Focused Review

Pulsed Radiofrequency for Occipital Neuralgia

Nicholas Manolitsis, MD[1], and Foad Elahi, MD[2]

From: [1]Dept. of Physical Medicine and Rehabilitation, Mercy Medical Center, Des Moines, Iowa; [2]The University of Iowa Hospitals and Clinics, The Center for Pain Medicine & Regional Anesthesia, Iowa City, Iowa

Address Correspondence:
Nicholas Manolitsis, MD
Mercy Medical Center
Dept. of Physical Medicine and Rehabilitation
1111 6th Avenue, East Tower, Level B
Des Moines, Iowa
E-mail:
nicholas.manolitsis@gmail.com

Disclaimer: There was no external funding in the preparation of this manuscript. Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received: 07-17-2013
Revised manuscript received: 07-13-2014
Accepted for publication: 07-16-2014

Free full manuscript:
www.painphysicianjournal.com

Background: The clinical application of pulsed radiofrequency (PRF) by interventional pain physicians for a variety of chronic pain syndromes, including occipital neuralgia, is growing. As a minimally invasive percutaneous technique with none to minimal neurodestruction and a favorable side effect profile, use of PRF as an interventional neuromodulatory chronic pain treatment is appealing.

Occipital neuralgia, also known as Arnold's neuralgia, is defined by the International Headache Society as a paroxysmal, shooting or stabbing pain in the greater, lesser, and/or third occipital nerve distributions. Pain intensity is often severe and debilitating, with an associated negative impact upon quality of life and function. Most cases of occipital neuralgia are idiopathic, with no clearly identifiable structural etiology. Treatment of occipital neuralgia poses inherent challenges as no criterion standard exists. Initially, conservative treatment options such as physical therapy and pharmacotherapy are routinely trialed. When occipital neuralgia is refractory to conservative measures, a number of interventional treatment options exist, including: local occipital nerve anesthetic and corticosteroid infiltration, botulinum toxin A injection, occipital nerve subcutaneous neurostimulation, and occipital nerve PRF. Of these, PRF has garnered significant interest as a potentially superior, safe, non-invasive treatment with long-term efficacy.

Objective: The objective of this article is to provide a concise review of occipital neuralgia; and a concise, yet thorough, evidence-based review of the current literature concerning the use of PRF for occipital neuralgia.

Study Design: Review of published medical literature up through April 2013.

Setting: The Center for Pain Medicine and Regional Anesthesia, the University of Iowa Hospitals and Clinics.

Results: A total of 3 clinical studies and one case report investigating the use of PRF for knee occipital neuralgia have been published worldwide. Statistically significant improvements in pain, quality of life, and adjuvant pain medication usage have been demonstrated.

Limitations: Lack of randomized control trials, small study sample sizes, an absence of diagnostic block imaging guidance, and the use of outcome measures that are inherently subjective, limiting objectivity and introducing an unquantifiable degree of bias.

Conclusion: Clinical studies to date examining the efficacy of PRF as a treatment for occipital neuralgia have yielded promising results, demonstrating sustained improvement in pain, quality of life, and adjuvant pain medication usage. Despite these encouraging clinical studies, conclusive evidence in support of PRF as an interventional treatment option for occipital neuralgia awaits to be seen.

Key words: Occipital neuralgia, pulsed radiofrequency, PRF, greater occipital nerve, lesser occipital nerve, chronic pain, interventional pain management

Pain Physician 2014; 17:E709-E717

The clinical application of pulsed radiofrequency (PRF) by interventional pain physicians for a variety of chronic pain syndromes, including occipital neuralgia, is growing. As a minimally invasive percutaneous technique with none to minimal neurodestruction and a favorable side effect profile, use of PRF as an interventional neuromodulatory chronic pain treatment is appealing. At this time, clinical research regarding the efficacy of PRF is limited but gradually accumulating. The objective of this article is to provide a concise review of occipital neuralgia; and a concise yet thorough evidence-based review of the current literature concerning the use of PRF for occipital neuralgia.

Background

Clinical Features

Occipital neuralgia, also known as Arnold's neuralgia, is defined by the International Headache Society (IHS) as a unilateral or bilateral paroxysmal, shooting or stabbing pain in the posterior part of the scalp, in the distribution of the greater occipital nerve (GON), lesser occipital nerve (LON), or third occipital nerve (TON), sometimes accompanied by diminished sensation or dysesthesia in the affected area and commonly associated with tenderness over the involved nerve(s) (1). Pain classically originates in the suboccipital region and radiates toward the posterior and/or lateral scalp over the vertex (2); however, pain may also be perceived retro-orbitally and over the neck, temple, and frontal regions (3). Paroxysms may occur frequently, while pain intensity can be severe and debilitating (4). Pressure over the GON and LON distributions may amplify the pain, while cervical extension and rotation may occasionally serve as a pain trigger (5). Associated symptoms may include photophobia, tinnitus, dizziness, nausea, and nasal congestion (4,6). Patients may also avoid activities such as brushing their hair, wearing a hat, or lying on a pillow (7).

