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Effectiveness of craniocervical training and manipulative therapy in patients with cervicogenic headache: A randomized controlled trial

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Abstract
Background and Objectives: Cervicogenic headache, accounting for 4%-22% of all the clinical headaches, is associated with considerable disability and decline in the quality of life. Multifaceted approach needs to successful management but its acute rehabilitation physical and manual modes of therapy have been validated as important therapeutic modalities. Though certain studies have suggested the beneficial effects of combining craniocervical training program and manipulative therapy for the long-term prevention and control of headaches, there is no conclusive evidence to validate the findings. The present study was aimed at evaluating the effectiveness of craniocervical training and manipulative therapy in patients with cervicogenic headache as individual and combined management strategies.
Materials and Methods: Multi-center, randomized prospective comparative study was conducted and 120 patients mean age group 25-40 were included in the study. Based on study criteria's patients were randomly allocated into 4 groups, comprising of 30 patients, as given below: Patients in Group1: receiving craniocervical training program, Group2: undergoing a manipulative therapy, Group3: undergoing a combination of craniocervical training and manipulative therapy and Group 4:(control group)not receiving any treatment. The patients were assessed for pain intensity, disability of neck and headache intensity using VAS scale, NDI, and the HFHDI respectively.
Results: A significant difference in the pre, post and one-month post training mean VAS scores was noted in group3. The comparison of the pre-training VAS scores for all the study groups showed that the control/no training group had the highest mean VAS score. The highest mean one-month post-training VAS score was noted in the group3, compared to all other groups. In group 3 more reduced HDI post training and one-month post training than the other groups. In group3 and group2 Patients had reduced NDI post training. However, it was comparatively higher than group 1.
Conclusion: Craniocervical training, manipulative therapy, and combination of both are effective for the long-term management of cervicogenic headache. Combined therapy group demonstrated significant effect in patient-reported outcomes with respect to the three scores- VAS, NDI and HDI.

Keywords: Cervicogenic headache (CEH), Craniocervical training, manipulative therapy

Introduction
Headache is one of the most prevalent neurologic disorders [1]. It has large impact on the day-to day-activities of individuals. There are around 300 types of headache, among which cervicogenic headache and TTH are the most common [2, 3]. The CEH accounts for 4%-22% of all the clinical headaches [4]. However, compared to the TTH, CEH is less prevalent, affecting only 0.4% to 2.5% of the general population [5]. The patients with CEHs like those migraine and TTHs have considerable decline in the quality of life. Additionally, patients with CEH encounter loss of physical functioning [6].
The American migraine foundation defines CEH as "the referred pain (pain perceived as occurring in a part of the body other than its true source) perceived in the head, from a source in the neck" [7]. The term was introduced by Sjaastad *et al*. in 1983.[8] Sjaastad and colleagues referred CEH as 'secondary headache', resulting from other underlying illness or physical issues (neck joint problem) [4, 7, 8]. In patients with CEH, the pain arises from a disorder of the cervical spine and its component elements such as vertebrae, disks or the soft tissue.[7]This headache is perceived over the occipital region, extending to the oculo- frontotemporal areas. The presence of unilateral headache and the aggravation of headache with neck movement are considered as the cardinal signs of CEH [9].

CEH arises from the sensitized structures in the neck [10]. Usually, it results from the musculoskeletal dysfunction of the three upper cervical segments [11]. Studies suggest that CEH are caused by structures in the mid and lower cervical spine [12]. Cooper *et al.* have showed that second and the third cervical spine facet joints are the main source of origin of CEH pain, followed by the fifth and sixth facet joints [13]. CEH is a heterogeneous group of headaches in which the pain generated in regions like cervical joints, muscles and nerves are transmitted to various regions of the head.[5]The relationship between the afferents of the upper three cervical nerves and those of the trigeminal nerve accounts for the anatomic basis of CEH [14]. The headache is perceived on both the cervical and trigeminal dermatomes due to the convergence of the afferent fibers of the trigeminal nerve and the upper three cervical nerves with the second-order sensory neurons at the dorsal horn of the upper cervical spinal cord [15-16]. The sources of CEH can include any structure innervated by the C1-C3 spinal nerves, intervertebral discs down to the C7 level, dorsal roots from C1 through C7, the greater and lesser occipital nerve, the zygapophyseal joints from C2-3 to C6-7, the major auricular nerve and the third occipital nerve [17]. CEH is more common in women, with 4-fold increased preponderance compared to men [6]. The incidence of CEH is more in individuals belonging to 18-30 years age group. However, people with a mean age of 42.9 years has been reported to be more susceptible to CEHs [5]. Zito *et al.* have reported that among all the chronic headache, CEH is estimated to affect around 14%-18% of the population [18]. Martelletti *et al*. suggested that CEH is a common type of headache, with an estimated prevalence ranging from 0.7% to 13.8% [19]. Sjaastad *et al*., in 2008 reported a 4.1% prevalence of CEH in European population [20]. Thakur *et al.* have reported a prevalence of CEH as high as 15.6% in population with frequent headache, and a prevalence of 1.7% in general population [21]. Haldeman *et al*. also reported a prevalence between 15% to 20% in patients with chronic headaches [22]. The varied rates of CEH observed are due to the use of different methodologies, diagnostic criteria and population [5]. The diagnosis of CEH is often challenging, as the symptoms are often un-differentiable from the primary headache disorders like hemicrania continua, TTH and migraine [23]. The notable symptoms of primary headache disorders include cervical muscle tenderness and neck pain [24]. However, in case of CEH, the bony structure of the neck or the soft tissues are the source of pain generation [8]. CEH is often differentiated from migraine and TTH by comprehensive musculoskeletal examination [25]. The common presentations of the headaches include unilateral dominant headache, aggravating with neck movement and certain postures, tenderness in the three upper cervical spine joints, weakness in the deep neck flexor etc [26]. Patients manifest increased tightness and trigger points in the upper trapezius, splenius capitis, levator scapulae, sternocleidomastoid and suboccipital extensors [27-29]. The first ICHD was issued by The IHS in 1988. Later in 2004 and 2013, the society published the revised editions. As per the current ICHD III beta version, CEH is classified as a secondary headache arising from the musculoskeletal disorders in the cervical spine, which is frequently accompanied by neck pain [30-32]. As per the IHS 2013, the diagnostic criteria for CEH are as follows [33]. A. Any headache fulfilling criterion C, 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 able to cause headache, C. Evidence of causation demonstrated by at least two of the following:

1. Headache has developed in temporal relation to the onset of the cervical disorder or appearance of the lesion.
2. Headache has significantly improved or resolved in parallel with improvement in or resolution of the cervical disorder or lesion.
3. Cervical range of motion is reduced and headache is made significantly worse by provocative maneuvers.
4. Headache is abolished following diagnostic blockade of a cervical structure or its nerve supply.

D. Not better accounted for by another ICHD-3 diagnosis. The criteria revised by the CEH International Study Group, for diagnosing CEH, is as follow [34]: Major criteria-I. Symptoms and signs of neck involvement, a) precipitation of comparable symptoms by: 1) neck movement and/or sustained, awkward head positioning, and/or 2) external pressure over the upper cervical or occipital region, b) Restriction of range of motion in the neck, c) ipsilateral neck, shoulder or arm pain, II. Confirmatory evidence by diagnostic anesthetic block and 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 or lack of effect of indomethacin; only marginal or lack of effect of ergotamine and sumatriptan; female gender; not infrequent history of head or indirect neck trauma, usually of more than 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”) swallowing difficulties f) ipsilateral edema, mostly in the periocular are. On physical examination, a patient with CEH shows restriction in the mobility of the upper cervical spine, muscle tightness and cervical pain.[18] The performance of the manual examination of the vertebral segment, like passive physiological intervertebral and passive accessory intervertebral motion, is of prime importance in determining the cause of headache from the dysfunctional spinal cervical spine segment, in patients with CEH [35]. Pain, headache, stiffness and limitation in the motion indicates the dysfunctional segment, during manual assessment [15-25]. The gold standard for the diagnosis of CEH is the use of diagnostic blockade [36]. The symptoms of the CEH are manageable using cervical rami blocks at the second and third cervical rami [37]. Therapies used for the management of CEH ranges from the less invasive drug- based therapy to the highly invasive surgical-based therapy. The study by Martelletti *et al*., suggested that therapies involving the repeated injections of type A botulinum toxin are safe and effective for the treatment of CEH [19]. The management involves the use of cervical epidural steroid injections, nerve blocks, physical therapy, exercise and medications [24]. Various anatomical and physiological dysfunction necessitate the need for manipulative therapies in patients with CEH [38]. The use of injections and surgery provides only moderate success and several randomized control trials have suggested the use of cervical manipulation, botulinum toxin injection and transcutaneous electrical nerve

stimulation [5]. The generally employed physical treatment modalities that have shown to be effective for CEH include cervical spine manipulation and mobilization, strengthening exercises involving the upper quarter muscles and deep neck flexor, thoracic spine thrust exercise and manipulation and C1-C2 self-sustained Natural Apophyseal Glide (SNAG) [23, 39, 40]. Zito *et al*., in 2006 evaluated the clinical tests of musculoskeletal dysfunction in the diagnosis of CEH. The study inspected the presence of cervical musculoskeletal impairment in 77 subjects, among which 27 subjects had CEH, 25 had migraine with aura and another 25 subjects served as control. The study assessed the posture, range of motion, pressure pain threshold, cervical manual examination, muscle length, and the performance in the cervical kinesthetic sense and cranio-cervical flexion test. The study demonstrated that subject with CEH had lesser range of cervical flexion/extension and higher incidence of painful upper cervical joint dysfunction, compared to the subjects with migraine and those belonging to the control group, when assessed by muscle tightness and manual examination. Moreover, the study showed that the manual examination can discriminate between people with CEH and migraine with aura, and the control group with 80% sensitivity [18]. One of the characteristic features of CEH is muscle dysfunction [41]. The muscle dysfunction encompasses loss of postural alignment and neuromuscular control, muscle weakness, extensibility and endurance [42]. Impaired muscle strength and endurance of the deep neck flexors are considered as the defining features of CEH, as they are absent in migraine and TTHs [18]. Several studies have reported the existence of muscle tightness and trigger points associated with CEH [43]. Zito *et al*. have reported muscle tightness in 35% of the CEH patients compared to only 17% and 16% noted in subjects with migraine and TTH respectively.[18]Studies have shown that restricted neck movement, impairment in the deep neck flexors and evidence on manual examination of upper cervical joint dysfunction are 100% sensitive and 94% specific in identifying CEH [44]. Several studies have evaluated the effectiveness of physiotherapy including CCT program and MT in the treatment of CEH. However, there is no conclusive evidence on their effects on frequency, intensity, and duration of headaches, and the influence of overall quality of life and disability. The present study was intended to evaluate the effectiveness of CCT and MT in reducing pain and disability in patients with CEH as individual and combined management strategies.

