

Efficacy of Neurectomy of Peripheral Branches of the Trigeminal Nerve in Trigeminal Neuralgia: A Critical Review of the Literature

V. Yuvaraj¹ · B. Krishnan²  · Beena Agnes Therese³ · T. S. Balaji⁴

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Abstract

Introduction Of the many chronic painful conditions, trigeminal neuralgia (TN) affecting the orofacial region needs the particular attention of physicians and surgeons, especially those specialising in the maxillofacial region. Treatment protocols for the management of classic TN include pharmacology and surgical intervention. Oral and maxillofacial surgeons have traditionally employed the peripheral neurectomy in the surgical management of TN. This review aims to evaluate the efficacy of peripheral neurectomy in the management of TN with regard to (a) the

relief of symptoms in comparison with standard neurosurgical procedures and (b) the duration of pain relief and complications observed compared to standard neurosurgical procedures.

Methods The review of the literature was done according to PRISMA guidelines and included randomised controlled trials, reviews and prospective clinical studies involving surgical procedures for the management of TN. The primary outcomes evaluated were (a) initial relief of pain, (b) duration of relief of pain, (c) complications observed with ablative procedures and (d) recurrence of symptoms. A total of 43 studies fulfilled the inclusion criteria.

Results In a total of 7913 patients from the 43 studies, central procedures were found to have best results for both quality and duration of pain relief. Percutaneous and peripheral procedures were associated with increased recurrence rates. The consolidated rates of complication for peripheral, percutaneous and central procedures were 39.46, 65.42 and 10.41%, respectively. The use of peripheral neurectomy alone in the management of classic TN was observed in 10 studies.

Conclusion Peripheral neurectomy in TN is associated with lesser quality of pain relief in comparison with central neurosurgical procedures. It also provides only short- to medium-term pain relief. Most studies with the use of peripheral neurectomy involved only a small group of patients with short follow-up periods. Oral and maxillofacial surgeons must not consider the peripheral neurectomy as the first surgical option in the management of classic TN. Long-term results can be achieved better with appropriate central neurosurgical procedures and pharmacotherapy.

Keywords Trigeminal neuralgia · Facial pain · Peripheral neurectomy · Surgical

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✉ B. Krishnan
krishident@yahoo.co.uk
V. Yuvaraj
getyuv@gmail.com
Beena Agnes Therese
beenaagnestherese@gmail.com
T. S. Balaji
jupiterbalu@gmail.com

- ¹ Department of Oral and Maxillofacial Surgery, Sri Venkateshwaraa Dental College and Hospital, Pondicherry, India
- ² Department of Dentistry, Jawaharlal Institute of Post Graduate Medical Education and Research (JIPMER), 74, 4th Cross, Thanthai Periyar Nagar, Pondicherry 605005, India
- ³ Department of Oral and Maxillofacial Surgery, Indira Gandhi Institute of Dental Sciences, Pillaiyarkuppam, Pondicherry, India
- ⁴ Department of Oral and Maxillofacial Surgery, Sri Venkateshwaraa Dental College, Ariyur, Pondicherry, India

Introduction

Response to painful noxious stimuli is a critical evolutionary phenomenon; albeit protective in nature, it instils apprehension in both the sufferer and healer. From time immemorial, healthcare providers have strived to relieve patients of pain with all the means available to them. Of the many chronic painful conditions, trigeminal neuralgia (TN) affecting the orofacial region needs the particular attention of physicians and surgeons, especially those specialising in the maxillofacial region. This painful debilitating condition has been described in myriad terms ranging from “stabbing”, “suicidal”, “lancinating” and “electric shock-like” and is defined by the International Association for the Study of Pain (IASP) as a “sudden usually unilateral severe brief stabbing recurrent pains in the distribution of one or more branches of the fifth cranial nerve” [1]. The pathophysiology of TN has been attributed to the short circuiting of the demyelinated axons resulting in the paroxysms of pain [2]. Another popular theory is the “ignition hypothesis” according to which abnormal firing is resultant to an injury to the myelin layer of the trigeminal nerve due to compression at its point of entry in the posterior fossa [3].

TN has been classified into “classic” and “symptomatic” based on the aetiology by the International Classification of Headache Disorders [4]. While symptomatic TN is caused by tumours, infections and arteriovenous malformations and is amenable to surgical intervention, classic TN is idiopathic with no specific guidelines for management.