Table 1. *Potential causes of occipital neuralgia.*

1. Vascular
- Irritation of the nerve roots C1/C2 by an aberrant branch of the arteria inferior posterior cerebelli (posterior inferior cerebellar artery)
- Dural arteriovenous fistula at the cervical level
- Bleeding from a bulbocervical cavernoma
- Cervical intramedullary cavernous hemangioma
- Giant cell arteritis
- Fenestrated arteria vertebralis pressing on C1/C2 nerve roots
- Aberrant course of the arteria vertebralis

2. Neurogenic
- Schwannoma in the area of the craniocervical junction: schwannoma of the nervus occipitalis
- C2 myelitis
- Multiple sclerosis

3. Muscular/tendinous

4. Osteogenic
- C1/C2 arthrosis, atlantodental sclerosis
- Hypermobile arcus posterior of the atlas
- Cervical osteochondroma
- Osteolytic lesion of the cranium
- Exuberant callus formation after fracture C1/C2

Etiology

Most cases of occipital neuralgia are idiopathic, with no clearly identifiable structural etiology (5,8,9). In many cases, compressive irritation or damage to the GON, LON, and or TON is implicated (7,10,11). Potential causes of irritation or damage may be vascular, neurogenic, muscular/tendinous, or osteogenic (Table 1) (4). The GON is more frequently involved (90%), whereas the LON is less frequently involved (10%). Both the GON and LON are involved in 8.7% of cases (12). Involvement of the TON—either alone or in combination with the GON and or LON—is not known. The TON is by far the least referenced of the 3 nerves defined to potentially contribute to occipital neuralgia and was only recently added to the updated diagnostic criteria in the International Classification of Headache Disorders 3rd edition (1,11). There are no epidemiologic studies documenting the incidence and prevalence of occipital neuralgia.

Clinically Relevant Anatomy

The GON arises from the dorsal primary ramus of the second cervical nerve with contribution from the third cervical nerve (Fig. 1) (13,14). It supplies sensory innervation to the medial portion of the posterior scalp as far anterior as the vertex, while also supplying motor innervation to the semispinalis capitis. Although the course of the GON is described with much variability, the most common site for compression occurs where the nerve penetrates the aponeurosis of the trapezius (15,16).

The LON arises from the ventral primary ramus of the second cervical nerve with contribution from the third cervical nerve (Fig. 1) (13,14). The LON traverses superiorly along the posterior border of the sternocleidomastoid muscle, supplying cutaneous innervation to the lateral portion of the scalp and the cranial surface of the auricle (13). Its most common location of compression is not defined in the literature.

