the chest with the elbows aligned in a superoinferior direction. The therapist contacted the transverse processes of the lower vertebrae of the target motion segment with the thenar eminence and middle phalanx of the third digit. The upper lever was localized to the target motion segment by adding rotation away and side-bend towards the therapist while the underside hand used pronation and radial deviation to achieve rotation toward and side-bend away moments, respectively. The space inferior to the xiphoid process and costochondral margin of the therapist was used as the contact point against the patient's elbows to deliver a manipulation in an anterior to posterior direction targeting T1-2 bilaterally (Fig. 2).

Mobilization and exercise group

Mobilizations targeting the right and left C1-2 articulations and bilateral T1-2 articulations were performed on at least one of the 6–8 treatment sessions. On other treatment sessions, therapists either repeated the C1-2 and/or T1-2 mobilizations or targeted other spinal articulations (i.e., C0-1, C2/3, C3-7, T2-9, ribs 1–9) using mobilization. The selection of the spinal segments to target was left to the discretion of the treating therapist and it was based on the combination of patient reports and manual examination. However, in order to avoid a "contact" or "attention effect" when compared with the manipulation group, therapists were instructed to mobilize one cervical segment (i.e., right and left) and one thoracic segment or rib articulation on each treatment session.

The mobilization targeting the C1-2 articulation was performed in prone. For this technique, the therapist performed one 30 s bout of left-sided unilateral grade IV PA mobilizations to the C1-2 motion segment as described by Maitland [7]. This same procedure was repeated for one 30 s bout to the right atlanto-axial joint. In addition, and on at least one session, mobilization directed to the upper thoracic (T1-2) spine with the patient prone was performed. For this technique, the therapist performed one 30 s bout of central grade IV PA mobilizations to the T1-2 motion segment as described by Maitland [7]. Therefore, we used 180 (i.e., three 30 s bouts at approximately 2 Hz) end-range oscillations in total on each subject for the mobilization treatment. Notably, there is no high quality evidence to date to suggest that longer durations of mobilization result in greater pain reduction than shorter durations or dosages of mobilization [59, 60].

Cranio-cervical flexion exercises [11, 61–63] were performed with the patient in supine, with the knees bent and the position of the head standardized by placing the craniocervical and cervical spines in a mid-position, such that a line between the subject's forehead and chin was horizontal, and a horizontal line from the tragus of the ear bisected the neck longitudinally. An air-filled pressure biofeedback unit (Chattanooga Group, Inc., Hixson, TN) was placed suboccipitally behind the patient's neck and preinflated to a baseline of 20 mmHg [63]. For the staged exercises, patients were required to perform the craniocervical flexion action ("a nod of the head, similar to indicating yes") [63] and attempt to visually target pressures of 22, 24, 26, 28, and 30 mmHg from a resting baseline of 20 mmHg and to hold the position steady for 10 s [61, 62]. The action of nodding was performed in a gentle and slow manner. A 10 s rest was allowed between trials. If the pressure deviated below the target pressure, the pressure was not held steady, substitution with the superficial flexors (sternocleidomastoid or anterior scalene) occurred, or neck retraction was noticed before the completion of the 10 s isometric hold, it was regarded as a failure [63]. The last successful target pressure was used to determine each patient's exercise level wherein 3 sets of 10 repetitions with a 10 s isometric hold were performed. In addition to mobilizations and cranio-cervical flexion exercises, patients were required to perform 10 min of progressive resistance exercises (i.e., using Therabands® or free weights) to the muscles of the shoulder girdle during each treatment session, within their own tolerance, and specifically focusing on the lower trapezius and serratus anterior [11].

Sample size

The sample size and power calculations were performed using online software from the MGH Biostatistics

Center (Boston, MA). The calculations were based on detecting a 2-point (or 20 %) difference in the NPRS (headache intensity) at the 3 months follow-up, assuming a standard deviation of three points, a 2-tailed test, and an alpha level equal to 0.05. This generated a sample size of 49 patients per group. Allowing for a conservative dropout rate of 10 %, we planned to recruit at least 108 patients into the study. This sample size yielded greater than 90 % power to detect a statistically significant change in the NPRS scores.

Data analysis

Descriptive statistics, including frequency counts for categorical variables and measures of central tendency and dispersion for continuous variables were calculated to summarize the data. The effects of treatment on headache intensity and disability were each examined with a 2-by-4 mixed-model analysis of variance (ANOVA), with treatment group (manipulation versus mobilization and exercise) as the between-subjects variable and time (baseline, 1 week, 4 weeks, and 3 months follow-up) as the within-subjects variable. Separate ANOVAs were performed with the NPRS (headache intensity) and NDI (disability) as the dependent variable. For each ANOVA, the hypothesis of interest was the 2-way interaction (group by time).

An independent *t*-test was used to determine the between group differences for the percentage change from baseline to 3-month follow-up in both headache intensity and disability. Separate Mann–Whitney *U* tests were performed with the headache frequency, GRC, headache duration and medication intake as the dependent variable. We performed Little's Missing Completely at Random (MCAR) test [64] to determine if missing data points associated with dropouts were missing at random or missing for systematic reasons. Intention-to-treat analysis was performed by using Expectation-Maximization whereby missing data are computed using regression equations. Planned pairwise comparisons were performed examining the difference between baseline and follow-up periods between-groups using the Bonferroni correction at an alpha level of .05.

We dichotomized patients as responders at the 3-month follow-up using a cut score of 2 points improvement for headache intensity as measured by the NPRS. Numbers needed to treat (NNT) and 95 % confidence intervals (CI) were also calculated at the 3 months follow-up period using each of these definitions for a successful outcome. Data analysis was performed using SPSS 21.0.

Results

Two hundred and fifty-one patients with a primary complaint of headaches were screened for possible eligibility. The reasons for ineligibility can be found in Fig. 3, the flow diagram of patient recruitment and retention. Of the 251 patients screened, 110 patients, with a mean age of 35.16 years (SD 11.48) and a mean duration of symptoms of 4.56 years (SD 6.27), satisfied the eligibility criteria, agreed to participate, and were randomized into manipulation ($n = 58$) and mobilization and exercise ($n = 52$) groups. Baseline variables for each group can be found in Table 1. Twelve therapists from 8 outpatient physical therapy clinics each treated 25, 23, 20, 14, 13, 7, 6 or 2 patients, respectively; furthermore, each of the 12 therapists treated approximately an equal proportion of patients in each group. There was no significant difference ($p = 0.227$) between the mean number of completed treatment sessions for the manipulation group (7.17, SD 0.96) and the mobilization and exercise group (6.90, SD 1.35). In addition, the mean number of treatment sessions that targeted the C1-2 articulation was 6.41 (SD 1.63) for the manipulation group and 6.52 (SD 2.01) for the mobilization and exercise group, and this was not significantly different ($p = 0.762$). One hundred seven of the 110 patients completed all outcome measures through 3 months (97 % follow-up). Little's Missing Completely at Random (MCAR) test was not statistically significant ($p = 0.281$); therefore, we used the Expectation-Maximization imputation technique to replace missing values with predicted values for the missing 3-month outcomes.

