Cervicogenic Headache

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Key Points

- The initial assessment of the headache patient should be focused on ruling out a secondary cause.
- The diagnosis of cervicogenic headache is made based on specific criteria that rely on evidence of causation as well as diagnostic blockade.
- The pathophysiology of cervicogenic headache likely involves cervical nociceptive stimulation relayed via the trigeminocervical complex.
- Noninterventional treatments for cervicogenic headache, including pharmacotherapy and exercise techniques, are supported by limited substantive evidence.
- Interventional treatments for cervicogenic headache include trigger point injections, occipital nerve blockade, medial branch blockade, and radiofrequency ablation.

Introduction

Spine specialists will encounter patients with headache and must be prepared to deliver an adequate evaluation. Cervicogenic headache, while less common than migraine and tension-type headache, is not uncommon with a 1-year prevalence of about 4.1%. It is especially common following whiplash injury. Patients should be examined for underlying myofascial pain, facetogenic pain, and occipital neuralgia. Pharmacotherapy is generally extrapolated from treatments for tension-type headache and myofascial pain. Common interventional treatments for cervicogenic headache include trigger point injections, occipital nerve blocks, and medial branch radiofrequency ablation. One particularly common pain generator in cervicogenic headache is the C2/C3 facet joint, which can be treated with third occipital nerve radiofrequency ablation. In this chapter we explore these forms of treatment and additionally discuss evidence about botulinum toxin and neuromodulation.

Approach to the Patient with Headache

Headache is ubiquitous and has a broad range of etiologies, from benign to life-threatening. The first step in approaching a headache patient is determining whether the headache is secondary to an underlying disease or whether it is a primary headache such as migraine, tension-type headache, or cluster headache. This is ascertained by taking a thorough history and performing a neurologic exam while being aware of potential alarming "red flag" signs and symptoms warranting further diagnostic workup [1].

An adequate headache history focuses on headache onset, characteristics [location, quality, and intensity], duration, frequency, and associated features [1]. Associated features can include migrainous features [photophobia, phonophobia, nausea, vomiting, and visual aura] and autonomic features. Patients may describe both headache triggers and relieving factors such as emotional stress and relaxation techniques, respectively [2].

A detailed physical and neurologic examination is important to detect any alarming signs although the majority of headache patients will present with a normal exam. Abnormalities in vital signs raise concern for a secondary headache such as fever in meningitis or elevated blood pressure in hypertensive encephalopathy. With that being said, a patient may present with hypertension and tachycardia as a result of pain. Body habitus may be a clue toward diagnosis; obesity is a known risk factor for migraine and idiopathic

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intracranial hypertension, while tall and thin features may point toward a connective tissue disorder such as Marfan syndrome which may be a risk factor for spontaneous intracranial hypotension. The presence of a bruit on auscultation of the carotid or vertebral artery can signify the presence of a dissection. Palpable superficial temporal artery tenderness is likely to be present in temporal arteritis, wherein cervical tenderness and decreased range of motion are described in cervicogenic headache. Papilledema on funduscopic exam and cranial nerve palsies may reflect increased intracranial pressure [2]. The remainder of the neurologic assessment consists of mental status, cranial nerves, motor (bulk, tone, strength,), reflexes, coordination, sensation (pain and temperature, vibration and position), and gait exams; derangements in any of these capacities may indicate a lesion somewhere along either the central or peripheral nervous system.

There are four categories of primary headache as per the International Classification of Headache Disorders (ICHD), version 3: migraine, tension-type headache, trigeminal autonomic cephalalgias (TAC), and other uncommon primary headache disorders [3].

