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Chronic Headache: a Review of Interventional Treatment Strategies in Headache Management

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Abstract

Purpose of the Review To provide an overview of current interventional pain management techniques for primary headaches with a focus on peripheral nerve stimulation and nerve blocks.

Recent Findings Despite a plethora of treatment modalities, some forms of headaches remain intractable to conservative therapies. Interventional pain modalities have found a niche in treating headaches. Individuals resistant to common regimens, intolerant to pharmaceutical agents, or those with co-morbid factors that cause interactions with their therapies are some instances where interventions could be considered in the therapeutic algorithm. In this review, we will discuss these techniques including peripheral nerve stimulation, third occipital nerve block (TON), lesser occipital nerve block (LON), greater occipital nerve block (GON), sphenopalatine block (SPG), radiofrequency ablation (RFA), and cervical epidural steroid injections (CESI).

Summary Physicians have used several interventional techniques to treat primary headaches. While many can be treated pharmacologically, those who continue to suffer from refractory or severe headaches may see tremendous benefit from a range of more invasive treatments which focus on directly inhibiting the painful nerves. While there is a plethora of evidence suggesting these methods are effective and possibly durable interventions, there is still a need for large, prospective, randomized trials to clearly demonstrate their efficacy.

Keywords Cervicogenic headache · Peripheral nerve stimulation · Radiofrequency ablation · Greater occipital nerve block · Lesser occipital nerve block · Sphenopalatine block

Introduction

Headaches are among the most common nervous system disorders with a prevalence of more than 48% in the general population. The incidence of headaches is slightly higher in females than males [1]. Despite a plethora of treatment modalities, some forms of headaches remain intractable to conservative therapies. Interventional pain modalities have found a niche in treating headaches. Individuals resistant to common regimens, intolerant to pharmaceutical agents, or those with co-morbid factors that cause interactions with their therapies are some instances where interventions could be considered in the therapeutic algorithm [2].

Headaches are classified into primary, secondary, and other painful cranial neuropathies [3••]. Based on the International Classification of Headache Disorders (ICHD), primary headaches have many forms. The most common are migraines, tension-type headaches (TTH), and the trigeminal autonomic cephalalgias (TACs). Other primary headache disorders can be associated with cough, exercise, cold, and even sexual activity. Despite constituting about 98% of all headache disorders, primary headaches are not life-threatening, and do not include serious underlying pathology. A diagnosis of primary headache is made after excluding pathology and secondary headaches.

Secondary headaches can be due to trauma, cranial or cervical vascular disorders, intracranial non-vascular disorders, substance abuse, and withdrawal, among others [4]. Cervicogenic headaches also are considered a secondary

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headache. The management for such headaches is focused on treating the underlying condition or pathology. The ICHD includes painful cranial neuropathies, other facial pains, and other headaches into a tertiary category. Lesions involving the trigeminal nerve, glossopharyngeal nerve, and also occipital nerve in addition to other headaches such as central post-stroke pain make up part of this group.

Physicians have used interventional techniques to treat headaches in all classifications. These techniques include peripheral nerve stimulation, third occipital nerve block (TON), lesser occipital nerve block (LON), greater occipital nerve block (GON), sphenopalatine block (SPG), radiofrequency ablation (RFA), and cervical epidural steroid injections (CESI). While some of these techniques have shown strong promise, others have mixed data and more trials are needed before their efficacy can be fully understood.

Primary Headache Disorders

Among the most prevalent primary headache disorders are tension-type headaches (TTH), chronic migraines (CM), and trigeminal autonomic cephalgias (TACs). TTH are more common and affect 60–80% of the general population. Migraines have a prevalence of 15% in the general population and affect gender differently as 7.6% of males and 18.3% of females have been diagnosed [1]. Cluster headaches, a type of TAC, are present in only 0.1% of individuals and remain an uncommon headache disorder that is commonly misdiagnosed or mistreated [3••].

Patients frequently describe TTH as a tight band firmly wrapped around the head, or a dull-aching tightness in the head [1]. These headaches are almost always episodic, and very rarely chronic. Unlike CM, TTH do not lead to chronic disruptions in a patient's life [5].

