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Novel Interventional Nonopioid Therapies in Headache Management

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Abstract

Purpose of Review Headaches encompass a broad-based category of a symptom of pain in the region of the head or neck. For those patients who unfortunately do not obtain relief from conservative treatment, interventional techniques have been developed and are continuing to be refined in an attempt to treat this subset of patients with the goal of return of daily activities. This investigation reviews various categories of headaches, their pathophysiology, and types of interventional treatments currently available.

Recent Findings Injection of botulinum toxin has been shown to increase the number of headache free days for patients suffering from chronic tension-type headaches. Suboccipital steroid injection has been demonstrated as a successful treatment option for patients suffering from cluster headache. Occipital nerve stimulation (ONS) has been described as a treatment for all types of trigeminal autonomic cephalgias. Percutaneous ONS is a minimally invasive and reversible approach to manage occipital neuralgia performed utilizing subcutaneous electrodes placed superficial to the cervical muscular fascia in the suboccipital area. Radiofrequency lesioning is another commonly used treatment in the management of chronic pain syndromes of the head and neck. If a diagnostic sphenopalatine ganglion block successfully resolves the patient's symptoms, neurolysis can be employed as a more permanent solution.

Summary Although many patients who suffer from headaches can be treated with conservative, less-invasive treatments, there still remains at present an ever-increasing need for those patients who are refractory to conservative measures and thus require interventional treatments. These procedures are continually evolving to become safer, more precise, and more readily available for clinicians to provide to their patients.

Keywords Headache · Botulism toxin · Sphenopalatine ganglion block · Suboccipital steroid injection · Occipital nerve stimulation · Trigeminal autonomic cephalgias

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Introduction

Headaches encompass a broad-based category of a symptom of pain in the region of the head or neck. There are many different types and sub-types of headaches, but they are similar in the fact that they are all debilitating to the patient. Some patients deal with headaches on a monthly, weekly, and daily basis to the point that it interrupts their ability to maintain living a normal life. A lot of research has been directed over the years to find safe, efficient, and fast ways to alleviate or even eliminate a patient's headache as soon as it presents or when there is identification of its impeding presentation. In the past, the majority of treatments were pharmacologically directed along with various other conservative measures. For those patients who unfortunately do not obtain relief from conservative treatment, interventional techniques have been developed and are continuing to develop in an attempt to help

treat this subset of patients to return function. This review breaks down various categories of headaches, their pathophysiology which results in pain in the form of a headache, and types of interventional treatments currently available, along with efficacy of these techniques.

Migraine Headaches

Migraine headaches are prevalent in the USA and lead to more emergency room and outpatient visits than any other condition [1••]. These attacks can be extremely disabling for patients and often result in time away from work. Migraines are characterized by episodic moderate-to-severe pain lasting between 4 and 72 h, typically unilateral, pulsating, aggravated by physical activity, and often associated with nausea and/or visual symptoms [2]. They are approximately three times more likely to occur in females, affecting up to 17% of females and 6% of males in North America [3•, 4]. Chronic migraine is further classified as those who suffer headache on ≥ 15 days per month for at least 3 months, with features of migraine on ≥ 8 days per month [2]. Risk factors for the development of chronic migraine include mood disorders, anxiety, medication overuse, female gender, obesity, and low education level [3•].

Pathophysiology

An understanding of the mechanisms leading to onset of pain is important for the development of treatment modalities. The pathophysiology of migraines is thought to stem from activation of the trigeminovascular system, a nerve plexus arising from the trigeminal ganglion which innervates the cerebral and pial arteries, venous sinuses, and dura matter. Once triggered, the neurons in this system release substance P, neurokinin A, and calcitonin gene-related peptide (CGRP), which result in neurogenic inflammation and vasodilation [4].

Treatment

First-line treatments for migraine are often aimed at decreasing inflammation, stimulating vasoconstriction, and the inhibition of pain pathways. The most commonly used medications to combat acute migraine include nonsteroidal anti-inflammatories, caffeine, combination analgesics, anti-emetics, corticosteroids, and 5HT1B/D serotonin agonists, triptans, and ergot alkaloids [3•]. There are side effects to each of these mentioned oral medications, and patients suffering from chronic migraine are at risk for the development of medication overuse headache, a severe rebound headache which develops as a result of withdrawal from chronic analgesics [2].

