Prospective Study

Is it Possible to Distinguish Cervicogenic Headache from Neck Pain with Cervicospinal Posture? A Single-Blind, Prospective Cross-Sectional Trial

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Disclaimer: There was no external funding in the preparation of this manuscript.

Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received: 03-14-2020
Revised manuscript received: 04-26-2020
Accepted for publication: 05-15-2020

Free full manuscript: www.painphysicianjournal.com

Background: Cervicogenic headache (CEH) is a type of headache that is considered to be originated from the upper cervical spine. There are conflicting results in studies showing changes in the cervical spine in patients with CEH.

Objectives: We aimed to compare the cervical radiographs of patients with CEH and nonspecific neck pain.

Study Design: A single-blind, prospective study.

Setting: The department of neurosurgery and physical medicine and rehabilitation in a university hospital.

Methods: In this cross-sectional study; 45 women with CEH and 45 women with neck pain were involved. The pain assessment of the patients was done by the Visual Analog Scale (VAS), and the disability assessment was tested with the Neck Disability Index (NDI). General cervical lordosis (GCL) and upper cervical lordosis (UCL) angles were calculated on the lateral cervical x-ray. Clinical parameters including age, weight, height, pain (VAS), disability (NDI), and disease duration were recorded. Patients with CEH and neck pain were compared. Correlations between GCL, UCL, and pain assessment were analyzed.

Results: Both groups were demographically similar. There was no significant difference at the lateral cervical x-ray measurements between CEH and neck pain groups (CEH group mean GCL = 19.2, UCL = 13.6; neck pain group mean GCL = 19.1, UCL= 14.8). The positive correlation between GCL and UCL in the neck pain group (r = 0.453; $P = 0.002$) was not found in the CEH group ($P > 0.05$).

Limitations: Anesthetic blockade was not used for the diagnosis. Also, the whole spinal alignment was not evaluated.

Conclusions: According to cervical lateral x-ray, there was no significant difference in posture in patients with CEH and neck pain.

Key words: Cervical lordosis, cervicogenic headache, gender, neck pain, posture

Pain Physician 2020: 23:E687-E694

Cervicogenic headache (CEH) is a type of symptomatic headache that is characterized by chronic unilateral headache secondary to cervical spine dysfunction. Generally it gets worse by neck movements, continuous placement of the head in an awkward position, and exposure to external pressure on the upper cervical or occipital region (1). The prevalence of this type of headache in the

population with any headaches is 53% and is generally variable between 0.4% and 20% and is most commonly seen after whiplash injuries (2). The condition that is considered to cause the problem can be considered as a valid cause of headache provided that it is proven to be the case clinically and/or by imaging studies.

CEH is pain originated from the cervical structures innerved by the upper 3 cervical spinal nerves. It is considered to occur by convergence of the nociceptive afferents of the trigeminal and upper 3 cervical spinal nerves with secondary sensorial neurons in the trigeminal-cervical nucleus that are present in the upper spinal cord. The headache is considered to be directed from the cervical region up to the head (1). Anaesthetic blockage to the cervical region or related nerve causing pain temporarily decreases the pain, indicating that the pain is of cervical origin. Although degenerative changes in the cervical spine have been demonstrated to not always be associated with pain (1), cervical dysfunction due to impaired posture has been suggested to be one of the causes or aggravating etiology of this condition (3). Among the possible causes of CEH are disorders of the atlanto-occipital joint, atlantoaxial joint, zygapophysial joint, intervertebral disc, and upper cervical spinal nerve. Lower cervical discs and spinal nerve roots (such as C5/6) have been demonstrated in some studies to result in CEH but most studies point to the upper cervical region (1,4,5). Although disturbed cervical alignment has been determined in tension headache and migraine (3), there are few studies with controversial results in the literature investigating the effects of the change in cervical lordosis on CEH. These contradictory results strongly influence the decision of whether exercise should be added to the treatment protocol in CEH and also creation of an appropriate treatment program by the clinicians. In light of this background, the aim of this study was to compare the cervical radiographs of patients with CEH and patients with neck pain without a headache. The hypothesis in this study is that nonspecific neck pain and cervical headache will have a different cervical alignment.With this conclusion, it may be possible to apply a more accurate therapeutic exercise program in the treatment of patients with CEH.