CM are the second most commonly encountered type of headache and are characterized by attacks of unilateral pulsating or throbbing, moderate to severe pain that is sustained for 4 to 72 h. Between events, the person may be completely pain free, which characterizes an episodic headache. Accompanying symptoms with CM pain can be nausea, vomiting, and light or sound sensitivity. CM can be provoked by sensitivity to certain smells. The emergence of a CM treatment modality that is cost-effective, readily available, easy to administer, evidence-based, and safe has yet to be discovered [6].

Cluster headaches are the most prevalent subtype of trigeminal autonomic cephalgias (TACs), which are a group of headaches characterized by short duration, strict unilaterality, and association with autonomic manifestations such as rhinorrhea, lacrimation, ptosis, and conjunctival injection. The prevalence of cluster headaches is higher in young males than females (3.5:1), and in smokers (65%). They are usually episodic, and only 10–20% of patients have a chronic component [1]. Some patients will have a cluster headache as infrequently as once every few days, while others might experience episodes up to 8 times per day. Cluster headaches are known for their excruciating pain, hence the term "suicidal headaches," and patients often become agitated at the beginning of an attack and may begin to sweat profusely [1]. The attacks have a circadian rhythm and alcohol will almost always trigger a classic attack in a cluster headache patient [3••].

Cervicogenic headaches (CGH), a secondary headache disorder, originate in the areas innervated by the cervical spine nerves (C1–C3). The Cervicogenic Headache International Study Group (CHISG) defines CGH as having at a minimum of the following: (1) demonstration of pain with neck movement or sustained awkward positioning or (2) demonstration of pain with applied pressure over the upper cervical or occipital region on the affected side, and finally (3) a positive response to anesthetic blockade of the cervical spine nerves. The CHISG diagnostic criteria also include unilateral pain (though bilateral pain is possible) and restriction in neck range of motion [7••]. This definition was recently updated by the ICHD requiring objective evidence of a cervical disorder or lesion in the spine causing headaches. It must also include two of the following four requirements: (1) a temperal relationship of disorder to causing headaches, (2) the headache improves with resolution of the lesion, (3) cervical range of motion is reduced and provocative measures cause headaches, and finally (4) a diagnostic nerve block abolishes the headache. The difficulty of fulfilling these criteria and the controversial nature of CGH have made diagnosis and management of CGH challenging [8].

The cervical spine is innervated by multiple sources: the cervical sinuvertebral nerves, the vertebral nerve, and branches of the cervical sympathetic trunk. Of note, Substance P is found within these nerve fibers, suggesting they may be nociceptive, or able to relay sensations of pain [9]. Anatomic studies have shown that stimulation of these nerves leads to referred pain in the scapular region extending through the occipital area and symptoms of a headache may result [10]. Cervical discs differ from thoracolumbar discs in that they lack a posterior annulus, which allows for greater range of motion. They also lack the gelatinous nucleus and circumferential annulus, and are thus not as susceptible to internal disruption. Rather, they are more prone to ligamentous sprains.

Although not technically classified as a headache, intervertebral cervical disc disease can cause referred pain to the head and scapula. A recent review by Peng et al confirms cervical disc disease as a significant etiology of headaches and neck and shoulder pain. [11•] What has proven particularly challenging in understanding intervertebral cervical discs as a source of headache is a lack of distinct clinical or radiographic diagnostic features. The disc pathology which leads to pain is also unclear. While degenerative disc disease and spondylosis can lead to pain, they are quite common radiographic findings found in people who are not experiencing any pain. Currently, the only diagnostic mechanism is a fairly invasive procedure that involves inserting a stimulating needle into the intervertebral disc space to try to reproduce painful symptoms. Currently, the only mechanism of treating painful cervical discs is surgical: an anterior cervical discectomy and fusion (ACDF), which in itself is controversial, as it typically only partially reduces symptoms [11•].

Therapeutic Options

Pharmaceutical agents are currently the cornerstone of headache management [12]. However, during the past few decades, several interventional therapies have emerged as treatments to headaches refractory to medications, (e.g., stimulation of occipital nerve, sphenopalatine ganglion block, deep brain stimulation, radiofrequency ablation, nucleus caudalis dorsal root surgery) [13] (See Table 1).