Interventional techniques are gaining popularity as a treatment for chronic migraine patients. Botulinum toxin (BTX) injection was approved by the FDA in 2010 for chronic migraine sufferers, with headaches lasting ≥ 4 h. BTX acts by inhibiting the release of acetylcholine from the presynaptic nerve terminal of motor neurons, resulting in muscle relaxation and decreased pressure on the trigeminal nerve. Additionally, BTX type A inhibits release of local neuropeptides (substance P, CGRP, glutamate, and vanilloid 1), which cause neuron inhibition and interference of central and peripheral sensitization of nociceptive fibers [5].

Injection of BTX type A into pericranial muscles has been demonstrated to successfully reduce the number of headache days, and overall headache severity, for patients suffering from chronic migraine [6]. For the treatment of frontal migraines, 35–40 U of BTX is injected into the frontalis, corrugator supercilii, and procerus muscles. For temporal migraines, 20–25 U BTX is injected on the anterior aspect of the temporalis bilaterally. For occipitalis injection, just 10–20 U BTX is introduced just superior to the occipital protuberance bilaterally [5]. Effects of BTX last approximately 90 days, after which injections should be repeated.

Trigeminal Autonomic Cephalgias

Trigeminal autonomic cephalgias (TAC) are a group of severe unilateral pain attacks that encompasses cluster headaches, paroxysmal hemicrania, short-lasting unilateral neuralgiform headache with conjunctival injection (SUNCT), and short-lasting neuralgiform headache attacks with autonomic symptoms (SUNA) [4]. Overall, these headaches are rare as compared to migraine and tension headaches.

Cluster Headache

The most common TAC is cluster headache, which has an overall prevalence of 0.1–0.3% and is more frequent in males, aged 20–40 [3•, 4]. Cluster headaches typically present in a short-lived episodic fashion, as 1–8 excruciating unilateral episodes per day, lasting between 15 min and 3 h, occurring in periods of 2 weeks to 3 months. These episodes are known to occur at about the same time each year, often awakening the patient from sleep and are associated with ipsilateral parasympathetic autonomic hyperactivity [3•]. Cluster headaches are classified as either episodic or chronic. Ten to 20% of cluster headache patients are classified as chronic, experiencing either no periods of remission or remission periods lasting < 1 month/year [7].

Pathophysiology

The pathophysiology of cluster headache is largely unknown but hypothesized to be the result of neurogenic inflammation. Because of the very short duration of cluster headaches, the episodes typically resolve before the onset of oral abortive

medications. Prophylaxis with calcium channel blockers, anticonvulsants, antidepressants, beta-blockers, corticosteroids, and NSAIDS aim to interrupt the cycle of cluster. For acute attacks, inhalational oxygen (at 12 l/min via nonrebreather mask) is the standard treatment [4].

Interventional Treatment

Suboccipital steroid injections have been described as a successful treatment option for patients suffering from cluster headache. To perform this procedure, a mixture of 1.5 ml of long-acting betamethasone diproprionate salt (12.46 mg), rapid acting betamethasone disodium phosphate (5.26 mg), and 0.5 ml of xylocaine 2% is injected into the suboccipital fossa halfway between the inion and mastoid process. A double-blind, placebo-controlled study revealed that 80% of cluster headache patients treated with a single bolus injection of betamethasone near the greater occipital nerve had a pain-free interval of at least 1 month [8].

Paroxysmal Hemicrania

Pathophysiology

Paroxysmal hemicrania is an uncommon but severe condition characterized by orbitofrontal attacks associated with ipsilateral autonomic features. These headaches are of short duration, lasting only a few minutes, and are more common in females. Indomethacin has been enormously effective for hemicrania patients and often results in complete resolution of symptoms [3•].

Interventional Treatment

There have been reports describing success in treating hemicranias patients with greater occipital nerve block using a mixture of 3 ml of 2% lidocaine and 80 mg of methylprednisolone, injected into the midpoint between the mastoid process and occipital tubercle [9]. This procedure has not been well studied, likely because most patients have such a profound and complete response to indomethacin, with most patients experiencing complete resolution by 2 days [8].