The overall group by time interaction for the primary outcome of headache intensity was statistically significant for the NPRS ($F_{(3,106)} = 11.196$; $p < 0.001$; partial eta squared = 0.24). Between-group differences revealed that the manipulation group experienced statistically significant greater improvement in the NPRS at both the 1-week (2.1, 95 % CI: 1.2, 2.9), 4-week (2.3, 95 % CI: 1.5, 3.1) and 3-month (2.1, 95 % CI: 1.2, 3.0) follow-up periods (Table 2). In addition, an independent samples *t*-test revealed the between-group difference in percentage change in headache intensity (36.58 %, 95 % CI: 22.52, 50.64) from baseline to 3-month follow-up was statistically significant ($t_{(108)} = 5.156$; $p < 0.001$) in favor of manipulation. See Table 3 for the percentage of subjects gaining 50, 75, and 100 % reduction in headache intensity at 3 months.

For secondary outcomes a significant group by time interaction existed for the NDI ($F_{(3,106)} = 8.57$; $p < 0.001$; partial eta squared = 0.20). At each follow-up period the manipulation group had superior outcomes in disability reduction as compared to the mobilization and exercise group. An independent samples *t*- test revealed the between-group mean percentage change in disability (35.56 %, 95 % CI: 24.95, 46.17) from baseline to 3 months follow-up was statistically significant ($t_{(108)} = 6.646$, $p <$

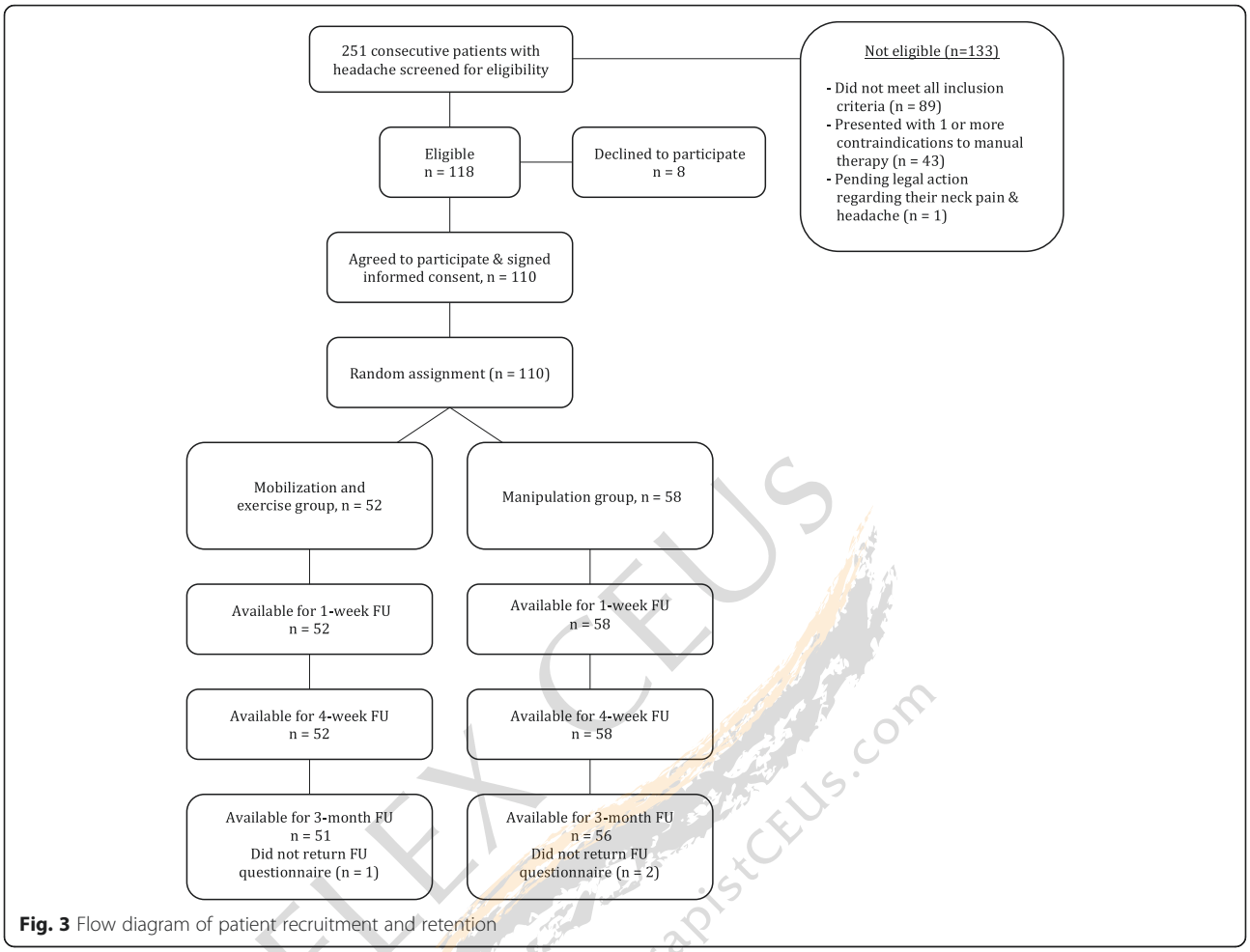

Fig. 3 Flow diagram of patient recruitment and retention

0.001); indicating the manipulation group experienced a significantly greater percentage in disability reduction (Table 3).