Pharmacologic Management

Current limitations with the pharmacologic approach is that many agents cannot be used in light of co-morbid medical conditions or medication interactions. For these patients, interventional procedures can be dramatically effective.

Peripheral nerve procedures fall into four general categories: nerve stimulation, localized nerve blocks, radiofrequency ablation, and localized steroid injections.

Peripheral Nerve Stimulation

Peripheral nerve stimulation (PNS) is an effective modality for variable forms of chronic primary headaches refractory to medical treatment, notably CM and cluster headaches. The mechanism by which PNS provides a decrease in frequency or pain severity is unclear, but perhaps involves activation of central endogenous pain modulation networks [14••].

Several studies have shown how effective PNS can be on chronic primary headaches. Popeney et al. studied the role of PNS on 25 chronic migraine patients and demonstrated an 88.7% improvement in headache quality as assessed by the MIDAS (Migraine Disability Assessment) scale, with only minimal residual disability seen in 15 out of 25 patients [15]. Matharu et al. reported significant improvement in six out of eight patients and Schwedt et al. showed significant improvements in a multitude of indices including headache frequency (improvement of 25 days from a baseline of 89/90 days), headache intensity (2.4 points from a baseline of 7.1 points), MIDAS scores (70 points from a baseline of 179 points), HIT-6 (11 points from a baseline of 71 points), and BDI-II scores (8 points from a baseline of 20 points) at a mean follow-up of 19 months [16, 17].

The first prospective trial that evaluated the efficacy of occipital nerve stimulation (ONS), the Occipital Nerve Stimulation for the Treatment of Intractable Migraine (ONSTIM) study, demonstrated a sharp 50% reduction in headache frequency and/or a three-point intensity scale decrease in 39% of 66 patients treated with active PNS for 12 weeks [18]. A double blinded, randomized controlled trial on the treatment of refractory migraine, the Precision Implantable Stimulator for Migraine (PRISM) study, showed a mean decrease of 5.5 migraine days/month in 63 patients who received active stimulation and a decrease of 3.9 days in 62 patients who received sham stimulation at 12 weeks. Although the difference was not statistically different, a subanalysis showed a 5.0 headache day reduction in the active group and a 2.6-day reduction in the sham group not overusing acute headache medication [14••].

Silberstein et al. studied the effect of neurostimulation near occipital nerves in patients with CM. Although they found no significant difference in the percentage of responders in the active compared with the control group (95% lower confidence bound (LCB) of − 0.06; $p = 0.55$), there was a significant difference in the percentage of patients that achieved a 30% reduction ($p = 0.01$) in headaches. Importantly, compared with sham-treated patients, there were also significant differences in reduction of number of headache days (active group = 6.1, baseline = 22.4; control group = 3.0, baseline = 20.1; $p = 0.008$), migraine-related disability ($p = 0.001$), and direct reports of pain relief ($p = 0.001$) [14••]. While the accepted standard for pain reduction has traditionally been 50%, in 2008, the Initiative on Methods, Measurements, and Pain Assessment in Clinical Trials (IMMPACT) panel and the HIS established a 30% reduction in pain as clinically meaningful [19]. PNS has been shown to have a benefit in the treatment of headaches especially if even modest (< 50%) reduction is considered a significant improvement. Summary of noteworthy studies on occipital nerve stimulation is provided in Table 2.

Table 1 Interventional approaches to treatment of headache

Interventional treatment options
Peripheral nerve stimulation (PNS)
Third occipital nerve (TON) block
Lesser occipital nerve (LON) and greater occipital nerve (GON) blocks
Sphenopalatine ganglion (SPG) block
Radiofrequency ablation (RFA)
Cervical epidural steroid injections (CESI)

Nerve Blocks

Third Occipital Nerve Block The third occipital nerve (TON block), emerged from the theory supporting the concurrent irritation of the 3rd occipital nerve, and the greater occipital nerve (GON) are the causes of CGH [2].