SUNCT and SUNA Headaches

Pathophysiology

SUNCT and SUNA headaches present as brief episodes of sharp, stabbing pain associated with conjunctival injection, tearing, and rhinorrhea, lasting between 5 s and 5 min, with up to 30 episodes per hour. These are extremely rare and tend only to affect males [3•]. SUNCT headaches are difficult to treat but can be prophylactically prevented with oral anticonvulsants [4].

Interventional Treatment

Occipital nerve stimulation (ONS) has been described as a treatment for all types of TACs, including SUNCT and SUNA patients who have failed medical management. At a median 2-year follow-up, six of seven patients treated with bilateral ONS had at least 50% resolution of symptoms lasting at least 6 months. Four patients reported complete resolution of symptoms, and the only recognized adverse event was the development of hemicrania in one patient, which was successfully treated with indomethacin [7].

Tension Headaches

Tension-type headaches (TTH) are the most common headache occurring in the general population, with a lifetime prevalence as high as 70–80%. These headaches are characterized by a dull, mild-moderate intensity, poorly localized, pressure-type pain that lasts several hours to days [3•, 4]. TTH is further classified into TTH with or without pericranial muscle tenderness and chronic TTH (CTTH) for those experiencing headache on ≥ 15 days/month or ≥ 180 headaches per year [4]. These headaches can be associated with other headache classifications (migraine, vascular headaches), myofascial pain syndromes, coexisting mood-disorders, and disorders of the neck and spine [3•, 4].

Pathophysiology

The pathophysiology of TTH is not well understood, and proposed mechanisms have not been supported by independent data. Certain researchers believe that the same mechanisms behind migraine and cluster are responsible for tension-type headache, which would explain why TTH responds well to similar classes of medications used to treat other headache disorders. Others believe that the cause of TTH is secondary to extended muscle contraction of the pericranial and cervical muscles [4].

Interventional Treatment

Choice patients may find relief in physical therapy, cognitive behavioral therapy, stress management, and acupuncture, but these treatments are not universally effective for all patients suffering from TTH. Oral agents including aspirin, ibuprofen, acetaminophen, tricyclic antidepressants, muscle relaxants, butalbital, and codeine have shown success in the prevention and treatment of tension headaches, and the addition of caffeine to these analgesics can increase their efficacy [3•, 4].

BTX injection has been demonstrated to increase the number of headache-free days for patients suffering from CTTH. For relief of tension headaches, BTX is injected into the temporalis, pericranial, and cervical muscles of the neck for 18 months [5]. This technique is most effective when BTX is introduced specifically into the patient's most tender muscles and trigger points [4]. BTX type A injection can also be used as prophylaxis for patients suffering from mixed headaches with features consistent with both migraine and TTH [3•].

Postdural Puncture Headache

According to the Headache Classification Committee of the International Headache Society, postdural puncture headache (PDPH) is defined as "bilateral headaches that develop within 5 days after the dural puncture. It is usually accompanied by neck stiffness and/or subjective hearing symptoms. It remits spontaneously within two weeks, or after sealing of the leak with autologous epidural lumbar patch" [10]. The time frame of onset is usually first 24–48 h after the dural puncture; however, literature has been reported of headache presenting as much as 7 days later [11]. The presenting symptoms include, but are not limited to, nausea, vomiting, neck stiffness, photophobia, diplopia, scalp paresthesia, tinnitus, hypoacousia, and mental status changes [12]. The symptoms resolve within 7 days or less in the majority of patients but in the minority may persist for weeks to months [13].

Factors affecting incidence of PDPH include needle size, needle design, and orientation of needle bevel during meningeal puncture and patient-specific factors. The smaller the needle size, the smaller the dural defect. The incidence of headache is much lower with the use of 24 to 27-gauge needles (5–12%) compared with 20 to 22-gauge needles (20–40%) [14]. Cutting tip needle cuts the dural fibers, while blunt tip needle divides and does not disrupt the continuity of the dural fibers. The estimated incidence of PDPH with 20–22 gauge cutting needle is 36% vs less than 2% with 22-gauge atraumatic needle [15]. The bevel orientation during dural puncture has been proposed as a potential factor affecting the CSF leakage and incidence of PDPH. In a meta-analysis study by Richman et al. showed statistically significant lower incidence of PDPH of 10.9 vs 25.8% in parallel vs perpendicular needle insertion, respectively, when using the cutting needles [16]. Patient-specific factor includes higher incidence in women vs men, pregnancy and young age groups (20–50 years), and patients with low body mass index. The higher rate of PDPH in pregnant women may be attributed to reduced CSF density and an increased intra-abdominal pressure, both of which may promote increased CSF leakage [17].