Treatment protocols for the management of classic TN include pharmacology and surgical intervention. Surgical intervention is considered only in intractable TN failing to respond to appropriate pharmacologic therapy [5] (Fig. 1). While most surgical interventions are the domain of neurosurgeons, oral and maxillofacial surgeons have traditionally employed the peripheral neurectomy in the surgical management of TN. With a better understanding of the pathology and advancement in imaging and neurosurgical interventions, the efficacy of peripheral neurectomy in TN has been questioned. This review aims to evaluate the role of peripheral neurectomy in the management of TN and its efficacy in relief of symptoms in comparison with standard neurosurgical procedures.

Objectives

1. To evaluate the comparative effectiveness of peripheral neurectomy and standard neurosurgical procedures towards pain relief and recurrence in the management of classic TN.

2. To compare the duration of pain relief and complications observed with peripheral neurectomy and standard neurosurgical procedures in the management of classic TN.

Methods

Protocol

The review was done according to PRISMA guidelines, and the final document checked according to the checklist provided on the website <http://www.prisma-statement.org>.

Inclusion Criteria

1. All randomised controlled trials, prospective clinical studies, reviews and questionnaire follow-up studies in the management of classic TN were included in this review. Case reports and retrospective studies were excluded.
2. Surgical interventions for TN either at
 - “Periphery” at the trigger zone area—neurectomy, alcohol injection and bupivacaine injections.
 - “Gasserian ganglion level”—percutaneous radiofrequency thermocoagulation (PRTC), glycerol rhizolysis, balloon compression and gamma knife surgery (GKS).
 - “Posterior fossa surgery”—microvascular decompression (MVD), partial sensory rhizotomy, gamma knife surgery (GKS).

Outcome Measures

Primary Outcomes

1. Initial pain relief following the intervention.
2. Duration of pain relief following the intervention.
3. Recurrence of pain following the intervention.
4. Complications of ablative procedures.

Search Methods for Identification of Studies

We searched the Cochrane, PubMed, MEDLINE databases from the years 1948–December 2016. The search terms used were “Neurosurgery”, “Trigeminal Neuralgia”, “Peripheral neurectomy”, “Peripheral Ablative Procedures”, “Surgical Management of Trigeminal Neuralgia”, “Gamma Knife Surgery”, “Radiofrequency Thermocoagulation”, “Balloon Compression”, “Posterior Fossa Surgery”, “Glycerol Rhizolysis”, “Microvascular Decompression”,