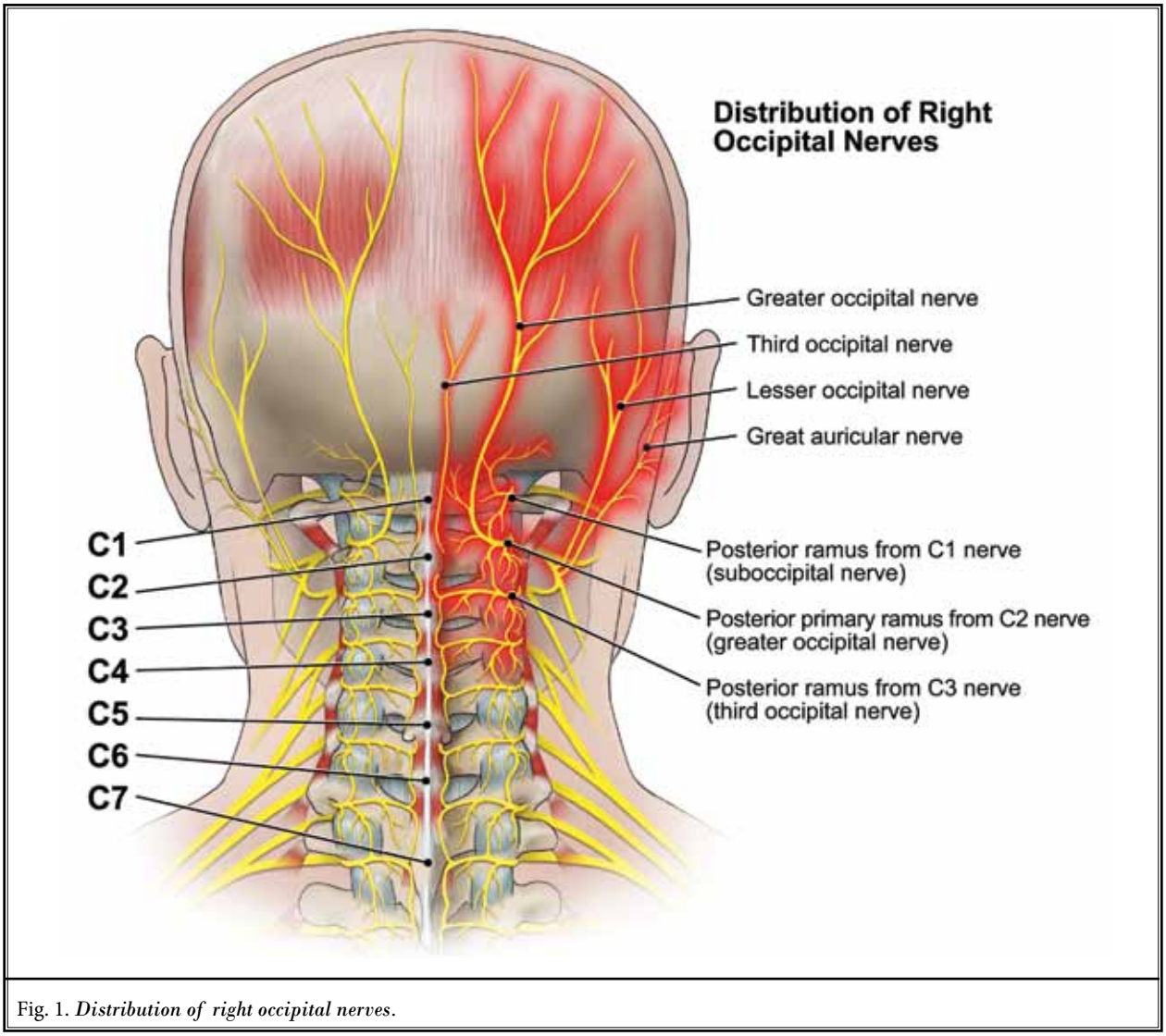

Fig. 1. *Distribution of right occipital nerves.*

The TON arises deep to the trapezius from the medial branch of the dorsal ramus of the third cervical nerve (Fig. 1) (14,17). The TON ascends medial to the GON and is connected to it both over the occiput and as the GON rounds the inferior edge of the inferior capitis oblique. It supplies sensory innervation to the skin over the rostral end of the neck and the occiput near the external occipital protuberance (17). A commonly implicated area concerning TON compression lies at the C2-3 facet joint (18-21).

Diagnosis

Distinguishing occipital neuralgia from other common headache syndromes — notably, migraine headache, tension headache, cluster headache, and cervicogenic headache — can be challenging in light of their many shared clinical manifestations. Other less common conditions that may also cause similar pain in the occiput region include greater auricular neuralgia, C2/3 radiculopathy, hemicrania continua, giant cell arteritis, and tumors of the cervical spinal column (5,22,23). As such, performance of a thorough history and physical examination is imperative for accurate diagnosis (24). On physical examination hypo- or dysesthesia over the greater and or lesser occipital nerve distribution may be noted. Furthermore, tenderness over the GON and or LON along with a positive Tinel's sign can be observed. In 85% of occipital neuralgia cases the clinical

Table 2. *The International Headache Society diagnostic criteria for occipital neuralgia.*

A. Unilateral or bilateral pain fulfilling criteria B—E
B. Pain is located in the distribution of the greater, lesser, and/or third occipital nerves
C. Pain has 2 of the following 3 characteristics:
1. Recurring in paroxysmal attacks lasting from a few seconds to minutes
2. Severe intensity
3. Shooting, stabbing or sharp in quality
D. Pain is associated with both of the following:
1. Dysesthesia and/or allodynia apparent during innocuous stimulation of the scalp and/or hair
2. Either or both of the following
a. tenderness over the affected nerve branches
b. trigger points at the emergence of the greater occipital nerve or in the area of distribution of C2
E. Pain is eased temporarily by local anesthetic block of the affected nerve
F. Not better accounted for by another ICHD-3 diagnosis
Comments: The pain of occipital neuralgia may reach the fronto-orbital area through trigeminocervical inter-neuronal connections in the trigeminal spinal nuclei.

presentation is unilateral (10). A clinical presentation consistent with the above noted history and physical examination findings in addition to temporary improvement after diagnostic blockade of the GON, LON, and/or TON with local anesthetic confirms the diagnosis (1). The IHS diagnostic criteria for occipital neuralgia are listed in Table 2 (1).

Treatment

The treatment of occipital neuralgia poses inherent challenges as no criterion standard exists. Initial treatment options focus upon conservative measures, with a goal of reducing secondary muscle tension and improving posture. These initial treatments may include physical therapy, massage, acupuncture, and heat (25,26). Pharmacologic treatments that may also be trialed initially include non-steroidal anti-inflammatory drugs (NSAIDs), tricyclic antidepressants, antiepileptics, and possibly opioids.

In cases where occipital neuralgia is refractory to conservative measures, a number of interventional treatment options exist, including local occipital nerve anesthetic and corticosteroid infiltration, botulinum toxin A injection, occipital nerve subcutaneous neurostimulation, and occipital nerve PRF. Of these, PRF—as is evidenced by the accumulation of recent studies—has garnered significant interest as a potentially safe, non-invasive treatment with long-term benefits for occipital neuralgia. In the discussion that follows, we will provide a concise yet thorough evidence-based review of the current literature concerning the use of PRF for occipital neuralgia. Procedural technique details on the performance of PRF for occipital neuralgia are beyond the scope of this focused review article.

Methods

To evaluate the use of PRF specifically for occipital neuralgia, a computer-aided search of PubMed, Ovid, and Scopus databases was performed using "pulsed radiofrequency" and "occipital neuralgia" as key word search terms. The search was open for original clinical studies, including case reviews, case series, and randomized control trials. Non-clinical basic science articles and review articles were excluded. An open date range was used.