Methods

The general demographics, pain status, and cervical radiologic evaluations of the patients was performed in this prospective, cross-sectional, single-blind study evaluating 2 different disease groups compatible in age and gender; the 2 groups were compared. The study was carried out at Hitit University Erol Olcok Training and Research Hospital, Department at Neurosurgery and Physical Medicine and Rehabilitation from March to September 2019. It included 45 women with CEH with an age of 18 to 50 years and 45 women with only nonspecific neck pain (6) in same the ages who presented to the neurosurgery outpatient clinic. The trial was registered with ClinicalTrials.gov under the number of NCT04242290. The institutional ethics approval was obtained from the ethics committee of Gaziosmanpasa University Medical School (approval date: 19/03/2019, project number: 19-KAEK-064). Oral and written informed consents were obtained from all patients. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Selection

For inclusion in the CEH group, inclusion criteria determined by the Cervicogenic Headache International Study Group (CHISG) were used. CHISG criteria includes (1) unilateral headache, starting from the upper neck/occipital region and spreading to the oculofrontotemporal area on the symptomatic side; (2) pain triggered by neck movements and/or continuous awkward positions; and (3) decreased joint range of motion in the cervical vertebra (2). For inclusion in the nonspecific neck pain group, patients had present pain in the posterior and lateral aspect of the neck between the superior nuchal line and the spinous process of the first thoracic vertebra. Patients with any of the following criteria were excluded: for the CEH group, previously diagnosed to have any other syndromes of headache (migraine, tension headache, etc.) or presence of bilateral headache; for the neck pain group, presence of 2 or more neurologic symptoms (decreased upper extremity muscle strength, decreased reflexes, and hypoesthesia compatible with the dermatome regions) suggesting nerve root compression (radiculopathy, plexopathy) as the specific cause for neck pain (e.g., clinical signs of infection, inflammatory disorder, tumor, osteoporosis, fracture, or a traumatic injury); for both groups, presence of any signs suspicious of central nervous system involvement (hyperreflexia, nystagmus, decreased vision, etc.) and reluctance to participate in the study.

Physical Examination

The motor strength, sensation, and reflexes of all patients in the study were evaluated by the same clinician. Physical examination maneuver (Spurling) was

performed. Cervical range of motion was measured. Spinous process palpation and paraspinal tenderness were evaluated as a part of the neck routine musculoskeletal examination.

Pain Assessment

Symptoms of all patients were questioned in detail and physical examinations were performed. After obtaining demographic information, such as age, height, and weight, patients were questioned about the severity and duration of pain, and the Neck Disability Index (NDI) was used for pain-related disability measurement. The pain severity was assessed with the Visual Analog Scale (VAS). The VAS is used to measure and monitor pain severity. The VAS is a 10-cm ruler on which it is written "painless" at one end and "the most severe pain" at the other. The patient scores between 0 and 10 for pain; a high score indicates the severity of pain. The NDI is the most widely used questionnaire to investigate the disability associated with neck pain. It was produced as a variation of the Oswestry Disability Index used for low back pain. There are 10 different headlines in total. Each section is scored from 0 (no disability) to 5 (heavy disability present). The total score ranges from 0 to 100. The closer the score to 100, the greater the disability. The topics evaluated include pain intensity, self-care, heavy lifting, reading, headache, concentration, work, driving, sleeping, and leisure activities. The validity and reliability of the Turkish version was made by Kesiktas et al (7).

Radiographic Assessment

Cervical radiographs of the patients were obtained and measurements on them were taken after a general assessment was performed. To facilitate generalization in clinical practice, 2 standard views of the cervical spine (anterior-posterior and lateral view, both upright) were obtained. Radiographic images and instructions were consistent with a standard cervical radiographic series as in clinical radiography practice. All the graphics and positions were performed by the same radiology technician. Patients were asked to stand in a comfortable position looking across with arms on the sides. The images were taken after a "stop breathing now" command after a series of normal breathing cycles. Forced expiratory and thoracic expansion, which were not allowed for the patient during radiographs, were obtained. All patients had standing cervical lateral spine x-rays from a 178-cm distance. Cervical radiographic analysis was evaluated measuring general cervical lordosis (GCL) and upper cervical lordosis (UCL) on lateral standing x-rays using Surgimap (Nemaris Inc. New York, USA).

