Cervicogenic headache: Pathophysiology, diagnostic criteria and treatment

Nurten İnan*, Yeşim Ateş**

SUMMARY
Cervicogenic headache is a relatively common and still controversial form of headache arising from structures in the neck. Cervicogenic headache is a unilateral fixed headache characterised by pain that starts in the neck and spreads to the ipsilateral oculo-fronto-temporal area. The pathophysiology of cervicogenic headache probably depends on the effects of various local pain-producing or eliciting factors, such as intervertebral dysfunction, cytokines and nitric oxide. A reliable diagnosis of cervicogenic headache can be made based on the criteria established in 1998 by the Cervicogenic Headache International Study Group or the International Headache Society's most recent International Classification of Headache Disorders (2004). Various therapies have been used in the management of cervicogenic headache. These range from lowly invasive, drug-based therapies to highly invasive, surgical-based therapies. Unfortunately, the paucity of experimental models for cervicogenic headache and the relative lack of biomolecular markers for the condition mean much is still unclear about cervicogenic headache and the disorder remains inadequately treated.

Key words: Cervicogenic headache, headache

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Introduction

The term of cervicogenic headache (CEH) has been first introduced by Sjaastad et al. in 1983. In this time headache syndrome has been described, indicating that the pain is believed to originate from the neck (Sjaastad et al. 1998a, 1983). The estimated prevalence of the disorder varies considerably ranging from 0.7 % to 13.8 % (Martelletti and van Suijlekom 2004).

The pathophysiological model for this kind of referred head pain, described by Kerr, has been used to explain the pain in CEH (Bovim 1993, Kerr 1961, Kerr and Olafsen 1961). Pain generated in any location within the trigemino-cervical territory can be referred to the frontal region via the trigemino-cervical nucleus (Taren and Kahn 1962, Kerr 1961). It has also been shown that, GON (greater occipital nerve) stimulation causes an increased neuronal activity in both the cervical and trigeminal neuronal systems (Bartsch and Goadsby 2002, Goadsby et al. 1997).

Neuroanatomical Basis and Pathophysiology of CEH

The neuroanatomical basis for CEH is the “trigemino-cervical nucleus” in the spinal grey matter of the spinal cord at the C1-C3 level, where there is a convergence on the nociceptive second order neurons receiving both trigeminal and cervical input. C1 spinal nerve has some ectopic sensory ganglia and it innervates the short muscles of the suboccipital triangle (Bogduk 1982). The C2 spinal nerve gives sensory supply to the median and lateral atlantoaxial joints; to several neck muscles (prevertebral, sternocleidomastoid, trapezius, semispinalis and splenius muscles); to the dura of the posterior cranial fossa and the upper spinal canal. Both the C2 and C3 spinal nerves supply the zygapophyseal joints and discs of the adjacent segments. The atlantoaxial ligaments and the dura mater of the spinal canal are innervated by the sinuvertebral nerves stemming from the C1-C3 spinal nerves. The origin is sympathetic, the nerves contain nociceptive, proprioceptive, vaso-motor and vaso-sensory fibers (Mendel 1992).

The intervertebral discs at the C2-C3 and C3-C4 levels have been the target of neurosurgical treatment of CEH (radiofrequency lesions of the discs, cervical discectomy and fusion). Several cervical structures, such as cervical muscles and their attachments to the bone; as well as the capsule of the intervertebral joints and discs, ligaments, nerves and nerve roots are thought to be pain generating candidates in CEH (Pöllman et al. 1997, Jansen et al. 1989). Nociceptive stimuli from these structures are primarily mediated by the upper three spinal nerves. The greater occipital (GON), the lesser or minor occipital (LON), the third occipital nerve and possibly the greater auricular nerve have been implicated in CEH (Pöllman 1997).

Nerve-Vessel compression on the C2 root, where the ventral ramus crosses the upper cervical segment of the vertebral artery, was hypothesized as a cause for CEH (Lucas 1994). Osseous compression of the nerves was not supported by radiological studies in CEH patients, or in morphological studies, but a potentially compressive venous plexus surrounding the C2 root and ganglion has been observed during microsurgical decompression (Pikus 1995).

The morphological evidence for compression of the upper cervical roots as a cause of CEH is only indirect, but the applied methods are too crude to exclude its presence (Andersen 2003).

Sensory Thresholds in CEH

A possible peripheral dysfunction in the C2-C3 region was observed ipsilateral to the headache side in CEH patients. These findings suggest a possible ipsilateral C2-C3 nerve or nerve root involvement in CEH, and possible secondary central somatosensory dysfunction in CEH (Sjaastad et al. 1998b, Sjaastad 1990).