Mann–Whitney *U* tests revealed that patients in the upper cervical and upper thoracic manipulation group experienced less frequent headaches at 1 week ($p < 0.001$; median 2.0 versus 3.0), 4 weeks ($p < 0.001$; median 1.0 versus 3.0) and 3 months ($p < 0.001$; median 1.0 versus 2.5) than patients in the mobilization and exercise group. Headache duration was significantly lower

Table 1 Baseline variables: demographics and outcome measures

Baseline Variable	Manipulation Group ($n = 58$)	Mobilization & Exercise Group ($n = 52$)
Age (years): Mean (SD)	34.1 (12.6)	36.4 (10.0)
Gender (female): number (%)	41 (71 %)	33 (64 %)
Duration of symptoms (days): Mean (SD)	1693.7 (2357.7)	1633.8 (2229.9)
BMI (kg/m^2): Mean (SD)	24.2 (3.8)	24.0 (3.3)
Headache intensity (NPRS 0–10): Mean (SD)	6.4 (1.6)	6.0 (2.1)
Disability (NDI 0–50): Mean (SD)	18.1 (7.9)	19.2 (7.8)
Headache frequency (0–7 days): Median	4	4
Headache duration: Median	3	3
Medication intake: Median	3	3

NPRS Numeric Pain Rating Scale, 0–10, lower scores indicate less pain; *NDI* Neck Disability Index, *0–50*, lower scores indicate greater function; Headache frequency = number of headache days in the last week, 0–7, higher scores indicate worsening; Headache duration = total headache hours in the last week, 1 = 0–5 h, 2 = 6–10 h, 3 = 11–15 h, 4 = 16–20 h, 5 = 21–25 h, 6 = 26 or more hours, higher scores indicate worsening; Medication intake = frequency of pain medication use in the past week, 1 = not at all, 2 = once a week, 3 = once every couple of days, 4 = once or twice a day, 5 = three or more times a day

Table 2 Changes in headache intensity (NPRS) and disability (NDI) with 95 % confidence intervals for both groups and between-group differences

Variable	Manipulation	Mobilization and Exercise	Between-Group Differences
Headache Intensity (NPRS 0–10)			
Baseline: Mean (SD)	6.4 (1.6)	6.0 (2.1)	
1-Week: Mean (SD)	3.1 (1.9)	4.9 (1.8)	
Change Score: Baseline to 1-Week	3.2 (2.6, 3.8)	1.2 (0.6, 1.7)	2.1 (1.2, 2.9); $P < 0.001$
4-Week: Mean (SD)	1.8 (1.6)	3.8 (2.0)	
Change Score: Baseline to 4-Week	4.5 (4.0, 5.1)	2.2 (1.7, 2.8)	2.3 (1.5, 3.1); $P < 0.001$
3-Month: Mean (SD)	2.0 (1.8)	3.8 (1.9)	
Change Score: Baseline to 3-Month	4.3 (3.7, 4.9)	2.2 (1.6, 2.9)	2.1 (1.2, 3.0); $P < 0.001$
Disability (NDI 0–50)			
Baseline: Mean (SD)	18.1 (7.9)	19.2 (7.8)	
1-Week: Mean (SD)	11.9 (8.5)	16.1 (7.5)	
Change Score: Baseline to 1-Week	6.2 (4.8, 7.6)	3.1 (2.0, 4.1)	3.1 (1.4, 4.9); $P < 0.001$
4-Week: Mean (SD)	6.5 (5.4)	13.0 (7.5)	
Change Score: Baseline to 4-Week	11.6 (9.7, 13.4)	6.1 (4.9, 7.4)	5.4 (3.2, 7.7); $P < 0.001$
3-Month: Mean (SD)	6.3 (5.9)	13.5 (7.8)	
Change Score: Baseline to 3-Month	11.7 (9.7, 13.8)	5.7 (4.2, 7.2)	6.0 (3.5, 8.6); $P < 0.001$

NPRS Numeric Pain Rating Scale, 0–10, lower scores indicate less pain; *NDI* Neck Disability Index, 0–50, lower scores indicate greater function

at 1 week ($p = 0.005$; median 2.0 versus 3.0, 4 weeks ($p < 0.001$; median 1.0 versus 2.0) and 3 months ($p < 0.001$; median 1.0 versus 2.0) in the manipulation group. Additionally, patient perceived improvement as measured by the GRC was significantly greater at 1 week ($p < 0.001$, 4.0 versus 1.0), 4 weeks ($p < 0.001$, 6.0 versus 3.0) and 3 months ($p < 0.001$, 6.0 versus 3.0) than patients in the mobilization and exercise group. At 3 months, patients receiving upper cervical and upper thoracic manipulation experienced significantly ($p < 0.001$) greater reductions in medication intake as compared to the mobilization and exercise group. Based on the cutoff score of 2 points on the NPRS, the NNT was 4.0 (95 % CI: 2.3, 7.7) in favor of the manipulation group at 3-month follow-up.

We did not collect any data on the occurrence of "minor" adverse events [48, 49] (transient neurological symptoms, increased stiffness, radiating pain, fatigue or other); however, no "major" adverse events [48, 49] (stroke or permanent neurological deficits) were reported for either group.

Discussion

Statement of principal findings

To our knowledge, this study is the first randomized clinical trial to directly compare the effectiveness of both

Table 3 Percentage of subjects gaining 50, 75 and 100 % reduction in headache intensity (NPRS) and disability (NDI) as well as the numbers needed to treat at 3 months

Variable	Manipulation ($n = 58$)	Mobilization & Exercise ($n = 52$)
Headache Intensity (NPRS 0–10)		
50 % Reduction	74.1 %	38.5 %
75 % Reduction	48.3 %	13.5 %
100 % Reduction	29.3 %	3.8 %
Number of individuals achieving at least a 2 point improvement in pain	53	33
Numbers Needed to Treat	4.0 (95 % CI: 2.3, 7.7)	
Disability (NDI 0–50)		
50 % Reduction	74.1 %	23.1 %
75 % Reduction	43.1 %	9.6 %
100 % Reduction	19.0 %	1.9 %

cervical and thoracic manipulation to mobilization and exercise in patients with CH. The results suggest 6–8 sessions of manipulation over 4 weeks, directed mainly to both the upper cervical (C1-2) and upper thoracic (T1-2) spines, resulted in greater improvements in headache intensity, disability, headache frequency, headache duration, and medication intake than mobilization combined with exercises. The point estimates for between-group changes in headache intensity (2.1 points) and disability (6.0 points or 12.0 %) exceeded the reported MCIDs for both measures. Although the MCID for the NDI in patients with CH has not yet been investigated, it should however be noted that the lower bound estimate of the 95 % CI for disability (3.5 points) was slightly below (or approximated in two cases) the MCID that has been found to be 3.5 [65], 5 [66], and 7.5 [45] points in patients with mechanical neck pain, 8.5 [33] points in patients with cervical radiculopathy, and 3.5 [44] points in patients with mixed, non-specific neck pain. However, it should be recognized that both groups made clinical improvement. In addition, the NNT suggests for every four patients treated with manipulation, rather than mobilization, one additional patient achieves clinically important pain reduction at 3 months follow-up.

Strengths and weaknesses of the study

The inclusion of 12 treating physical therapists from 8 private clinics in 6 different geographical states enhances the overall generalizability of our findings. Although significant differences were recognized up to 3 months, it is not known if these benefits would have been sustained at long-term. In addition, we used high-velocity, low-amplitude manipulation techniques that employed bidirectional thrusts into rotation and translation simultaneously and Maitland based grade IV PA mobilization techniques; thus, we cannot be certain that these results are generalizable to other kinds of manual therapy techniques. Some might argue that the comparison group might have not received adequate intervention. We sought to balance internal and external validity so standardized treatment for both groups and provided a very explicit description of the techniques used which will also allow for replication. Furthermore, we did not measure minor adverse events and only asked about two potential major adverse events. Another limitation is that we included multiple secondary outcomes. Therapist preferences as to which technique they thought would be superior was not collected and potentially could impact the results.