Results

As of the time of our literature search, a total of 3 clinical studies and one case report investigating the use of PRF for knee occipital neuralgia have been published worldwide: one in South Korea, one in Belgium, and 2 in the United States (Table 3) (10,27-29). Of these clinical studies, 2 study designs were prospective, non-randomized, and without a control group; while one study design was a retrospective, observational, non-randomized, and multi-centered. Study sizes included 10, 19, and 102 participants, respectively. Diagnostic block protocols were heterogenous amongst the case report and clinical studies. Variation was noted in the number of diagnostic blocks performed, the type of anesthetic used, the inclusion of corticosteroid, the volume infiltrated, and the specific nerves blocked (Table 3) (10,27-29). Consensus criterion of at least 50% pain relief was deemed to be a positive diagnostic block, although a small group of 10 patients having less than 50% improvement were included in the Huang et al (29) study. PRF treatment protocols were also heterogenous amongst the case report and clinical studies, with variations noted in the number and duration of

Table 3. *Occipital neuralgia, PRF studies.*

Study (y)	Study Design	Diagnosis/Diagnostic Test Block Utilized	Intervention	Outcome Measures	Assessment Interval	PRF Treatment Results
1. Navani, et al 2006 (27)	Case Report	Dx: Greater Occipital Neuralgia **Diagnostic Test Blocks:** 1st block: Left GONB, 4.5mL of 0.25% Bupivicaine & 20mg of Triamcinalone Result: 95% pain relief for 3 days. 2nd block: Left GONB, 3mL of 0.25% Bupivicaine & 40mg of Triamcinalone Result: 95% pain relief for 9 days.	PRF to the GON **PRF Settings** Impedence: 470 Ω Sensory stimulation noted at: 0.6 V PRF performed at 42°C for 4 min Treatment interval: 4 months Number of treatments: 2 N = 1	Verbal Analog Scale	Not known	1. 60-70% pain relief noted for 4 months after the first treatment 2. 60-70% pain relief noted for 5 months after the second treatment
2.Vanelderen, et al 2010 (10)	Prospective Non-randomized Longitudinal Non-controlled	Dx: Occipital Neuralgia **Diagnostic Test Blocks:** 0.5% Bupivacaine 2mL per nerve Infiltration sites: GON, LON, or both, Number of cycles: 1 Positive block criteria: ≥50% pain reduction on VAS	PRF to the GON and/or LON **PRF Settings** Sensory stimulation noted at: < 0.5 V PRF current of 20 msec bursts with frequency of 2 Hz at 45 V, applied for 4 min. per nerve PRF probe did not exceed 42°C N = 19	VAS MBPQ MQS	1,2 & 6 months	1. Improvement in VAS noted at 1, 2 & 6 months. 2. Improvements in disturbances of: - daily activity - mood - sleep noted at 1, 2 & 6 months. 3. Improvement in MQS noted at 1, 2 & 6 months.
3. Choi, et al 2012 (28)	Prospective Non-randomized Longitudinal Non-controlled	Dx: Occipital Neuralgia **Diagnostic Test Blocks:** 1% Lidocaine & Dexamethasone Infiltration sites: GON & LON Number of cycles: 2 Diagnostic test block interval: one week apart Positive block criteria: ≥ 50% pain reduction on VAS	PRF to the GON and LON **PRF Settings** Sensory stimulation occurred at: < 0.5 V PRF performed at 42°C for 4 min. at both GON & LON N = 10	VAS TPI	Mean monthly follow-up: 7.5 months	1. Significant improvements in VAS and TPI noted in months 1-6. 2. Analgesic cessation noted at last follow-up in 8 out of 10 patients post-PRF treatment
4. Huang, et al 2012 (29)	Observational Retrospective Multi-center Longitudinal Non-controlled	Dx: Occipital Neuralgia or Migraine Headache with Occipital Nerve Tenderness **Diagnostic Test Blocks:** Bupivacaine, with or without lidocaine and depo-methylprednisolone. Number of cycles: 1, 2, 3 or more Diagnostic test block interval: not specified Positive block criteria (variable): ≥ 80% pain relief 45% of patients 50% – 79%, pain relief 41% of patients < 50% pain relief 10% of patients	PRF to the GON and/or LON **PRF Settings** Electrical stimulation performed at lowest possible voltage. Impedence range: 150-500 Ω # of PRF cycles: variable Voltage output: 40 – 60 V Frequency: 2 Hz Pulse Duration: 20 msec Cycle Duration: 4 minutes Temperature: 42°C N = 102	NRS Primary Outcome Measure: ≥ 50% pain relief for > 3 months Secondary Outcome Measure: Procedural Satisfaction	Variable	1. 51% experienced ≥ 50% pain relief and satisfaction lasting at least 3 months. 2. Variables associated with positive outcome: a. traumatic inciting event b. lower diagnostic block volumes c. multiple rounds of PRF d. isolated GON involvement 3. Factors correlating with treatment failure: a. extension of pain anterior to scalp apex b. ongoing secondary gain issues

