General

Literature Review: Pericranial Nerve Blocks for Chronic Migraines

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Purpose of Review

Headaches, especially migraines, are one of the most pervasive neurological disorders affecting up to 15.9% of the population. Current methods of migraine treatment include lifestyle changes, pharmacologic, and minimally invasive techniques such as peripheral nerve stimulation (PNS) and pericranial nerve blocks (PNB).

Recent Findings

PNBs are used to treat and prevent migraines and involves injection of local anesthetics with or without corticosteroids. PNBs include the greater occipital, supraorbital, supratrochlear, lesser occipital, auriculotemporal, sphenopalantine ganglion, and cervical root nerve blocks. Of the PNBs, the most extensively studied is the greater occipital nerve block (GONB) which has been shown to be an efficacious treatment for migraines, trigeminal neuralgia, hemi-crania continua, and post-lumbar puncture, post-concussive, cluster, and cervicogenic headaches but not medication overuse and chronic tension type headaches.

Summary

In this review, we aim to summarize the recent literature on PNBs and their efficacy in the treatment of migraines including a brief discussion of peripheral nerve stimulation.

INTRODUCTION

Headache is one of the most pervasive disabling neurological diseases[1] affecting roughly 15.9% of the population with women having a higher predisposition than men.[2] Migraine is a subcategory of headache with specific diagnostic criteria and genetic implications, as patients with family members who experience migraine are three times more likely to develop migraines themselves.[3] Triggers such as stress, missed meals, hormonal changes, and changes in weather correlate with the development of migraine headaches.[4] Current methods of migraine treatment include pharmacologic, lifestyle, minimimally invasive techniques such as pericranial nerve blocks (PNB) and peripheral nerve stimulation (PNS), and surgical decompression reserved as a last resort.

PNBs have been used for decades to treat and prevent migraines and involves injection of local anesthetics and/or the addition of corticosteroids.[5] Of note, a randomized comparison study revealed that addition of triamcinalone to the PNB, did not improve patients' migraines.[6] PNBs include the greater occipital, supraorbital, supratrochlear, lesser occipital, auriculotemporal, sphenopalatine ganglion (SPG), and cervical root nerve blocks.[7] Of the various PNBs, the most studied is the greater occipital nerve block (GONB),[7] as it has demonstrated efficacy in both treatment and prophylaxis.[8,9] Furthermore, evidence has demonstrated GONB to be efficacious in the treatment of post-

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Table 1. SNOOP4 mnemonic categorizing underlying findings concerning for secondary causes of migraine/ headache

Symptom	History or Exam findings
(S) Systemic	• Immunosuppression • HIV • Malignancy • Evidence of infection
(N) Neurologic	• Aberrant neurologic exam • Deviation in mood
(O) Onset (sudden)	• Maximum intensity in less than 60 seconds (thunderclap headache)
(O) Older age	• New onset after 50 years of age
(P1) Pattern change	• Change in characteristics based on previous migraines/headaches • Progression of disease
(P2) Precipitated by Valsalva	• Worsened with Valsalva maneuver (herniation and increased ICP)
(P3) Postural	• Worsened based on postural change
(P4) Papilledema	• Visual changes, diplopia, loss of vision, or fundoscopic imaging

lumbar puncture headache,[10] trigeminal neuralgia,[11] hemicrania continua,[12] post-concussive headache,[13] cluster headaches,[14] and cervicogenic headache.[15,16] It is noteworthy that GONB has not been successful in treating medication overuse headache and chronic tension type headache.[17,18] In this review, we aim to summarize the recent literature on PNBs and their efficacy in the treatment of migraines including a discussion of peripheral nerve stimulation as treatment.

MIGRAINE DIAGNOSIS

The diagnosis of migraine is made clinically via patient history, clinical examination, and diagnostic criteria. Prior to the diagnosis of primary migraine, underlying pathology causing secondary migraine must be ruled out; the SNOOP4 mnemonic (Table 1) can be used in ruling out secondary migraine causes.[19]