Secondary headache is initially considered or excluded in the differential diagnosis based on alarming symptoms in the history or signs on neurologic exam. The following mnemonic, *SNOOP4*, is a useful tool for making this distinction:

Systemic symptoms, signs, and secondary causes
- Fever, chills, myalgias, and night sweats
- Nuchal rigidity, rash, and weight loss
- Immunocompromised state/infection (i.e., HIV), inflammatory disease (i.e., giant cell arteritis), and malignancy

Neurologic symptoms and signs
- Altered mental state, diplopia, loss of consciousness, tinnitus, and visual loss (i.e., IIH)

Onset sudden
- Arterial dissection, cerebral venous sinus thrombosis, reversible cerebral vasoconstriction syndrome, and subarachnoid hemorrhage

Onset older than 50 years
- Infection, inflammatory disease (i.e., giant cell arteritis), and malignancy

Pattern change
- Progressive headache
- Precipitated by Valsalva maneuver (i.e., Chiari malformation)
- Position (i.e., intracranial hypo-/hypertension, neck movements associated with cervicogenic headache)
- Papilledema [4]

Cervicogenic headache has been defined based on two separate, but similar, sets of criteria. In 1998 the Cervicogenic Headache International Study Group put forth the following major criteria:

I. Symptoms and signs of neck involvement:
   (a) Precipitation of head pain, similar to the usually occurring one:
      1. By neck movement and/or sustained awkward head positioning
      2. By external pressure over the upper cervical or occipital region on the symptomatic side
   (b) Restriction of the 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.

II. Confirmatory evidence by diagnostic anesthetic blockades

III. Unilaterality of the head pain, without sideshift [5]

As per the International Classification of Headache Disorders, 3rd edition, the diagnosis of cervicogenic headache can be made according to the following:

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 [3]

Epidemiology of Cervicogenic Headache

The best epidemiological evidence with regard to the prevalence of cervicogenic headache comes from the Vågå study. In this cross-sectional study performed by Sjaastad in 2007, 1838 Norwegian inhabitants of the commune of Vågå were interviewed to establish prevalence data for cervicogenic headache. Of this group, 75 individuals (4.1%)

met the Cervicogenic Headache International Study Group criteria. Forty-one of these participants (2.2%) had exclusively met cervicogenic headache criteria without meeting criteria for another headache disorder as well (termed "core cases"). The remaining 34 (1.8%) composed the "extra" headache group; 23 had migraine without aura, 16 had migraine with aura, and 9 had tension-type headache. Migrainous features in this cohort included nausea and vomiting, photophobia and phonophobia, pulsatile quality, and exacerbation with exercise. Autonomic features were rare and consisted of lacrimation; conjunctival injection and nasal secretion were not reported. While duration and frequency varied greatly, 61% of cervicogenic headache events exceeded 72 hours, and attacks occurred at a mode of 1 per 2–4 weeks. The headache was continuous in 54% of these patients [6].

There was a male predominance (female/male ratio of 0.71) among the 41 subjects with pure cervicogenic headache and a slight female predominance (female/male ratio 1.06) among the entire cohort. In comparison, migraine has a 1-year prevalence of about 12% with a female-to-male ratio of 3:1. In this study the mean age of onset of cervicogenic headache was 32.7 years; migraine age of onset is usually during the teenage years or twenties [6, 7].

In another study, 21.4% of those with cervical spine disease necessitating surgery were found to suffer from cervicogenic headache [8]. Over 50% of patients with whiplash injuries may experience cervicogenic headache [9].

Pathophysiology of Cervicogenic Headache

The anatomy involved in other headache disorders including migraine is likely also involved in the pathogenesis of cervicogenic headache. The trigeminocervical complex contains second-order neurons that receive afferent stimulation from both the meninges and upper cervical roots. Central sensitization of this complex can result from excessive dural stimulation, in the case of migraine, and in turn render hypersensitivity to cervical afferents. Both dural-based and cervical nociceptive sensitization may yield a self-perpetuating circuit wherein neck pain and headache can trigger one another [10]. It is postulated that this pathway is complicit in cervical hyperesthesia that is frequently comorbid with migraine headache [11]. Possible pain-generating structures that can contribute to cervicogenic headache include soft tissues, bones, facets, nucleus pulposus, adjacent neural structures such as the greater occipital nerves (GON) and lesser occipital nerves (LON), cervical nerve roots, and more. Episodic neck pain and cutaneous allodynia can also be symptoms of migraine, potentially mimicking cervicogenic headache [11, 12].

