Systematic Review

Use of Radiofrequency Ablation for the Management of Headache: A Systematic Review

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Background: Headache is a very common condition that affects 5-9% of men and 12-25% of women in North America and Europe. Globally, the prevalence of active headaches among adults is 47%. The most common type of headache is tension headaches (38% of adults), followed by migraines (10%), and chronic headaches (3%). While the majority of headaches are benign, the disorder can severely negatively influence a patients' quality of life, which is directly reflected in societal costs.

Objective: The objective of this review was to summarize available evidence behind radiofrequency ablation (RFA) for headache, including pain outcome measures, secondary outcomes, and complications.

Study Design: Systematic review.

Setting: This systematic review examined studies that applied the use of RFA for management of headache.

Methods: This systematic review was reported following the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA). Two reviewers independently scored the methodological quality of the selected studies. Due to heterogeneity of studies, a best-evidence synthesis of the available prognostic factors was provided.

Results: In the present investigation, we evaluated 18 studies composed of 6 randomized controlled trials (RCTs), 6 prospective studies, and 6 retrospective studies. All the studies assessed pain improvement with RFA in patients with headache. Most studies targeted the occipital nerve for treatment. Complications were mostly mild and self-limiting, including eyelid swelling, rash, superficial infection of the procedural site, and worsening of headache.

Limitations: A large variability in definitions of trigeminal neuralgia, radiofrequency technique, and patient selection bias was observed in our selected cohort of studies. In addition, there is a paucity of strong longitudinal RCTs and prospective studies.

Conclusion: Our review discusses several studies that suggest the efficacy of RFA in the treatment of headaches. Outcomes varied based on the difference in approaches regarding continuous radiofrequency versus pulsed radiofrequency, temperature, and duration of administration. The majority of the studies discussed in this review indicate a therapeutic benefit of RFA for headaches over a short-term period. Pain outcomes beyond one year are understudied and further studies are needed to determine the long-term effects of RFA for headaches.

Key words: Headache, radiofrequency ablation

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Headache is a very common condition that affects 5%-9% of men and 12%-25% of women in North America and Europe (1). Globally, the prevalence of active headaches among adults is 47%; the most common are tension headaches (38% of adults), followed by migraines (10%), and chronic headaches (3%) (2). While the majority of headaches are benign, the disorder can severely negatively affect patients' quality of life, which directly results in numerous societal costs. The economic burdens of headaches are mostly related to work absence or decrease productivity due to headache symptoms, with indirect costs estimated at $14.4 billion annually (2). Direct costs, i.e., the medications and medical investigation associated with headache conditions, account for a smaller portion of this burden (e.g., approximately $1 billion annually). While headaches are, in general, not associated with increased mortality, the World Health Organization ranked it as the 19th leading global cause of disability-adjusted life years among women aged 15-44 (2).

The exact pathophysiology of headaches is unclear. Literature reviews of tension headache mechanisms suggest that underlying pathophysiology results from sensitization of peripheral myofascial nociceptors, which can sensitize the central nervous system and cause misinterpretation of benign stimuli as pain (3,4). Hypersensitivity can be caused by sensitization of neurons of the spinal dorsal horn and decreased inhibition of pain transmission from supraspinal structures (4). Newer research has linked migraine headaches with mediation or modulation through activation of trigeminal nerves releasing calcitonin generelated peptides and other peptides, which release proinflammatory mediators.

Patients typically initially manage headaches with conservative measures, such as medications. Based on systematic reviews, there is evidence to suggest that acetaminophen and ibuprofen are effective abortive therapies for tension headaches (5,6). The use of radiofrequency ablation (RFA) is quite common in the management of several chronic pain conditions (7-9). Patients refractory to medical treatment could be good candidates for surgical interventions such as RFA. The evidence behind RFA use for headaches has been inconclusive (10,11). However, there has also been evidence supporting the efficacy of RFA use for headaches, showing a success rate of up to 90% (12). RFA, directed toward the target nerves, may be administered as continuous radiofrequency (CRF). This works by inducing coagulative necrosis through high frequency alternating currents (13). Probes are set to high temperatures of 60°C - 80°C (13). This method of RFA is more prone to complications such as hyperalgesia, facial numbness, and corneal hypoesthesia (14). Pulsed radiofrequency (PRF) works by administering short, high-voltage bursts and is less likely to cause complications, but theoretically may be less effective due to less administered heat (13).

The aim of this review, therefore, is to summarize available evidence behind RFA, including pain outcome measures, secondary outcomes, and complications.

Methods

Systematic Literature Search

The authors searched Medline, PubMed, the Cochrane Database of Systematic Reviews, PROSPERO, and the Cochrane Central Register of Controlled Trials for relevant publications. We also searched Google Scholar and the clinical trial registry (clinicaltrials.gov) for additional publications. These database searches were completed on June 25, 2019. Our EMBASE and MEDLINE searches included both controlled terms (MeSH, EMBASE, Emtree, MEDLINE) and free text that included the following: "radiofrequency ablation," "radio-frequency,", "RF," "RFA,", "radiofrequency lesioning," "ablation," "neurolysis," "radiofrequency therapy," "headache,", "analgesia," and "pain," in the English literature. Bibliographies of the published papers were screened for various chronic pain pathologies that received radiofrequency treatment of the trigeminal nerve.