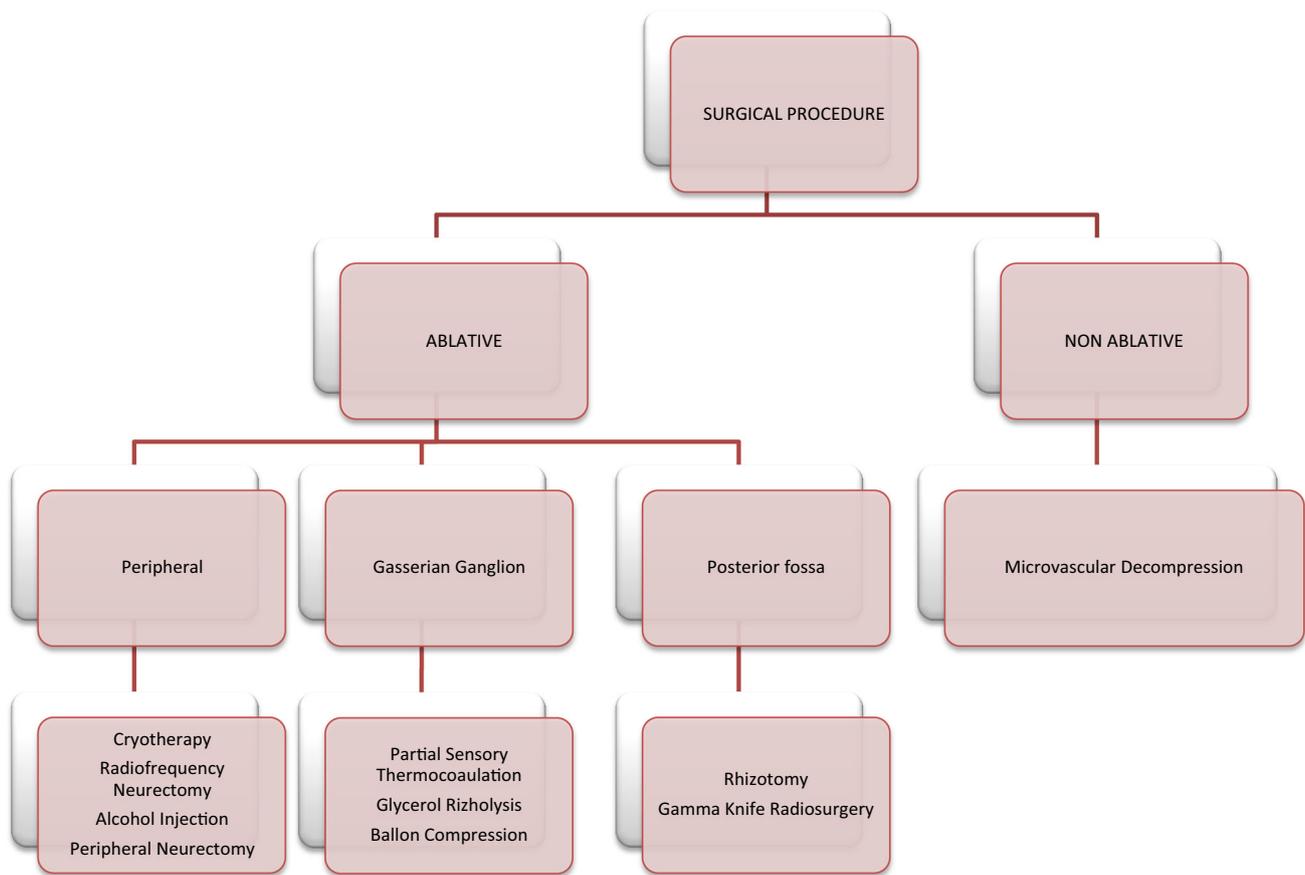


Fig. 1 Surgical interventional procedures in the management of classic trigeminal neuralgia

“Sensory Rhizotomy”, “peripheral injections in trigeminal neuralgia”, “neurovascular compression in trigeminal neuralgia”.

Data Collection and Analysis

Two senior authors independently read the data from the identified studies like title, abstract and when available, the full reports. The authors independently assessed the quality of trials using the format prescribed in the PRISMA guidelines using the domains: Title, Abstract, Introduction, Objectives, Participants, Interventions, Comparisons, Outcomes, and Study design (PICOS). In methodology section, protocol and registration, eligibility criteria, information sources, study selection, data collection, bias and summary were assessed.

Of the 45 studies initially selected, two studies were excluded due to the lack of availability of sufficient information.

Details of Included Studies

Forty-three studies were selected based on the inclusion criteria previously mentioned. One significant finding of the studies was that while neurosurgeons had authored the neurosurgical procedures, all peripheral neurectomy articles were authored by oral and maxillofacial surgeons, excepting for 2, which included both the maxillofacial surgeon and neurosurgeon [6, 7].

Results

A total of 7913 patients were included in the review. For the analysis of results, numerical data are critical for the comparison of outcomes. However, on a comparison of the included studies, it was observed that all four primary outcome measures were not analysed. This anomaly meant that the primary outcomes could not be summarised against a common denominator of the patient population included in the review. To overcome this, we were advised to perform a working analysis for every outcome measure based on the consolidation of the available quantitative data for

that particular outcome measure. The summative value of a particular outcome measure was arrived by adding the numerical data of only those studies which had quantified the outcome measure and dividing by only that number of patients in whom the outcome had been analysed. An illustrative example of the working analysis is given in Table 1.

Central procedures were found to have best results for both quality and duration of pain relief. Percutaneous and peripheral procedures were associated with increased recurrence rates (Table 2). The consolidated rates of complication for peripheral, percutaneous and central procedures were 39.46, 65.42 and 10.41%, respectively (Table 3).

The use of peripheral neurectomy alone in the management of classic TN was observed in 10 studies. Most of these studies lacked clarity on the criteria for arriving at the diagnosis of TN. No information on possible odontogenic causes of facial pain was available. Further, critical data such as a definite exclusion of central pathology, pre-operative investigations performed and results thereof, pharmacology therapy and its duration and efficacy, reasons for abandoning the medical management were not described in most studies. The unavailability of such data meant that the decision to employ peripheral neurectomy as the exclusive surgical option could not be evaluated scientifically in most studies.