Noninterventional Treatments for Cervicogenic Headache

There is a large and diverse pharmacologic armamentarium for headache treatment, which varies based on headache type. Tables 15.1, 15.2, 15.3, and 15.4 present a series of examples delineated by diagnosis and drug class of both acute management and preventative therapy.

While NSAIDs, antidepressants, antiepileptics, and muscle relaxants are commonly prescribed, there is no substantial

Table 15.1 Acute therapy for migraine [13]

Drug	Class
Acetaminophen	NSAID (nonsteroidal anti-inflammatory drug)
Almotriptan	$5HT_{1B/D}$-agonist
Aspirin	NSAID
Chlorpromazine	Antiemetic
Diclofenac	NSAID
Dihydroergotamine	Ergot alkaloid
Domperidone	Antiemetic
Eletriptan	$5HT_{1B/D}$-agonist
Ergotamine	Ergot alkaloid
Frovatriptan	$5HT_{1B/D}$-agonist
Ibuprofen	NSAID
Metoclopramide	Antiemetic
Metamizol	NSAID
Naproxen	NSAID
Naratriptan	$5HT_{1B/D}$-agonist
Prochlorperazine	Antiemetic
Rizatriptan	$5HT_{1B/D}$-agonist
Sumatriptan	$5HT_{1B/D}$-agonist
Zolmitriptan	$5HT_{1B/D}$-agonist

Table 15.2 Preventative therapy for migraine [14]

Drug	Class
Amitriptyline	Antidepressant
Atenolol	Beta blocker
Candesartan	Angiotensin receptor blocker (ARB)
Coenzyme Q10	Other
Divalproex sodium	Anticonvulsant
Feverfew	Other
Fluoxetine	Antidepressant
Frovatriptan	Triptan
Gabapentin	Anticonvulsant
Lisinopril	Angiotensin-converting enzyme (ACE) inhibitor
Methysergide	Serotonin antagonist
Metoprolol	Beta blocker
Nortriptyline	Antidepressant
Nadolol	Beta blocker
Onabotulinumtoxin A	Neurotoxin
Petasites	Other
Riboflavin	Other
Timolol	Beta blocker
Topiramate	Anticonvulsant
Venlafaxine	Antidepressant

Table 15.3 Acute therapy for tension-type headache [15]

Drug	Class
Acetaminophen	NSAID
Aspirin	NSAID
Caffeine	Other
Ibuprofen	NSAID
Ketoprofen	NSAID
Naproxen sodium	NSAID

Table 15.4 Preventative therapy for tension-type headache [15]

Drug	Class
Amitriptyline	Antidepressant
Mirtazapine	Antidepressant
Tizanidine	Muscle relaxant
Venlafaxine	Antidepressant

evidence supporting the use of oral pharmacotherapy for cervicogenic headache [16, 17].

Trials on exercise techniques for neck pain, including cervicogenic headache, were appraised in a Cochrane Review published in 2015. This review classified the evidence supporting the use of craniovertebral stretch and range of motion exercises as low quality. Additionally, evidence of static and dynamic cervical strengthening and endurance exercises including pressure biofeedback was considered moderate quality [18].

Interventional Treatments for Cervicogenic Headache

Myofascial Pain

Myofascial pain affects millions of Americans and results from excessively shortened or contracted muscle whose focus is localizable to a trigger point. Trigger points are small firm nodules that elicit radiating soft tissue pain on palpation. While this syndrome may result from trauma, strain, deconditioning, or posture, the exact pathogenesis of trigger points is uncertain [19, 20].

Trigger point injections (TPIs) are commonly used therapies which involve needling and may include injecting a medication into the trigger point (Figs. 15.1, 15.2 and 15.3). The most common TPI injectate is composed of local anesthetics, but some practitioners also include corticosteroids [21]. To date there is no clear evidence demonstrating the efficacy of standardized TPIs as a form of monotherapy for myofascial pain [21]. Likewise for the treatment of headache, there is heterogeneity of both pharmacotherapy and technique with a paucity of randomized controlled trials (RCT) [22].