The Role of Muscle in the Pathophysiology of CEH

The role of musculoskeletal system in the pathophysiology of CEH has been discussed in many studies (Andersen et al. 2003, Bansevicius et al. 1999). Electromyographic (EMG) activity recorded over trapezius with surface electrodes was significantly higher on the symptomatic side compared to the non-symptomatic side before and during a mental stress test in CEH patients. Side differences in EMG activity could not be registered in the temporal muscles, although pain was significantly more severe on the symptomatic side. This can be explained by a referred pain mechanism in the temporal region and a more direct involvement of the shoulder and neck muscles in CEH. It is not known whether the difference in trapezius EMG response between the symptomatic and non-symptomatic side in CEH patients contributes to the pathogenesis of CEH.
or if it is a secondary phenomena (Andersen et al. 2003).

**Skin and Connective Tissue Changes in CEH**

Skin-fold tenderness and thickness have also been measured in CEH, tension type headache and migraine without aura. Significant asymmetry in skin-fold tenderness was found only in the CEH group and side difference was limited to the trapezius region. The authors concluded that such measures are of supportive value in some CEH cases, although they were not a reliable diagnostic test (Bansevicius and Pareja 1998).

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**Tenderness and Pressure Pain Threshold (PPT) Studies**

Bovim found lower PPT in CEH compared to migraine, tension-type headache (TTH) and control groups (Bovim 1992). The lowest PPT was measured in the occipital region and on the symptomatic side in CEH patients. No statistically significant difference was found between migraine, TTH and control groups (Bovim 1992). According to these results the pathophysiology of CEH is different from migraine, cluster and tension-type headache.

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**Table 1:** Cervicogenic headache diagnostic criteria (Sjaastad et al. 1998b).

**Major Criteria**

I. Symptoms and signs of neck involvement; it is obligatory that one or more of the phenomena 1a to 1c are present.
   Ia) Precipitation of head pain, similar to the usually occurring one:
      Ia1) By neck movement and/or sustained, awkward head positioning, and/or:
      Ia2) 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 anesthetic blockages.

III Unilaterality of the head pain, without sideshift.

**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 indomethacin
   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 photo-phobia
   c) Dizziness
   d) Ipsilateral 'blurred vision'
   e) Difficulties on swallowing
   f) Ipsilateral edema, mostly in the periocular area
Diagnostic Criteria

International Headache Society and International Cervicogenic Headache Study Group have both developed different classification systems for the diagnosis of CEH. There are some slight differences between them however one can realize similar main points. They are both used and referred frequently.

Revised diagnostic criteria of the International Cervicogenic Headache Study Group are shown in Tables 1 and 2 (Sjaastad et al. 1998b).

According to the International Headache Society's most recent International Classification of Headache Disorders (2004) the diagnostic criteria of CEH are as follows (Göbel et al. 2004):

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:
   1. Demonstration of clinical signs that implicate a source of pain in the neck.
   2. 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.

According these criterias;

1. Tumors, fractures, infections and rheumatoid arthritis of the upper cervical spine have not been validated formally as causes of headache, but are nevertheless accepted as valid causes when demonstrated to be so in individual cases. Cervical spondylosis and osteochondritis are not accepted as valid causes fulfilling, criteria B. When myofascial tender spots are the cause, the headache should be coded under 2. Tension-type headache.

2. Clinical signs acceptable for criterion C1 must have demonstrated reliability and validity. The future task is the identification of such reliable and valid operational tests. Clinical features such as neck pain, focal neck tenderness, history of neck trauma, mechanical exacerbation of pain, unilaterality, coexisting shoulder pain, reduced range of motion in the neck, nuchal (pertaining to the back of the neck) onset, nausea, vomiting, photophobia, etc. are not unique to cervicogenic headache, but they do not define the relationship between the disorder and the source of the headache.

3. Abolition of headache means complete relief of headache, indicated by a score of zero on a visual analogue scale (VAS). Nevertheless, acceptable as fulfilling criterion C2 is >90% reduction in pain to a level of <5 on a 100-point VAS.