Discussion

A clinical diagnosis of TN in a patient with orofacial pain may be quite obvious, yet challenging. Coexisting pathological conditions involving the dentition and oral tissues, sinuses and orbit may mimic symptoms and confuse the

clinician. Spending adequate time in the patient interview and physical examination of the regions supplied by the trigeminal nerve is important. Neurological conditions like multiple sclerosis, atypical facial pain may always be considered before a final diagnosis of classic TN. As this condition has no pathognomonic radiological features, the use of plain X-rays and computed tomography scans is mainly to exclude other pathological conditions (space-occupying lesions, bony compression of the nerve, etc.) responsible for the neuralgia of the trigeminal nerve. Magnetic resonance imaging (MRI) and MR angiography can identify intracranial conditions and identification of vascular structures encroaching on the trigeminal nerve root entry zone [8]. Pharmacotherapy is almost always the first line of management in practically all cases of classic TN and is used only for pain relief with no attempt to “cure” TN. Carbamazepine is usually the first drug of choice, but long-term therapy is fraught with risks such as drowsiness, nausea and vertigo, hematopoietic disturbances and liver dysfunction [9]. Diagnostic administration of carbamazepine is no longer advocated as relief of pain does not exclude the presence of a tumour, cyst or multiple sclerosis without regard to patient’s age [9]. Other drugs such as gabapentin, pregabalin, dilantin sodium have also been used either single or in combination therapy [9]. Surgical procedures are considered when the patient does not attain pain relief after adequate trials of 2 or 3 medications, or when pain relief is attained, but patient requires medication dosing at levels that result in a significant drug toxicity [10].

Toda has cautioned on the pitfalls of comparison amongst procedures for TN as diagnostic criteria for TN in each study are not the same and clinicians often underreport pain recurrence and post-operative complications. Further, comparisons amongst procedures for TN are

Table 1 Illustrative example of the method of consolidation used in the working analysis

	Number of patients undergoing procedure (N)	First outcome (initial pain relief) (IPR)	Second outcome (duration of pain relief) (DPR)	Third outcome (recurrence rate) (RR)	Fourth outcome (complications rate) (CR)
Article 1	N 1	IPR 1	Not given	Not given	CR 1
Article 2	N 2	Not given	DPR 2	Not given	CR 2
Article 3	N 3	IPR 3	DPR 3	RR 3	Not given

$$\text{Summary of first outcome (initial pain relief)} = \frac{\text{IPR1} + \text{IPR3}}{\text{N1} + \text{N3}}$$

$$\text{Summary of second outcome (duration of pain relief)} = \frac{\text{DPR1} + \text{DPR3}}{\text{N2} + \text{N3}}$$

$$\text{Summary of third outcome (recurrence rate)} = \frac{\text{RR3}}{\text{N3}}$$

$$\text{Summary of fourth outcome (complications rate)} = \frac{\text{CR1} + \text{CR2}}{\text{N1} + \text{N2}}$$

Table 2 Pain recurrence rates following surgical intervention in trigeminal neuralgia

Nature of procedure	Pain relief (in %)	Duration of pain relief (in years)	Rate of recurrence (in %)
Peripheral	53.13	2	15.34
Percutaneous procedures	62.38	2.4	18.33
Central procedures	76.062	10	7.81

Table 3 Complications following surgical management of trigeminal neuralgia

Nature of procedure	Complications reported	Consolidated rate of complications (in %)
Peripheral	Hypoesthesia, dysesthesia, paresthesia High requirement of analgesics Persisting paroxysms several days after neurectomy	39.46
Percutaneous	Diminished corneal reflex Anaesthesia dolorosa Masseter weakness and paralysis Permanent palsy of the abducent nerve CSF leakage Aseptic meningitis Carotid cavernous fistula	65.42
Central	Deaths (0.2%) Brain stem infarction (0.1%) Ipsilateral hearing loss (1%) Hypoesthesia, disappearance of corneal reflection, masticatory atonia, paraesthesia, trachyphonia, hearing loss, vertigo or tinnitus CSF leakage, hearing loss and persistent diplopia Facial numbness (36%) Persistent paresthesia (15.8%)	10.41