Methods

A multicenter randomized prospective comparative study of 120 patients (both male and female) using simple random sampling and allocation with computerized table method was done. Sample size calculation was done by estimating the difference between means of populations with specified precision [35]. The sample size was calculated based on the pilot study as a minimum requirement of 30 subjects for each group. The following formula was used to calculate sample size.

$$\text{Sample size} = \frac{Z^2 2\sigma^2}{d^2}$$

Where, Z= level of statistical significance,95% confidence interval Z score= 1.96,d=absolute precision,$\sigma^2 = \frac{(n_1-1)s_1^2+(n_2-1)s_2^2}{n_1+n_2-2}$, n_1 and n_2- sample sizes for population 1 and 2 respectively,s_1^2- sample variance from population 1,s_2^2- sample variance from population 2. Patients which were diagnosed with cervicogenic headache aged between 25-40 years included according to inclusion and exclusion criteria. The intervention craniocervical training program, a manipulative therapy and combination of craniocervical training and manipulative therapy were given once in a day, 5 days/week/ for two weeks and each session lasts for 30 min. the inclusion criteria for this study were patients both male and female belonging to 25-50 years of age, who those willing to participate in this study, unilateral or one-sided overwhelming side-predictable headache related to neck pain, which may exacerbate by specific neck position or neck movement, joint delicacy at least in one of the three upper cervical joints, as distinguished by manual palpation, recurrent headache at least once every week, persisting for a period of 2 months to 10 years, mechanical neck pain involving the initial three cervical vertebrae and exclusion criteria for this study who were Age <25 and >50, bilateral headaches (typifying tension headache), features suggestive of migraine, vertebra-basilar insufficiencies, tumors, cervical canal stenosis or herniation's, traumatic causes, neurological cause, any condition that might contraindicate MT, non-musculoskeletal pain, signs of neurological involvement, cervical dis prolapse, spinal stenosis, previous neck surgery, spasmodic torticollis, fibromyalgia, cervical radiculopathy, uncooperative patient, whiplash injuries.

Outcome measures

VAS Scale

VAS scale valid and reliable universally accepted 0-10 rating scale used to assess pain intensity. The patients were instructed to mark the scale based on the intensity of the pain pre and post-intervention. Resting pain, pain at the time of wake up, and at the time of exacerbation were also recorded for pre-and post-comparison [45].

NDI

NDI is a self-report questionnaire comprising of 10 questions on the following domains: pain intensity, headaches, lifting, reading, concentration, personal care, driving, work, sleeping, and recreation. It is the most widely used index for evaluating self-rated disability in patients with neck pain [46-48]. Each question contains six possible choices, scored from 0 (no disability) to 5 (complete disability). Finally, scores of all section are summed up to report on a 0-50 scale, 0 being the best possible score and 50 being the worst. The score can also be reported from 0-100. The score is often reported as a percentage (0-100%) [47-49]. Higher scores indicate the expanded levels of functional disability. The features of the index include test-retest dependability, solid legitimacy, consistency and great responsiveness [47].

HFHDI

Henry Ford Headache Disability Inventory was used to assess headache intensity. The study received approval from the central ethical committee of NITTE University (No. NU/CEC/02/2009)