Treatment

Conservative treatment in CEH includes several modalities:

A) Non invasive methods:
   1) Pharmacological treatment
   2) Physiotherapy
   3) Transcutaneous electrical nerve stimulation

B) Invasive methods:
   1) Therapeutic local anaesthetic blocks of the GON

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<th>Table 2: Cervicogenic headache minimum requirements for the diagnosis (Sjaastad et al. 1998b).</th>
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| Definite CEH
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| 2. Positive anesthetic blockage effect
| 3. Unilaterality without side-shift
| Provisional CEH
| 1. Reduced range of neck motion
| 2. Ipsilateral shoulder/arm pain
| 3. Positive anesthetic blockage effect
| 4. Unilaterality without side-shift |

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2) Local anesthetic and Botulinum toxin type A injections
3) Transforaminal and epidural steroid injections
4) Treatment of CEH by means of radiofrequency procedures
5) Dorsal column stimulation
6) Other treatment alternatives
7) Surgery

**Pharmacological Treatment**

CEH patients often use non-steroidal anti inflammatory drugs (NSAIDs). There are no convincing clinical studies to determine the efficacy of these drugs. Morphine-like drugs have only a marginal effect and are generally not recommended for CEH patients. Ergotamine or oxygen inhalation is not effective in CEH (Bovim and Sjaastad 1993). The new 5HT1D agonists generally seem to be ineffective, but this needs to be established scientifically in CEH. Indomethacin treatment may be given to exclude hemicrania continua.

**Physiotherapy**

Physiotherapy has the enormous advantage of being 'universally' available. Moreover, such therapy is innocuous. Physiotherapy will, therefore, in many settings be an initial therapy in many headache forms including CEH (Jay et al. 1989). The treatment modalities will necessarily vary, according to experience, and may also include traction and mobilization.

Any beneficial effect of physiotherapy largely unsubstantiated, but, nevertheless one can give it a try, since good treatment alternatives are few and far between in the early stages of the disorder. Manual therapy has also been given to patients with a possible CEH diagnosis. A demand must be that MRI imaging has been carried out prior to treatment and that particular cautiousness is exercised (Inan and Inan 2003).

**Transcutaneous Electrical Nerve Stimulation (TENS)**

The introduction of the gate control concept by Melzack in 1965 has facilitated the development of afferent stimulation techniques for alleviation of pain, such as TENS. Electrical stimulation for pain in this area was first used by Shealy as Dorsal Column Stimulation, according to Wall and Melzack's Gate Control Theory (Shealy et al. 1967). Later, the technique has been modified, and the transcutaneous electrical stimulator is nowadays commonly used for pain relief. The duration of pulses and frequencies can be adjusted, and it is possible to stimulate different type fibers by chosen stimulation parameters. It is possible to stimulate selectively Aα, b and g fibers carrying touch and position sensation, and it is possible to block pain at the spinal level, or to stimulate Aδ and C fibers carrying pain and it blocks the pain in upper level (Tarhan et al. 1999).

The application of TENS as a pain-relieving method has been used in several types of headache by several authors. Farina et al. applied TENS therapy in 10 patients with CEH, 15 patients with occipital neuralgia, and 35 patients with mixed headache (Farina et al. 1986). Assessment was performed before and after the treatment. This study demonstrated that TENS was effective in 70-80% of the patients in all three groups. A randomized, clinical trial in patients with CEH was performed by Tarhan and Inan (Tarhan 1999). Pain severity was assessed by VAS and headache frequency during the study was recorded. They found significant improvement in the treatment group during the 1st, 2nd, and 3rd months after the treatment, when compared to placebo.

In this study, the daily treatment session lasted 30 minutes, and the total number of sessions was ten. Current frequency was 100 Hz, and the wave duration was 50 ms. the power was adjusted to cause a tingling sensation. The stimulator was placed in the paravertebral, suboccipital region bilaterally.

**Local Anesthetic and Botulinum Toxin Type A Injections**

Local anesthetics have been used as intramuscular injection for the treatment of CEH. Medical and injection therapies in acute and chronic mechanical neck disorders have been recently reviewed in a Cochrane database systematic review (Peloso et al. 2005). At short-term follow-up, intramuscular injection of lidocaine was found superior to placebo or dry needling, but similar to ultrasound. However in chronic mechanical neck disorders with radicular findings, epidural methylprednisolone and lidocaine reduced neck pain and improved function at one-year follow-up compared to the intramuscular route.
Botulinum toxin inhibits the release of the neurotransmitter acetylcholine at the neuromuscular junction thereby inhibiting striatal muscle contractions. Besides the reduction in muscle tone, Botulinum toxin type A tends to reduce pain in pain syndromes associated with muscle spasm. In addition, Botulinum toxin type A has been proposed as an analgesic, suggesting alternative non-cholinergic mechanisms of action (Sycha 2004). Although there is no agreement on the dose and site of administration of Botulinum toxin type A injections for the treatment of CEH, it was found promising by many authors (Sycha et al. 2004, Haldeman and Dagerais 2001).

In a recent review on the effect of medical and injection therapies participants with chronic mechanical neck disorders with or without radicular findings or headache, there was moderate evidence from five high quality trials showing that Botox A intramuscular injections were not better than saline in improving pain (Peloso et al. 2005).