Pathophysiology

The pathophysiology of the PDPH is not completely understood, but there are several proposed theories that exist. One hypothesis is mechanical traction. CSF leak secondary to dural puncture leads to loss of CSF volume which impairs buoyancy of the brain. This creates caudal shifting of the brain and causes intracranial tension on the pain-sensitive intracranial structures and causes headache. These structures include cranial nerves V, IX, and X, the dura, and the bridging veins [18]. The cervical dural punctures are not generally associated with PDPH because as the level of puncture goes up in the spine, there is a less hydrostatic pressure at the dural puncture site. Another hypothesis is based on Monro-Kellie rule which proposes that in intact skull, sums of the volumes of brain, blood, and CSF are constant. Thereby, reduction in intracranial CSF volume leads to compensatory increase in intracranial blood volume by causing cerebral vasodilation which results in headache [19]. The standing position further decreases intracranial pressure, which causes more venous distention resulting in worsening headache [18].

Interventional Treatment

The initial treatment for PDPH is usually conservative, which includes noninvasive and pharmacologic interventions. Reported effective noninvasive measures are hydration, caffeine, oral nonopioid medications, and bed rest. Interventional treatment includes epidural administration of blood, saline, colloids, or fibrin glue [20]. Epidural blood patch (EBP) is the gold standard treatment of PDPH [21]. It usually requires two people, one to obtain the blood and one to locate the epidural space. Patient positioning could be sitting or lateral decubitus depending on patient's tolerance in upright position. It is observed that 15 ml of blood spreads six segments cephalad and three segments caudal, or 1.6 ml of blood is required for one segment. Therefore, it is common to select a site caudal to the suspected dural tear. Reported ideal target volume is 20 ml. Less volume can be placed if patient starts complaining excessive back or leg pain [22]. Patient should remain supine with the legs slightly elevated after the EBP and can receive IV fluids during this time. A study by Martin et al. found that being in supine position for 2 h resulted in 100% relief vs 60% relief in patients who were in supine position for 30 min [23]. The incidence of long-term relief of PDPH after initial EBP is 61–75% [24]. It is very important to assess patient's coagulation status and must be within normal limits to avoid risk of an epidural hematoma [25].

It is unclear how long after EBP one can safely perform epidural/spinal procedures such as spinal anesthesia for procedures or epidural steroid injection in patients with lumber disc disease. According to a study by DiGiovanni et al. in Angora goats, dural scar tissue achieves maximum thickness

2 weeks after EBP and thins out to normal dural thickness approximately 3 months after the EBP in these goats [26]. Shaparin et al. have suggested that it is best to consider epidural procedure in patients who clear this time frame, the duration of which is not exactly not known in humans. Further studies are needed in humans to determine the healing process timeline after EBP to safely administer epidural anesthesia/analgesia [27].

Spontaneous Intracranial Hypotension

Spontaneous intracranial hypotension (SIH) is a syndrome with symptoms similar to meningeal puncture headache but without the previous history of meningeal puncture. It can occur at any age including adolescents, but female in late middle age are most predisposed [28]. Patients with certain disease states such as Marfan syndrome, Ehler–Danlos syndrome, neurofibromatosis, and disc disease are also predisposed to develop SIH [29]. Trivial trauma to the cervical spine, including manipulation, may precipitate intracranial hypotension, although the latter is more likely to be performed as treatment after the onset of headaches [30]. This syndrome can also be suspected in a patient with postural headache that occurs after a fall, trauma, whiplash, exercise, or violent coughing [31].