Inclusion and Exclusion Criteria

We included randomized controlled trials (RCTs), open nonrandomized controlled studies, prospective studies, and retrospective studies for this systematic review. We limited our search to publications of original studies that investigated the application of either continuous radiofrequency (CRF) or pulsed radiofrequency (PRF) treatment in adult patients with a history of headache lasting for at least one month. We excluded the following: research that was only available in abstract or poster forms, animal studies, non-English papers, nonradiofrequency technology, book chapters, case reports, unclear diagnosis, and the pediatric population.

Data Extraction and Synthesis

Data synthesis and analysis were performed, including assessment of the risk of bias or quality of individual studies, outcomes assessment, and qualitative and quantitative analysis. Our final evaluation included retrospective, prospective, and RCTs. The reference population, diagnostic group, and outcomes were extracted from these articles using a prespecified, standardized extraction form. The information extracted from each study includes: the author's last name, publication year, study design, number of arms, sample size, radiofrequency technique (pulse versus continuous), temperature range and duration, duration of pain relief, secondary outcomes, side effects, and conclusion. We also extracted the mean and standard deviations for the pain scores when reported. If not reported, we included the paper for thorough analysis and additional discussion purposes.

Quality of Evidence

The quality of each individual article used in this analysis was assessed using the Cochrane Review rating system (Table 1) and Interventional Pain Management Techniques -- Quality Appraisal of Reliability and Risk of Bias Assessment Tool (IPM – QRB) for RCTs (Table 2), and Interventional Pain Management Techniques– Quality Appraisal of Reliability and Risk of Bias Assessment for nonrandomized or observational studies (IPM-QRBNR) (Table 3).

Utilizing the Cochrane Review criteria, studies meeting at least 9 of the 13 inclusion criteria were considered high-quality. Those meeting 5 to 8 criteria were considered moderate-quality, and those meeting fewer than 5 criteria were considered low quality and were excluded. Studies of high quality based on Cochrane Review criteria, IPM-QRB, and IPM-QRBNR criteria were included. Studies of moderate quality based on Cochrane Review criteria, IPM-QRB, and IPM-QRBNR criteria were also included.

Based on the IPM-QRB and IPM-QRBNR criteria, studies meeting the inclusion criteria but scoring less than 16 were considered low quality and were excluded; studies scoring from 16 to 31 were considered moderate quality; and studies scoring from 32 to 48 were considered high quality and were included.

Methodologic quality assessment of each manuscript was performed by 2 review authors. The assessment was carried out independently in an unblinded, standardized manner to assess the methodologic quality and internal validity of all the studies considered for inclusion. If discrepancies occurred, a third reviewer performed an assessment, and a consensus was reached. Further remaining issues were discussed by all reviewers and were then resolved.

Table 1. *Methodological quality assessment of 6 randomized trials utilizing Cochrane review criteria.*

	Bakshi (2017)	Celiker (2011)	Cohen (2015)	Haspeslagh (2006)	Stovner (2004)	Yang (2015)
Randomization adequate	Y	Y	Y	U	Y	Y
Concealed treatment allocation	Y	Y	Y	Y	Y	Y
Patient blinded	N	N	Y	N	Y	Y
Care provider-blinded	N	N	Y	N	N	N
Outcome assessor blinded	N	N	Y	N	N	Y
Drop-out rate described	Y	Y	Y	Y	Y	Y
All randomized participants analyzed in the group	N	N	N	Y	Y	N
Reports of the study free of suggestion of selective outcome reporting	Y	Y	Y	Y	Y	Y
Groups similar at baseline regarding most important prognostic indicators	Y	Y	N	Y	Y	Y
Co-interventions avoided or similar	Y	Y	Y	Y	Y	Y
Compliance acceptable in all groups	Irrelevant (Procedure)	Irrelevant (Procedure)	Irrelevant (Procedure)	Irrelevant (Procedure)	Irrelevant (Procedure)	Irrelevant (Procedure)
Time of outcome assessment in all groups similar	Y	Y	Y	Y	Y	Y
Are other sources of potential bias likely	Y	Y	Y	Y	Y	Y
Score	8/12	8/12	10/12	8/12	10/12	10/12

Y = Yes; N = No; U = Unclear

Table 2. *Methodological quality assessment of 6 randomized trials utilizing IPM - QRB.*

		Bakshi (2017)	Celiker (2011)	Cohen (2015)	Haspeslagh (2006)	Stovner (2004)	Yang (2015)
I.	TRIAL DESIGN AND GUIDANCE REPORTING						
1.	CONSORT or SPIRIT	3	2	3	2	3	3
II.	DESIGN FACTORS						
2.	Type and Design of Trial	2	2	2	2	2	2
3.	Setting/Physician	1	1	1	1	1	2
4.	Imaging	NA	NA	NA	NA	NA	NA
5.	Sample Size	2	2	2	1	0	1
6.	Statistical Methodology	1	1	1	1	1	1
III.	PATIENT FACTORS						
7.	Inclusiveness of Population	NA	NA	NA	NA	NA	NA
8.	Duration of Pain	1	0	2	2	2	2
9.	Previous Treatments	2	1	2	2	2	2
10.	Duration of Follow-up with Appropriate Interventions	2	2	1	2	3	2
IV.	OUTCOMES						
11.	Outcomes Assessment Criteria for Significant Improvement	2	2	2	1	4	2
12.	Analysis of all Randomized Participants in the Groups	1	1	1	1	1	1
13.	Description of Drop Out Rate	1	1	1	1	2	1
14.	Similarity of Groups at Baseline for Important Prognostic Indicators	2	2	1	2	2	2
15.	Role of Co-Interventions	1	1	1	1	1	1
V.	RANDOMIZATION						
16.	Method of Randomization	2	2	2	2	2	2
VI.	ALLOCATION CONCEALMENT						
17.	Concealed Treatment Allocation	2	2	2	2	2	2
VII.	BLINDING						
18.	Patient Blinding	0	0	1	0	1	1
19.	Care Provider Blinding	0	0	1	0	1	1
20.	Outcome Assessor Blinding	1	0	1	1	1	1
VIII.	CONFLICTS OF INTEREST						
21.	Funding and Sponsorship	2	2	3	2	2	2
22.	Conflicts of Interest	3	3	2	3	0	3
TOTAL		31	27	32	29	33	34