Strengths and weaknesses in relation to other studies: important differences in results

Jull et al. [11] demonstrated treatment efficacy for manipulative therapy and exercise in the management of CH; however, this treatment package included both mobilization and manipulation. The current study may provide evidence that the management of patients with CH should include some form of manipulation despite the fact it is often suggested that cervical manipulation should be avoided because of the risk of serious adverse events [67, 68]. Furthermore, it has been shown that individuals receiving spinal manipulation for neck pain and headaches are no more likely to experience a vertebrobasilar stroke than if they received treatment by their medical physician [69]. Additionally, after reviewing 134 case reports, Puentedura et al. concluded that with appropriate selection of patients by careful screening of red flags and contraindications, the majority of adverse events associated with cervical manipulation could have been prevented [70].

Meaning of the study: possible explanations and implications for clinicians and policymakers

Based on the results of the current study clinicians should consider incorporating spinal manipulation for individuals with CH. A recent systematic review found both mobilization and manipulation to be effective for the management of patients with CH but was unable to determine which technique was superior [8]. Additionally, clinical guidelines reported that manipulation, mobilization and exercise were all effective for the management of patients with CH; however, the guideline made no suggestions regarding the superiority of either technique. [71] The current results may assist authors of future systematic reviews and clinical guidelines in providing more specific recommendations about the use of spinal manipulation in this population.

Unanswered questions and future research

The underlying mechanisms as to why manipulation may have resulted in greater improvements remains to be elucidated. It has been suggested that high-velocity displacement of vertebrae with impulse durations of less than 200 ms may alter afferent discharge rates [72] by stimulating mechanoreceptors and proprioceptors, thereby changing alpha motorneuron excitability levels and subsequent muscle activity [72–74]. Manipulation might also stimulate receptors in the deep paraspinal musculature, and mobilization might be more likely to facilitate receptors in the superficial muscles [75]. Biomechanical [76, 77], spinal or segmental [78, 79] and central descending inhibitory pain pathway [80–83] models are plausible explanations for the hypoalgesic effects observed following manipulation. Recently, the biomechanical effects of manipulation have been under scientific scrutiny [84], and it is plausible that the clinical benefits found in our study are associated with a neurophysiological response involving temporal sensory

summation at the dorsal horn of the spinal cord [78]; however, this proposed model is currently supported only on findings from transient, experimentally induced pain in healthy subjects [85, 86], not patients with CH. Future studies should examine different manual therapy techniques with varying dosages and include a 1-year follow-up. Furthermore, future studies examining the neurophysiological effects of both manipulation and mobilization will be important for determining why there may or may not be a difference in clinical effects between these two treatments.

Conclusion

The results of the current study demonstrated that patients with CH who received cervical and thoracic manipulation experienced significantly greater reductions in headache intensity, disability, headache frequency, headache duration, and medication intake as compared to the group that received mobilization and exercise; furthermore, the effects were maintained at 3 months follow-up. Future studies should examine the effectiveness of different types and dosages of manipulation and include a long-term follow-up.

Manual therapies for cervicogenic headache: a systematic review

Abstract This paper systematically reviewed randomized clinical trials (RCT) assessing the efficacy of manual therapies for cervicogenic headache (CEH). A total of seven RCTs were identified, i.e. one study applied physiotherapy ± temporomadibular mobilization techniques and six studies applied cervical spinal manipulative therapy (SMT). The RCTs suggest that physiotherapy and SMT might be an effective treatment in the management of CEH, but the results are difficult to evaluate, since only one study included a control group that did not receive treatment. Furthermore, the RCTs mostly included participant with infrequent CEH. Future challenges regarding CEH are substantial both from a diagnostic and management point of view.

Keywords Randomized clinical trials · Manual therapies · Physiotherapy · Chiropractic · Cervicogenic headache · Treatment

Introduction

Cervicogenic headache (CEH) is a secondary headache characterized by unilateral headache and symptoms and signs of neck involvement [1–5]. It is often worsened by neck movement, sustained awkward head position or external pressure over the upper cervical or occipital region on the symptomatic side [1, 3].

The prevalence of CEH varies in the general population depending on the diagnostic criteria, i.e. 1.0 % applying six positive criteria of the Cervicogenic Headache International Study Group (CHISG) and 4.6 % when only five criteria were used, while it was 2.5 % applying the International Headache Society (IHS) criteria [3, 5–8]. A recent epidemiological survey found that the prevalence was 0.13 % in men and 0.21 % in women applying three or more major CHISG criteria [9, 10]. Thus, along with different diagnostic criteria, it is likely that other methodological differences play a role.

The pathogenesis of CEH may originate from various anatomic structures in the cervical spine. Convergence of afferents of the trigeminal and upper three cervical spinal nerves onto the second-order neurons in the trigeminocervical nucleus in the upper cervical spinal cord is likely to lead to the headache [11, 12]. The craniovertebral junction is stabilized by joint capsules, tectorial membrane, transverse and alar ligaments [13]. A proton-weighted magnetic resonance imaging (MRI) study of people with CEH, whiplash-associated headache or migraine was analyzed blinded and identified no significant differences in the three groups [14]. Furthermore, the site of the CEH was not correlated with the site of signal intensity changes of the alar and transverse ligaments. One study suggests that lower cervical disc prolapse may cause CEH [15], but the results could not be confirmed as no specific MRI changes of cervical discs or craniovertebral ligaments were found in CEH [14]. Muscle tenderness is likely to play a role and is more pronounced on the pain than the non-pain site, i.e. pericranial tenderness was recorded according to the tenderness score of eight pairs of pericranial muscles and tendon insertion points, each scored on a four-point scale

(0–3) at each location, and the tenderness score on the pain and non-pain sides was compared [10]. However, so far the pathogenesis and etiology of CEH remain a challenge.

Due to insufficient pharmacological treatment strategies, medication overuse is frequent and likely secondary to the pain rather than a confounding factor, as the medication overuse is of shorter duration than the duration of the CEH [10]. A 3-year follow-up of people with CEH from the general population found no improvement [16], while people from the general population with headache attributed to chronic rhinosinusitis or medication overuse headache improved after a short advice [16, 17].