Pathophysiology

The commonly accepted mechanism for the development of SIH is the leakage of CSF through a weakness in the spinal meninges, e.g., meningeal diverticulum or small tears in the root sleeves or perineural cysts known as Tarlov cysts. This mechanism of its etiology can, therefore, be compared with the headache that often follows postdural puncture, in both cases hydrodynamics of the CSF space is destroyed and the ability of the fluid to provide buoyancy and support for the brain within the cranial cavity is lost [29].

Low CSF pressure on lumber puncture and meningeal enhancement on the MRI are diagnostic. MRI of the cranium typically demonstrates uniform pachymeninginеal contrast uptake, subdural fluid collection, and caudal displacement of the cerebellar tonsils [32]. Other modalities such as MRI mylography, CT mylography, and radionucleoide cysternography can also aid in diagnosis [33].

Interventional Treatment

Epidural blood patch (EBP) is the treatment of choice; however, it appears that EBP is less effective in SIH than in postdural puncture headache. The lower success may be related to the multiple CSF leaks, injection of the blood away from the site of the CSF leak, and location of CSF leak at the anterior aspect of the dura or the nerve root sleeve which is rare [34]. According to different studies, site of leak can be located anywhere in the spine [35, 36]. In the absence of exact location, most pain management physicians inject blood at the mid-thoracic area to cover upper lumber and lower thoracic levels. CT mylography is warranted if one or two EBPs are not helpful [37]. Surgical intervention is required if multiple EBPs are ineffective and condition of the patient deteriorates [38].

Cervicogenic Headache

Cervicogenic headache (CGH) is a clinical syndrome defined as unilateral headache that originates in the neck, provoked by neck movement or pressure over the tender points in the neck with reduced range of movements in cervical spine. Features of CGH can be difficult to differentiate from migraine or tension-type headaches based only on clinical criteria [39]. The International Headache Society (HIS) set forth the following diagnostic criteria for CGH [10]:

1. 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
2. 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
3. Evidence that the pain can be attributed to the neck disorder or lesion based on at least one of the following

(a) Demonstration of clinical signs that implicate a source of pain in the neck
(b) Abolition of headache following diagnostic blockade of a cervical structure or its nerve supply using placebo- or other adequate controls

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

Pathophysiology

CGH is referred pain arising from cervical structures innervated by upper three cervical nerves (C1–C3). The possible pain generators are atlanto-occipital joint, atlantoaxial (AA) joint, C2–C3 zygapophyseal joint, C2–C3 intervertebral disc, and upper cervical spinal nerves and roots themselves [40]. The suboccipital nerve which is the dorsal ramus of C1 innervates the atlanto-occipital joint. Therefore, any pathologic condition or injury to this joint is a potential source for head pain that is referred to the occipital region. The C2 spinal nerve and its dorsal root ganglion innervate the atlantoaxial and C2–C3

zygapophyseal joints; therefore, trauma to or pathologic changes to these joints can be a source of referred head pain. The third occipital nerve which is the superficial medial branch of dorsal ramus of C3 also innervates C2–C3 zygapophyseal joint. Pain from C2–C3 and third occipital nerve is referred to the occipital region as well as frontotempral and periorbital regions [41, 42]. This joint and the third occipital nerve appear most vulnerable to trauma from whiplash injuries of the neck. Pain originating from the C2–C3 joint accounts for 27% of the patients presenting with CGH after whiplash injury. The majority of CGH in patients with whiplash injuries resolves within a year of the injury [43].

Interventional Treatment

Lateral AA Joint

The lateral AA joint accounts for approximately 16% of the patients with CGH. The common pathology is secondary to osteoarthritis or as a result from trauma [44]. Clinical presentation includes occipital or suboccipital pain, focal tenderness over the suboccipital area, restricted painful rotation of C1 on C2, and pain provocation by passive rotation of C1 [40]. However, these clinical presentations are not specific. Lateral AA joint intra-articular injection with steroids can be effective for diagnosis as well as short-term pain relief. Narouze et al. showed favorable long-term outcome after both pulsed and thermal radiofrequency lesioning of the AA joint capsule [45]. Strict caution should be exercised during AA joint injections to avoid injuries to vertebral artery, C2 dorsal root ganglion, and nerve root to avoid serious complications. Injection of the contrast agent should be performed using real-time fluoroscopy, preferably with digital subtraction, prior to the injection of the local anesthetic, as negative aspiration is of low sensitivity. Narouze also reported an ultrasound-assisted AAJ injection in an effort to add more safety to the procedure because ultrasound can identify the relevant soft tissue structures near the joint (vertebral artery and C2 dorsal root ganglion) [46].