Results

Search Result

Our final search methodology yielded 18 studies that investigated the use of radiofrequency treatment for headache (12,15-31). The search and study selection flow chart is displayed at Fig. 1. After duplicates were removed, studies were screened based on our inclusion and exclusion criteria. The details of the 18 studies are described in Table 4. Eighteen studies, comprising 6 RCTs (15-17,22,29,31), 6 prospective studies (18,19,25-27,30), and 6 retrospective studies (12,20,21,23,24,28), are summarized in Table 3.

Targeted Nerves

All publications had patients with a diagnosis of headache. The occipital nerve was the most commonly targeted nerve using CRF or PRF treatment (12,17,19,21-25,29,31). Another group of nerves identified as the sphenopalatine ganglion were also ablated in 3 of the publications included in this review (18,26,27).

Table 3. *IPM checklist for assessment of 12 nonrandomized or observational studies of IPM techniques utilizing IPM-QRBNR.*

		Abd-Elsayed et al. (2019)	Fang et al. (2016)	Govind et al. (2003)	Halim et al. (2010)	Hamer et al. (2014)	Huang et al. (2012)	Lang et al. (2010)	Lee et al. (2007)	Narouze et al. (2009)	Salgado-Lopez et al. (2019)	Shabat et al. (2013)	Van Suijlekom et al. (1998)
I.	STUDY DESIGN AND GUIDANCE REPORTING												
1	STROBE or TREND Guidance	3	3	3	3	3	3	3	2	3	3	3	2
II.	DESIGN FACTORS												
2	Study Design and Type	1	2	2	1	1	1	1	2	2	2	1	2
3	Setting/Physician	1	2	2	2	1	2	1	1	2	1	1	1
4	Imaging	NA	2	NA	NA	NA	NA	NA	NA	3	NA	NA	NA
5	Sample Size	1	0	0	0	0	1	0	0	0	0	0	0
6	Statistical Methodology	2	2	2	2	2	2	2	2	2	2	2	2
III.	PATIENT FACTORS												
7	Inclusiveness of Population	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
8	Duration of Pain	2	2	2	2	2	2	2	2	2	2	2	2
9	Previous Treatments	1	2	2	2	2	2	2	2	2	2	2	1
10	Duration of Follow-up with Appropriate Interventions	4	3	2	3	3	2	4	3	4	4	3	3
IV.	OUTCOMES												
11	Outcomes Assessment Criteria for Significant Improvement	2	2	2	2	2	2	2	4	2	2	2	2
12	Description of Drop Out Rate	2	1	1	1	1	1	2	1	1	2	1	1
13	Similarity of Groups at Baseline for Important Prognostic Indicators	0	0	0	0	0	0	2	0	0	2	0	0
14	Role of Co-Interventions	2	2	2	2	2	2	2	2	2	2	2	2
V.	RANDOMIZATION												
15	Method of Assignment of Participants	3	4	4	3	3	3	1	4	4	4	1	4
VI.	CONFLICTS OF INTEREST												
16	Funding and Sponsorship	2	1	1	2	2	1	2	1	1	1	2	1
TOTAL		26	28	25	25	24	24	26	26	30	29	22	23