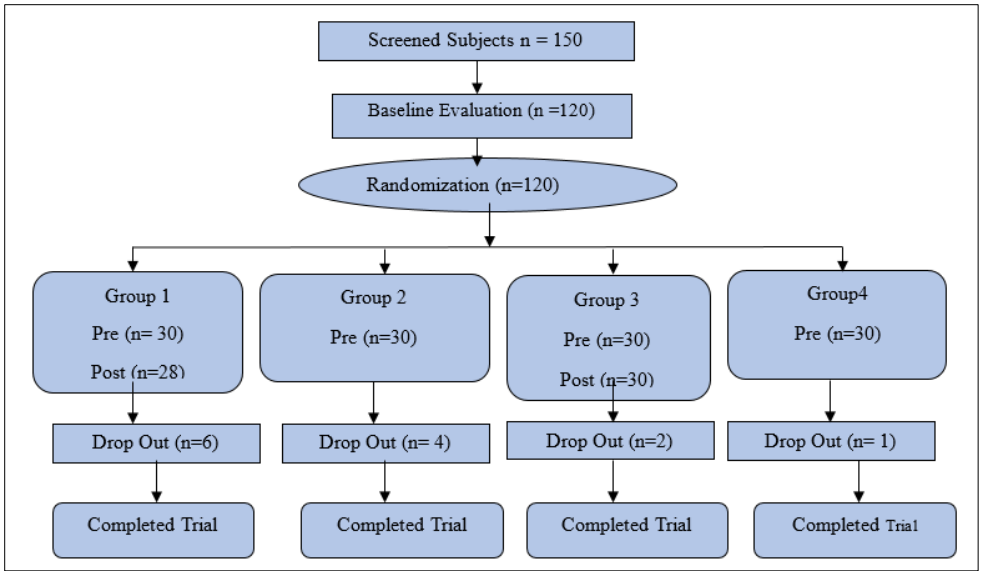


Fig 1: Flow chart representing the procedure of selection of patients

Results

Paired t test and Unpaired t test (Kruskal-Wallis test, chi-square test, ANOVA) were applied to analyze the data. All statistical analysis was done with utilizing the SPSS ver. 22 and Microsoft excel.

VAS Score

The mean difference in group1 (CCT)-pre- 6.750, post-3.750 and 1 month -3.583 with (95% Confidence interval) lower bound (6.401, 3.358 and 3.159) and upper bound (7.099, 4.142 and 4.008) respectively, group 2 (MT)-pre-7.115, post-4.115 and 1month-4.038 with (95% Confidence interval) lower bound (6.780, 3.739 and3.631) and upper bound (7.450, 4.492 and 4.446) respectively, group3 (CCT&MT) -pre-6.929, post-2.786 and 1month-2.857 with (95% Confidence interval) lower bound (6.606, 2.423 and 2.464) and upper bound (7.251, 3.149 and 3.250) respectively and in group 4 (control group) -pre-7.138, post-4.621 and 1 month-3.966 with (95% Confidence interval) lower bound (6.821, 4.264 and 3.579) and upper bound (7.455, 4.978 and 4.352) respectively.

NDI

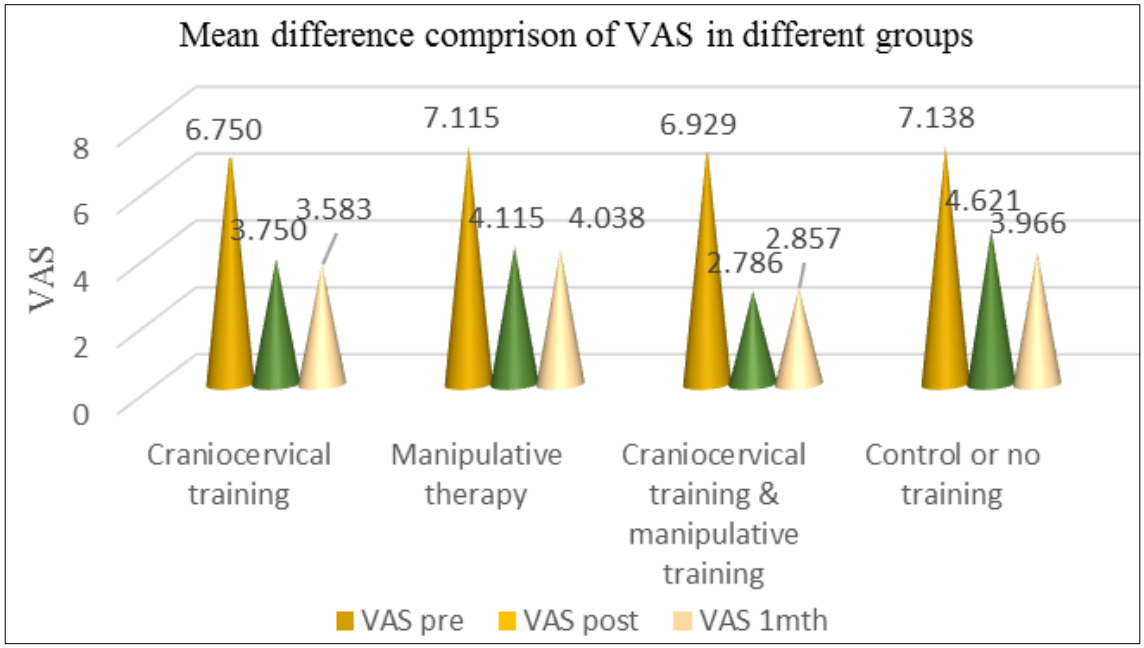
The mean difference in group1(CCT)-pre-47.208, post-34.542 and 1 month -31.375 with (95% Confidence interval) lower bound (44.270, 31.470 and 27.840) and upper bound (50.147, 37.613 and 34.910) respectively, group2 (MT)-pre-53.077, post-38.769 and 1 month - 35.346 with (95% Confidence interval) lower bound (50.254, 35.818 and 31.950) and upper bound (55.900, 41.720 and 38.742) respectively, group3(CCT & MT)-pre-55.321, post-35.107 and 1 month-29.643 with (95% Confidence interval) lower bound (52.601, 32.263 and 26.370) and upper bound (58.042, 37.951 and 32.915) respectively and in group4 (control)-pre-55.379, post-44.690 and 1 month-42.172 with (95% Confidence interval) lower bound (52.706, 41.895 and 38.957) and upper bound (58.053, 47.484 and 45.388) respectively.