For the diagnosis of migraines, patients require 5 or more lifetime headaches lasting between 4-72 hours.[20] These headaches must have 2 or more of the following symptoms: unilateral in nature, pulsating pain, patient-reported moderate to severe pain, and/or pain that is aggravating or results in avoidance of activities that exacerbate symptoms.[20] Additionally, patients should have 1 more of the following concomitant symptoms such as nausea, emesis, photophobia, or phonophobia during an episode.[20] Subcategories of migraines include migraines with aura and chronic migraines. The diagnosis of migraine with aura requires a minimum of 2 or more episodes lasting between 4-72 hours with 1 or more of the following reversible aura symptoms affecting the following systems: brainstem, motor, retinal, sensory, speech/language, and visual.[20] Withal, patients require a minimum of 3 of the following 6 characteristics: 1 aura being unilateral, 1 aura being positive, 2 or more symptoms occurring subsequently, 1 aura symptom spreading gradually over 5 or more minutes, each aura symptom lasting between 5 to 60 minutes, or the aura is followed by a headache within 60 minutes.[20] Once symptoms persist for 15 or more days in a month for 3 or more months, the migraine is classified as chronic.[20]

PHARMACOLOGICAL MANAGEMENT

Pharmacological treatment of migraines is categorized as either abortive in the acute setting or prophylactic for prevention of recurrent migraines. Abortive treatment ranges from over-the-counter medications, namely acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs), to more specific migraine therapy such as triptans, calcitonin-gene related peptide (CGRP) antagonists, ergots, and lasmiditan.

ACETAMINOPHEN, ASPIRIN, AND CAFFEINE

Regarding oral acetaminophen, 1000 mg versus placebo in patients with acute migraines demonstrated superior 2-hour headache relief as well as significantly higher two-hour headache free rates.[21] A meta-analysis of randomized placebo-controlled trials using a combination of aspirin, acetaminophen, and caffeine (APC) showed that APC was superior to placebo at 2-hour pain relief (54.3% vs. 31.2%, RR 1.7, 95% CI 1.6–1.9) as well as pain free response at 2 hours (19.6% vs. 9.0%, RR 2.2, 95% CI 1.4– 3.3).[22]

TRIPTANS

Triptans are serotonin 1b/1d agonists that inhibit the release of vasoactive peptides, ultimately blocking brainstem pain pathways and promoting vasoconstriction. Sumitriptan, naratriptan, rizatriptan, eletriptan, zolmitriptan have all been shown to be effective in treating acute migraines. In a systematic review including 133 randomized controlled

trials, triptans relieved headaches within 2 hours in 42-76% of patients, and 18-50% of patients had 2 hours of sustained relief from headache pain.[23]

CALCITONIN-GENE RELATED PEPTIDE ANTAGONISTS

CGRP antagonists target calcitonin gene receptors which are implicated in migraine pathophysiology and are often used in patients who tolerate triptans.[24] Dihydroergotamine, an alpha-adrenergic and potent $5HT_{1b/1d}$ receptor agonist, has been shown to be effective for abortive migraine therapy.[24] Lastly, lasmiditan, a $5\text{-}HT_{1F}$ receptor agonist involved in the trigeminal system, is a relatively new migraine abortive agent.[24]

Additional pharmacologic therapies with established efficacy in preventing migraines include medications from several drug classes such as beta blockers, anticonvulsants, and antidepressants.[24] Of note, beta blockers metoprolol, propranolol, and timolol are recommended by the American Academy of Neurology (AAN) for preventative migraine therapy.[24] Recommended anticonvulsants for migraine prevention include sodium valproate and topiramate with several placebo-controlled trials demonstrating their efficacy.[24] Tricyclic antidepressants (TCA) such as amitriptyline and serotonin norepinephrine reuptake inhibitors (SNRI) such as venlafaxine are described as probably effective by the AAN in migraine prevention.[25]

NON-INVASIVE MIGRAINE INTERVENTIONS

Emerging non-invasive interventions are hypothesized to treat migraines by targeting the abnormal cortical response seen in migraine patients.[26] One such intervention is transcranial magnetic stimulation (TMS), a form of brain stimulation, which involves magnetic field changes that induce weak electrical currents in the brain. This is done by placing a metal coil on the scalp through which an alternating electrical current is passed. Transcranial direct current stimulation (tDCS) is another form of brain stimulation that delivers weak currents to the brain through two sponge electrodes placed on the scalp, ultimately modulating the resting membrane potential of neural fibers. Moreover, both treatments have been used in the diagnosis and treatment of psychiatric disorders such as depression for several years and continue to be explored in migraine therapy.