The most commonly chosen TPI location for headache is the trapezius, whose pain is typically referred in an ipsilateral and hemicranial distribution [22, 23]. The trapezius, splenius, and semispinalis capitis as well as cervicum all compose the

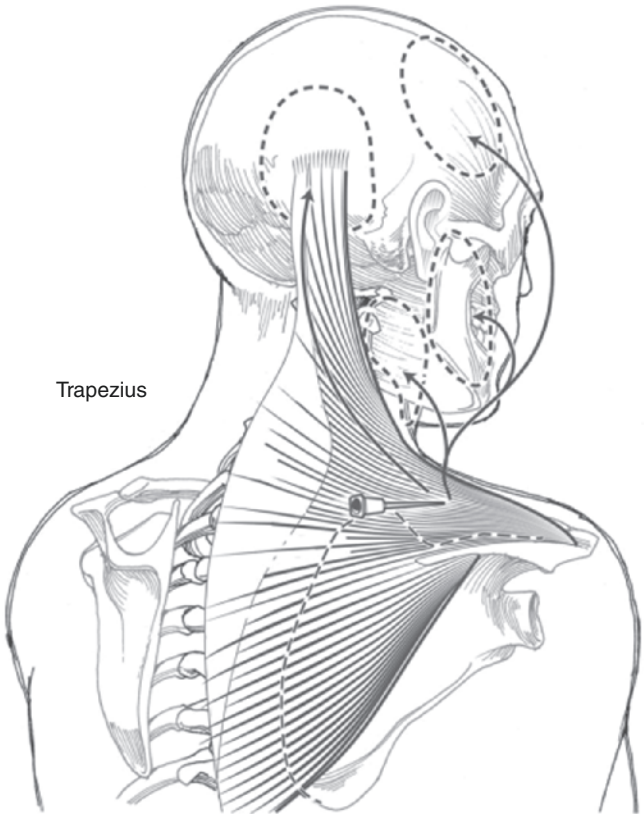

Fig. 15.1 Common trigger point injection location in the trapezius, as indicated by the needle. Pain referral trajectories and destinations are represented by the arrows and dotted lines, respectively. (Reproduced from Robbins et al. [22]; with permission from John Wiley and Sons)

cervical paraspinal muscles. Cervical paraspinals can potentially refer pain in a holocephalic pattern as well as to the shoulders and neck. Frequent tension in the neck, however, may be explained by myofascial pain derived from the levator scapulae. The sternocleidomastoid is another common injection site which potentially refers pain in a circumferentially cranial distribution including the anterior and lateral regions of the neck [22, 23]. Other muscle groups in which trigger point injections can be performed for cervicogenic headache include the temporalis and masseter muscles [22]. In a systematic literature review of the efficacy of dry needling, used interchangeably with acupuncture, for cervicogenic headache, the available evidence was classified as level D (poor) given limited studies on this treatment modality [24].

Botulinum toxin A injection was shown to decrease headache when applied to myofascial pain in cervical and shoulder girdle muscle groups in a randomized, double-blind, placebo-controlled trial in a population enriched for treatment responders. Baseline data on headache prevalence, frequency of headache, and headache diagnosis was not included. In this study, 54 participants responsive to an initial injection of botulinum toxin A in anterior neck flexor and posterior neck extensor muscles were randomized to either a second dose or saline placebo. Subjects