Thus, due to muscle tenderness and possibly not yet identified local factor in the cervical spine, it might be that manual therapies can alleviate CEH, along with blockage of the greater occipital nerve (GON), which is the only effective pharmacological treatment so far [18, 19]. This paper systematically review randomized clinical trials (RCT) assessing the efficacy of manual therapies for CEH.

Methods

The literature search was done on CINHAL, Cochrane, Medline, Ovid and PubMed. Search words were cervicogenic headache and chiropractic, manipulative therapy, massage therapy, osteopathic treatment, physiotherapy or spinal mobilization. All RCT written in English using either of the manual therapies on CEH were evaluated. CEH was preferentially classified according to the criteria of the IHS from 1988 or its revision from 2004, or according to the Cervicogenic Headache International Study Group (CHISG) [1–5]. Table 1 shows the diagnostic criteria for CEH. The studies had to evaluate at least one CEH outcome measure, i.e. pain intensity, frequency, or duration. The methodological quality of the included RCT studies was assessed by the first author. Table 2 shows that the evaluation covers study population, intervention, measurement of effect, data presentation and analysis and the maximum score is 100 points, and ≥50 points is considered to be methodology of good quality [20–23].

Results

The literature search identified seven RCT on CEH that met our inclusion criteria. One study applied physiotherapy ± temporomadibular mobilization techniques and six studies applied cervical spinal manipulative therapy (SMT) [24–30]. Four studies were conducted by chiropractors, two studies by physiotherapists and one by a physician. RCTs studies on massage therapy, spinal mobilization or osteopathic intervention on CEH were not identified.

Methodological quality of the RCTs

Table 3 shows the methodological score of the included RCT studies. The score varied from 50 to 81 points.

Randomized controlled trials (RCT)

Table 4 shows details from the seven RCT studies regarding study population, intervention and results in relation to headache frequency, duration and intensity, while other results are presented in the text.

Physiotherapy

The Dutch study was conducted by experienced physiotherapists with unblinded treatment and outcome measures [30]. The participants were diagnosed with CEH by a neurologist according to the criteria of the International Headache Society (IHS) [5]. Participants were excluded, if ever received temporomandibular disorder (TMD)/orthodontic treatment or experienced neuropathic head pain. The primary end point was headache intensity while TMD complaints (mouth opening, pain and range, deviation, sounds and pain threshold of anterior temporal muscles) and neck disability were secondary end points. Both TMD complaints and neck disability improved statistically significantly in the experimental group as compared to conventional physiotherapy group at 3- and 6-month follow-up ($p < 0.001$ in both comparisons).

Cervical spinal manipulative therapy

The Danish study was conducted by a chiropractor with unblinded treatment and blinded analysis of outcome measures [24]. The participants were diagnosed by a physician according to the criteria of the IHS excluding the radiographic criterion [1]. Participants whom had not previously received SMT or had conditions contraindicated to SMT were excluded from the study. The primary end-points were change in headache intensity, headache duration and NSAIDs consumption from pre-treatment at 2 weeks to post-treatment at week 6. The consumption of NSAIDs was significantly reduced from pre-treatment to post-treatment in the cervical SMT group ($p < 0.0005$), but not in the soft tissue (ST) group, however, the reduction in consumption of NSAIDs was not statistically significantly different in the cervical SMT and ST groups ($p = 0.14$).

The 2nd Danish study was based on an extended study population from the 1st Danish study [24, 25]. The methodology and end-points were similar, except that the pre-treatment period was reduced from 2 to 1 week and the statistical calculation was based on median rather than mean

Table 1 Diagnostic criteria of cervicogenic headache

Cervicogenic Headache International Study Group [3]

Major criteria[a]	1. Symptoms and signs of neck involvement
	a. Precipitation of head pain, similar to the usually occurring one:
	i. By neck movement and/or sustained awkward head positioning, and/or:
	ii. By external pressure over the upper cervical or occipital region on the symptomatic side
	b. Restriction of range of motion (ROM) in the neck
	c. Ipsilateral neck, shoulder, or arm pain of a rather vague nonradicular nature or, occasionally, arm pain of a radicular nature.
	2. Confirmatory evidence by diagnostic anesthetic blockade
	3. Unilaterality of the head pain, without side shift
Head pain characteristics	4. a. Moderate-severe, non-throbbing, and non-lancinating pain, usually starting in the neck.
	b. Episodes of varying duration
	c. Fluctuating, continuous pain
Other characteristics of some importance	5. a. Only marginal effect or lack of effect of indomethacin
	b. Only marginal effect or lack of effect of ergotamine and sumatriptan
	c. Female sex
	d. Not infrequent occurrence of head or indirect neck trauma by history, usually of more than only medium trauma
Other features of lesser importance	6. a. Nausea
	b. Phonophobia and photophobia
	c. Dizziness
	d. Ipsilateral "blurred vision"
	e. Difficulties swallowing
	f. Ipsilateral edema, mostly in the periocular area

International Classification of Headache Disorders-II [5]

A. Pain, referred from a source in the neck and perceived in one or more regions of the head and/or face, fulfilling criteria C and D

B. Clinical, laboratory and/or imaging evidence of a disorder or lesion within the cervical spine or soft tissues of the neck known to be, or generally accepted as, a valid cause of headache

C. Evidence that the pain can be attributed to the neck disorder or lesion based on at least one of the following:

i. Demonstration of clinical signs that implicate a source of pain in the neck

ii. Abolition of headache following diagnostic blockade of a cervical structure or its nerve supply using placebo- or other adequate controls

D. Pain resolves within 3 months after successful treatment of the causative disorder or lesion

[a] It is obligatory that one or more of phenomena 1a-1c are present

change. The consumption of NSAIDs was significantly reduced from pre-treatment to post-treatment in the cervical SMT group, but not in the ST group, however, the median reduction in consumption of NSAIDs was not statistically significantly different in the cervical SMT and ST groups ($p = 0.14$).

The Australian multicenter study was conducted by 25 experienced physiotherapists with unblinded treatment and blinded outcome measures [26]. The study participants were diagnosed according to the diagnostic criteria of CHISG by GPs or physiotherapists [4]. Those with bilateral headache, conditions that contraindicated to spinal manipulative treatment (SMT) or whom had received physiotherapy or chiropractic treatment for headache within the previous year were excluded. The primary end-point was a change in headache frequency from baseline to immediately after treatment and 12 months after the intervention, while headache intensity, duration and neck pain were secondary end-points. Neck pain was reduced immediate post-treatment in the all intervention groups ($p < 0.001$–0.01), but was only maintained at 12-month follow-up in the exercise group and combined SMT and exercise group ($p < 0.001$–0.01). The median medication intake comparing baseline with 12-month follow-up was reduced 93 % in the combined SMT and exercise group, 100 % in the SMT and exercise groups, while it increased 33 % in the control ($p < 0.015$ for all). The authors suggest that the treatment effect may be underestimated since 46 % of controls received active intervention (unspecified) for their headache within the trial period.