Table 2 Summary of noteworthy studies on occipital nerve stimulation for chronic headache

Author	Study	Design	Number of subjects	Follow-up period	Results	Evidence	Comments
Peripheral nerve stimulation							
Silberstein et al. (2012) [14••]	Occipital nerve stimulation for chronic migraine	Multicenter RCT	Active ($n = 105$) Sham ($n = 52$)	12 weeks	No difference in percentage of responders in both the groups Showed 30% reduction in headaches	Level 1b	Failed to show difference in primary endpoint, i.e., 50% reduction in pain
Mekhail (2017) [20••]	Occipital nerve stimulation	Single-center RCT	20	52 weeks	60% of patients received 30% reduction in pain	Level 1b	50% of adverse events were hard-ware related
Dodick (2014) [21••]	Neurostimulation near occipital nerves for chronic migraine	Multicenter RCT	Active ($n = 105$) Sham ($n = 52$	52 weeks	30% headache reduction in 60% of patients. 50% reduction in 48% of patients.	Level 1b	This open-label study of Silberstein et al. (additional 40 weeks) showed headache-free days and disability at 12 months High adverse events rate (40% required surgical intervention) were reported
Saper (2011) [18]	Occipital stimulation for intractable migraine	Multicenter RCT Assigned to 3 different groups	75	3 months	50% reduction in headache frequency	Level 1b	Lead migration rate was high (24%)
Fontaine (2017) [22]	Occipital nerve stimulation Chronic cluster headache	Observational prospective study	44	12 months	Headache decreased by > 50% in 59% of patients 47.8% were excellent responders	Level 4	~ 70% responded to ONS In responders, heath-related quality of life improved significantly 33% patients had minor surgical complications
Rodrigo (2017) [23]	Occipital nerve stimulation for refractory migraine	Long-term open-label, prospective	37	7 years	Significant reduction in pain over the follow-up period	Level 4	7/35 implants were removed for various reasons. Difficult to make clear recommendations because of uncontrolled design and not all patients completed a 7-year follow-up
Miller (2016) [24]	Occipital nerve stimulation	Uncontrolled, open-labeled prospective	53	42 months	> 30% reduction in monthly headaches were observed in 45% of patients	Level 4	Mixed headache types were included in the cohort
Popeney (2003) [15]	C1–C3 stimulation for chronic migraine	Case series	25	18 months	88% improvement in MIDAS Score	Level 4	Significant reduction in headache severity, frequency, and disability
Schwedt et al. (2007) [17]	Occipital nerve stimulation	Retrospective case series	15	19 months	Fewer headache days associated with mean pain reduction by 52%	Level 4	60% of patients required revision within a year

RFA radiofrequency ablation, *MIDAS* migraine disability assessment score, *ONS* occipital nerve stimulation

TON is a superficial branch from the dorsal ramus of C3 which courses deep to the semispinalis capitis muscle and is unique when compared to other cervical occipital nerves. Along its proximal one third, it lies adjacent to the greater occipital nerve (GON), allowing both to be blocked easily. The TON is the primary afferent channel along which the second and third cervical zygapophysial joints send their sensory input. The remaining cervical zygapophysial joints are innervated by two medial branches that arise from the dorsal rami of the two successive spinal nerve roots [2].

Bupivacaine, mepivacaine, lidocaine, and prilocaine are all commonly used in treatment of refractory primary headaches. Lidocaine is most commonly used, with a concentration of 1%, onset of action is within 4–8 min after injection, and sustainability of local anesthesia occurs for 1 to 2 h. Bupivacaine has a more profound effect, and quite longer duration of action (i.e., 4 to 8 h), with a solution concentration of 25% or 50%, and onset within 8 to 12 min after infiltration [25]. Some physicians prefer to combine both agents in a 1:1 solution.

Ashkenazi et al. concluded that addition of local steroids to the LA agents had no significant added short- or long-term benefits whatsoever on patients given GON block for treatment of headache [26], although some still choose to add it as a local anti-inflammatory agent. Some preparations combine LA agent with local vasoconstrictors, such as epinephrine, to decrease bleeding in a surgical field, but this is neither recommended nor necessary in nerve block procedures [26].