Third Occipital Neurolysis

As stated above, the third occipital nerve supplies C2–C3 zygapophyseal joint as it crosses the joint laterally [46]. Third occipital radiofrequency ablation (RFA) has been shown to be effective in the treatment of this headache. The third occipital nerve has variable anatomy, and incomplete lesioning is not unusual [47]. Therefore, use of the three needles technique to include all the variations from just lateral to the joint line to above or below the joint and in a way creating continuous lesions within one electrode width from adjacent lesions has shown to improve results markedly [48].

Cervical Epidural Steroid Injection (CESI) in CHG

CESI is the widely accepted treatment in patients with cervical radicular pain or radiculopathy. Two prospective studies demonstrated promising results of the CESI in CGH patients in both short- and long-term pain relief, particularly for patients with clinical and radiographic evidence of upper cervical spinal nerve root irritation [49, 50]. Further studies designed to include such patients with treatment protocols to target upper cervical nerve roots may provide additional evidence that CESI is an effective treatment for CGH [51].

Occipital Neuralgia

Pathophysiology

Occipital neuralgia is categorized separately under cranial neuralgias according to the second edition of ICH disorders, but it can produce symptoms indistinguishable from CGH. It typically presents as a sharp pain in the occipital region which arises from greater and lesser occipital nerves. Segmental nerve blocks are required for diagnosis and treatment in some cases [52]. Cryoneurolysis, RFA, and C1–C3 rhizotomy showed variable responses [53–55]. Occipital neurostimulation may be an option for persistent headache due to occipital neuralgia [56].

Interventional Treatment

Percutaneous ONS is the relatively low-risk, minimally invasive, and reversible approach to manage occipital neuralgia and some types of intractable primary headache. It is performed using the subcutaneous electrodes placed superficial to the cervical muscular fascia in the suboccipital area. Permanent implant may be performed if trial is effective. It is carried out using the same electrode lead type or paddle type surgical lead and attached to a pulse generator which can be implanted in the infraclavicular, flank, upper buttock, or abdomen area. Lead migration is the most frequent complication necessitating the revision [57, 58]. The other potential complication is a painful muscle contraction secondary to stimulation if implanted lead is deep at the level of suboccipital muscles. Ultrasound has also been deemed promising in placement of lead under direct vision in the correct superficial plane to the muscles [46].

Cervical Myofascial Pain

Traditionally, myofascial pain is defined as a pain that derives from myofascial trigger points (MTrP). MtrPs are small, highly sensitive areas in muscle characterized by hypersensitive, palpable, taut bands of muscles that are tender on palpation,

reproduce patient's symptoms, and cause referred pain [59]. There are four most common muscles responsible for cervical myofascial headache that include the trapezius, sternocleidomastoid, the splenius capitis, and temporalis [60]. The headaches causally associated with cervical myofascial tender spots are coded as episodic or chronic tension-type headache as per ICHD [10].

Pathophysiology

One of the proposed mechanisms of development of myofascial trigger points is related to an excess release of acetylcholine which leads to sustained contraction of the muscle and formation of a trigger point [59]. This sustained contraction can lead to a significant increase in the concentration of inflammatory and nociceptive transmitters within the trigger point. Constant peripheral muscle nociceptive activation by these inflammatory and nociceptive compounds forms the permanent stimulus that facilitates pain neurotransmission which results in central sensitization and glial activation [61].

Interventional Treatment

Traditional interventional therapy includes trigger point injections (TPI), in which needles are inserted directly into trigger point regions which have been identified on physical exam. Various substances have been used including saline, corticosteroids, local anesthetics, and dry needling [62]. Evidence suggests that there is no advantage to use one drug compared to other and any drug over dry needling. A systemic review by Cummings revealed that the effect of TPI is likely by the needle itself rather than any specific drug. No difference was shown in therapeutic benefit between "wet" needling vs "dry" needling. No difference has been found in pain reduction between saline vs local anesthetics. Studies have not demonstrated superiority for the addition of corticosteroids to local anesthetic vs using local anesthetics alone [60]. There are no clear cut guidelines regarding the number of injection points, frequency of the injection, and volume or type of injectate.