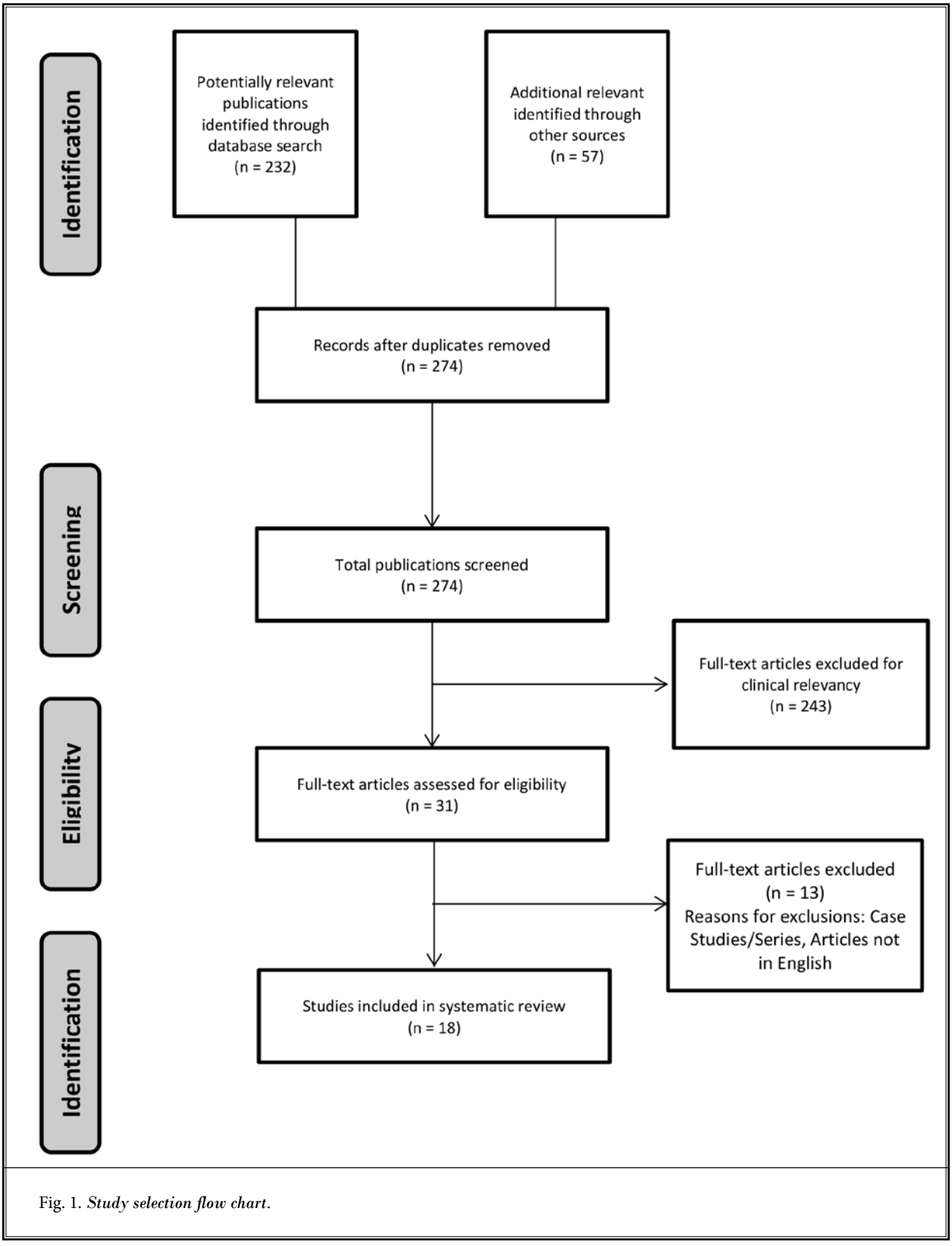

Fig. 1. *Study selection flow chart.*

Table 4. *Characteristics of studies included in systematic review.*

Author (year)	Diagnosis	Sample Size (N)	Age, mean	Men (%)	Study Design	Ablation Technique	Ablated Nerve	Duration of Pain Relief	Secondary Outcome	Side Effects	Conclusion
Abd-Elsayed et al. (2019)	Neuralgia-associated headache conditions	168 pts, 244 ablations	43.6	24.4%	Retrospective Study	Continuous 80°C for 180 s	Greater and lesser occipital nerve	Mean pain score pre-RFA = 5.69 +/- 2.23, then significant reduction to 2.86 +/-2.29 post-RFA. Mean duration of pain relief = 182.2 days +/- 154.5 days	Mean % pain improvement = 62.6% +/-33.7. Maximum duration of pain relief was 831 days. 89.3% of RFAs led to some degree of improvement; remaining 10.7% had no improvement.	3 pts developed eyelid swelling after supraorbital + supratrochlear RFAs. 2 pts had worsening of HA-symptoms. 1 patient had superficial infection at procedure site, treated with antibiotics.	RFA is a safe and effective treatment for pts with chronic headache conditions associated with peri-cranial neuralgias.
Bakshi et al. (2017)	Nasal obstruction secondary to bilateral inferior turbinate hypertrophy	RFA: 44 turbinoplasty: 42	RFA: 33.8 TP: 35.6	RFA: 50 TP: 43.2	Randomized Clinical Trial	350 J delivered for 50-60 s	Anterior, middle, and posterior end of turbinate	75% of RFA and 87.1% of TP had improvement in HA by 1 year. Relief of HA in RFA was significant by 3 months.	N/A	RFA: 9 pts had bloody nasal discharge; 5 pts had persistent burning sensation of the nose	RFA more effective than TP for treating nasal obstruction, equally effective in managing sneezing. Not significantly better for HA relief.
Celiker et al. (2011)	Chronic nasal obstruction	84	N/A	60.7	Randomized Clinical Trial	N/A	Inferior nasal concha	At 3 months, RF turbinate reduction was superior to nasal steroids for nasal blockage, HA, and snoring. RF turbinate reduction + nasal steroids better for headaches vs. RF turbinate reduction alone	RF turbinate reduction group had better nasal flow post treatment.	N/A	RF turbinate reduction is superior than nasal steroids for improving symptoms associated with nasal obstruction.
Cohen et al. (2015)	Occipital neuralgia	81	41.6	52	Double Blind Comparative-Effectiveness Study	PRF 42°C, 40-60V, 2Hz, 20 ms pulses in 1 s cycle; 120s duration per cycle. Control: sham PRF.	Greater occipital nerve	Pts who received PRF had better pain relief compared to pts who received steroids. PRF group had greater change from average occipital pain, and worst occipital pain. Difference in worst occipital pain stopped being significant for PRF at 6 months.	Reduction in HA frequency did not reach significance at any time point between groups. Use of rescue medications for occipital neuralgia and migraines + occipital nerve tenderness did not differ at any follow-up. PRF group had significant reduction in insomnia score.	PRF group: one report of worsening HA, one of swelling, and one of rash.	PRF is superior to steroid injections for pain relief in occipital neuralgia but no difference for other outcomes.