Lesser Occipital Nerve and Greater Occipital Nerve Blocks The pain in CGH is thought to arise from the convergence of upper cervical and trigeminal sensory pathways to the head and face. Anesthetic blocks of the LON and facial (FN) can be used to diagnose CGH, and have been found effective in providing temporary relief in CGH. A FN blockade can be added for patients with more extensive pain [27].

Blocks are typically performed in a similar manner to the TON block, with the use of a localizing nerve stimulator. GON blockade is used for patients with pain in the parietal and occipital areas. LON blockade is used for patients with pain in the frontal and temporal areas, and FN blockade added for pain extending into the orbital area [27].

A randomized, double blinded study of LON, GON, and FN blockade for 50 people with CGH demonstrated statistically significant reduction in pain, analgesic consumption, and associated symptoms in the blockade group. Two weeks after the procedure, the intervention group reported a nearly 50% improvement on standardized headache severity assessments, compared to both their baseline and the control group. They also reported a decrease in frequency and in symptoms such as nausea, photophobia, and phonophobia. Intervention patients reported relief for an average of 3.67 days, whereas the control group reported relief for 1.52 days. Those that received the FN block had a significantly longer period of relief (3.93 days) compared with those who had LON and GON only (3.22 days) [27].

Sphenopalatine Ganglion Block The pterygopalatine ganglion (also known as the sphenopalatine ganglion, or Meckel's ganglion) is a complex structure that functions as a reliable point for not only parasympathetic pathways but also many sensory and sympathetic nerve pathways [28••]. The sphenopalatine ganglion (SPG) is located in the pterygopalatine fossa that is thought to be involved in the pathophysiology of cluster headaches, making it a useful target. A SPG block results in anesthesia of a relatively large surface area supplied by the maxillary branch of the 3rd cranial nerve, i.e., the trigeminal nerve [25]. Percutaneous radiofrequency ablation of the SPG was shown to have encouraging results in patients with intractable cluster headaches [28••].

The SPG block can be performed using 2 main methods. First, an injection can be placed around the ganglion either through an intraoral pass way or alternatively topical placement of a LA agent on the nasal mucosa overlying the SPG in the postero-lateral nasal wall [28••, 29].

Sanders et al. conducted a retrospective analysis of patients with refractory cluster headaches treated by radiofrequency lesion of the SPG. The authors studied 56 patients with episodic cluster headaches and ten patients with chronic cluster headaches over a period of 12–70 months. In the episodic cluster headache group, 60.7% of subjects experienced complete pain relief, but only three of ten patients with chronic cluster headaches had the same result [30]. Additionally, Narouze and colleagues reported favorable outcome after intractable chronic cluster headaches as well as acute headaches. Significant improvement was seen in both mean attack intensity and mean attack frequency for up to 18 months in 15 patients [31]. Furthermore, Narouze et al. has described that application of LA agents to the nasal mucosa can have similar results with the added benefit of patients being able to perform such a procedure by themselves in the home-based setting [29].

Using radiofrequency on sphenopalatine ganglion was initially described by Salar et al. [32]. Compared to the short-lived effect of SPG block, SPG radiofrequency ablation tends to have a longer duration of effect. While Narouze et al. reported improvement in symptoms up to 18 months in patients who underwent SPG radiofrequency ablation, studies reporting on the SPG block showed a more modest duration of relief [33]. A systematic review by Ho and colleagues evaluated 15 studies on the topic of SPG radiofrequency ablation. One study was a small but positive prospective cohort study for cluster headaches, while the other 14 studies were case reports and case series. There were no controlled studies. The authors concluded that because there is not yet a randomized controlled study to test the efficacy of RFA on the SPG, their recommendations for its use was a grade B [34]. SPG is a useful target for treatment of cluster headaches and may be the option of choice for individuals unable to tolerate refractory to oral medication, but stronger evidence is needed before a firm conclusion can be made.

Radiofrequency Ablation

Radiofrequency ablation (RFA) acts by destruction of the peripheral pain–generating nervous tissue (i.e., TON, and cervical medial branch nerve in CGH, and occipital nerve in occipital neuralgia) [35]. The aim of this technique is to generate a thermal current within the culprit nerve, thereby causing destruction of the afferent pain pathway [36].