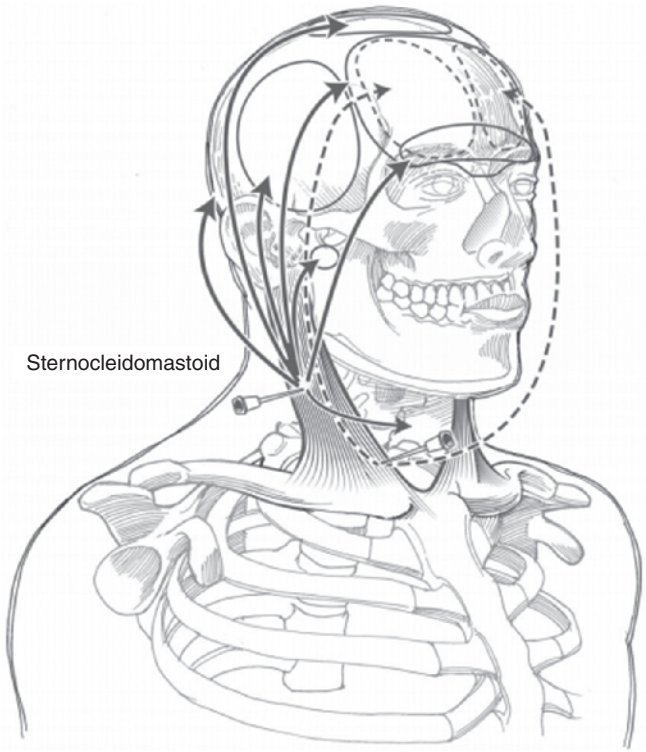

Fig. 15.2 Common trigger point injection locations in the sternocleidomastoid, as indicated by the needles. Pain referral trajectories and destinations are represented by the arrows and dotted lines, respectively. (Reproduced from Robbins et al. [22]; with permission from John Wiley and Sons)

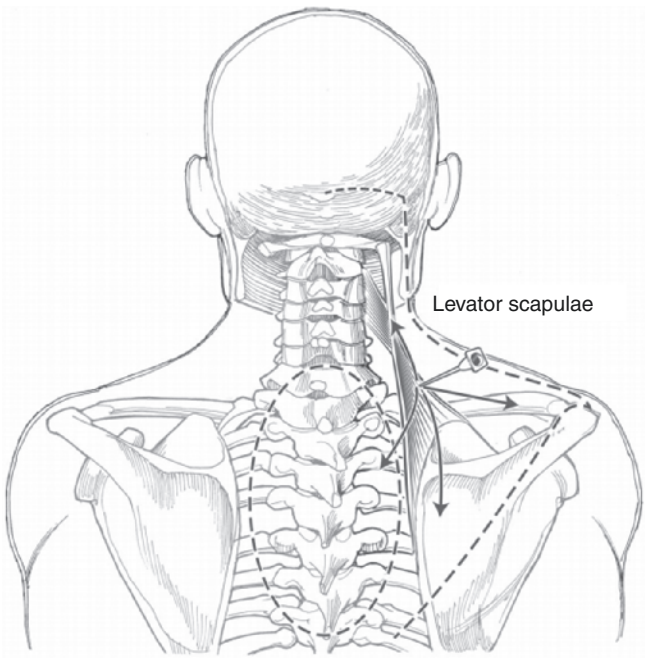

Fig. 15.3 Common trigger point injection location in the levator scapulae, as indicated by the needle. Pain referral trajectories and destinations are represented by the arrows and dotted lines, respectively. (Reproduced from Robbins et al. [22]; with permission from John Wiley and Sons)

received up to 300 units of botulinum toxin A. Headache frequency, duration, and Numerical Scale (NS) pain scores at baseline and 26 weeks were compared as secondary outcome measures. A significant reduction in headaches experienced per week was found in the treatment group in addition to a trend in reduction of worst NS pain scores (p = 0.07); there was no difference in headache duration between the two groups [25]. While only from a single RCT not specifically studying cervicogenic headache, the results of this study suggest that off-label use of botulinum toxin A may be beneficial for cervicogenic headache with concomitant myofascial pain of the neck and shoulder girdle. Unfortunately, access to this treatment is often limited, as botulinum toxin A does not have a US Food and Drug Administration (FDA) indication for myofascial pain or cervicogenic headache.