GON = Greater Occipital Nerve; LON = Lesser Occipital Nerve; GONB = Greater Occipital Nerve Block; Dx = Diagnosis; PRF = pulsed radiofrequency; VAS = Visual Analog Scale; MBPQ = Modified Brief Pain Questionnaire; MQS = Medication Quantification Scale; TPI = Total Pain Index; NRS = Numerical Rating Scale

PRF cycles, as well as the nerves treated. PRF treatment duration ranged from 120 msec to 240 msec, while PRF treatment cycles ranged between 1 – 3 per nerve. In the case report by Navani et al (27), only the left GON was treated; in the study by Vandelderen et al (10), either the GON or the LON was treated; in the studies by Choi et al (28) and Huang et al (29), the GON and/or the LON were treated. PRF treatments were noted to have not exceeded 42 degrees Celsius in the case report and the clinical studies. Several validated outcome measures were utilized to gauge the clinical efficacy of PRF for occipital neuralgia. These included the Verbal Analogue Scale, Visual Analogue Scale (VAS), Modified Brief Pain Questionaire, Medication Quantification Scale, and Total Pain Index.

Discussion

The available research to date reveals encouraging results, with statistically significant improvement in pain, quality of life, and adjuvant pain medication usage. Specifically, Navani et al (27) demonstrated 60% – 70% pain relief that was sustained for 4 months after initial treatment and for 5 months after the second treatment. Vanelderen et al (10) demonstrated that 68.4%, 57.9%, and 52.6% of patients reported pain relief of at least 50% or more at one, 2, and 6 month assessment intervals, which correlated with VAS score improvement from a mean baseline score of 7.5 to mean posttreatment scores of 3.5, 3.5, and 3.9 at the aforementioned assessment intervals; improvement in sleep disturbance, mood disturbance, and disturbance of daily living—3 parameters reflective of quality of life—at one, 2, and 6 month assessment intervals; and a decrease in the median medication score from 11.2 before treatment to 4.4, 3.4, and 2.2 at the one, 2, and 6 month assessment intervals. Choi et al (28) demonstrated improvement in mean VAS scores with a decline from 6.9 to 1.2 and 0.8 at the one and 6 month assessment intervals, as well as an improvement in mean Total Pain Index scores with a decline from 232.7 to 53.7 and 40.6 at the one and 6 month assessment intervals. Huang et al (29) demonstrated that 51% of patients experienced positive treatment outcomes, defined as greater than or equal to 50% pain relief lasting at least 3 months. Factors found to be associated with a positive outcome included using lower diagnostic block anesthetic volumes, performing multiple rounds of PRF, having isolated GON involvement, and having a traumatic inciting event. Conversely, factors found to correlate with treatment failure included having pain radiate anterior to the apex of the skull and ongoing secondary gain issues.

The mechanism of action underlying the utility of PRF in interventional pain medicine is uncertain. Unlike conventional continuous radiofrequency ablation, whose pain relief effects are mediated through nonselective, temperature-dependent, neurodestruction, PRF is widely believed to act through a temperature-independent, neuromodulatory process, altering synaptic transmission and pain signaling via the emission of electric fields, with none to minimal resultant tissue destruction. Given the nondestructive nature of PRF, deafferentation pain—a feared complication of continuous radiofrequency ablation—is not a potential risk. A growing number of basic science studies support the hypothesized neuromodulatory effects of PRF. For instance, Erdine et al (30) were able to demonstrate that PRF can have a disruptive effect on axonal microtubules, microfilaments, and mitochondria, with the greatest disruption evident in nociception mediating, unmyelinated type C fibers, followed by myelinated type A-delta and type A-beta fibers. Furthermore, Hagiwara et al (31) demonstrated that PRF may modulate neuropathic pain through enhancement of descending noradrenergic and serotonergic inhibitory pathways.

Research investigating other interventional treatment options for occipital neuralgia has also been performed. Studies evaluating the infiltration of the occipital nerves with local anesthetic and or corticosteroid have yielded results suggestive of short-term pain relief. For instance, a prospective study by Kuhn et al (32) identified that 70% of patients receiving corticosteroid infiltration experienced pain recurrence within 2 weeks, while prolonged pain relief of greater than 2 months was observed in only 20% of patients. Similar results suggestive of short-term pain relief were also found in a study performed by Hammond and Danta (12), in which a single infiltration of local anesthetic resulted in less than one week of pain relief in 64% of patients, whereas only 36% of patients experienced pain relief beyond one month. Meanwhile, studies evaluating the use of botulinum toxin type-A for occipital neuralgia have yielded mixed results. In a small, prospective study, Taylor et al (33) noted relief in the sharp, shooting pain associated with occipital neuralgia without any effect on the dull, aching pain. Additionally, no significant decrease in adjuvant pain medication usage was demonstrated, while quality-of-life measures did exhibit some improvement. On the contrary, a small retrospective study by Kapural et al (34) demonstrated improvement

in VAS scores—with a mean duration of pain relief of 16.3 ± 3.2 weeks—as well as an improvement in Pain Disability Index scores. Lastly, several studies investigating subcutaneous neurostimulation of the occipital nerves have also been performed. In a seminal study, Wiener et al (35) implanted subcutaneous neurostimulators in 13 patients with medically refractory occipital neuralgia, resulting in greater than 50% pain relief and requiring little to no pain medication in 12 of 13 patients. Follow-ups ranged from 18 months to 6 years. In a similar study, Slavin et al (36) implanted subcutaneous neurostimulators in 10 patients with therapy-resistant occipital neuralgia, resulting in greater than 50% pain relief in 70% of the patients after a mean follow-up of 22 months. Comparable results have been reported in other studies as well (37-39).