In pulsed radiofrequency ablation (PRF), the current is applied in a pulsatile manner with short pulses of high-voltage electrical current applied as "bursts" [35, 36]. A systematic review by Grandhi et al. reviewed 10 articles between 1966 and 2017 which investigated the use of RFA and PRF for the management of CGH. The review concluded that RFA and PRF provide very limited benefit in the management of CGH. Furthermore, the authors claimed that at the time of publication, there was no high-quality RCT and/or strong non-RCTs to support the use of these techniques, despite numerous case reports which had demonstrated benefit [37•]. In 2018, Abd-Alsayed et al. conducted a retrospective analysis on the use of RFA for pericranial nerves to treat chronic headache conditions. The study showed that of the 57 patients who received 72 RFAs for pericranial nerves to treat a headache or pericranial neuralgia, 90.3% of patients had improvement in their headache condition after receiving RFA. In addition, pain scores decreased from 6.6 ± 1.7 preprocedure to 1.9 ± 1.9 postprocedure ($p < 0.001$) [38].

Additionally, in 2018, Cohen and colleagues reported the results of a double-blind randomized control trial comparing PRF to steroid injections for occipital neuralgia or migraines with occipital nerve tenderness. Forty-two participants were randomized to receive local anesthetic and saline, and 3–120-s cycles of PRF per targeted nerve. The other 39 participants were randomized to receive local anesthetic mixed with deposteroid and 3 rounds of sham PRF. Patients, treating physicians, and evaluators were blinded to interventions. The PRF group experienced a greater reduction in average occipital pain at 6 weeks (mean change from baseline -2.743 ± 2.487 vs -1.377 ± 1.970; $p < 0.001$), than the steroid group, which persisted through the 6-month follow-up. Comparable benefits favoring PRF were obtained for worst occipital pain through 3 months (mean change from baseline -1.925 ± 3.204 vs -0.541 ± 2.644; $p = 0.043$), and average overall headache pain through 6 weeks (mean change from baseline -2.738 ± 2.753 vs -1.120 ± 2.1; $p = 0.037$). The authors concluded that although PRF can provide greater pain relief for ON and migraine with occipital nerve tenderness than steroid injections, the superior analgesia may not be accompanied by comparable improvement on other outcome measures [39••].

Although considered weak evidence, there have been case reports that have demonstrated efficacy of PRF in treatment of CGH. A case report by Odonkor et al. claimed pain relief at 12 weeks after C1–C2 joint ablation for CGH [40]. Fadayomi et al. utilized an ultrasound–guided approach for a C2 PRF in a patient with cluster headaches and reported ongoing pain relief 8-month post procedure [41].

The literature is not completely supportive of RF for treatment of headaches but as pointed out by Grandhi et al., this may be due to the lack of strong RCTs that clearly show a benefit. A systematic review on this topic done by Nagar et al. reviewed the existing literature on the topic and also concluded that there is poor evidence to support PRF for CGH [42•]. The few studies that have been conducted recently point to a partial benefit but more studies are needed. Summary of noteworthy studies on RF for treatment of headaches is provided in Table 3.

Cervical Epidural Steroid Injections

Injection of steroids into the epidural space is a known treatment of radicular pain and radiculopathies, and subsequently, interlaminal injection of steroids into the cervical epidural space has also proven effective in managing CGH.

Injection of the cervical epidural space is typically at C6/7 or C7/T1, under fluoroscopic guidance. Injected fluid flows preferentially along the dural sheath and exits the spinal canal through adjacent intervertebral foramina [49••].

Current data around efficacy of CESI is not robust; however, a literature review by Wang et al. demonstrates some preliminary data that CESI may be effective for short- and long-term pain relief in CGH, particularly in patients with clinical and radiographic evidence of upper cervical spinal nerve root irritation [49••]. Martellettie et al. showed CESI to be effective up to 4-week post procedure, but not effective at 6 months [50]. He et al. showed both a decrease in the average number of days patients experienced pain, the occurrence of severe pain, and daily NSAID usage at both 3 and 6 months. The author also demonstrated that CESI is particularly effective for CGH when known upper cervical disc pathologies are present [51]. Of note, neither study found any post procedural complications or long-term sequelae [49••].