HDI

The mean difference in group1 (CCT)-pre-59.41, post-2.917 and 1 month-37.250 with (95% Confidence interval) lower bound (56.300,40.050 and 34.911) and upper bound (62.533, 45.783 and 39.589) respectively, group2(MT)-pre-52.000, post-38.923 and 1 month-38.846 with (95% Confidence interval) lower bound (49.006, 36.169 and 36.598) and upper bound (54.994, 41.677 and 41.094) respectively, group3(CCT&MT)-pre-56.64, post-37.214 and 1 month-33.929 with (95% Confidence interval) lower bound (53.758, 34.561 and 31.763) and upper bound (59.528, 39.868 and 36.094) respectively and in group4 (control)-pre-52.759, post-41.448 and1month-39.931with (95% Confidence interval) lower bound (49.924, 38.841 and 37.803) and upper bound (55.594, 44.056 and 42.059) respectively.

Table 1: Mean difference Comparison of VAS score pre, post and one month in different groups

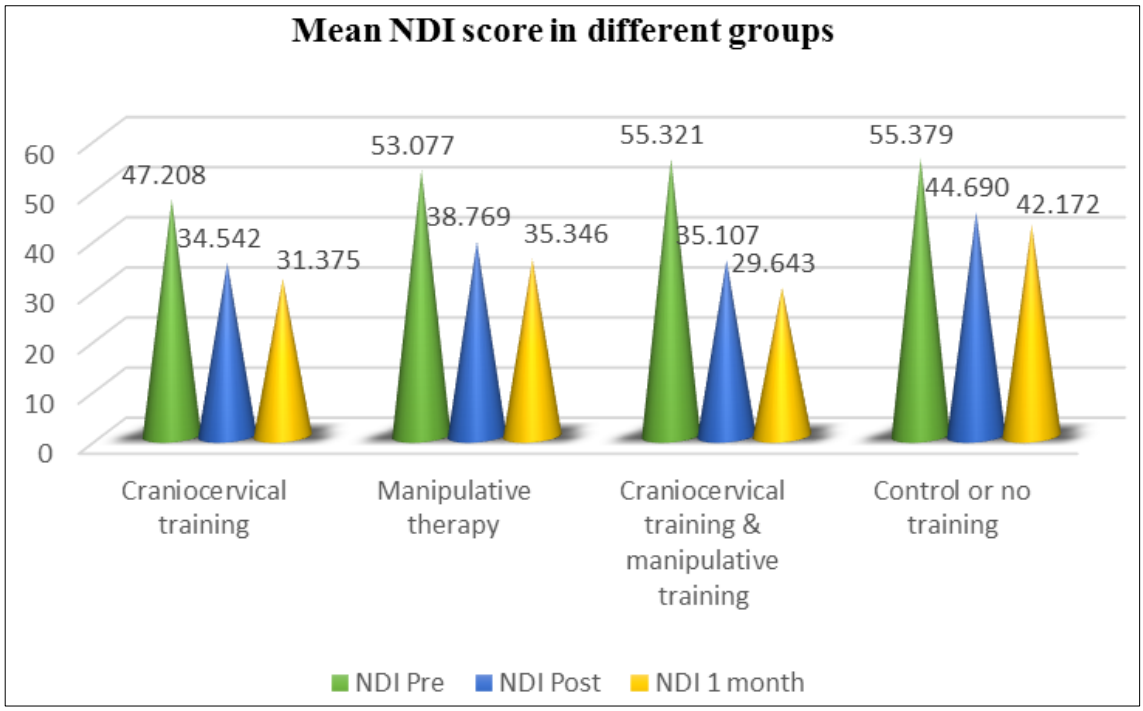
Training group	VAS	Mean	95% Confidence interval	
			Lower bound	Upper bound
CCT	VAS pre	6.750	6.401	7.099
	VAS post	3.750	3.358	4.142
	VAS 1mth	3.583	3.159	4.008
MT	VAS pre	7.115	6.780	7.450
	VAS post	4.115	3.739	4.492
	VAS 1mth	4.038	3.631	4.446
CCT&MT	VAS pre	6.929	6.606	7.251
	VAS post	2.786	2.423	3.149
	VAS 1mth	2.857	2.464	3.250
Control/no training	VAS pre	7.138	6.821	7.455
	VAS post	4.621	4.264	4.978
	VAS 1mth	3.966	3.579	4.352



Graph 1: Mean VAS score pre-, post- and one-month post training in different groups

Table 2: Mean difference Comparison of NDI score pre, post and one month in different groups