When balancing clinical effectiveness to side-effect and complication risk, PRF possesses a superior and safer profile in comparison to the aforementioned occipital neuralgia treatment options (10,28). Although infection and bleeding are possible complications of any percutaneous intervention, potential complications associated with occipital nerve infiltration include temporary dizziness and gait disturbance, injection site soreness, bradycardia, and focal alopecia (40-43). Additionally, a case report by Lavin and Workman (44) chronicled the development of Cushing's syndrome—with signs and symptoms of intermittent hypertension, severe muscle weakness, and fluid retention—after serial occipital nerve blocks containing corticosteroid. Similarly, neurostimulation has been associated with several potential complications, including lead migration, hardware erosions, electrode fractures, disconnections, and sepsis (36). Moreover, the cost and skill necessary for neurostimulation lends preference to other less invasive options (4). In contrast, 3 of the 4 PRF studies to date reported no adverse effects (10,27,28), while one study reported minor complications in 6 out of 102 subjects, 5 of which consisted of temporary worsening of pain and one patient who experienced a new painful sensation behind the ear and cheek that resolved within 3 weeks (29).

Several limitations concerning the available studies examining the use of PRF for occipital neuralgia warrant consideration. First, despite the utilizations of validated outcome measures for the quantification of pain in each of the aforementioned studies, each outcome measure is subjective and dependent upon personal interpretation, which inherently limits study objectivity and introduces an unquantifiable degree of bias. Second, small study sample sizes—varying from 10, 19, and 102 patients—limit the power of outcome observations. Third, no randomized controlled trials—which in various evidence classification schemes worldwide are viewed as gold standard evidence of treatment effectiveness (45)—have been performed to date. Rather, all studies to date have utilized uncontrolled study designs, which have been known to overestimate treatment effects (10). However, a "lack of evidence" supported by randomized controlled trials should not be dogmatically interpreted as "evidence for the lack of effectiveness" (46). In fact, several inherent challenges to the performance of randomized controlled trials in interventional pain medicine exist, ranging from ethical dilemmas associated with the performance of sham trials in the pain medicine populace, to study design difficulties associated with the etiologic heterogeneity and natural history of pain disorders. In recognition of these practical obstacles, several pain physicians have begun to advocate for the application of "comparative effectiveness research" (47) and application of rigorously conducted observational studies (48) for clinical guidance. Lastly, none of the studies utilized imaging guidance in the performance of diagnostic blocks. Although all 4 studies relied upon surface landmarks for target nerve guidance, current pain medicine practice guidelines advocate use of imaging guidance to improve reproducibility (precision), diagnostic accuracy, and safety (49). Undoubtedly, diagnostic block imaging guidance would minimize unwanted type I error, and thus maximize accurate interpretation of PRF efficacy for occipital neuralgia. Discussion of the advantages and/or disadvantages of specific imaging modalities available for diagnostic block performance, such as ultrasound or fluoroscopy, is beyond the scope of this focused review article

When the studies examining the efficacy of PRF as a treatment for occipital neuralgia are assessed through the evidence classification scheme described by Guyatt et al (50), they are found to collectively comprise an encouraging body of evidence scored as 2 C+. While this score does provide evidence in support of PRF as an interventional treatment option that harbors potential therapeutic effectiveness, evidence in support of PRF as a first-line interventional treatment option is lacking. From a financial perspective, PRF may confer an additional cost saving benefit to third party payers when compared to conservative, chronic pharmacologic management (51).

Many important unanswered questions concerning the clinical utilization of PRF for occipital neuralgia remain:

- What is the mechanism of action underlying the pain modulating effects of PRF?
- What is the optimal diagnostic block protocol to maximize diagnostic specificity? How many diagnostic blocks are ideal? What is the optimal volume of anesthetic agent?
- What is the optimal PRF treatment protocol? Should the GON, LON, and or TON be treated individually or collectively? How many cycles of PRF are ideal?
- What are the optimal PRF treatment settings? What is the ideal duration of PRF electric field exposure?

Well-designed randomized control trials, as well as comparative-effectiveness trials involving PRF and the aforementioned interventional treatment options are needed to further support the use of PRF for occipital neuralgia. According to clinicaltrials.gov, one comparative-effectiveness trial involving PRF vs. local anesthetic and corticosteroid infiltration is currently underway in the United States. With much anticipation, we await the results of this trial and future randomized control trials to further elucidate efficacy and delineate optimal PRF diagnostic and treatment protocols.

Conclusion

Evidence in support of PRF as a safe and effective interventional treatment option for occipital neuralgia appears promising. Clinical studies to date have demonstrated sustained improvement in pain, quality of life, and adjuvant pain medication usage. Despite these encouraging studies, conclusive evidence in support of therapeutic efficacy is lacking. Further research is needed to support the use of PRF for occipital neuralgia.