Botulinum toxin serotype A inhibits release of Ach at the motor endplate and thereby causes sustained and prolonged relaxation of muscles and is itself an analgesic inhibiting central sensitization [63]. Although this therapy seems promising, results of randomized controlled trials and studies have been mixed. A study reported by Ferrante et al. showed no statistically significant improvement in cervicothoracic myofascial pain in injection of botulism A vs placebo [64, 65]. In a study by Harden et al., there was short-term (12-week) reduction in myofascial pain of chronic tension-type headache with botulism toxin compared to placebo [66]. In a randomized control trial (RCT) of botulism A vs 0.5% bupivacaine, Graboski et al. found no significant difference, as both were equally effective in reducing myofascial pain below the baseline pain level [66]. A recent RCT by Nicole A et al. demonstrated effectiveness of botulism A in reducing pain scores and improving quality of life compared to placebo in a patients with cervical and shoulder girdle myofascial pain. In this study, the researchers used enriched protocol wherein all the study subjects were given initial botulism injections in trigger points. Six weeks after the injections, those patients who had a clinical response according to their study criteria entered into second phase of randomized study with placebo [67]. New theories emphasize the selection of patients with overlap of symptoms of cervical myofascial pain, headache, and spasmodic torticollis for botulism A treatment as opposed to injection into trigger points. It is hypothesized that these patients benefit from botulism A therapy by restoring the aberrant biomechanics and postural abnormalities in association with physical therapy [68].

Sphenopalatine Ganglion

Sphenopalatine blocks and neurolysis techniques are essential components in the management of chronic pain syndromes of the head and neck that have failed traditional management. These conditions include migraines, trigeminal autonomic cephalalgias, and cluster headaches but have also been applied to the treatment of atypical facial pain, complex regional pain syndromes, temporomandibular joint pain, and pain secondary to cancers of the head and neck [1, 2, 68].

Pathophysiology

The anatomy of the sphenopalatine ganglion helps elucidate the constellation of symptoms associated with these pain syndromes and provides a functional understanding for the pain practitioner employing sphenopalatine nerve block or stimulation. The sphenopalatine is a collection of neurons residing within the pterygopalatine fossa, lying inferior to the maxillary nerve as it crosses the sphenopalatine fossa [69]. It has parasympathetic, sensory, and sympathetic contributions, which derives from the greater petrosal branches of the facial nerve, sphenopalatine branches of the maxillary nerve, and deep petrosal nerves, respectively [68]. Though only the parasympathetic branches synapse within the ganglion [70], this unique anatomy allows trigeminal afferents to stimulate parasympathetic neurons within the sphenopalatine ganglion causing autonomic symptoms such as lacrimation and rhinorrhea [71]. For this reason, the sphenopalatine ganglion has been evaluated for its role in chronic pain syndromes of the head and neck, particularly those with autonomic symptoms.

Interventional Treatment

Patients suffering from these symptoms may find relief through a sphenopalatine ganglion block. The procedure is most commonly performed intranasally but may also be achieved via an infrazygomatic approach. Rarely, blocks may also be achieved via a trans-oral or lateral infratemporal approach [69]. Related to the proximity of the sphenopalatine ganglion to the middle nasal turbinate and lateral nasal mucosa, the intranasal approach may be safely achieved in the office and by employing anatomical landmarks. This approach involves measuring the distance from the patient's nares to mandibular notch, which corresponds to the distance to the middle nasal sinus. The patient then assumes a supine position, and a pain practitioner soaks two cotton-tipped q-tips in 4% lidocaine before inserting them into the nares and directing them towards the middle nasal turbinate at an angle roughly parallel with the zygoma [68]. These q-tips remain in place for approximately 30–45 min to allow for absorption of the local anesthetic [68]. Subtle variations of this procedure exist, and practitioners may choose another local anesthetic such as bupivacaine or ropivacaine with or without steroids or neosynephrine [70]. Additionally, one study demonstrated that patients with chronic pain secondary to cancers of the head and neck can be taught to perform intranasal sphenopalatine ganglion blocks independently, at home, with a statistically significant improvement in their pain (visual analog score 8.57 ± 1.31 to 2.46 ± 1.23 ($P < 0.0001$)) [72]. As a successful sphenopalatine ganglion block takes effect, patients report ipsilateral autonomic symptoms including lacrimation, rhinorrhea, and conjunctival injection. Absolute contraindications to sphenopalatine ganglion block include patient refusal, local infection or sepsis, and severe allergic reaction to any medication used [68]. Relative contraindications include facial trauma, pre-existing neurological deficits, coagulopathy, and mild or moderate allergies to the involved medications [1].