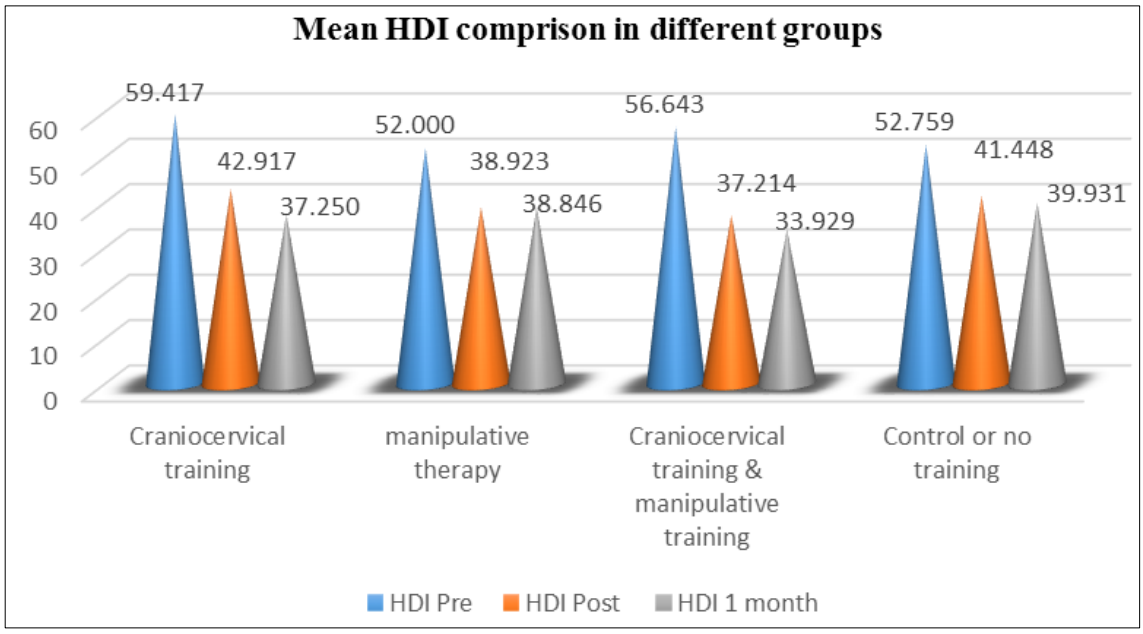
Training group	NDI	Mean	95% Confidence interval	
			Lower bound	Upper bound
CCT	NDI pre	47.208	44.270	50.147
	NDI post	34.542	31.470	37.613
	NDI one-month	31.375	27.840	34.910
MT	NDI pre	53.077	50.254	55.900
	NDI post	38.769	35.818	41.720
	NDI one-month	35.346	31.950	38.742
CCT&MT	NDI pre	55.321	52.601	58.042
	NDI post	35.107	32.263	37.951
	NDI one-month	29.643	26.370	32.915
Control or no training	NDI pre	55.379	52.706	58.053
	NDI post	44.690	41.895	47.484
	NDI one-month	42.172	38.957	45.388



Graph 2: Mean NDI score pre-, post- and one-month post training in different groups

Table 2: Mean difference Comparison of HDI score pre, post and one month in different groups

Training group	HDI	Mean	95% Confidence interval	
			Lower bound	Upper bound
CCT	HDI pre	59.417	56.300	62.533
	HDI post	42.917	40.050	45.783
	HDI 1 month	37.250	34.911	39.589
MT	HDI pre	52.000	49.006	54.994
	HDI post	38.923	36.169	41.677
	HDI 1 month	38.846	36.598	41.094
CCT&MT	HDI pre	56.643	53.758	59.528
	HDI post	37.214	34.561	39.868
	HDI 1 month	33.929	31.763	36.094
Control or no training	HDI pre	52.759	49.924	55.594
	HDI post	41.448	38.841	44.056
	HDI 1 month	39.931	37.803	42.059



Graph 3: Mean HDI score pre-post- and one-month post training in different groups

Discussion

The present study findings indicate that CCT, MT and the combination of both CCT and MT are effective in reducing pain, NDI and HDI in people with CEH. The additive effect of the two training programs were also noted to be statistically significant in reducing the VAS score and HDI score in the CEH patients, compared to the individual training programme, but not the NDI score.

Craniocervical training and cervicogenic headache

The present study has noted a significant decrease in the mean VAS, NDI and HDI scores in patients receiving CCT compared to the control group with no treatment. However, the training alone was less effective in reducing the pain and HDI score in the CEH patients, compared to both CCT and MT. The CCT was found to be more significantly effective than the combined therapy and MT in reducing the NDI in CEH patients. The training significantly decreased the mean NDI scores, one-month after the training, compared to patients who did not receive any training. The within-group comparison revealed a significant difference in the mean VAS, NDI and HDI scores before and after the training, and before and one-month after the training in subjects who had CCT. Additionally, there was a significant increase in the HDI scores during one-month follow-up period, compared to the pre-training scores. CEH arises from the upper cervical and the atlanto-occipital joints, and radiates to the frontal-temporal and possibly to the supraorbital region [50, 51]. Management of CEHs is benefited if the appropriate therapeutic methods are directed towards the cervical nociceptor structures [52]. CCFEx targets deep neck flexors such as the longus capitis and colli muscles, as they provide significant support to the cervical region.[5] Jull *et al*. in 2009 reported the effectiveness of CCT exercise in patients with chronic neck pain and its ability to alter the spatial and temporal characteristics of the deep cervical flexor muscles [53]. O'Leary *et al*. in 2007 proposed that, in comparison to the cervical flexion exercise, the CCFEx has a more potential influence on the pain sensitive structures of the upper cervical region. The study showed that specific CCFEx provides instantaneous changes in the mechanical hyperalgesia, rendering pain relief [54]. Several randomized controlled trials have validated the effectiveness of CCT programme in treating cervicogenic and other types of headache. Iqbal *et al*. (2013) studied the effectiveness of training on deep cervical flexor muscles in patients with neck pain, belonging to an age group of 25-45 years. The study reported a significant alleviation in the pain and disability after performing deep cervical flexor muscle training for four weeks with pressure biofeedback (craniocervical flexion training) [55]. These observations corroborate with the present study results showing a