GCL (Fig. 1) is basically measured by the "Cobb" method. In the lateral graph, the angle between the 2 lines drawn perpendicular to the lines passing on the inferior end plate of the C2 and C7 vertebrae is considered as the "general cervical lordosis angle." Higher values indicate increased cervical lordosis (3). For the measurement of UCL (Fig. 2), a line is drawn from the uppermost posterior point of the odontoid process to the lowermost posterior point of C2. The second line is drawn to pass between the lowermost-posterior portions of the C3 and C4 cervical vertebrae. The angle between these 2 lines is considered the "upper cervical lordosis angle" (3). The evaluation of cervical lateral radiography was performed by a researcher blind to the study groups and who had been evaluating radiographs in similar patient populations for 9 years. The radiographs of the patients were measured again 2 weeks after the first measurement by the same investigator and intrarater reliability between the 2 measurements was evaluated.

Statistical Analyses

The SPSS 25.0 package program (IBM Corporation, Armonk, NY) was used for statistical analyses of the findings obtained in the study. Descriptive statistical methods (frequency, percentage, mean, standard deviation [SD]) were used for the evaluation of study data in addition to Kolmogorov-Smirnov distribution test for the evaluation of normal distribution. In the comparison of the quantitative data between the 2 groups, the Student t-test and the Mann-Whitney U test were used in normally distributed variables and nonnormally distributed variables, respectively. The Spearman correlation test was used to investigate the relationship between the 2 quantitative data because normal distribution was not observed. Intraclass correlation coefficient (ICC) was used for intrarater reliability for measurements of cervical radiographies. $P < 0.05$ was considered to be significant.

Results

Of the 145 patients with headache and 170 patients with neck pain who were evaluated for suitability for the study, 45 female patients, each for the CEH group (mean age 42.8 ± 7.3 years) and for the neck pain group (mean age 39.3 ± 9.5 years), respectively, were included in the study. The most important reason of exclusion

Fig. 1. *GCL (Cobb angle between C2 and C7) measurement on cervical lateral x-ray.*

was bilateral headache and cervical radiculopathy for CEH and neck pain groups, respectively. The general characteristics of the patients are summarized in Table 1.

Evaluation of Pain

Duration of pain was similar in both groups (mean duration: 22 months). No difference was found between the 2 groups in pain intensity (mean VAS: 7.8). A significant difference was found in mean NDI scores between the 2 groups (26.6 in the CEH and 21.3 in the neck pain group, $P = 0.023$).

Radiographic Evaluation

GCL and UCL measurements on cervical lateral radiographies were similar in the 2 groups ($P > 0.05$). Mean GCL and UCL in the total series was found to be 17.17 (±12) and 14.4 (±7,6), respectively (Table 1). Evaluation

