Archives of Anesthesiology and Critical Care (In Press); x(x): xx-xx.

Available online at http://aacc.tums.ac.ir

Case Report

Prolonged Pulsed Radiofrequency Treatment in Resistant Trigeminal Neuralgia: A Case Report

Seyyed Masoud Hashemi[1], Faranak Behnaz[2], Sina Hassannasab[1], Sogol Asgari[3]*

[1]Department of Anesthesiology, School of Medicine, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[2]Department of Anesthesiology, School of Medicine, Shohada-e-Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[3]Department of Anesthesiology, Anesthesiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

ARTICLE INFO

Article history:
Received 16 October 2024
Revised 06 November 2024
Accepted 20 November 2024

Keywords:
Pain management;
Prolonged pulsed radiofrequency;
Extended duration pulsed radiofrequency;
Trigeminal neuralgia;
Trigeminal ganglion

ABSTRACT

Trigeminal neuralgia (TN) is one of the most severe painful conditions known to man. Contradictory results regarding the effectiveness of pulsed radiofrequency (PRF) treatment of the trigeminal ganglion have been published in the literature. In the past few years, reports in support of prolonged (extended duration) radiofrequency treatment of the trigeminal ganglion have been emerging. Unlike most other interventional procedures that include nerve or ganglion destruction and its resultant potential complications, PRF treatment is believed to be much safer. Working toward the establishment of effective PRF protocols proves highly valuable in the management of TNs refractory to medical treatment. This article showcases the successful control of two cases of refractory trigeminal neuralgia (TN) through extended duration pulsed radiofrequency treatment. Recent studies, however, suggest prolonged PRF ablation may provide a more durable solution. PRF offers a potentially safer alternative to traditional interventions by minimizing nerve destruction.

Introduction

The trigeminal nerve, which is the largest of the cranial nerves, arises from the pons. The nerve has three main branches: the ophthalmic (V1), the maxillary (V2), and the mandibular (V3), hence the name trigeminal.

The ophthalmic and maxillary nerves are purely sensory, while the mandibular nerve possesses both sensory and motor functions [1]. TN, or "tic douloureux," is sudden, severe, brief, stabbing pain in the trigeminal nerve distribution that usually affects one side of the face. It affects 4 out of every 100,000 people in the general population [2]. TN can be classified into two categories: classic and symptomatic TN. Classic TN is the most common form. An offending vessel—most commonly a segment of the superior cerebellar artery—is compressing the nerve in this form. In symptomatic TN, the patient has all signs and symptoms of TN, but no offending vessel to the nerve is identifiable [3-4].

The ultimate goal of any treatment modality for TN is to reduce pain and relieve symptoms. Anticonvulsant medications, such as carbamazepine, are the first line of treatment for TN. Oxcarbazepine is commonly accepted as the second choice and has a more favorable side effect profile. Topiramate, phenytoin, baclofen, and gabapentin, among others, are some of the medications tried in TN. We reserve surgical methods for cases where we have exhausted all medical options [4].

Microvascular decompression (MVD), percutaneous trigeminal balloon compression (PBC), gamma knife surgery (GKS), radiofrequency treatment (RF), and glycerol or alcohol gangliolysis are some non-medical ways to treat TN [5–9]. Once an offending vessel is present, MVD of the trigeminal root proves to be highly

The authors declare no conflicts of interest.

*Corresponding author.
E-mail address: drasgari98429@gmail.com

effective. Success figures as high as 98% have been claimed for immediate pain relief after this procedure, and up to 68% of such patients may remain in remission up to 8-10 years after the procedure [4]. Percutaneous balloon compression (PBC) of the trigeminal ganglion is a percutaneous intervention performed under general anesthesia. This procedure is believed to produce results comparable to MVD [4, 10]. Reports of RF treatment of the trigeminal ganglion suggest the same high success rate for RF treatment as claimed for MVD and PBC for trigeminal neuralgia. There is also disagreement about the best ways to use different types of RF treatment, such as continuous radiofrequency (CRF), pulsed radiofrequency (PRF), and combined continuous and pulsed radiofrequency (CCPRF) treatments [4, 11–13].

Gamma knife radiosurgery (GKS) is a minimally invasive approach to the treatment of TN with a success rate comparable to that of MVD. Patients typically experience pain relief 1 to 2 months after the procedure [14]. Glycerol gangliolysis is a percutaneous procedure that requires minor sedation. Reports have indicated short-term success rates as high as 80% for this procedure. The procedure is safe, and complications are negligible [4].