References

1. Headache Classification Committee of the Internatinal Headache Society: International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia* 2013; 33:629-808.
2. Afridi SK, Shields KG, Bhola R, Goadsby PJ. Greater occipital nerve injection in primary headache syndromes—prolonged effects from a single injection. *Pain* 2006; 122:126-129.
3. Sulfaro MA, Gobetti JP. Occipital neuralgia manifesting as orofacial pain. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1995; 80:741-745.
4. Valelderen P, Lataster A, Levy R, Mekhail N, van Kleef M, Van Zundert J. Occipital neuralgia. *Pain Pract* 2010; 10:137-144.
5. Barna S, Hashmi M. Occipital neuralgia. *Pain Management Rounds* 2004; 1.
6. Kuhn WF, Kuhn SC, Gilberstadt H. Occipital neuralgias: Clinical recognition of a complicated headache. A case series and literature review. *J Orofac Pain* 1997; 11:158-165.
7. Dougherty C. Occipital neuralgia. *Curr Pain Headache Rep* 2014; 18:411
8. Magnusson T, Ragnarsson T, Bjornsson A. Occipital nerve release in patients with whiplash trauma and occipital neuralgia. *Headache* 1996; 36:32-36.
9. Cohen SP, Plunkett AR, Wilkinson I, Nguyen C, Kurihara C, Flagg A II, Morlando B, Stone C, White RL, Anderson-Barnes VC, Galvagno SM Jr. Headaches during war: Analysis of presentation, treatment, and factors associated with outcome. *Cophalalgia* 2010; 32:94-108.
10. Vanelderen P, Rouwette T, De Vooght P, Puylaert M, Heylen R, Vissers K, Van Zundert J. Pulsed radiofrequency for the treatment of occipital neuralgia: A prospective study with 6 months of follow-up. *Regional Anesthesia and Pain Medicine* 2010; 35:148-151.
11. Tubbs RS, Mortazavi MM, Loukas M, D'Antoni AV, Shoja MM, Chern JJ, Cohen-Gadol AA. Anatomical study of the third occipital nerve and its potential role in occipital headache/neck pain following midline dissections of the craniocervical junction. *J Neurosurg Spine* 2011; 15:71-75.
12. Hammond SR, Danta G. Occipital neuralgia. *Clin Exp Neurol* 1978; 15:258-270.
13. Waldman SD. *Atlas of Interventional Pain Management.* Elsevier Inc., Philadelphia, 2009, pp 29-31.
14. "Occipital Neuralgia." Illustration. *MedicalExhibits.com.* Amicus Visual Solutions, 2007. Web. June 3, 2013.
15. Tubbs RS, Salter EG, Wellons JC, Blount JP, Oakes WJ. Landmarks for the identification of the cutaneous nerves of the occiput and nuchal regions. *Clin Anat* 2007; 20:235-238.
16. Ashkenazi A, Levin M. Three common neuralgias. How to manage trigeminal, occipital, and postherpetic pain. *Postgrad Med* 2004; 116:16-18, 21-24, 31-32 passim.
17. Tubbs RS, Salter EG, Wellons III JC, Blount JP, Oakes WJ. Landmarks for the identification of the cutaneous nerves of the occiput and nuchal regions. *Clinical Anatomy* 2007; 20:235-238.
18. Bogduk N. The clinical anatomy of the cervical dorsal rami. *Spine* 1982; 7:319-330.
19. Bogduk N, Marsland A. On the concept of third occipital headache. *J Neurol Neurosurg Psychiatry* 1986; 49:775-780.
20. Ehni G, Benner B. Occipital neuralgia and the C1-2 arthrosis syndrome. *J Neurosurg* 1984; 61:961-965.
21. Trevor-Jones R. Osteo-arthritis of the paravertebral joints of the second and third cervical vertebrae as a cause of occipital headaches. *S Afr Med J* 1964; 38:392-294.