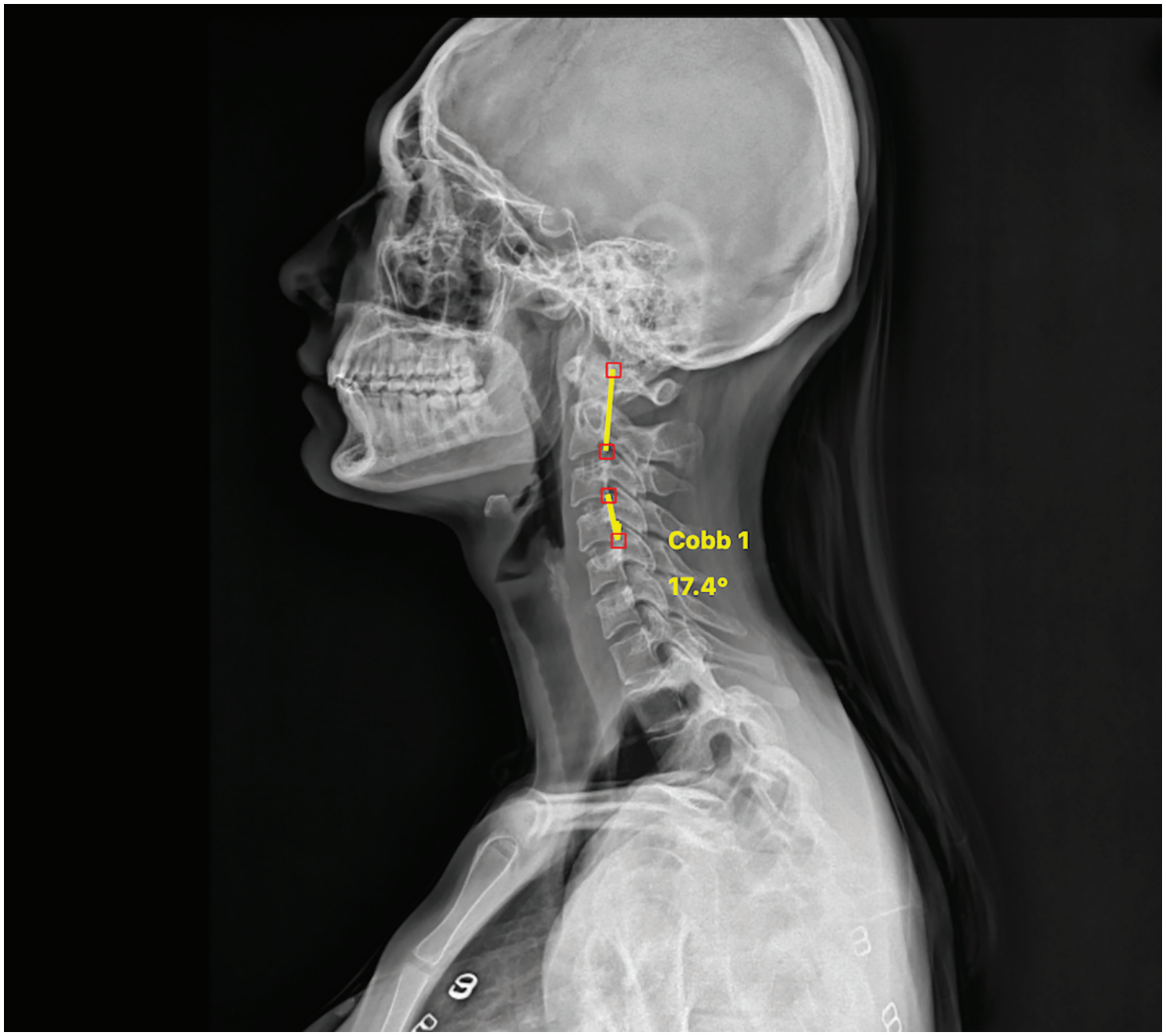

Fig. 2. *UCL measurement on cervical lateral x-ray (the measurement method is described in detail in the method section).*

of the associations between cervical measurements and pain scales revealed no significant correlation between change in the pain, UCL, and GCL in the CEH group ($P > 0.05$), whereas a positive correlation was determined between GCL and UCL in the neck pain group ($r = 0.453$; $P = 0.002$) (Table 2). Radiographic measurements were repeated in a randomly selected group of 20 patients 2 weeks after the initial evaluation of the cervical vertebra. These evaluations resulted in an ICC for inter-rater reliability of 0.948 (95% confidence interval [CI], 0.871–0.979) for GCL, and 0.885 (95% CI, 0.782–0.952) for UCL.