Case Report

Case 1:

A 43-year-old lady who was suffering from episodic sharp stabbing attacks of pain in the right mandibular region was diagnosed with third division (V3) trigeminal neuralgia. Her symptoms appeared in the winter of 2009. Initially, doctors treated the pain as a dental issue. The patient had cycles of pain attacks with up to 30 pain episodes per day with periods of remission in between those cycles. Tooth brushing was a notable inciting factor for pain attacks. The V2 and V3 branches, which were more dominant in the V3 territory, were involved in the 2011 diagnosis of TN. At the time, the patient received medical treatment with carbamazepine 1200 mg and pregabalin 450 mg per day. A temporary and partial improvement of symptoms was achieved, followed by an uncontrollable relapse of symptoms 2 years later, which led to MVD surgery in June 2013.

The procedure achieved high initial success, resulting in the discontinuation of medications for several months. Nine months later, the patient was again started on carbamazepine and pregabalin, and by 2015, the pain was refractory to medical therapy. A second MVD surgery was performed in early 2015, which absolutely failed to alleviate symptoms. In autumn 2015, the patient underwent CT-guided gamma knife radiosurgery that resulted in a reduction of pain intensity and extent of distribution. In 2016, 2017, and August 2018, the patient received three PRF treatments, of which the last one was according to a prolonged (extended duration) PRF protocol. Before the implementation of the prolonged (extended duration) PRF treatment, the patient was on carbamazepine 1200 mg and pregabalin 450 mg per day, and oxycodone 2.5 mg three times per day. Over a time span of 8 weeks, medications were reduced to carbamazepine 200 mg daily. The patient was highly satisfied with her results until July 2019, when she returned with occasional episodes of sharp stabbing pain. At the present time her pain is controllable with carbamazepine 400 mg and pregabalin 150 mg per day.

Case 2:

A 58-year-old lady who was suffering from left-sided attacks of sharp stabbing pain in the upper jaw was diagnosed with second division (V2) trigeminal neuralgia since April 2018. Touching, speaking, and tooth brushing were strong inciting factors. Posterior fossa MRI had excluded the presence of any offending vascular structure. The patient was started on medical therapy for 4 months (carbamazepine 800 mg and pregabalin 450 mg per day) with inadequate response before undergoing a combined PRF-CRF treatment. The procedure had included three PRF treatments followed by one CRF ablation in the same session. The patient was pain-free for 4 months following the combined PRF-CRF treatment, and during this period, she only took carbamazepine 200 mg per day. With the reappearance of painful attacks, her medication dose was raised to carbamazepine 800 mg and pregabalin 450 mg. With inadequate response to medical treatment, six months after the first RF treatment, the patient underwent a prolonged (extended duration) PRF treatment. Her response to PRF treatment was almost immediate, and within 10 days her medication dose was reduced to carbamazepine 200 mg and pregabalin 75 mg per day, the latter of which was discontinued one week later. In her follow-ups until the present time, she has experienced good control of her pain attacks with carbamazepine 200 mg per day. No attempt on discontinuation of carbamazepine has been considered till the present.

Procedure:

Minimal sedation with fentanyl 50 mcg and midazolam 1 mg was given before the procedure in both instances. A 22 G, 10 cm RF needle with a 5 mm active tip (EPIMED, R-FTM Needles) was used. Upon entry to the foramen ovale, motor stimulation at 0.8 V, 2 Hz resulted in contraction of the lower jaw. Sensory stimulation at 50 Hz was carried out. A successful elicitation of paresthesia within the relevant sensory distribution at 0.3 V in each patient showed that the active tip of the RF needle was close enough to the target of treatment. Subsequently, 7 cycles of PRF (duration: 120 sec, temperature: 42°C) were delivered. Fifteen-second intervals were allowed between each cycle of PRF application. Upon completion of the procedure, dexamethasone 4 mg was administered through the RF needle.

Discussion

Medical therapy is the first step in pain alleviation in TN. Several medications, including carbamazepine, oxcarbazepine, phenytoin, gabapentin, lamotrigine, topiramate, baclofen, ketamine, and pimozide, are used in the treatment of TN [4, 15].