Table 1 (con't). *Characteristics of studies included in systematic review.*

Author (year)	Diagnosis	Sample Size (N)	Age, mean	Men (%)	Study Design	Ablation Technique	Ablated Nerve	Duration of Pain Relief	Secondary Outcome	Side Effects	Conclusion
Fang et al. (2016)	Cluster headache	16	44.6	87.5	Prospective Observational Study	Pulsed with max temp of 42°C for 120 {ms?}	Sphenopalatine ganglion	85% (11/13) of episodic cluster headache cases showed positive treatment outcomes. 33% (1/3) of chronic cluster headache cases showed positive treatment outcomes. Mean remission pre-RFA was 8.7+/-2.9 months; mean remission post-RFA was 16.6+/-5.2 months. Mean cluster duration pre-RFA was 2+/-0.9 months; mean cluster duration post-RFA was 05+/-0.3 months.	One patient underwent 3 PRF treatments as symptoms recurred 3 times. 15% (2) ECH and 67% (2) CCH pts did not respond to PRF treatment at one month f/u.	N/A	RFA of sphenopalatine ganglion is effective and safe for relief of episodic cluster headaches.
Govind et al. (2003)	Occipital headache	49 (51 nerves)	43	42.9	Prospective Observational Study	80°C for 90 s	Occipital nerve	88% (43) pts achieved > 90 days of pain relief. 13% (6) pts did not achieve pain relief lasting > 90 days, 6% (3) pts had headache recurrence that were manageable by simple analgesics. Median duration of complete pain relief was 297 days, with 8 pts having ongoing relief. Median duration of complete pain relief with repeat neurotomy was 217 days, with 6 pts having ongoing relief.	N/A	97% numbness, 95% ataxia, 55% dysesthesia, 15% hypersensitivity, 10% itch	RF neurotomy provides relief of occipital headache though the relief may be limited in duration and can require repeated procedures.
Halim et al. (2010)	Cervicogenic headache	86	50	37	Retrospective Study	PRF: 45 V, 2 Hz, 10 ms for 10 mins	C1-C2 joint	50% (43) pts had ≥ 50% relief at 2 months. 50% (43) pts had ≥ 50% relief at 6 months. 44.2% (38) pts had ≥ 50% relief at one year. Long-term pain relief (6 months, one year) were reliably predicted by ≥ 50% relief at 2 months.	Duration of pain preprocedure and baseline pain score were nonsignificant predictors of ≥ 50% pain relief at 2 months, 6 months, and one year.	One patient experienced increased severity of occipital headache lasting several hours.	PRF of lateral C1-C2 facet joint is a safe technique in pts with cervicogenic headache.

Table 1 (con't). *Characteristics of studies included in systematic review.*

Author (year)	Diagnosis	Sample Size (N)	Age, mean	Men (%)	Study Design	Ablation Technique	Ablated Nerve	Duration of Pain Relief	Secondary Outcome	Side Effects	Conclusion
Hamer et al. (2014)	Cervicogenic headache and/or occipital neuralgia	40	46.9	11.4	Retrospective Study	80°C for 90 s	C2 dorsal root ganglion, and/or third occipital nerve	90% (36) pts reported ≥ 50% pain reduction after treatment. 35% (14 pts) reported 100% pain relief, 70% (28 pts) reported ≥ 80% relief. 7.5% (3) pts reported zero pain relief, 2.5% (1) of pts reported 30% relief. 48% (19 pts) reported <6 months of pain relief. 52% (21) pts reported > 6 of pain relief. Mean duration of improvement was 22.35 weeks; 24.16 weeks if pts with no pain relief are excluded.	Most frequent procedure: bilateral C2 ganglion RFA. Next most common: bilateral C2 and third occipital nerve ablations.	2.5% reported hyperesthesia along greater occipital and lower occipital nerves, lasting 1-6 months. One patient reported occipital hyperesthesia that was worse than her headache after unsuccessful ablation.	RFA of C2 dorsal root ganglion and/or third occipital nerve can provide many months of ≥ 50% pain relief in majority of recipients, with expected duration of symptom improvement of 5-6 months.
Haspeslagh et al. (2006)	Cervicogenic headache	30 (15 in RFA)	48.3	26.7	Randomized controlled trial	RFA of facet: 67°C for 60 s; RFA of cervical segmental nerves: 50 Hz and 2 Hz threshold; RFA of cervical facet joint, followed by cervical dorsal root ganglion	Greater occipital nerve	Differences in VAS pain scores, effect scores, and quality of life scores between 2 groups were not statistically significant at any time point. After 16 weeks, success rate of RFA was 66.7% vs. 55.3% of the steroid group.	N/A	N/A	RFA of cervical facet joints and upper dorsal root ganglions is not a better treatment for TN than treatment of greater occipital nerve.
Huang et al. (2012)	Occipital neuralgia	102	51.2	26.5	Retrospective Study	PRF: 42°C plateau temps; 40-60 V, 2 Hz, 20 ms pulses in a 1-second cycle, 120 s duration per cycle	Greater and/or lesser occipital nerve	51% (52) pts experienced ≥ 50% pain reduction after treatment for at least 3 months.	Factors associated with procedural success: inciting event, presence of greater occipital neuralgia by itself, lower injectate volumes during diagnostic blocks, multiple cycles of PRF.	6 pts: temporary worsening pain, new painful sensation behind ear and cheek which resolved in 3 weeks	PRF may provide intermediate-term benefit in occipital neuralgia to a significant proportion of refractory cases.