An American study conducted by three experienced chiropractors evaluated the dose response for chiropractic care of cervicogenic headache [27]. The participants were diagnosed according to the IHS criteria except the radiographic criterion [1]. Participants were excluded if SMT was contraindicated or if the participants had complicated condition that might have been related to clinical outcome. The primary end-point was a change in mean headache intensity from baseline to 4- and 12-week follow-up recorded on 100 points modified Von Korff pain scale. The headache intensity score is the average of headache intensity today, worst headache intensity within the last 4 weeks and average headache intensity within the last 4 weeks. Headache frequency, disability, and neck pain were secondary end-points. Although the participants were allowed to seek consultations outside the trial, only few used that opportunity. The main results of the RCT were that several consultations seem to be advantageous over few consultations in the treatment of cervicogenic headache (Table 2). At 4- and 12-week follow-up headache disability was reduced 44, 50, 76 % and 14, 52, 55 % in the SMT 1, 3 and 4 times a week groups, while neck pain was reduced by 31, 50, 55 % and 30, 54, 38 %, respectively. Comparison of the SMT 1 time a week group with SMT 3 and 4 times a week groups was not statistically significant.

Table 2 Criteria list of methodological quality assessment of randomized controlled trials (RCTs) [22]

1. Study population (30 points)
   a) Description of inclusion and exclusion criteria (1 point). Restriction to a homogeneous study population (1 point)
   b) Comparability of relevant baseline characteristics: duration of complaint (1 point), value of outcome measures (1 point), age (1 point), recurrences (1 point), and radiating complaints/associated symptoms (1 point)
   c) Description of the randomization procedure (2 points). Randomization procedure which excluded bias, i.e. random numbers table (2 points)
   d) Description of dropouts for each group and their reasons (3 points)
   e) Loss to follow-up: less than 20 % loss to follow-up (2 points), OR less than 10 % loss to follow-up (4 points)
   f) Sample size: greater than 50 subjects in the smallest group after randomization (6 points), OR greater than 100 subjects in the smallest group after randomization (12 points)
2. Interventions (30 points)
   g) Correct description of the manual intervention (5 points). All interventions described (5 points)
   h) Pragmatic study: comparison with an existing treatment modality (5 points)
   i) Co-interventions avoided in the design of the study (5 points)
   j) Comparison with a placebo control group (5 points)
   k) Mention of the experience of the therapist (5 points)
3. Measurement of effect (30 points)
   l) Placebo controlled studies: patients blinded (3 points), blinding evaluated and fully successful (2 points) OR Pragmatic studies: patients fully naive, evaluated and fully successful (3 points), time restriction of no manual treatments for at least 1 year (2 points)
   m) Outcome measures: pain assessment (2 points), global measure of improvement (2 points), functional status (2 points), spinal mobility (2 points), medical consumption (2 points)
   n) Each blinded outcome measure mentioned under item M earns 2 points
   o) Analysis of post-treatment data (3 points), inclusion of a follow-up period longer than 6 months (2 points)
4. Data presentation and analysis (10 points)
   p) Intention-to-treat analysis when loss to follow-up is less than 10 % OR intention-to-treat analysis as well as worst-case analysis for missing values when loss to follow-up is greater than 10 % (5 points)
   q) Corrected presentation of the data: mean or median with a standard deviation or percentiles for continuous variables (5 points)

Table 3 Quality score of the analyzed randomized controlled trials (RCTs) using manual therapies for treatment of CEH

Study	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	Total
Piekartz and Lüdtke [30]	2	3	4	3	2	0	10	5	0	0	5	2	6	6	3	0	5	56
Nilsson [24]	2	2	4	3	4	0	10	5	5	0	0	2	4	4	3	0	5	53
Nilsson et al. [25]	2	2	4	3	4	0	10	5	5	0	0	2	4	4	3	0	5	53
Jull et al. [26]	2	5	4	3	4	0	10	5	5	5	5	2	8	8	5	5	5	81
Haas et al. [27]	2	4	4	3	4	0	10	5	0	0	5	2	6	0	3	5	5	58
Borusiak et al. [28]	2	2	4	0	4	0	10	0	5	5	5	2	6	0	0	0	5	50
Haas et al. [29]	2	4	4	3	4	0	10	5	0	5	5	2	6	0	3	5	5	63

The letters correspond with letters from the criteria list (Table 2)

The German study was conducted by a physician with blinded participants and unblended treatment and outcome measures [28]. The study followed the guidelines of the IHS with slight modifications, as the diagnosis CEH according to the criteria can only be given retrospectively after resolution of the symptoms [5]. Participants were allowed to have co-occurrence of migraine and/or tension-type headache. Participants were excluded if ever exposed to SMT or diagnosed with secondary headaches other than CEH. Main outcome measures were headache frequency, duration, intensity, medication consumption and days of absence from school. No statistical significant change was observed in the treatment or sham group between baseline and at 2-month follow-up in relation to medicine consumption or days of absence from school due to headache.

The 2nd American pilot study was conducted by four experienced chiropractors while additional chiropractors in

Table 4 Randomized controlled trials (RCTs) of physiotherapy and spinal manipulative therapy for CEH