Discussion

To our knowledge, this single-blind, prospective and cross-sectional study can be regarded as one of the pioneering studies in the literature comparing patients with CEH to patients with neck pain, according to the change in cervical lordosis. The results demonstrated no difference between cervical lateral radiographs of patients with CEH and nonspecific neck pain. Angles of GCL and UCL were found to be similar in patients with CEH and neck pain. To the best of our knowledge, there is no study in the literature comparing these 2

Table 1. *Evaluation of demographic characteristics, pain, and radiographic features between groups.*

	CEH Group	Neck Pain	*P* Value	Overall
Patient characteristics				
Age (min-max)	42.8 (23-50)	39.3 (18-50)	0.074[1]	41.1 (18-50)
Weight (min-max)	72.5 (48-90)	74.4 (50-105)	0.513[2]	73.4 (48-105)
Height (min-max)	160 (145-175)	162.4 (145-180)	0.142[2]	161.2 (145-180)
Pain assessment				
Pain duration (mean±SD)	18.8 ± 20.8	17.15 ± 23.2	0.360[1]	22.12 ± 22.1
VAS (mean±SD)	8.3 ± 1.5	7.4 ± 2	0.057[1]	7.8 ± 1.8
NDI (mean±SD)	26.6 ± 8.4	21.3 ± 9.6	0.023[1]	23.4 ± 9.2
Cervical radiography features				
GCL (C2-C7) (mean±SD)	19.2 ± 11.4	19.1 ± 12.5	0.397[2]	17.17 ± 12
UCL (C2-C3/4) (mean±SD)	13.6 ± 6.7	14.8 ± 8.3	0.574[2]	14.4 ± 7.6

[1]Mann-Whitney *U* test. [2]Student *t*-test.

Table 2. *Correlation of radiographic and pain parameters for CEH and neck pain group.*

	GCL r Value	UCL r Value
CEH group		
Pain duration	0.162	0.041
VAS	0.207	-0.094
NDI	0.119	-0.165
Upper cervical cobb	0.229	
Cervical pain group		
Pain duration	0.017	0.020
VAS	0.137	0.053
NDI	0.022	0.057
UCL	0.453 ($P = 0.002$)	

groups so far. Jouibari et al (8) compared the cervical sagittal parameters with the control group in patients with neck pain. Also, Farmer et al (3) examined the cervical spinal posture of the healthy population with the CEH patient group. In both mentioned studies, no significant difference was found between the cervical sagittal parameters and patient groups in line with our results.

Craniovertebral angle (CVA) was demonstrated to be reduced by tilting the head forward in pediatric patients with CEH in a previously published study. This change in cervical posture was not observed in the asymptomatic group (9). There is a study in the literature showing a decrease in CVA in patients with adult CEH (10), whereas no association was found between headache and cervical alignment in the remaining studies performed (11-13). However, cervical alignment was not evaluated by lateral cervical radiography in any of the studies published. Lateral cervical radiography and lordosis was measured in a single study by the Cobb method similar to our study by Farmer et al (3); similar to the results of this present study, no difference was found between the CEH and the control groups in terms of cervical lordosis. The reason for the similarity in the radiologic evaluation between the CEH and neck pain groups in this present study might be the method of evaluation of symptoms of short and long duration together without discriminating them. Inclusion of patients with chronic and/or subchronic disease might have led to changes in the spinal alignment.

Magnetic resonance imaging (MRI) is another imaging method examining posture in patients with CEH. No significant difference was observed between the groups in a study evaluating the changes in intensity of the craniovertebral and cervical junction, and transverse and alar ligaments by MRI in patients with CEH, whiplash associated injuries, and migraine (1). The reason of this condition might be the frequent finding of the structural changes in alar ligaments and upper joints in asymptomatic patients (14). In a study investigating CVA and cervicomedullary angle (CMA) by MRI, pain and CVA and CMA values were found to decrease in the CEH group compared with the control group, and a negative correlation with pain and CVA and CMA values was determined (4). The trigeminal pain was suggested to be rarely associated with cervical disorders, although an association between CEH and neck posture has been demonstrated (15). In addition, Fukui et al (16) showed that trigeminal region was not included in the pain spread pattern of the zygapophysial joints between C2/3

and C7/Th1. C2/3 and C3 was reported to cause pain in the occipital region with no pain in the forehead (16). C2/3 zygapophysial joint was accepted as the source of pain by Bogduk (17). These studies have demonstrated that it is unclear whether anatomic changes in the neck or any misalignments are the source of CEH. However, conservative treatments, especially exercise programs with or without manual therapy, are important for treatment (17,18).