Occipital Neuralgia, Occipital Nerve Blocks, and Occipital Nerve Stimulation

Occipital pain is present in many headache disorders including migraine and cervicogenic headache. In a retrospective study of 64 patients treated with peripheral nerve blocks for headache management, nearly half of the cohort endorsed GON tenderness [26]. Occipital pain can be referred from other locations via the trigeminocervical complex or may be intrinsic to the distribution of the greater or lesser occipital nerves in the case of occipital neuralgia [27]. Occipital neuralgia (ON) can be unilateral or bilateral and is described by the International Headache Society as paroxysmal shooting or stabbing pain with subsequent dysesthesia [27]. The ICHD-3 diagnostic criteria are as follows:

A. Unilateral or bilateral pain in the distribution(s) of the greater, lesser, and/or third occipital nerves and fulfilling criteria B–D.
B. Pain has at least two of the following three characteristics:
   1. Recurring in paroxysmal attacks lasting from a few seconds to minutes
   2. Severe intensity
   3. Shooting, stabbing, or sharp in quality
C. Pain is associated with both of the following:
   1. Dysesthesia and/or allodynia apparent during innocuous stimulation of the scalp and/or hair
   2. Either or both of the following:
      (a) Tenderness over the affected nerve branches
      (b) Trigger points at the emergence of the greater occipital nerve or in the area of distribution of C2
D. Pain is eased temporarily by local anesthetic block of the affected nerve(s).
E. Not better accounted for by another ICHD-3 diagnosis [3].

There is significant overlap in the symptomatology of occipital neuralgia with other headache disorders. Because of this, the diagnosis may be challenging, rendering the importance of both criteria D and E [27].

Occipital nerve blocks are a nonspecific treatment; they have been found to attenuate migraines [28–31], cluster headaches [32–36], chronic daily headaches [32, 37, 38], and cervicogenic headaches [30, 39–43] along many studies of varying designs, utilizing medications spanning many drug classes. GON blockade has been found to provide immediate, intermediate, and long-term relief for cervicogenic headache [30, 39, 41]. In a single-arm unblinded study of 180 patients with non-whiplash-induced cervicogenic headache, 169 patients experienced full remission of pain lasting a mean 23.5 days when injected depot methylprednisolone in the GON and LON [43]. Occipital nerve blockade was found to yield a 50% improvement from baseline pain intensity in a double-blind RCT using a mixture of lidocaine, bupivacaine, epinephrine, fentanyl, and clonidine for GON, LON, and facial nerve blocks. Cervicogenic headache frequency and duration in addition to accompanying symptoms such as nausea, vomiting, photophobia, phonophobia, appetite, and normal daily activity were all significantly improved as compared to saline placebo [42]. This cohort of 47 patients then underwent a prospective noncomparative stimulator-guided nerve block trial using the same formula at the same anatomic locations. Ninety-six percent of patients achieved continuous pain relief for 6 months; 87% of these patients required repeated injections ranging from 2 to 13 total [41]. Both GON and C2/C3 nerve blockade were found equally effective in decreasing pain frequency and duration in a prospective study of 28 patients with cervicogenic headache. The minimum duration of pain relief was 2 months when using lidocaine 1% followed by bupivacaine 0.25% 1 week after [40].

The above studies were comprehensively reviewed by Ashkenazi et al. in 2010 [44]. In the interim there have been two RCTs displaying significant benefit of GON blockade in chronic migraine, both comparing bupivacaine to saline [45, 46], and two RCTs demonstrating a reduction in cluster headache frequency after suboccipital steroid injections [36, 47].

Another method for treating occipital pain is pulsed radiofrequency (PRF). In a double-blind RCT comparing PRF versus depomethylprednisolone for the treatment of ON and/or migraine with occipital nerve tenderness, average occipital pain among 42 patients had significantly diminished for 6 weeks as compared to 39 patients in the steroid group [48].

Facetogenic (Zygapophysial Joint) Pain

Facet arthropathy is most common in the cervical spine, with estimated point prevalence ranging from 45% to 55% [49, 50]. These patients may complain of axial neck discomfort accompanied by pain radiating in a facet referral pattern with an exam notable for paraspinal tenderness [49]. In a prevalence study utilizing pain maps in 194 patients with cervical facet pain, 36% of symptomatic joints were C2/C3 joints, followed by C5/C6 (35% of symptomatic joints) and C6/7 (17% of symptomatic joints). Fewer than 5% of symptomatic joints were at C1/C2, C3/C4, or C4/C5 [51]. Similarly, those with post-whiplash cervical facet pain were found to predominantly have symptoms emanating from C2/C3 and C5/C6 [52].