If a block is unsuccessful, it is possible that the sphenopalatine ganglion is too deep to be reached intranasally and an infrazygomatic approach might be required for success [73•]. The infrazygomatic approach requires light to moderate sedation and incorporates fluoroscopy, which has been shown to increase success rates, decrease procedure times, and decrease complication rates [68]. Therefore, an infrazygomatic approach is performed in a procedure suite or ambulatory setting at the practitioner's discretion. The patient is placed in a supine position and then prepped and draped with all relevant anatomical landmarks visible and marked. With fluoroscopy, a lateral image is obtained before initiating the procedure and the pterygopalatine fossa, which resembles a radiolucent funnel, is identified superior to the mandibular notch [69]. An experienced practitioner then inserts a large bore catheter, such as a 16-gauge angiocatheter, at the ramus of the mandible and directs it towards medial border of the pterygopalatine fossa [68]. It is helpful to frequently verify correct positioning with AP and lateral fluoroscopic imaging before inserting the block needle through the angiocatheter and advancing it towards the middle turbinate until it is adjacent to the palatine bone. If the injection of water-soluble contrast confirms proper placement under fluoroscopy, the local anesthetic of choice can be administered to accomplish a diagnostic or therapeutic sphenopalatine block.

Radiofrequency lesioning is another commonly used treatment in the management of chronic pain syndromes of the head and neck. If a diagnostic sphenopalatine ganglion block successfully resolves the patient's symptoms, neurolysis can be used as a more permanent solution. Two modalities exist: radiofrequency lesioning (RFTC) and a newer pulsed electromagnetic field radiofrequency lesioning (P-EMF) [68]. Either technology is administered via the infrazygomatic approach and is achieved via high-frequency alternating electrical currents (300–500 kHz), which cause local hemorrhage and demyelination [71]. After correct catheter positioning, RFTC is accomplished by administering local anesthetic, inserting an insulated radiofrequency needle, and using a trial stimulation to test for proper positioning. When positioned appropriately, the patient should experience nasal paresthesia with a low voltage trial of less than 0.3 V. If the patient experiences paresthesia to the teeth or hard palate, the radiofrequency tip should be repositioned caudo-medially or cephalon-medially, respectively, and positioning should again be tested [68]. If RFTC is performed, the practitioner should administer 2–3 ml local anesthetic prior to ablation to prevent damage to the surrounding nervous structures. This step is unnecessary with the P-EMF approach where temperatures do not exceed 40–42 °C. Contraindications to radiofrequency ablation include uncontrolled coagulopathy, sepsis, local infection, altered anatomy due to trauma or previous surgery, and failed sphenopalatine ganglion block [71].

Patients should be aware of potential complications to either SPG blocks or neurolysis. These include bleeding, bruising, infection, damage to surrounding nervous structures, and transient reflex bradycardia.

Conclusion

Patients who live and deal with headaches can have detrimental impacts on their daily lives. Although many patients who suffer from headaches can be treated with conservative, less-invasive treatments, there is still an ever-increasing need for those patients who are refractory to these conservative measures and thus require interventional treatments. These procedures are continually evolving to become safer, more precise, and more readily available for interventional pain physicians to provide to their patients.

Compliance with Ethical Standards

Conflict of Interest Omar Viswanath, Roxanna Rasekhi, Rekhaben Suthar, Mark Jones, Jacquelin Peck, and Alan D. Kaye declare no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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