There are many studies investigating cervical lordosis in patients with neck pain (8,19-21). Contradictory results were found in these studies examining cervical lordosis and pain. Grob et al (19) found no difference in cervical lordosis between groups of patients with neck pain and control, whereas Harrison et al (20) found a reduction in cervical lordosis in patients with neck pain. In another study, cervical muscle imbalance was associated with extensor muscle weakness and decreased cervical lordosis. In that study, muscle strength of the patients was observed to be decreased as cervical lordosis was decreased (21). In that retrospective study, cervical lordosis and muscle strength were examined in patients with neck pain only, without the evaluation of the severity of pain.

Jouibari et al (8) found no difference in lordosis when comparing patients with neck pain and asymptomatic patients. Only the T1 slope angle was found to be decreased in the patient group and was described to be an improved compensation mechanism to maintain the center of gravity of the head in the spinal region (8). No association was found in the severity of pain and disability score in cervical lordosis among patients with neck pain in that study evaluating pain, disability, and cervical lordosis. A study in normal population showed that UCL was associated with the subaxial cervical Cobb angle (22). When the correlations between pain and radiologic measurements were examined, a positive correlation between UCL and GCL angles was found in the neck pain group but not in the CEH group. The reason for this may be the disruption of the compensation mechanism between the upper cervical ligament, muscle and/or misalignment, and the subaxial cervical spine in the CEH group. However, the neck pain group was able to compensate by pulling the center of gravity of the head back to relax the paraspinal muscles and facilitate the head in an upright position.

There are several limitations to be mentioned in the study. First, diagnostic anesthetic blockade, the major criterion of CHISG, was not included as exclusion criteria for the CEH group. The reason for not including anesthetic blockage is to prevent complications of an invasive intervention and to avoid confusion in the diagnosis because injection might result resolution of trigger points and neck pain. This criterion was not included in previous studies investigating CEH either (3). Second, there were no male patients in the study group; the inclusion of both genders would reveal gender-related differences in the evaluation of cervical spinal curvature radiographs (23). Although there is no significant difference between the 2 genders in GCL, the UCL in men is shown to be smaller and the lower cervical lordosis is higher than in women (24). As a consequence, our results cannot be generalized to the male population with CEH. Also, psychological conditions that may affect head and neck pain and spinal alignment were not questioned. In addition, not all spinal locations that may affect cervical alignment have been examined. A possible thoracic, lumbar, or pelvic misalignment may lead to differences in GCL or UCL values (22). However, it is the main powerful aspect of this present study that it is one of the few studies investigating the relationship between spinal alignment and CEH in the literature. In addition, performing radiographic measurements via a professional computer program has led to more objective results, as can be understood from high interrater reliability values.

Conclusions

Focusing on only one structural change in the cervical spine may not be an appropriate diagnostic method for detecting possible pathological findings in patients with CEH. Finding the source of CEH is still vital to detect and treat the main pathology. Pain mechanisms need to be elucidated by detailed analysis of the whole spinal alignment using different methods investigating ligament, muscle, and spinal changes in the upper cervical region in this patient group.

Acknowledgments

The authors would like to thank all the participants in this study.