The atlanto-occipital joint is a potential pain generator for cervicogenic headache; however it is a rare focus of intervention given its proximity to vital structures. For example, the third segment of the vertebral artery passes posterior to the atlas and at this level has an anatomically variable course. This poses significant risk of unintended needle penetration and catastrophic consequences [53]. Caudally, the lateral atlantoaxial joint is also a potential pain generator for cervicogenic headache and also carries similar opportunities for iatrogenic injuries. Intervention at both locations can result in unintended dural puncture, breach of periforaminal arteries, direct nerve root damage, and spinal cord injury [54, 55].

The C2/C3 facet joint is innervated by the third occipital nerve (TON), which is the superficial medial branch of the C3 dorsal ramus [56]. Whiplash is a common cause of C2/C3 facet arthropathy. In a study in which subjects with whiplash received double-blind, comparative diagnostic TON blocks, the prevalence of TON headache among 100 subjects was 27%; 53% of subjects with headache as their predominant symptom were diagnosed with TON headache [9]. When this research group performed double-blind comparative diagnostic cervical medial branch blocks (MBB) at lower cervical levels in a post-whiplash cervical zygapophysial joint pain prevalence study, 31 of 52 patients (60%) suffered pain localizable to C2/C3 and below. Pain emanating from C2/C3 was found in 50% of patients with headache as the predominant symptom [52].

TON blocks and cervical MBBs serve to localize the origin of a patient's pain and prognosticate response to radiofrequency ablation (RFA). MBBs may be a final treatment step in those with long-standing analgesia, whereas RFA is offered to those whose relief from MBBs is transient [9, 57]. In a cadaveric study exploring a series of commonly recommended injectate volumes for ultrasound-guided TON blocks, vertical injectate spread was greater than the distance between the TON and GON using both 0.3 and 0.5 mL of methylene blue. A volume less than 0.3 mL was recommended for use given the likelihood of concomitant blockade at a greater quantity and thus lower specificity when evaluating patients for RFA [57].

The evidence supporting RFA for chronic C2/C3 facet pain is limited. While C2/3 RFA was at one time considered to be a technically difficult intervention, these difficulties

were overcome by increasing electrode diameter, fluoroscopically monitoring electrode placement, and allowing for no uncoagulated tissue between consecutive lesions. In a prospective observational study, 49 patients underwent RFA of TON after meeting the inclusion criterion of positive comparative diagnostic C2/C3 MBBs. Forty-three of forty-nine patients reported complete analgesia for at least 90 days, an initial success rate of 88% [58].

There have been two negative RCTs evaluating medial branch RFA for cervicogenic headache; however neither used MBB response to determine RFA candidacy. Stovner and colleagues randomized 12 subjects with cervicogenic headache to either C2–C6 medial branch RFA versus sham [59]. Haspeslagh et al. randomized 15 subjects to a protocol of C3–C6 facet joint denervation followed by dorsal root ganglion denervation based on physical exam and diagnostic blockade when necessary [60]. The remaining 15 subjects received GON blocks with local anesthetics and steroids followed by transcutaneous electrical nerve stimulation if needed.

Neuromodulation

Occipital nerve stimulation (ONS) and high cervical spinal cord stimulation may be considered for refractory cervicogenic headache. ONS has not been studied in cervicogenic headache, rather primarily in chronic migraine and to a lesser degree in cluster headache, short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT), and short-lasting unilateral neuralgiform headache attacks with cranial autonomic features (SUNA). There have been three RCTs studying ONS for refractory chronic migraine; all of these studies have shown promise in a minority of patients; however none have met their prespecified primary endpoints. Furthermore, lead migration rates were high [61–67].

High cervical spinal cord stimulation has also shown promise in small, single-arm studies for intractable migraine and cluster headache [68]. Neither of these neuromodulatory approaches have been studied to date in cervicogenic headache.

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