Country	Study population	Method	Intervention	Results
Physiotherapy				
The Netherland [30]	43 participants (16M, 27F) Age 18–65 years Mean age 36 years CEH mean duration >6 months and at least one of four signs of temporomandibular disorder (TMD) CEH diagnosed by neurologist	RCT of 7–7½ months duration conducted by a physiotherapist, i.e. Baseline evaluation 3- to 6-week treatment 6-month follow-up Comparison of baseline, post-treatment and at 6-month follow-up	Six interventions ≤30-min within 3–6 weeks The physiotherapist selected the technique and treatment and exercise he or she considered to be beneficial for the participant The experimental group received accessory (translatory) movements of temporomadibular region and/or masticatory muscle techniques such as trigger point treatment and muscle stretching. Active and passive movement facilitating optimal function of cranial nerve tissue, coordination exercises and home exercises. The therapist could also opt for additionally neuromusculoskeletal treatments for cervical region ($n = 20$) (7M, 13F) Conventional physiotherapy including manual techniques at the cranio-cervical region and exercises ($n = 18$) (6M, 12F) Drop outs ($n = 5$)	The experimental group showed a significant reduction in headache intensity 3- and 6-month post-treatment as compared to conventional physiotherapy ($p < 0.001$) The pain intensity was seven on a colored analog scale (comparable to VAS) at baseline and reduced to 3.2 and 2.1 at 3- and 6-month post-treatment in the experimental group, while the pain was stable around 6.8 in the conventional physiotherapy group at the three recordings
Spinal manipulative therapy (SMT)				
Denmark [24]	39 participants (17M, 22F) Age 20–57 years Mean 39 years Headache ≥5 days per month for at least 3 months CEH diagnosed by a physician and chiropractor	RCT of 6-week duration conducted by a chiropractor, i.e. 2-week baseline 3-week treatment 1-week follow-up Comparison of pre-treatment at week 2 and post-treatment at week 6 Headache diary	Cervical SMT by chiropractor i.e. toggle recoil at upper cervical and diversified technique at lower cervical determined by the chiropractor ($n = 20$) (9M, 11F) Soft tissue (ST) work including deep friction massage at cervico-thoracic area and laser therapy at upper cervical region ($n = 18$) (8M, 10F) Drop outs ($n = 1$)	Mean headache duration was reduced in both the CSMT and ST group ($p < 0.0001$ and $p < 0.002$, respectively), i.e. a 59 and 52 % reduction from pre- to post-treatment. Mean headache duration reduction was not statistically significant in the two groups Mean headache intensity was reduced in the cervical SMT group ($p < 0.001$), but not in ST group, i.e. a 36 and 22 % reduction from pre- to post-treatment Mean headache intensity reduction was not statistically significant in the two groups
Denmark [25]	54 participants (23M, 31F) Age 20–60 years Mean 37 years Headache ≥5 days per month for at least 3 months CEH diagnosed by physician and chiropractor	RCT of 5-week duration conducted by a chiropractor, i.e. 1-week baseline 3-week treatment 1-week follow-up Comparison of pre-treatmen at week 1 and post-treatment at week 5 Headache diary	Cervical SMT by chiropractor i.e. toggle recoil at upper cervical and diversified technique at lower cervical determined by the chiropractor ($n = 28$) (13M, 15F) Soft tissue (ST) work including deep friction massage at cervico-thoracic area and laser therapy at upper cervical region ($n = 25$) (10M, 15F) Drop outs ($n = 1$)	Median headache duration was reduced in both cervical SMT and ST group ($p < 0.0001$ and $p < 0.04$, respectively), i.e. a 69 and 37 % reduction from pre- to post-treatment Median headache duration was reduced more in the cervical SMT than in the ST group ($p < 0.03$) Median headache intensity was reduced in the cervical SMT group ($p < 0.0015$), but not in ST group, i.e. a 36 and 17 % reduction from pre- to post-treatment. Median headache intensity was reduced more in the cervical SMT than in the ST group ($p < 0.04$)

Table 4 continued

Country	Study population	Method	Intervention	Results
Australia [26]	200 participants (60M, 140F) Age 18–60 years Mean 36.7 years Mean headache duration 6.1 years CEH diagnosed by GPs or physiotherapists	RCT of 12-month duration conducted by physiotherapists i.e. 2-week baseline 6-week treatment 3-, 6- and 12-month follow-up Comparison of baseline, immediately following post-treatment and 12-month follow-up Headache diary recording	Cervico-scapular muscle exercise twice a day ($n = 52$) (9M, 43F) Cervical SMT a total of 8-12 treatments ≤30-min ($n = 51$) (19M, 32F) Combined cervical SMT and cervico-scapular muscle exercise ($n = 49$) (21M, 28F) Control group (no treatment) ($n = 48$) (11M, 37F) Drop outs ($n = 7$)	Headache frequency and intensity were reduced immediately following post-treatment and at 12-month follow-up in all intervention groups as compared to the control group ($p < 0.001$–0.05) A 50 % reduction in headache frequency was noted in 76 % in cervico-scapular muscle excercise group, 71 %, in the cervical SMT group, 81 % in the combined cervical SMT and exercise group and 29 % of the control group, while 100 % reduction was observed in 31, 33, 42 and 4 % of the four groups Headache duration was reduced in the cervical SMT and the combined cervical SMT and exercise group immediately following post-treatment ($p < 0.05$ and 0.001 respectively) and in the combined cervical SMT and exercise group at 12-month follow-up ($p < 0.05$)
USA [27]	24 participants (4M, 19F, 1 unknown) Mean age 40.3 years Mean headache duration >3 months CEH diagnosed by chiropractor	RCT of 12-week duration conducted by three chiropractors, i.e. baseline evaluation 3-week treatment Follow-up at weeks 4 and 12 Comparison of baseline, 4 (1 week post-treatment) and 12-week follow-up Headache diary recording	All participants received cervical SMT by the diversified technique, with an option for additional two physical modalities, i.e. heat and soft tissue therapy including massage and trigger point therapy. Treating chiropractor could also recommend modifications of daily activities and rehabilitative exercises SMT 1 time per week ($n = 7$) (2M, 5F) SMT 3 times per week ($n = 8$) (2M, 8F) SMT 4 times per week ($n = 8$) (8F) Drop outs ($n = 1$)	At 4-week follow-up headache intensity (see result text for details) was significantly reduced in SMT 4 times a week group as compared to SMT one time a week group, and at 12-week follow-up headache intensity was significantly reduced in both the SMT 3 and 4 times a week groups as compared to the SMT 1 time a week group At 4- and 12-week follow-up the mean headache intensity was reduced 21 and 4 % in the SMT 1 time a week group, 49 and 44 % in the SMT 3 times a week group and 58 and 38 % in the SMT 4 times a week group At 4- and 12-week follow-up the mean headache frequency improved 41, 45, 61 %, and 14, 36, 53 % in the SMT 1, 3 and 4 groups, respectively
Germany [28]	52 participants (21M, 31F) Age 7–15 years Mean age 11.6 years At least headache once a week for at least 6 months CEH diagnosed by physician	Prospective RCT of 4-month duration conducted by a physician, i.e. 2-month baseline One treatment 2-month follow-up Comparison of baseline, post-treatment, follow-up Headache diary recording	Cervical SMT by physician ($n = 24$) Sham cervical manipulation (Placebo) ($n = 28$) Drop outs ($n = 4$)	Both the treatment and sham group had a statistically significant reduction in headache days from baseline to 2-month follow-up ($p = 0.009$ and $p = 0.027$), i.e. from 40.4 to 30.7 % days with headache, and from 41.2 to 31.8 % days with headache Headache frequency, total duration and intensity showed no statistical significant change in neither of the two groups No statistically significant differences were found between the two group in relation to the headache variables described above