difficult because the commonly used terms “analgesia”, “hypoalgesia”, “paraesthesia” and “dysesthesia” are imprecise [11]. Selecting the appropriate surgical procedure to treat TN is dependent on patient’s physical and mental condition. While some patients want long-term pain relief at any cost, others will accept shorter pain-free periods in return for a few complications [12]. Peripheral surgical procedures such as neurectomy are well within the expertise of the oral and maxillofacial surgeon. Peripheral neurectomies are a destructive form of surgery but have the distinct advantages of being performed even under local anaesthesia with good tolerance by patients [13]. One of the prerequisites of peripheral neurectomy for injured peripheral nerves and neuromas is a complete relief of pain after repetitive local anaesthetic nerve blocks. Avoiding adrenaline in these nerve blocks is important as injured peripheral nerves and neuromas abnormally express adrenergic receptors, which are algogenic when activated and can, therefore, produce a false-negative response to

blockade [14]. The pain relief obtained with neurectomies is not only due to the removal of the sensory receptors of peripheral nerves but also as a result of the trauma that is produced resulting in temporary degenerative changes in the ganglionic cells [15]. The indications for peripheral neurectomy appear to be few and are to be considered only in a select group of patients, viz., (a) elderly patients with restricted life expectancy, (b) those unwilling to accept the anaesthesia that would result from a root or ganglion destruction, (c) when there is a delay in access to centres with neurosurgical expertise, (d) those unable to cooperate for neurosurgical procedures under dissociative anaesthesia/general anaesthesia and (e) when TN is refractory to medication or needs dosages that will result in significant side effects [11, 15–17]. In a questionnaire survey amongst oral and maxillofacial surgeons in the UK, a vast majority opted for medical management of TN as the first line of management with only a minuscule number preferring either peripheral procedures or immediate referral to a

neurosurgeon [18]. When questioned on management following a failure of medical therapy, options for peripheral procedures and referral to a neurosurgeon were preferred almost equally by the respondent surgeons. A closer examination of studies that have performed only peripheral neurectomies for supposedly elderly patients with TN shows that this peripheral procedure has been employed in a number of patients within 40 years of age and only five patients were over the age of 50 [7, 13]. In one study, a third of the neurectomies were performed under general anaesthesia contradicting one of the main advantages of this procedure being amenable to local anaesthesia [19]. Patients who were fit to undergo general anaesthesia would have probably been capable of undergoing a central neurosurgical procedure. This suggests that the peripheral neurectomy is perhaps being considered as the first option of treatment despite stating that it should be reserved only for a select group of patients. Central neurosurgical procedures such as MVD and GKS have been employed in a wide age range with the resultant pain relief not dependent on the age of the patient [20–22].

The immediate outcomes of peripheral neurectomies are usually excellent. While some studies report immediate relief of pain following the procedure, Agrawal et al. [15] mention that paroxysms often persisted for several days after surgery before subsiding completely. The long-term efficacy of peripheral neurectomies in classic TN is variable. One of the early documented studies on peripheral neurectomies in TN reported pain relief in 30 of 47 patients at the end of 1 year. This pain relief was observed in only ten patients at the end of the fourth year [23]. Grantham and Segerberg [24] on the evaluation of the role of palliative surgical procedures in TN reported a median pain-free period of 33.2 months in 55 neurectomies. Quinn and Weil [25] performed 162 neurectomies in 88 patients and documented median total pain relief period of 41 months with a mean of 52.1 months.

Results of peripheral neurectomy also appear to be dependent on the nerve branch on which the surgery has been performed. Khanna and Galinde [26] reported pain-free period of 24 and 26 months following infraorbital and mental neurectomies, respectively. However, Mason observed that infraorbital neurectomy was likely to be more successful than inferior alveolar neurectomy and attributed this to the occlusion of the infraorbital foramen with a resultant retardation of nerve regeneration [23]. A myriad of materials, such as fat, gold foils, silicone, have been used to occlude the foramen following peripheral neurectomy [16, 27, 28]. Failures of inferior alveolar neurectomy were often the result of the onset of symptoms in another branch or division of the trigeminal nerve, and a simultaneous lingual neurectomy has been advocated to reduce the incidence of failure [23, 25]. Oturai et al. [29] in

a comparative analysis of alcohol block, peripheral neurectomy and radiofrequency coagulation in TN observed that the time until half the patients had experienced recurrent pain was only 1 month for the 53 patients who were treated with neurectomy. A recently published study comparing the effects of obturation of mental/infraorbital foramen following peripheral neurectomy appeared to suggest a significant pain relief following obturation [17]. However, while no pain was present even after 24 months following placement of stainless steel screws in the foramina, similar pain-free period of 22 months was observed without obturation. The small sample size of 14 patients in the above study puts into question the statistical significance of the results.