significant reduction in the intensity of pain, NDI and HDI scores in CEH patients when CCT was followed-up for a period of one month. The improved NDI has been attributed to the reduction in the intensity of pain [55, 56]. In a recent study, Gallego *et al*. compared the effectiveness of craniocervical flexion training and cervical proprioception training in chronic neck pain, and found that the exercises substantially reduced the pain at rest and the disability for two months [57]. The present study also noted a significant decrease in the pain, NDI and HDI scores in patients who had CCT compared to the control group, after training and one-month after training. CCT exercises reduce the pain by increasing the endorphins, providing better neuromuscular control, activating stretch receptors through muscle contraction, and stimulating the secretion of beta-endorphins from pituitary gland, thereby blocking the peripheral and central pain [58]. Additionally, the research by Chung *et al*. (2011) concluded that craniocervical flexor training effectively improves the cross-sectional area of the longus colli muscle and absolute rotational angle, thereby reducing the NDI in chronic neck patients. The training was found to be beneficial in improving muscle function and retraining the muscles [59].

Manipulative therapy and cervicogenic headache

The present study noted that MT is significantly less effective when compared to the combined training (CCT and MT) in reducing the VAS score at one-month follow up. However, the training program was more effective than the control in reducing the NDI score at one-month follow-up. A significant difference was noted in the mean VAS, NDI and HDI scores before and after the training, and before and one-month after the training. The present observations are substantiated by several randomized controlled trials, wherein the application of spinal MT have shown notable effects on the frequency, intensity and consumption of medicine in the patients with CEH [35, 60, 61, 62, 63].

Piekartz *et al*., based on a randomized controlled trial conduced in CEH patients, suggested that the treatment of the temporomandibular region provides a long-term benefit in improving the headache [11, 5, 64]. A multicenter randomized controlled trial conducted by Jull *et al*., in 2002 on CEH patients reported that MT significantly reduced the frequency and intensity of the headache, with maintained effects, during a one-year follow-up assessment [35]. These observations substantiate the present study findings showing a significant decrease in the VAS, NDI and HDI scores before undergoing the training, post training and during the one-month post-training follow-up period.

The present study has noted a decrease by 57 % and 56% in the mean VAS score immediately after the treatment and during the one-month follow up. A decrease by 73% was noted in the post-training NDI score, and a decrease by 66% in the one-month follow-up. Similarly, the HDI score was reduced by ~ 75% immediately after training and during one-month follow-up, compared to the pre-training scores. The results are comparable to the findings of Jull *et al*., who reported a >50% reduction in the headache frequency in 71% of the participants and 100% reduction in 33% of the participants who received spinal manipulative therapy [35]. The study by Haas *et al*. in 2004 and 2010 reported a mean reduction of 43%, 29% and 40% in the intensity of headache at the 4, 12 and 24 weeks follow-up respectively, and corresponding reduction of 49%, 34% and 52% in patients who received spine manipulation therapy [26, 61]. Whereas, the Nilsson *et al*. have reported a reduction of 36% and 22% in the headache intensity post treatment and during one-week follow-up in the group undergoing cervical spine manipulation [63].

The safety of the spinal MT in patients with CEH has been recently validated by Chaibi and colleagues. The present study also reinforces the safety, as no adverse effects has been reported in any of the subjects who received spinal manipulative therapy. A single-blinded placebo, randomized controlled trial, enrolling a total of 19 participants, reported an improved headache frequency at all points in both the study groups. Headache index was noted to be enhanced in the group who had the spinal manipulation therapy at all time, but in the placebo group it improved at 6 and 12 months of follow-up. These observations are comparable to the present study findings [64].

Contradictory observations were reported by Borusiak *et al*., indicating that cervical spine manipulation training was inefficient in children and adolescent patients. The study concluded the training was not significantly different compared to the placebo, with respect to the main outcomes measured like percentage of days with headache, intensity of headache, duration of headache etc [8, 6, 62]. Limited literature evidence has been documented, comparing the effectiveness of MT, CCT and both MT and CCT with a control group in patients with CEH.