C2/C3 Facet Joint Injections and RFA for CGH

Another means of treating CGH is via C2–C3 facet joint injections. These are typically performed with a combination of steroids and local anesthetic agents, and target the TON, which innervates the C2–C3 zygapophysial joint. These injections are typically used to treat cervical pain rather than CGH, although there is some data pointing towards efficacy in CGH. A prospective analysis of C2–C3 injection for chronic

Table 3 Noteworthy studies on radiofrequency lesioning of cervical facet joints for chronic headache

Author	Study	Design	Number of subjects	Follow-up period	Results	Evidence	Comments
Cohen (2015) [39••]	Pulsed radiofrequency (PRF)	Multicenter RCT PRF ($n = 39$) Sham ($n = 42$)	81	3 months	Greater reduction in occipital pain in PRF group ($p < 0.001$)	Level 1b	Compared PRF to steroid injections in occipital pain and migraine Migraine group experienced significant difference in occipital pain with PRF No difference noted in headache disability and medication use in all groups
Gabrhelik (2011) [43]	Pulsed RF versus greater occipital nerve block	Randomized, blinded, pilot study	30	Evaluated at 3- and 9-month post-procedure	At 3 months, VAS and medication reduction and was similar between groups At 9 months, more PRF patients reported reduced VAS	Level 1b	VAS, medication quantification, and global perceived effect were assessed Greater occipital nerve block is safe and provides good analgesia
Stovner (2004) [44]	RFN of C2–C6 facet joints on the ipsilateral side	Randomized, double-blind, sham controlled study	12 (6 patients randomized to RFA)	24 months	RFN patients improved in the first 3 months but in the long-term both groups remained same	Level 1b	RFN of cervical facet joints s not beneficial in cervicogenic headache
Haspeslagh (2006) [45]	RFN and local anesthetic steroid injection in control group	RCT	30 RFN ($n = 15$) Control ($n = 15$)	48 weeks	No difference between treatment groups at any point in the trial	Level 1b	No evidence that RFN of upper cervical facets and upper dorsal root ganglion is better than local steroid injection of greater occipital nerve
Lee (2007) [46]	Conventional radiofrequency	Case series	30	12 months	> 75% reduction in pain at 12 months	Level 4	Patient selection was highly selective and uncontrolled. Included only patients who responded to (> 50% analgesia) with 2 diagnostic medial branch blocks
Van Suijlekorn (1998) [47]	RFN of cervical facet joints	Prospective case series	15	16.8 months	Significant reduction in pain and analgesic consumption	Level 4	More than 50% reduction in headache days/ week was reported but concluded that definitive conclusion can only be reached by an RCT
Govind (2003) [48]	Revised technique of RFN for third occipital headache	Prospective case series	49	~ 42 weeks	88% achieved successful outcome Median duration of analgesia was 297 days	Level 4	Revised technique consisted of larger gauge needle and maintaining minimum distance between the needles Complete pain relief for 90 days was considered a successful outcome

RFN radiofrequency neurotomy

headaches in whiplash patients demonstrated residual improvement through 12 months [52].

Likewise, percutaneous radiofrequency neurotomy targeting the TON via C2–C3 has been more commonly used for CGH. In RF neurotomy, as described above, the nerve is destroyed via a monopolar needle positioned parallel to the nerve. When an alternating current is applied, a thermal injury is produced at the target nerve, which ultimately coagulates [52]. In patients with diagnostically confirmed CGH, TON neurotomy has been shown to be effective in 88% of those treated, with a median duration of relief of 297 days [48].

Conclusion

Headaches comprise a prevalent and extraordinarily diverse group of neurological disorders. While many can be treated pharmacologically, those who continue to suffer from refractory or severe headaches may see tremendous benefit from a range of more invasive treatments which focus on directly inhibiting the painful nerves. While there is a plethora of literature suggesting these methods are effective and possibly durable interventions, there is still a need for large, prospective, randomized trials to clearly demonstrate their efficacy.

Compliance with Ethics Guidelines

Conflict of Interest Ruchir Gupta, Kyle Fisher, and Srinivas Pyati 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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