Table 4 continued

Country	Study population	Method	Intervention	Results
USA [29]	80 participants (16M, 64F) Mean age 36 years Mean headache duration >3 months CEH diagnosed by chiropractor	Prospective RCT of 6-month duration conducted by four chiropractors, i.e. Baseline evaluation 8-week treatment Follow-up at weeks 12 and 24 Comparison of baseline, 12- and 24-week follow-up Headache diary recording	All interventions received 10 min visits by chiropractors One cervical and upper thoracic SMT treatment every week, with prior optional 5 min moist heat pack and 2 min light massage and 8 visit including control physical examinations but no treatment ($n = 20$) (4M, 16F) Two cervical and upper thoracic SMT every week, with prior optional 5 min moist heat pack and 2 min light massage ($n = 20$) (4M, 16F) One 5 min of moist heat followed by 5 min light massage every week and eight control physical examination but no treatment ($n = 20$) (5M, 15F) Two 5 min of moist heat followed by 5 min light massage every week ($n = 20$) (3M, 17F) Drop outs ($n = 7$)	Headache intensity at 4, 12 and 24 weeks improved more in the SMT group than in light massage group that received treatment twice a week ($p < 0.05$), while a similar comparison among those whom received treatment once a week was not statistical significant At 24 weeks mean headache intensity was reduced 35 and 45 % in the SMT groups treated once or twice a week, while it was reduced 27 and 17 % in the similar light massage groups At 24 weeks a 50 % reduction in pain intensity was achieved by 28 and 47 % in the SMT groups treated once or twice a week, while it was 28 and 16 % in the similar light massage groups At 24 weeks mean headache frequency was reduced 48 and 56 % in the SMT groups treated once or twice a week, while it was reduced 35 and 31 % in the similar light massage groups

each clinic served as a backup therapist [29]. The treatment and outcome measures were unblinded. Participants were diagnosed according to the IHS excluding the radiographic criteria using a questionnaire [5]. Participants were excluded if they could not attend two visits per week for 8 weeks, took prophylactic prescribed medication for headache, had massage or SMT for their headache within the last 3 months or had complicated conditions. The primary end-point was headache intensity while secondary end-points were headache frequency, disability, neck pain and use of over the counter medication (OTC). 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. The authors concluded that only the SMT group treated twice a week had clinical important effect on mean neck pain and disability. Generally dose effects tended to be small.

Discussion

Methodological considerations

All seven RCTs studies ascertained the participants through clinical interviews which is considered to be the most valid method in establishing a precise headache diagnosis [31]. All the RCTs included relatively few participants except the Australian physiotherapy study [26]. However, due to participants were divided into four groups each with 48–52 participants, even the Australian study did not receive points for number of participants in the quality score (Table 3). The number of investigators in the seven RCTs varied from 1 to 25. The advantage with one investigator is elimination of inter-observer variability, which is likely to be present if there are two or more investigators. The 25 investigators in the Australian study might be a challenge in relation to the result [32]. The Dutch study was flawed by the participants not being blinded to the intervention, as well as co-intervention was allowed by the investigator which is a major risk for bias [30]. All the RCTs were considered to be of at least good methodological quality, i.e. score $\geq$50 (Table 3), with the Australian study standing out with an excellent 81 points score of the maximum 100 points.

According to the guidelines of the IHS, an intervention is recommended to last at least 3 months in chronic migraine trials [33]. All the RCTs had less than 3-month intervention, varying from a single treatment to 8-week treatment. In three of SMT the RCTs allowed non-trial treatment which can lead to biased results [26, 27, 29]. Two of the RCTs included participants with co-occurrence

of migraine and tension-type headache [28, 29], thus, the effect observed might not be exclusively due to improvement of the CEH.

Only one of the RCTs included a control group that did not receive treatment [26]. It is generally accepted that RCTs including a control group are advantages to pragmatic RCTs, as the effect in the placebo control group often is high [23]. True net effect is more accurately calculated when adding a control group. One RCT had had a successful blinding using SMT or sham treatment, the latter group was denoted as "control group" by the authors [28]. Future RCTs should include a placebo group, i.e. a group of participant that do not receive treatment, although, it is known that blinding adult participants in SMT trials is difficult [34]. Thus, the lack of control group that do not receive treatment makes interpretation of the results difficult, since many of the RCTs had "control groups" that receive a non SMT treatment that might had some effect.

Results

The Dutch study was considered to be of good methodological quality, although it had room for many improvements [30]. The experimental group had a statistically significant improvement in headache intensity as compared to conventional physiotherapy, an effect that must be considered to also be of clinical significance as the headache intensity was reduced >50 %. The study stands alone, since it also included TMD complaints that also improved. The study included multimodal treatment modalities such as exercise, and thus the results cannot with certainty be exclusive of manual intervention.

The two Danish studies were based on the same study population, with additional 15 participants in the 2nd Danish study [24, 25]. The 1st Danish study presented mean data and the 2nd Danish study presented median data. The median but not mean headache duration and intensity was statistically significantly reduced in the SMT group as compared to the ST group [24, 25]. The 59 and 52 % mean reduction of headache duration in the SMT and ST groups is clinically meaningful, and the 36 and 22 % mean reduction in headache intensity in the two groups is also likely to be clinically meaningful.

The Australian study showed a significant reduction in headache frequency and intensity in all active treatment groups as compared to the control group, an effect that was maintained at 12-month follow-up [26].

The 1st American RCT was a dose–response study without statistical significant results, but there was a tendency toward favouring SMT three or four times a week for SMT once a week [27]. The study did not avoid co-intervention in the any of the three groups leading to a possible bias.

The German RCT included children and adolescent and had only one treatment session, and found no statistically significant differences [28]. Due to the single treatment, it cannot be excluded that more treatment sessions might have given another result, considering that CEH is known to be difficult to treat.

The results of the 2nd American study favoured SMT for light massage (LM), and favouring SMT four times a week slightly over SMT three times a week [29].

One of the major problems in all the RCTs is the fact that the majority of participants had intermittent CEH [24–30]. However, CEH is often characterized by a continuous headache with an intensity that might fluctuate rather than being a paroxysmal disorder [10, 14]. The fact that CEH is often continuous makes sense, assuming that CEH is caused by local factors in the neck/cervical spine. Another major problem is the fact that clinical diagnostic criteria for CEH have not proved to be valid [35]. Although, applying the diagnosis criteria of CHISG not including a blockage of the greater occipital nerve (GON) is equally inter-observer reliable as the diagnosis of migraine and tension-type headache [36]. Thus, the validity of a GON blockage as a diagnostic criteria can be questioned. Medication is usually ineffective in CEH. So far there have not been conducted any RCTs on the effect of medicine in CEH. Blockage of the GON might be effective in CEH [10, 18, 19]. However, an operation of the peripheral course of GON with special attention to the trapezius insertion had no effect [37].

Conclusion

Current RCTs suggest that physiotherapy and SMT might be an effective treatment in the management of CEH. However, the RCTs mostly included participant with infrequent CEH. Future challenges regarding CEH are substantial both from a diagnostic and management point of view.

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