Carbamazepine is the commonly accepted first choice. Due to its potential serious toxicities, 6–8 weeks after achieving acceptable pain control, its dose must be lowered to the least amount that maintains pain control. People commonly regard oxcarbazepine as the second choice. While it is as effective as carbamazepine, it bears fewer adverse effects in comparison to carbamazepine. Phenytoin is another effective anticonvulsant medication in the management of TN. Effectiveness of this medication most often declines within 2 years [4, 16].

Other anticonvulsants that are used in patients with TN include lamotrigine, gabapentin, and topiramate. Lamotrigine is an anticonvulsant with a lighter side effect profile compared to carbamazepine. Gabapentin has a benign side effect profile and is used alone or in combination with other medications. Topiramate exerts its effect through both the voltage-gated sodium channels and gamma-aminobutyric acid receptors (GABA receptors). It has shown promising results in the management of TN. Other useful medications include sodium valproate, racemic ketamine, topical capsaicin, methadone, and tizanidine [4].

Patients who are resistant to medical management are suitable candidates for surgical and interventional management [12–13]. Neurovascular conflicts may be the underlying cause of TN. They most commonly occur between a segment of the superior cerebellar artery and the nerve root at its entry zone. In cases of such conflicts, microvascular decompression (MVD) is considered the optimal option. The short-term success rate for this procedure may be 90% and higher, although an annual recurrence rate of 3.5% may be expected [4, 15].

Retrogasserian gamma knife surgery is a safe and effective treatment modality in patients with trigeminal neuralgia. This procedure has claimed very high initial and long-term success rates in pain alleviation [14].

Percutaneous interventions, including retrograsserian glycerol injection, balloon compression of the trigeminal ganglion, CRF thermocoagulation, and PRF treatment, have been implemented in the management of TN.

Percutaneous balloon compression is a procedure that aims to inflict pressure damage on the Gasserian ganglion. This procedure requires general anesthesia and cannulation of the foramen ovale under fluoroscopic guidance. A Fogarty balloon is then inflated to a pressure of 650 to 950 mmHg to compress the Gasserian ganglion. The balloon remains inflated for 1 minute, as longer inflation times seem to hold no advantage in outcome [4, 15].

Continuous radiofrequency thermocoagulation (CRF) uses radiofrequency waves to produce heat through vibration and friction [11]. Temperature may rise up to 90°C in the target tissue with resultant thermocoagulation and necrosis. A systematic review of ablative neurosurgical techniques for the treatment of TN evaluated 166 studies reporting CRF thermocoagulation, glycerol rhizolysis, balloon compression of the trigeminal ganglion, and stereotactic radiosurgery and concluded that CRF thermocoagulation offers the highest rates of complete pain relief [17]. Various complications have been reported with CRF ablation of the trigeminal ganglion, and the higher the temperature, the more the likelihood of occurrence of complications [11].

Sluijter introduced the practice of pulsed radiofrequency treatment. The aim of pulsed applications of radiofrequency waves to tissue was to make a dissociation between the thermal and electromagnetic effects of the waves. Typically, pulses with a width of 20 milliseconds and a frequency of 500 kHz are applied to the tissue. Typically, we maintain the tissue temperature at 42°C or lower [18-19]. PRF treatment delivers short pulses of RF energy to the tissue. The time off between pulses allows the generated heat to dissipate. As a result, we can significantly lower the tissue temperature compared to CRF ablation [20]. The CRF creates a zone of thermal coagulation around the electrode tip, but the PRF does not damage tissue to the point where it permanently disrupts the nervous system [21].

Exertion of neuromodulatory effects on gene expression in sensory neurons by the pulsed electrical field, reversible disruption of impulse transmission in small unmyelinated sensory neurons, and modulation of noradrenergic and serotonergic pathways as well as the immune system are among the proposed mechanisms for the effects of PRF [22-23].

Opinions regarding the efficacy of PRF in TN are quite varied. Erdine et al. in a clinical trial constituting a total of 40 patients allocated into two groups decided that unlike CRF, PRF was not an effective treatment modality in pain management in patients suffering from TN [13].

Meanwhile, several other reports, both before and after that clinical trial, have supported the efficacy of CRF in TN. Van Zundert et al. in 2003, reported a case series of five patients suffering from TN who underwent PRF treatment. Three of the reported patients had excellent long-term alleviation of their symptoms (average of 17.5 months), while one had a partial response (requiring a repeat PRF) and the other only a short-term response [13].