PERIPHERAL NERVE BLOCKS (PNBS)

Migraines are primarily classified as a central nervous system (CNS) disorder; however, recent evidence has shown that scalp, pericranial, and trigger point tenderness extend extracranially beyond the skull base via afferent trigeminal nerve fibers; hence, the peripheral nervous system has become a potential target for effective management and improvement in pain and functional outcomes.[27-32] These procedures are of short duration, minimally invasive, cost effective, safe and can be performed in the procedure suite, inpatient, or outpatient settings. Commonly injected anesthetics are lidocaine or bupivacaine with or without the addition of corticosteroids.[33] After reported cases of lipoatrophy, skin hyperpigmentation and alopecia with the use of corticosteroids, they tend to be avoided or used sparingly.[34]

PNB SUBTYPES

GREATER OCCIPITAL NERVE BLOCK (GONB)

The most commonly used PNB is the GONB for both acute and chronic migraine treatment.[32,35] GON pathophysiology involves targeting referred pain to the frontal and orbital areas conferred by the convergence of C2 dermatomal and trigemino-vascular nerve bundles.[36] Rapid onset of GONB decreases the need for opioid and non-opioid bridging to pain relief. GON blocks can be performed routinely at an interval of 3 months or more. Risks include bleeding, nerve injury, intravascular injection necessitating knowledge of anatomical landmarks of the occipital nerve and CN V branches. The lesser and third occipital nerve stem from posterior C2/C3 cervical branches and innervate the occipital and upper cervical portions of the skull/head.[37] The C2 nerve forms the dorsal primary rami, the medial branch of which is the GON, and can be easily located by palpating the occipital protuberance and mastoid process approximately 2 cm lateral and 2 cm inferior to the occipital protuberance.[35] In one study, combined GON and superior occipital nerve (SON) blocks decreased pain in 7 out of 14 patients half an hour after injection.[38] GONB performed on patients with episodic or resistant migraines and allodynia with a 50-50 combination of lidocaine and bupivacaine resulted in almost 90% of patients demonstrating 46.8% and 65.7% reduction in headache intensity and allodynia after 20 minutes of injection, respectively.[39] In a double-blinded randomized control trial (RCT), patients were injected with either 0.5% bupivacaine or placebo with the bupivacaine cohort experiencing a higher level of efficacy in terms of number of headache days (reduced to 8.8 from 18.2) compared to placebo ($p < 0.001$).[40] A second study with ultrasound-guided bupivacaine injection had a significant reduction in average pain intensity score as compared to the control ($p = 0.003$).[41] In an RCT of episodic migraine patients, similar results in reduction of pain intensity were observed when lidocaine was used in combination with saline or triamcinolone suggesting, which other studies have been in agreement, that corticosteroids offer no further benefit.[42]

LESSER OCCIPITAL NERVE BLOCK (LONB)

Commonly targeted along with the GONB, the lesser occipital nerve (LON) is located two-thirds the distance between the occipital protuberance and mastoid process. The C2/C3 cervical nerves also form the ventral primary ramus which eventually forms the LON.[35] Interestingly, there is no evidence for lesser occipital nerve blocks for the treatment of migraines.[7]

SUPRATROCHLEAR NERVE (STN) AND SUPRAORBITAL NERVE (SON) BLOCKS

The superomedial aspect of the supraorbital ridge is the site of injection regarding the supratrochlear nerve (STN). It innervates the anterior scalp, upper eyelids and forehead. The V1 ophthalmic division of the trigeminal nerve (CN V) branches into the frontal nerve which in turn branches into the STN.[35]

One of the larger branches of the frontal nerve is the SON, easily located just above the supraorbital foramen of the frontal bone supplying the conjunctiva and upper eyelid. The supraorbital artery runs medially to the SON and must be avoided when performing this block.[35] Supraorbital and supratrochlear nerve blocks have shown efficacy in conjunction with GONB for both treatment and prophylaxis of migraine headaches.[43,44]

AURICULOTEMPORAL NERVE (ATN) BLOCK

The auriculotemporal nerve (ATN) can be easily localized in the anterior part of the tragus and supplies the temples, temporomandibular joint, tragus, and ear auricle. Trigeminal nerve branches into a mandibular division which further gives rise to the ATN from its posterior division.[35] There are few patients who have undergone ATN blocks and experienced relief from temporomandibular neuralgia, but current evidence does not show improvement in patients' pain from migraines.[7,45]