References

1. Knackstedt H, Krakenes J, Bansevicius D, et al. Magnetic resonance imaging of craniovertebral structures: Clinical significance in cervicogenic headaches. *J Headache Pain* 2012; 13:39-44.
2. Dunning JR, Butts R, Mourad F, et al. Upper cervical and upper thoracic manipulation versus mobilization and exercise in patients with cervicogenic headache: A multi-center randomized clinical trial. *BMC Musculoskelet Disord* 2016; 17:64.
3. Farmer PK, Snodgrass SJ, Buxton AJ, et al. An investigation of cervical spinal posture in cervicogenic headache. *Phys Ther* 2015; 95:212-222.
4. Coban G, Coven I, Cifci BE, et al. The importance of craniovertebral and cervicomedullary angles in cervicogenic headache. *Diagn Interv Radiol* 2014; 20:172-177.
5. Sillevis R, Swanick K. Musculoskeletal ultrasound imaging and clinical reasoning in the management of a patient with cervicogenic headache: A case report. *Physiother Theory Pract* 2019; 1-11.
6. Guzman J, Hurwitz EL, Carroll LJ, et al. A new conceptual model of neck pain: Linking onset, course, and care: The Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *J Manipulative Physiol Ther* 2009; 32:S17-S28.
7. Kesiktas N, Ozcan E, Vernon H. Clinimetric properties of the Turkish translation of a modified neck disability index. *BMC Musculoskeletal Disord* 2012; 13:25.
8. Jouibari MF, Le Huec JC, Ranjbar Hameghavandi MH, et al. Comparison of cervical sagittal parameters among patients with neck pain and healthy controls: A comparative cross-sectional study. *Eur Spine J* 2019; 28:2319-2324.
9. Budelmann K, von Piekartz H, Hall T. Is there a difference in head posture and cervical spine movement in children with and without pediatric headache? *Eur J Pediatr* 2013; 172:1349-1356.
10. Watson DH, Trott PH. Cervical headache: An investigation of natural head posture and upper cervical flexor muscle performance. *Cephalalgia* 1993; 13:272-284; discussion 232.
11. Dumas JP, Arsenault AB, Boudreau G, et al. Physical impairments in cervicogenic headache: Traumatic vs. nontraumatic onset. *Cephalalgia* 2001; 21:884-893.
12. Weber Hellstenius SA. Recurrent neck pain and headaches in preadolescents associated with mechanical dysfunction of the cervical spine: A cross-sectional observational study with 131 students. *J Manipulative Physiol Ther* 2009; 32:625-634.
13. Zito G, Jull G, Story I. Clinical tests of musculoskeletal dysfunction in the diagnosis of cervicogenic headache. *Man Ther* 2006; 11:118-129.
14. Pfirrmann CW, Binkert CA, Zanetti M, et al. MR morphology of alar ligaments and occipitoatlantoaxial joints: Study in 50 asymptomatic subjects. *Radiology* 2001; 218:133-137.
15. Vincent MB. Cervicogenic headache: The neck is a generator: Con. *Headache* 2010; 50:706-709.
16. Fukui S, Ohseto K, Shiotani M, et al. Referred pain distribution of the cervical zygapophyseal joints and cervical dorsal rami. *Pain* 1996; 68:79-83.
17. Bogduk N. The neck and headaches. *Neurol Clin* 2014; 32:471-487.
18. Park SK, Yang DJ, Kim JH, et al. Effects of cervical stretching and cranio-cervical flexion exercises on cervical muscle characteristics and posture of patients with cervicogenic headache. *J Phys Ther Sci* 2017; 29:1836-1840.
19. Grob D, Frauenfelder H, Mannion AF. The association between cervical spine curvature and neck pain. *Eur Spine J* 2007; 16:669-678.
20. Harrison DD, Harrison DE, Janik TJ, et al. Modeling of the sagittal cervical spine as a method to discriminate hypolordosis: Results of elliptical and circular modeling in 72 asymptomatic subjects, 52 acute neck pain subjects, and 70 chronic neck pain subjects. *Spine* 2004; 29:2485-2492.
21. Yoon SY, Moon HI, Lee SC, et al. Association between cervical lordotic curvature and cervical muscle cross-sectional area in patients with loss of cervical lordosis. *Clin Anat* 2018; 31:710-715.
22. Passias PG, Alas H, Lafage R, et al. Global spinal deformity from the upper cervical perspective. What is "abnormal" in the upper cervical spine? *J Craniovertebr Junction Spine* 2019; 10:152-159.
23. Guo GM, Li J, Diao QX, et al. Cervical lordosis in asymptomatic individuals: A meta-analysis. *J Orthop Surg Res* 2018; 13:147.
24. Been E, Shefi S, Soudack M. Cervical lordosis: The effect of age and gender. *Spine J* 2017; 17:880-888.