In a study with animals, Tanaka N. et al. looked at how pulsed radiofrequency treatment affected mechanical allodynia caused by resiniferatoxin (RTX). They observed that PRF treatment was more effective when applied in earlier stages of the development of mechanical allodynia and with higher durations [18].

Nicolas Hai Liang Chua and achieved substantial success in a series of 36 patients with TN. The patients had undergone extended PRF with the Gasserian ganglion. The applied pulse width was 10 milliseconds, and the frequency of pulses was 4 Hz. The temperature that was achieved was 42°C [20].

Subsequently, Thapa D. et al. presented the successful management of two patients with refractory TN with extended duration PRF (8 min). They applied 4 PRF cycles of 120 seconds each [24]. Nader A. et al. in a case report of a patient with refractory trigeminal neuralgia of the maxillary branch showed the effectiveness of PRF applied through the pterygopalatine fossa with ultrasonography guidance. They applied PRF for 90 seconds and reached a temperature of 42°C. Their subject reported complete (100%) and sustained (till publication of the article; 6 months) pain relief [25]. Researchers have proposed that an insufficient PRF dose may occasionally lead to an inadequate response with PRF [20]. The combined CRF and PRF (CCPRF) application has been successfully used in painful conditions [11].

Neuroablative procedures, including CRF, are associated with various complications. Impaired corneal reflex, neuroparalytic keratitis, anesthesia dolorosa, paresthesia and dysesthesia, masseter weakness, and transient paralysis of the oculomotor and abducens nerves are among such complications. Surgical approaches should also include inherent operative risks. Neuroparalytic keratitis and anesthesia dolorosa (a form of deafferentation pain) are two of the most serious of such complications [20, 26-28]. The presented patients had undergone surgical/neuroablative procedures earlier. Accordingly, in order to avoid imposing complications, a decision was made to use extended duration PRF treatment on the sGasserian ganglion in both instances.

Conclusion

Contradictory results regarding the effectiveness of pulsed radiofrequency (PRF) treatment of the trigeminal ganglion have been published in the literature. In the past few years, reports in support of prolonged (extended duration) radiofrequency ablation have been emerging. Unlike most other interventional procedures that include nerve or ganglion destruction and its potential complications, PRF treatment is believed to be much safer. Working toward the establishment of effective PRF protocols proves highly valuable in the management of TN refractory to medical treatment.

Abbreviations

TN: Trigeminal Neuralgia
MVD: Microvascular Decompressin
PBC: Percutaneous Trigeminal Balloon Compression
GKS: Gamma Knife Surgery
RF: Radiofrequency Treatment
CRF: Continuous Radiofrequency
PRF: Pulsed Radiofrequency
CCPRF: Combined Continuous and Pulsed Radiofrequency
GABA: Gamma-Aminobutyric Acid
TRX: Resiniferatoxin

Acknowledgements

We would like to thank anyone who contributed to this study. Data availability: The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

[1] Pearce JM. Trigeminal neuralgia (Fothergill's disease) in the 17th and 18th centuries. Neurol Neurosurg Psychiatry. 2003; 74(12):1688.
[2] Arnold M. Headache classification committee of the international headache society (IHS) the international classification of headache disorders. Cephalalgia. 2018; 38(1):1-211.
[3] HIS (International Headache Society), Classical trigeminal neuralgia, The International Classification of Headache Disorders 3rd edition. [Internet]. 2024. Available from: https://ichd-3.org.
[4] Punyani SR, Jasuja VR. Trigeminal neuralgia: An insight into the current treatment modalities. J Oral Biol Craniofac Res. 2012; 2(3):188-97.
[5] Burchiel, KJ, Trigeminal Neuralgia Surgery: Overview, Preparation, Technique, Medscape. [Internet]. 2019. Available from: https://emedicine.medscape.com/article/248933-overview?form=fpf.
[6] Revuelta-Gutierrez R, Martinez-Anda JJ, Coll JB, Campos-Romo A, Perez-Peña N. Efficacy and safety of root compression of trigeminal nerve for trigeminal neuralgia without evidence of vascular compression. World Neurosurg. 2013; 80(3-4):385-9.
[7] Emril DR, Ho KY. Treatment of trigeminal neuralgia: role of radiofrequency ablation. J Pain Res. 2010; 249-54.
[8] Vallejo R, Benyamin RM, Aliaga L. Radiofrequency vs. pulse radiofrequency: the end of the controversy. Tech Reg Anesth Pain Manag. 2010; 14(3):128-32.
[9] Eugene AR. Trigeminal neuralgia and radiofrequency lesioning. Brain: broad research in artificial intelligence and neuroscience. 2015; 6(1-2):91.
[10] Ying X, Wang H, Deng S, Chen Y, Zhang J, Yu W. Long-term outcome of percutaneous balloon compression for trigeminal neuralgia patients elder than 80 years: a STROBE-compliant article. Med. 2017; 96(39): e8199.
[11] Wu H, Zhou J, Chen J, Gu Y, Shi L, Ni H. Therapeutic efficacy and safety of radiofrequency ablation for the treatment of trigeminal neuralgia: a systematic review and meta-analysis. J Pain Res. 2019; 423-41.
[12] Van Zundert J, Brabant S, Van de Kelft E, Vercruyssen A, Van Buyten JP. Pulsed radiofrequency treatment of the Gasserian ganglion in patients with idiopathic trigeminal neuralgia. Pain. 2003; 104(3):449-52.
[13] Erdine S, Ozyalcin NS, Cimen A, Celik M, Talu GK, Disci R. Comparison of pulsed radiofrequency with conventional radiofrequency in the treatment of