Table 1 (con't). *Characteristics of studies included in systematic review.*

Author (year)	Diagnosis	Sample Size (N)	Age, mean	Men (%)	Study Design	Ablation Technique	Ablated Nerve	Duration of Pain Relief	Secondary Outcome	Side Effects	Conclusion
Lang et al. (2010)	Cervicogenic headache	31	46	61.3	Retrospective Study	80°C for 90 s	Occipital nerve	The mean percentage of pain relief on the first day after the RF neurotomy was 91.64%. The median duration of pain relief until recurrence of 50% of the pre-coagulation pain was 125.11 days (minimum 6 days, maximum 732 days).	Eight patients worked full-time after successful coagulation, 5 of them underwent re-coagulation subsequent to headache recurrence. The 2 patients who remained unable to work were in the arthritis group.	All patients complained of numbness in the neck or the occipital region, which subsided without treatment..	Our results indicate that this therapy is effective in patients with underlying diseases of primarily degenerative origin.
Lee et al. (2007)	Cervicogenic headache	30	54	53.3	Prospective Observational Study	80°C for 90 s	Occipital nerve	Number of patients who showed pain relief > 75% were 60% at one week, 83.3% at one month, 76.7% at 6 months and 73.3% at 12 months. The average number of headaches per week decreased from 6.2 to 2.8 post-operation.	There was a 70% reduction in analgesic intake/ week.	Twelve patients complained of soreness on the posterior neck for 2-7 days following the procedures, all of which resolved within a week.	RF neurotomy represents a moderate duration of pain relief without any serious side effects in the majority of these chronically disabling patients.
Narouze et al. (2009)	Chronic cluster headache	15	N/A	N/A	Prospective Observational Study	Two 80°C RF lesions for 60 s each	Sphenopalatine ganglion	At onemonth postoperation, the mean attack intensity decreased from 8.6 (on a scale of 1-10) to 2.6 and the mean attack frequency improved from 17 attacks/ week to 5.4.	Precise needle placement with the use of real-time fluoroscopy and electrical stimulation prior to attempting RF lesioning may reduce the incidence of adverse events.	50% (7/15) reported temporary paresthesia in the upper gums and cheek. One patient had a coin-like area of permanent anesthesia over his cheek.	Percutaneous RF ablation of the sphenopalatine ganglion is an effective modality of treatment for patients with intractable chronic cluster headaches.
Salgado-Lopez et al. (2019)	Chronic cluster headache	PRF: 24 RFA: 13	40	78.4	Prospective Observational Study	PRF: 80°C for 60 s; RFA: 42°C and 40 V for 120 s	Sphenopalatine Ganglion	The mean effectiveness period was slightly higher with radiofrequency ablation (5.21 months) than with pulsed radiofrequency (4.69 months) (P = 0.820).	A total of 5 patients (13.5%) experienced complete clinical headache relief of both pain and parasympathetic symptoms, 21 patients (56.7%) presented partial and transient relief, and 11 patients (29.7%) did not improve.	None reported	There are no statistical differences between RFA and PRF. Because of the similarity in efficacy and the greater theoretical risk of thermal complications, we recommend the use of PRF.

Table 1 (con't). *Characteristics of studies included in systematic review.*

Author (year)	Diagnosis	Sample Size (N)	Age, mean	Men (%)	Study Design	Ablation Technique	Ablated Nerve	Duration of Pain Relief	Secondary Outcome	Side Effects	Conclusion
Shabat et al. (2013)	Chronic headache	69	48	42	Retrospective Study	42°C for 120 s	Suprascapular nerve	After 4 weeks, 41 patients (59%) had improvement in their headache. After 3 months, 38 (55%) of the patients reported significant pain relief.	Thirty-one patients (45%) reported long-term pain relief for the headache (defined as reduction of VAS by at least 30%)	No complications were found except for mild discomfort in the treated area which spontaneously resolved up to 3 weeks after the procedure.	PRF for the suprascapular nerve is a safe and an effective procedure for patients who suffer from headache that is attributed to the lower cervical nerve roots
Stovner et al. (2004)	Cervicogenic headache	12	48	50	Randomized, Double Blind, Sham-controlled Study	3-4 lesions of 85°C for 60s	Greater occipital nerve	In month one both groups tend to be better, but in month 3 there seems to be a tendency that the RF-group is doing better than the sham group with regard to all variables except analgesics intake. In month 6 and later the two groups seem to be similar, but in month 24, the sham group is better on most variables.	All patients had at least a 50% effect on at least one of the blockades, but only 4 patients had more than 90% effect on at least one of the blockades.	More patients in the RF-group reported increased neck pain (4/6) than in the sham group (1/6) at discharge from the hospital 1–2 days after the procedure.	We do not find much evidence that RF-treatment of facet joints C2-C6 is a promising procedure for most patients fulfilling purely clinical criteria for cervicogenic headache.
Van Suijlekom et al. (1998)	Cervicogenic headache	15	N/A	N/A	Prospective Observational Study	N/A	N/A	There was a significant reduction in headache severity in 12 (80%) patients. Mean VAS decrease was 31.4 mm ($P < 0.001$) and 53.5 mm ($P < 0.0001$) respectively in 8 weeks and 16.8 months follow-up.	The average mean number of headache days per week decreased from 5.8 days to 2.8 days ($P = 0.001$).	N/A	A definitive conclusion about the clinical efficacy of this treatment can only be drawn from a randomized controlled trial.
Yang et al. (2015)	Chronic migraine	40	43.5	17.5	Randomized clinical trial	42°C for 120 s twice	Occipital nerve	The mean decrease of headache duration in the treatment group was 8.9 days per month at the 6-month follow-up. There was a significant difference in the decrease of headache duration between the treatment and the sham groups at the onemonth ($t = 8.14$, $P < 0.001$), 2-month ($t = 7.93$, $P < 0.001$), and 6-month ($t = 7.11$, $P < 0.001$) follow-up time points	The VAS differed significantly between the treatment and the sham groups at the 1-month ($t = 4.08$, $P < 0.001$), 2-month ($t = 4.86$, $P < 0.001$), and 6-month ($t = 3.27$, $P < 0.01$) follow-up periods	One patient in the treatment group reported mild pain at the injection site and the pain subsided within 6 hours without any treatment.	RF on the cervical 2-3 posterior medial branches could provide a satisfactory treatment that can reduce pain intensity, headache duration, and disability scores. The procedure was relatively easy to perform and resulted in few side effects.