**Therapeutic Local Anesthetic Blocks of the Greater Occipital Nerve (GON)**

GON blocks are frequently used in the diagnosis of CEH. Injections with a local anesthetic agent in the vicinity of the GON are also used as therapy. In a subgroup of patients with CEH, Vincent demonstrated a significant relief of headache complaints during a seven-day period after infiltration around the GON with bupivacaine 0.5 / 1-2 ml (Vincent 1998). Anthony suggests that the results of repeated local injections of an anesthetic agent around the GON may be more effective by combining it with local corticosteroids. In another study, repeated blocks proved to have a long-lasting effect in the treatment of this disorder; GON and C2/C3 blocks were found to be equally effective (Inan et al. 2001).

**Transforaminal and Epidural Steroid Injections**

Epidural corticosteroid injections are indicated if MRI reveals spinal stenosis of the central or lateral canal, or a disc herniation. Steroidshave anti-inflammatory effects and direct analgesic effects on theC fibers. Theyalsoallow a decrease in drug consumption. If the epidural provides good relief, the patient can be referred for more aggressive physical therapy and epidural injections may be repeated as needed up to a maximum of three times (Feng and Schofferman 2003). Transforaminal epidural steroid injections have also been used for the treatment of CEH. Since each method of treatment has an associated level of risk, these injections should also be used when indicated and with adequate care. Death of a patient has been reported due to perforation of a vertebral artery during transforaminal epidural steroid nerve root block (C7) (Rozin et al. 2003).

**Treatment of CEH by Means of Radiofrequency Procedures**

Pulsed radiofrequency is not a neuroablative procedure, it is neuromodulatory in nature and has not produced side effects. These advantages make it an excellent option for the treatment of referred pain involving the medial branches of the C1 and C2 dorsal rami (Racz et al. 2001). If there is excellent relief from the medial branch block and joint injections, they may be repeated when the steroids wear off. If there is good relief again, but pain recurs, medial branch radiofrequency neurotomy is recommended (Feng and Schofferman 2003). Neural blockade at the atlantooccipital and atlantoaxial joints is a very technically demanding technique and should be performed only in skilled hands.

Radiofrequency denervation of the medial branch nerves may also be performed in patients with CEH arising from the facet joints of the cervical vertebra. When pain relief following double diagnostic blocks was used an indication to radiofrequency denervation of cervical facet joints a median duration of pain relief for 422 days have been reported (Van Suijlekom 1998). However in a more recent study efficacy of radiofrequency denervation of facet joints ipsilateral to the CEH C2-C6 have been evaluated in a randomized, double-blind, sham-controlled study with no significant difference between the study and treatment groups after a three months period (Stovner et al. 2004).

**Dorsal Column Stimulation in CEH Treatment**

In this technique the needle is introduced with a midline dorsal incision, approximately 2-3 cm down to the fascia, at one of the upper thoracic segments. The electrode is brought into the epidural space with a modified loss of resistance technique. The electrode is then manipulated upwards as far as the C1-C2 level under fluoroscopic guidance. In the ideal case, on test stimulation, the patient should experience a tingling sensation in the area where the headache is felt. One prob-
lem with this technique has been to place the electrode as far cranially as one would like to have it, and thereby obtaining a tingling sensation in the whole pain area. After a successful test period of up to two weeks, a permanent pulse generator is placed in a subcutaneous pocket. The electrode can also be placed directly at the C2 level through an operation with cases where it was impossible to position the electrode in the correct position with the percutaneous technique (Fredrisen 2003).

**Surgical Procedures in CEH Treatment**

Operative procedures like ganglionectomy, ventral decompressive operation and fusioning, and dorsal decompressive laminectomy and laminoplasty are used in CEH patients.

Ganglionectomy was found to be helpful for CEH patients, with attacks triggered by vascular irritation or compression of upper nerve roots, especially the C2-root.

One or two segmental decompressive operations were performed on CEH patients with particularly strong and protracted headache.

In patients with severe CEH combined with more than two segmental cervical spinal stenosis, dorsal decompression was indicated. It was usually performed from the lamina C2 to C6 or C7 (Jansen 2003).

**Conclusion**

CEH is not merely a symptom; it is a rather complex syndrome. Correct diagnosis requires utilization of the diagnostic criteria mentioned in the text that have been recently developed by the International Cervicogenic Headache Study Group and further accepted and included in the classification of the International Headache Society. Most favorable treatment approach to CEH is carried out stepwise starting from non-invasive methods mentioned herein and advancing towards more invasive techniques until an optimal response is achieved. However repeated use of almost all of the treatment techniques may be required.

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