22. Handel T, Kaplan R. Occipital neuralgia. In: Frontea WR (ed). *Essentials of Physical Medicine and Rehabilitation.* Hanley and Belfus, Philadelphia, PA. 2002.
23. Maimone-Baronello M, Piccoli F, La Bella V. Great auricular neuralgia: A case report. *Headache* 2003; 43:1005-1006.
24. Anthony M. Headache and the greater occipital nerve. *Clin Neurol Neurosurg* 1992; 94:297-301.
25. Decheng C, Gale S. *Diseases Treated by Single Point of Acupuncture and Moxibustion.* Foreign Language Press, Beijing, 2001.
26. Xie Z. 51 cases of occipital neuralgia treated with acupuncture. *J Tradit Chin Med* 1992; 12:180-181.
27. Navani A, Mahajan G, Kreis P, Fishman SM. A case of pulsed radiofrequency lesioning for occipital neuralgia. *Pain Medicine* 2006; 7:453-456.
28. Choi, H J, Oh IH, Choi SK, Lim YJ. Clinical outcomes of pulsed radiofrequency neuromodulation for the treatment of occipital neuralgia. *J Korean Neurosurg Soc* 2012; 51:281-285.
29. Huang JHY, Galvagno SM Jr, Hameed M, Wilkinson I, Erdek MA, Patel A, Buckenmaier C III, Rosenberg J, Cohen SP. Occipital nerve pulsed radiofrequency treatment: A multi-center study evaluating predictors of outcome. *Pain Medicine* 2012; 13:489-497.
30. Erdine S, Bilir A, Cosman ER Sr, Cosman ER Jr. Ultrastructural changes in axons following exposure to pulsed radiofrequency fields. *Pain Practice* 2009; 9:407-417.
31. Hagiwara S, Iwasaka H, Takeshima N, Noguchi T. Mechanisms of analgesic action of pulsed radiofrequency on adjuvant-induced pain in the rat: Roles of descending adrenergic and serotonergic systems. *Eur J Pain* 2009; 13:249-252.
32. Kuhn SC, Kuhn WF, Gilberstadt H. Occipital neuralgias: Clinical recognition of a complicated headache. A case series and literature review. *J Orofac Pain* 1997; 11:158-165.
33. Taylor M, Silva S, Cottrell C. Botulinum toxin type-a (botox) in the treatment of occipital neuralgia: A pilot study. *Headache.* 2008; 48:1476-1481.
34. Kapural L, Stillman M, Kapural M, McIntyre P, Guirgius M, Mekhail N. Botulinum toxin occipital nerve block for the treatment of severe occipital neuralgia: A case series. *Pain Pract* 2007; 7:337-340.
35. Weiner R, Reed K. Peripheral neurostimulation for control of intractable occipital neuralgia. *Neuromodulation* 1999; 2:217-222.
36. Slavin KV, Nersesyan H, Wess C. Peripheral neuro-stimulation for treatment of intractable occipital neuralgia. *Neurosurgery* 2006; 58:112-119.
37. Slavin KV, Colpan ME, Munawar N, Wess C, Nersesyan H. Trigeminal and occipital peripheral nerve stimulation for craniofacial pain: A single-institution experience and review of the literature. *Neurosurg Focus* 2006; 21:E5.
38. Norenberg E, Winkelmuller W. The epifacial electric stimulation of the occipital nerve in cases of therapy-resistant neuralgia of the occipital nerve. *Schmerz* 2001; 15:197-199.
39. Kapural L, Mekhail N, Hayek SM, Stanton-Hicks M, Malak O. Occipital nerve electrical stimulation via the midline approach and subcutaneous surgical leads for treatment of severe occipital neuralgia: A pilot study. *Anesth Analg* 2005; 101:171-174.
40. Naja Z M, El-Rajab M, Al-Tannir MA, Ziade FM, Tawfik OM. Repetitive occipital nerve blockade for cervicogenic headache: Expanded case report of 47 adults. *Pain Pract* 2006; 6:278-284.
41. Saddah HA, Taylor FB. Sustained headache syndrome associated with tender occipital nerve zones. *Headache* 1987; 27:201-205.
42. Leinisch-Dahlke E, Jurgens T, Bogdahn U, Jakob W, May A. Greater occipital nerve block is ineffective in chronic tension type headache. *Cephalalgia* 2005; 25:704-708.
43. Afridi SK, Shields KG, Bhola R, Goadsby PJ. Greater occipital nerve injection in primary headache syndromes—prolonged effects from a single injection. *Pain* 2006; 122:126-129.
44. Lavin PJ, Workman R. Cushing syndrome induced by serial occipital nerve blocks containing corticosteroids. *Headache* 2001; 41:902-904.
45. Taylor R. Clinical Research in interventional pain management techniques: An epidemiologist/trialist's view. *Pain Practice* 2008; 8:439-445.
46. Shanthanna HA. Comprehensive evidence based review of pulsed radiofrequency in chronic pain. *Indian J Pain* 2010; 24:5-15.
47. Benyamin RM, Datta S, Falco FJ. A perfect storm in interventional pain management: Regulated, but unbalanced. *Pain Physician* 2010; 13:109-116.
48. Bogduk N, Fraifeld EM. Proof or consequences: Who shall pay for the evidence in pain medicine? *Pain Medicine* 2010; 11:1-2.
49. Manchikanti L, Boswell MV, Singh V, Benyamin RM, Fellows B, Abdi S, Buenaventura RM, Conn A, Datta S, Derby R, Falco FJ, Erhart S, Diwan S, Hayek SM, Helm S, Parr AT, Schultz DM, Smith HS, Wolfer LR, Hirsch JA; ASIPP-IPM. Comprehensive evidence-based guidelines for interventional techniques in the management of chronic spinal pain. *Pain Physician* 2009: 12:699-802.
50. Guyatt G, Gutterman D, Baumann MH, Addrizzo-Harris D, Hylek EM, Phillips B, Raskob G, Lewis SZ, Schünemann H. Grading strength of recommendations and quality of evidence in clinical guidelines: Report from an American college of chest physicians task force. *Chest* 2006; 129:174-181.
51. Giovannini V, Pusateri R, Russo V, Viscardi D, Palomba R. Economic evaluation of "pulse dose" radiofrequency in the treatment of occipital neuralgia headache. *Translational Medicine* 2012; 1:25-27.