Combined training and cervicogenic headache

Pharmacological management is considered as the first line treatment for primary chronic headache. However, this treatment approach is associated with drug overuse due to frequent episodes of headaches. A study conducted in Norwegian population has indicated overuse of medication is noted in nearly 47% patients with primary chronic headache. Hence both prophylactic medication and non-pharmacological management are considered as safer treatment approaches, as their use can cause only minor transient adverse events and no pharmacological interaction [65]. Headache disorders, as a whole, have been identified as a major public health concern, as it is associated with significant disability and economic burden on both individual and society. Headache has been reported as the most common cause for analgesic use in general population [66]. Chronic headache and overuse of different headache medicines can lead to a condition called medication-overuse headache, and the global prevalence of this condition is estimated to be around 1-2% [67]. Conservative therapies have been recognized as the first choice of management for headaches arising from cervical musculoskeletal disorders. MT is the key intervention used for managing upper cervical joint arthopathy associated with CEHs. There is inconclusive evidence on the effectiveness of MT and the available studies have evaluated only the short-term outcome. Moreover, there is insufficient literature evidence on the effect of exercise and very few studies have evaluated the combined effect of CCT and MT [35]. The non-invasive strategies employed for the management of CEH include transcutaneous electrical nerve stimulation (TENS), massage, exercise, manipulation and mobilization. Despite the availability of several treatment interventions, there is no clear consensus on the most effective form of non-invasive strategy for the management of CEH. The present study holds significant relevance, as it has reported a significant

reduction in VAS in patients who received craniocervical training and manipulative training on follow-up (2.786) and at 1 month (2.857) when compared to the other 3 groups. Though patients who received individual CCT or MT also demonstrated significant VAS reduction post training, it was much higher than patients who received combined training.

Similar to this finding, a multicenter, randomized controlled trial conducted by Jull *et al*. have demonstrated a significant decrease in headache frequency and intensity, and the neck pain at the 12-month follow-up assessment, in subjects who had undergone both exercise and MT. However, on contrary to the current result, the study has found that the effectiveness of combined therapy was not significantly superior when compared to individual therapies.

In the current study, the combined therapy group demonstrated significant reduction in mean scores for the VAS, NDI and HDI indices, thereby indicating a good treatment outcome. In concurrence with this finding, a systematic review by Racicki *et al*. have concluded that conservative physical therapy treatment techniques are effective for reducing the recurrence and severity of CEH. Based on the review findings, which considered six randomized clinical trial, the researchers have further suggested that a combination of manipulation, mobilization and cervico-scapular strengthening exercises may serve as the most effective intervention for managing CEH [68].

The present study findings substantiate the additive effects of both the therapies. Jull *et al*. have tried to elucidate the mechanism underlying the combined effect. The study has reported that response of both MT and low-load exercise on the pain system is similar. It has been speculated that modulation of pain perception in both the approaches is achieved through local afferent input. Studies suggest that this afferent input may serve as a stimulating factor at various levels of neural inhibitory systems [35, 69]. The afferent input is also speculated to play a key role in activating descending inhibitory pathways from the lateral periaqueductal gray area of the midbrain [70, 71]. However, the present study did not explore the multi mechanisms involved in conferring pain relief by these physical treatments.

The current study holds greater relevance, as the literature search indicates the study conducted by Jull *et al*. is the only randomized clinical trial that has evaluated the effects of exercise as well as thrust and non-thrust manipulation [68]. Chaibi *et al*. in 2014 have conducted the first systematic review of randomized clinical trials on manual therapies for primary chronic headaches. The study has highlighted the need of conducting future randomized clinical trials that comply with the International Headache Society's guidelines for clinical trials. The study has also reported that the efficacy of manual therapy for managing CEH is comparable to that of prophylactic medication with tricyclic antidepressant [65].

Conclusion

Craniocervical training, manipulative therapy, and combination of both are effective for the long-term management of cervicogenic headache. Combined therapy group demonstrated significant effect in patient-reported outcomes with respect to the three scores- VAS, NDI and HDI.

Study limitations

- If Patient Centered and Physical outcomes are viewed collectively, overlap is observed in the effects of the three treatments, making it apparent that particular treatments can have better effect on one outcome than another.
- There are concerns about the small yet substantial risks associated with cervical manipulative therapy. Increase in pain would have been one of the reasons for drop outs from the study.
- Drop out ratio was not calculated while determining the sample size.
- Mobilizations were limited to only the upper cervical segments, but if the other segments were also treated might have yielded in better results
- The study did not obtain the medication history of the subjects for CEH.
- Treatment duration was short (only two weeks).
- Follow-up was done only for a short period i.e. only two weeks from the last treatment session.
- Only one follow-up session was done and no further follow- up sessions were carried out.
- Objective outcomes were not assessed, which would have given a proper insight into the effects of treatment.
- Quality of life and mental stress were not assessed.

Recommendations for future work

- Further research focusing on evaluation of long-term outcomes of CCT program in patients with CEH need to be conducted.
- Randomized control trials can be conducted for comparing CCT with other soft tissue release techniques employed for managing myofascial pain syndromes common to neck, which in turn induces CEHs.
- Further research should focus on identifying valid objective measures and other scales to measure the quality of life and psychological status of patients, which may assist in better assessment of treatment results and outcomes.

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