idiopathic trigeminal neuralgia. Eur J Pain. 2007; 11(3):309-13.
[14] Wolf A, Kondziolka D. Gamma knife surgery in trigeminal neuralgia. eurosurg Clin. 2016; 27(3):297-304.
[15] Spina A, Mortini P, Alemanno F, Houdayer E, Iannaccone S. Trigeminal neuralgia: toward a multimodal approach. World Neurosurg. 2017; 103:220-30.
[16] Siddiqui MN, Siddiqui S, Ranasinghe SJ, Furgang AF. Pain management: trigeminal neuralgia. Hosp Physician. 2000; 1:64-70.
[17] Lopez BC, Hamlyn PJ, Zakrzewska JM. Systematic review of ablative neurosurgical techniques for the treatment of trigeminal neuralgia. Neurosurg. 2004; 54(4):973-82.
[18] Arakawa K, Kaku R, Kurita M, Matsuoka Y, Morimatsu H. Prolonged-duration pulsed radiofrequency is associated with increased neuronal damage without further antiallodynic effects in neuropathic pain model rats. J Pain Res. 2018; 11:2645.
[19] Sluijter ME. Radiofrequency. FlivoPress, 2001.
[20] Chua NHL, Halim W, Beems T, Vissers KCP. Pulsed Radiofrequency Treatment for Trigeminal Neuralgia. Anesth Pain. 2012; 1(4):257-61.
[21] Maurer AJ, Candido KD, Knezevic NN. Radiofrequency Treatment. Pain: A Review Guide. 2019; 869-72.
[22] Imani F. Using Pulsed Radiofrequency for Chronic Pain. Anesth Pain. 2012; 1(3):155-6.
[23] Sluijter ME, Imani F. Evolution and mode of action of pulsed radiofrequency. Anesthesiol Pain Med. 2013; 2(4):139-41.
[24] Deepak Thapa DN, PDCC VA, Christopher Dass MB, Verma P. Management of refractory trigeminal neuralgia using extended duration pulsed radiofrequency application. Pain Phys. 2015; 18: e433 5.
[25] Nader A, Bendok BR, Prine JJ, Kendall MC. Ultrasound-guided pulsed radiofrequency application via the pterygopalatine fossa: a practical approach to treat refractory trigeminal neuralgia. Pain Phys. 2015; 18(3): e411-5.
[26] Cheng JS, Lim DA, Chang EF, Barbaro NM. A review of percutaneous treatments for trigeminal neuralgia. Oper Neurosurg. 2014; 10(1):25-33.
[27] Blomstedt PC, Bergenheim AT. Technical difficulties and perioperative complications of retrogasserian glycerol rhizotomy for trigeminal neuralgia. Stereotact Funct Neurosurg. 2003; 79(3-4):168-81.
[28] Kanpolat Y, Savas A, Bekar A, Berk C. Percutaneous controlled radiofrequency trigeminal rhizotomy for the treatment of idiopathic trigeminal neuralgia: 25-year experience with 1600 patients. Neurosurg. 2001; 48(3):524-34.