Quality of Evidence

Of the 18 manuscripts meeting inclusion criteria (12,15-31), 6 were randomized trials (15-17,22,29,31). Tables 1 and 2 show the methodologic quality assessment and risk of bias in each of these trials utilizing the Cochrane review criteria and the IPM-QRB criteria respectively.

Assessment by the Cochrane review criteria showed 3 moderate-quality and 3 high-quality randomized trials. Likewise, assessment by IPM-QRB showed 3 moderate-quality and 3 high-quality randomized trials (15-17,22,29,31).

Table 3 shows the assessment of the included non-randomized or observational studies, utilizing IPM-QRB-NR criteria. All 12 studies included in this category were shown to be of moderate quality (12,18-21,23-28,30).

Outcome

Pain outcomes were reported as the Visual Analog Scale (VAS) or Numeric Rating Scale by most of the publications included in this review. Simultaneously, the functional outcome measures were also reported by most publications. The most commonly reported secondary outcomes included a reduction in analgesic intake postprocedure, the need for a repeat procedure, and complications.

Discussion

This review of 18 publications that investigated the use of RFA on patients with headaches suggests that RFA can provide immediate, short-term, and long-term pain relief.

Pain Relief and Secondary Outcome: Efficacy of RF treatment in Randomized Control Trials

The randomized studies in this review were performed by Bakshi et al (15), Celiker et al (16), Cohen et al (17), Haspeslagh et al (22), Stovner et al (29), and Yang et al (31). Bakshi et al's study (15) revealed that 75% of patients undergoing RFA reported improvement in their headaches at one year postprocedure, with the relief becoming significant at 3 months. This study compared turbinoplasty with RFA for relief of various pains secondary to turbinate hypertrophy; it concluded that RFA was equally as effective as turbinoplasty for headache relief. Celiker et al's randomized controlled trial (16) found that RF turbinate reduction was superior to nasal steroids in treating headaches at 3 months follow-up; RF turbinate reduction in conjunction with nasal steroids is even more effective than RF alone.

Another randomized trial by Cohen et al (17) described patients who underwent PRF had greater pain relief of occipital neuralgia compared to those who received only steroid injections. Patients who received PRF had a greater change of pain scores compared to average occipital pain and worst occipital pain. However, the differences in worse pain stopped being significant at 6 months. The authors conclude that while PRF is superior to steroid injections for pain relief in occipital neuralgia, there were no differences for other outcomes.

Haspeslagh et al's (22) trial investigated patients who received RFA of the cervical facet joint versus RFA of the greater occipital nerve. The differences in pain scores, effect scores, and quality of life between the 2 groups were not statistically significant at any time point. The authors conclude that RFA of the cervical facet joints and dorsal root ganglion is not superior to RFA of the greater occipital nerve for treatment of cervicogenic headache. Stovner et al's (29) study also used RF treatment of the C2-C6 facet joints. At 3-months follow-up, the RF treated group had superior outcomes in all variables except analgesic intake compared to the sham group. However, by 6-months follow-up, the RF group and sham group were comparable; by 24 months, the sham group had superior outcomes. The study concluded that the evidence for treating cervicogenic headache with RF treatment of facet joints was not promising.

The randomized study conducted by Yang et al (31) found that the mean decrease of headache duration in the RF treated group was 8.9 days/month at 6-months follow-up. Compared to the sham group, there was a significant decrease of headache duration in the RF-treated group at the one month ($t = 8.14$, $P < 0.001$), 2-month ($t = 7.93$, $P < 0.001$), and 6-month ($t = 7.11$, $P < 0.001$) follow-up time points. The VAS scores also differed significantly between the RF treatment and the sham groups at the one month ($t = 4.08$, $P < 0.001$), 2-month ($t = 4.86$, $P < 0.001$), and 6-month ($t = 3.27$, $P < 0.01$) follow-up periods. The authors conclude that RF treatment of the C2-C3 posterior medial nerve branches reduces pain intensity, headache duration, and disability score with few side effects.