One of the purported advantages of peripheral neurectomy has been the ease of performing a repeat surgery when required. Freemont and Millac [16] recorded an average pain-free period of 26.5 and 59 months following single neurectomy and multiple neurectomies, respectively. However, there is also evidence to suggest that repeat neurectomies are associated with a marked decrease in the duration of the pain-free period, and more than three neurectomies on the same nerve are not recommended [30]. Cerovic et al. [19] published their experience with multiple peripheral neurectomies in 36 patients. An average of 2.2 operations for the infraorbital nerve and 1.77 operations for the inferior alveolar/mental nerve was required. The results of their study indicated that there was a clear trend of a decreasing time of remission in repetitive neurectomies and most patients presented with recurrent pain after relatively short periods of time. They concluded that peripheral neurectomies are not a very effective method and are an almost obsolete surgical technique. Further, all attempts should be made to apply conservative measures as long as possible between repeat neurectomies. Better outcomes following peripheral neurectomy have been observed in patients who underwent the peripheral surgery due to pain recurrence following neurosurgical procedure. Murali and Rovit [7] noticed good to excellent pain relief lasting for at least 5 years in all 28 patients who underwent a peripheral neurectomy procedure following percutaneous radiofrequency thermocoagulation. It is hypothesised that axonal regrowth after a neurectomy, which is the usual cause of pain recurrence, is impaired or delayed in patients due to the presence of a radiofrequency lesion in the Gasserian ganglion.

As many patient symptoms are adequately controlled with medication, a more pragmatic approach of neurosurgical reference of all patients who wish to have non-medical management early, or in whom medical management has failed, is reasonable [18]. Prolonged medical therapy may result in irreversible damage to the nerve and a reduction in the efficacy of eventual surgery [31]. Further,

results of central neurosurgical procedures are inferior when there has been a delay between first diagnosis and treatment, and also when other operations have been tried first [32, 33].

Summary of Results

In general, the choice of the surgery is dependent on patient preference, surgeon experience and expertise available. The conclusions drawn related to peripheral neurectomy are:

(A) Initial pain relief and recurrence:

1. The overall results have shown that peripheral neurectomy is associated with lesser quality of pain relief in comparison with central neurosurgical procedures.
2. Multiple neurectomies are associated with poor outcomes.

(B) Duration of pain relief:

Peripheral neurectomies provide only short- to medium-term pain relief. Pain usually recurs within 2 years due to axonal regeneration. In contrast, central neurosurgical procedures provide satisfactory long-term pain relief.

(C) Complications:

Complications with peripheral neurectomies tend to be more localised in comparison with the morbidity associated with percutaneous and central neurosurgical ablative procedures.

Conclusion

Peripheral neurectomies cannot be recommended for routine use as most studies involved an only small group of patients with short follow-up periods [34]. Further, it provided lesser quality and duration of pain relief in comparison with standard neurosurgical procedures. The possibility of an undiagnosed central pathology may partly explain the unsatisfactory results with the use of peripheral neurectomies. Performing a peripheral ablative procedure, in the beginning, may affect the efficacy of the central neurosurgical procedure. Surgical ablation of the peripheral branches of the trigeminal nerve must be considered only as a last resort in exceptional situations (debilitated patients unfit or unwilling for neurosurgical procedures, emergency relief of pain when a neurosurgeon is not available, elderly patients with a limited life span after the failure of other interventional procedures) [7, 18].

The personal opinion of the authors is that all patients with suspected TN, when seen by a dental/maxillofacial surgeon, should be evaluated with dental panoramic radiographs to rule out confounding odontogenic causes of facial pain. Attempts must be made to eliminate any suspected dental causes of facial pain. Care should be taken to avoid any harmful or unnecessary dental care. The medical management of TN is best performed under the monitored care of a physician/neurologist. Performing peripheral neurectomies for suspected TN without radiological evidence ruling out central lesions or vascular compressions is not scientifically acceptable. A judicious combination of appropriate central neurosurgical procedures and pharmacotherapy (as decided by the physician/neurologist/neurosurgeon) may provide better long-term outcomes.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no competing interests.

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