SPHENOPALATINE GANGLION (SPG) AND CERVICAL ROOT NERVE BLOCKS

The SPG block is less invasive and involves the application of local anesthetic to the SPG located in the lateral nasal cavity. The block was first described in 1908 by Sluder and subsequent case and retrospective studies have demonstrated improvement in acute migraine treatment with a decrease in patient pain scores at 15 minutes, 2 hours, and 24 hours.[46] Moreover, SPG blocks have been shown to also improve trigeminal neuralgia, cluster headaches, and postherpetic neuralgia.[47,48]

Cervical root nerve blocks result in improvement in patient pain scores with cervicogenic headaches due to cervical radiculopathy and whiplash injury, but the evidence for its use in migraine treatment is limited and requires further evaluation.[49,50]

PERIPHERAL NEUROSTIMULATION/ PERIPHERAL NERVE STIMULATION (PNSL)

There has been an increase in the usage of peripheral nerve stimulation (PNS) for the treatment of migraine headaches. The proposed mechanism of action involves A-beta afferent fibers in the dorsal horn of the spinal cord.[51-55]

NON-INVASIVE PNS

TRANSCUTANEOUS SUPRAORBITAL NERVE STIMULATION (TSNS)

Transcutaneous supraorbital nerve stimulation (tSNS) is a portable device used for migraine prophylaxis but no data or trials have been undertaken to prove its efficacy in abortive treatment. In a recent double-blinded RCT evaluating prophylactic treatment, the treatment group had an almost 50% responder rate, and the mean number of headache days per month had been significantly reduced ($p < 0.05$) in the treatment group as compared to the control group.[32,56,57]

TRANSCUTANEOUS VAGUS NERVE STIMULATION (TVNS)

Recent preliminary development via an open label and randomized pilot study suggests that the gammaCore device (a transcutaneous vagus nerve stimulator (tVNS)) was effective in treating acute migraine attacks in 21% of the patients; whereas, the pilot study demonstrated at least a 50% reduction of the headaches in 4/26 patients.[58]

INVASIVE PNS

Invasive approaches have been explored in chronic migraine patients who are treatment resistant and continue to be used despite insufficient data demonstrating efficacy.

OCCIPITAL NERVE STIMULATION (ONS)

Three large RCTs examined the safety and efficacy of occipital nerve stimulation (ONS). Sixty-six patients were enrolled in the ONSTIM study (Occipital Nerve Stimulation for the treatment of chronic migraine headaches). During a 12-week follow-up period, there was a 50% reduction in the headache frequency observed in all patients. 39% of the patients had a decrease in headache intensity as compared to the control group.[59] One of the largest RCTs with 157 patients did not reach its primary end point of 50% reduction of mean daily headache intensity; however, there was a 30% reduction in the mean headache days ($p < 0.05$) and a significant decline in the migraine-related disability score (MIDAS) ($p < 0.05$) in patients treated with ONS as compared to the sham cohort.[60]

VAGUS NERVE STIMULATION (VNS)

The effects of vagus nerve stimulation (VNS) in refractory epilepsy is well established; however, there is insufficient evidence for the usage of VNS in patients with migraines. In a retrospective study of 10 epilepsy patients with VNS implant, 8 patients had at least a 50% decrease in the headache frequency at a 6-month follow-up.[61]

COMPLICATIONS AND PROGNOSIS

Complications for PNBs can be categorized by generalized, due to corticosteroids, and due to technique (based on

provider skill level). The most identified generalized complications are pain at the site of injection, dizziness, allergy to local anesthetic, and vasovagal episodes.[35,62] If corticosteroids are used, common complications include hyperpigmentation, alopecia, and cutaneous atrophy.[62] Other minor side effects include infection at the site of injection, intravascular injection of local anesthetic, puncture of surrounding vasculature (with concomitant sequalae of disrupted perfusion), and nerve damage.[35,62]

CONCLUSION

Migraines are a common and debilitating neurological disorder that affects patients' lives drastically. Management involves avoiding triggers and prophylactic medication to prevents migraines. Once a migraine occurs, patients have several options for pharmacological abortive therapy. Non-pharmacological, minimally invasive treatment options include PNS and PNBs. PNBs are quick to perform, minimally invasive, cost effective, safe and can be performed in the procedure suite, inpatient, or outpatient settings. PNBs offer patients an alternative treatment option for migraines especially those who fail conservative pharmacological management.

AUTHOR CONTRIBUTIONS

All authors were involved in the writing and editing of the manuscript.

DISCLOSURES

There are no conflict of interests with the authors.

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