Duration of Analgesic Effect: Short-term Pain Relief

Short-term pain relief can be defined as pain reduction lasting up to 12 weeks. Lang et al's (24) study noted immediate pain relief and revealed a 91.64%

mean pain relief on the first day after RF neurotomy. Eight out of the 18 studies demonstrated short-term pain relief (16,19,20,23,24,26,28,30). Lee et al's (25) prospective study found that 50% of patients experienced > 75% pain relief as soon as one week follow-up after RFA of the occipital nerve. Five studies reported that patients experienced pain relief for at least 12 weeks (23,24,26,28,30). These studies investigated the RFA of the occipital nerve (2 studies), sphenopalatine ganglion (one study), and the suprascapular nerve (one study). Narouze et al (26) also found that at one month follow-up, the mean attack intensity had decreased from 8.6 (out of 10) to 2.6, with the mean attack frequency decreasing to 5.4 attacks/week from 17.

Duration of Analgesic Effect: Long-term Pain Relief

Long-term pain relief can be defined as pain reduction that lasts for greater than 12 weeks. Eight out of the 18 studies demonstrated long-term pain relief (12,19-21,24,25,30,31). Abd-Elsayed et al (12) conducted continuous RF of the occipital nerve and found the mean duration of pain relief was 182.2 days +/- 154.5 days, with the maximum duration being 831 days. Patients received continuous RFA of the occipital nerve in Govind et al's (19) study; their findings indicate that 88% of patients achieved > 90 days of pain relief, with a median duration of pain relief of 297 days. The retrospective study by Halim et al (20) investigated PRF therapy of the C1-C2 joint and found that 50% of patients had > 50% pain relief at 6 months, and 44.2% of patients continued to have > 50% pain relief at one year.

Hamer et al's (21) retrospective study investigated CRF treatments of the C2 dorsal root ganglion and/or third occipital nerve. They found that 52% of patients had > 6 months of pain relief, with the median duration being 22.35 weeks. Lang et al's (24) study of CRF of the occipital nerve found the median duration of pain relief was 125.11 days, with a minimum of 6 days, and a maximum of 732 days. Lee et al's (25) study of RF neurotomy of the occipital nerve found that 76.7% of patients had pain relief at 6 months, with 73.3% at 12 months. The prospective comparison study by Salgado-Lopez et al (27) found that RFA of the sphenopalatine ganglion resulted in 5.21 months of pain relief, compared with PRF, which resulted in 4.69 months of pain relief. Yang et al's (31) trial of RF treatment on the occipital nerve revealed significantly decreased VAS scores when compared to the sham group at 6 months.

Outcomes with Continuous Versus Pulsed RF Ablation Treatment

Salgado-Lopez et al (27) conducted a prospective study comparing PRF versus RFA of the sphenopalatine ganglion. The mean period of effectiveness was slightly higher with RFA versus PRF (5.21 vs. 4.69 months, $P = 0.820$); the authors conclude that as there are no statistical differences, PRF is recommended given the risk of thermal complications. Six out of the 18 studies in this review used PRF treatment for headache (17,18,20,23,28,31). All 6 studies concluded that PRF is a safe and effective treatment. Grandhi et al's (10) systematic review of RF and PRF treatments noted that there were no high-quality RCTs to support the use of either. Stover et al's (32) RCT using continuous RFA did not recommend RF treatment of the C2-C6 facet joints as treatment.

Targeted Nerves

Nine out of the 18 studies targeted the occipital nerve. Three studies targeted the sphenopalatine ganglion. The remainder of the studies investigated RF treatment of nasal turbinates, nasal concha, cervical facet joints, and the suprascapular nerve.

Safety Profile and Complications

There were multiple types of side effects reported from the 18 studies in this review. Patients who received RFA of the occipital nerve experienced a variety of side effects, including eyelid swelling, rash, superficial infection of the procedural site, and worsening of headache (12,17). Govind et al's (19) study with third occipital neurotomy did not report any complications but did report self-limited side effects that did not require interventions: numbness, ataxia, dysaesthesia, hypersensitivity, and itching. Similarly, Huang et al (23) reported 6 patients received PRF to the occipital nerve and experienced temporary worsening pain and new pain behind the ear/cheek, which resolved in 3 weeks.

Lang et al's (24) retrospective study on RFA of the occipital nerve reported that all 31 patients complained of numbness in the neck of the occipital region, which resolved without treatment. Lee et al's (25) prospective study found 12 patients who experienced posterior neck soreness following the procedure, which self-resolved within a week. Halim et al's (20) retrospective analysis of PRF treatment of the C1-C2 found one patient who experienced an increased severity of occipital headache symptoms, lasting several hours. Narouze's (26) prospective study with RF of the sphenopalatine

ganglion noted that 50% of patients reported temporary paresthesias in the upper gums and cheek; one patient was left with a permanent coin-sized area of anesthesia on his cheek.

Limitations

There are a few findings that arise when evaluating the data and conclusions from the selected studies. There is a lack of consistency in the procedural approach and characteristics, making it difficult to make a comparison to other standard of care treatment protocols. In addition, there is also a lack of prolonged follow-up for the pain and disability scores for the patients that were treated with RFA.

Conclusion

The present investigation reviews several studies that suggest the efficacy of RFA in the treatment of headaches. The approach (continuous versus pulsatile), temperature, and duration of administration require further trials to elucidate differences in outcomes. Given different etiologies and characteristics of headaches, larger studies focused on different subsets of patients with headache are warranted in order to clarify more precisely benefits and best practice strategies. The majority of the studies indicate the benefit of RFA or PRF over a short period, but did not investigate outcomes beyond one year duration or any long-term implications.

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