



Review Article

## Unraveling the Mystery of Trigeminal Neuralgia: Insights into Diagnosis and Management—An Overview

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### ABSTRACT

A rare and painful condition known as trigeminal neuralgia, this condition is typified by abrupt, unbearable, paroxysmal, piercing, stabbing pain that is frequently unilateral throughout the trigeminal dermatomes. While the illness generally is not lethal, it is debilitating and can occasionally end in psychological disorders. This disorder diminishes the quality of everyday life. To ease the pain and suffering patient's agony, a precise diagnosis and an effective therapeutic approach are essential. A comprehensive examination of the diagnosis, management, and rehabilitation of trigeminal neuropathy is given in this article. This includes pharmaceutical administration, surgical management, alternative recently discovered methods of treatment and a screening approach. Latest innovations and newer guidelines of treatment are also discussed to enhance clinical outcomes and improve patients' prognoses.

**Keywords:** nerve compression, anticonvulsant, radiosurgery, facial pain, and surgical intervention

### INTRODUCTION

Uncommon dentofacial distress, recognized as trigeminal neuralgia (TN), is frequently brought by compaction caused by arteries and veins. A global headache association explains it as repeated, unambiguous, brief, electric shock-like discomfort that stops on its own is abruptly initiated, restricted to the branching of several nerve divisions, or is induced by harmless stimuli. Fothergill identified the ailment as tic douloureux after diagnosing the first case of it in 1756. initially, he called it a painful affection of the face, but later, John Hunter clarified that he meant it to be a type of nerve illness. This condition was medically managed with powdered mercury and the drugs opium and arsenic in the 19th and 18th centuries.<sup>[1]</sup> In 1994, phenytoin delivered useful outcomes for TN. The precise physiology or the development of this condition is still in debate. However, thorough research has been conducted mostly on classical TN. The condition starts when the trigeminal fibres in the pons or dorsal root entrance zone sustain damage to their core myelin; the "ephapsys" caused by these myelinated nerve fibre losses permit all tactile proprioceptive and temperature stimuli to be converted into pain. An overwhelming amount of pain stimuli sensitizes the trigeminal cells, causing them to fire continuously. Nerves become hyper-excited in the peripheral because of more pain stimuli, and sensitivity in the center advances. Non-painful stimuli can activate these hyperexcitable nerve cells, which causes them to react with semi-epileptic painful episodes. Paroxysmal attacks become less frequent as the damage gets worse and persistent neuropathic pain starts.<sup>[2]</sup> Neurovascular constriction induced by an aberrant artery or

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blood vessel, arteriovenous abnormalities, vestibular tumor, meningioma, epidermoid cyst, and other cysts and tumors, and vessel aggregation in the area anterior to the pons at the nerve root entrance zone. Other arteries or veins may also contribute to 5th cranial nerve compaction.<sup>[3,4]</sup>

Along with identifiable sources of facial discomfort, this kind of disorder is typified by the existence of trigger zones devoid of any observable neurological deficiency. An innocent touch to the cheek, while cleaning teeth, or when opening the mouth may cause this pain. It is possible to characterize the discomfort as electric shock-like, acute, stabbing, sporadic, abrupt, severe, piercing, and paroxysmal. Before determining the exact cause, a physician must rule out other possible reasons for facial pain. These may include:

*Crack tooth:* An incomplete breakage and crack in a crucial dental region affecting the connective tissue and nerves is known as crack tooth syndrome. When the patient expresses their suffering, it closely resembles trigeminal neuropathy. The pain is commonly characterized as burning or jabbing, and it is identified as TMJ disorders or similar oral-facial difficulties. Among widely accepted methods that rule out crack teeth syndrome were selective biting testing and transillumination.<sup>[5]</sup>

*Post-traumatic trigeminal nerve impairment* is the term used to refer to discomfort that develops within locations related to the trigeminal nerve post-injury to the dentofacial region and exhibits all the characteristics of facial nerve damage. This could be the consequence of regular surgeries like endodontic procedures, tooth extractions, or various iatrogenic and physical traumas. People who are affected frequently describe the discomfort as shooting, pyrogenic, or recurring. A precise diagnosis can be reached with the aid of a careful or thorough background recording.

*Glossopharyngeal Neuralgia* is a unique kind of mouth awkwardness that does not look like trigeminal nerve pain. It produces abrupt bursts of tenderness throughout the neck or throat region; individuals usually describe it as a stabbing knife-like feeling in these areas and sporadically extending discomfort to the ears. The position of the pain—which must occur in the rear segment of the lingual apparatus, tonsillar cavity, angle of the mandible, or the ears—is the main difference between TN and glossopharyngeal neuropathy.<sup>[5]</sup>

*Nervus Intermedius neuralgia:* A rare condition called nerve intermedius neuropathy can cause brief bursts of ear discomfort, which may radiate to the parieto-occipital region. Once it leaves the brainstem, this neuron enters the internal auditory meatus. To differentiate between nervus intermedius neuralgia and TN, it is critical to consider the primary complaint of the patient.<sup>[6]</sup>

*Short-lasting unilateral neuralgiform headache with conjunctival injections and tearing (SUNCT):* An atypical entity that mostly impacts individuals who are in the middle decades of life range. The pain with this condition produces is usually scorching, shooting, or electric, which can range in severity from moderate to extreme. It affects both the eye and periocular regions. The presence of conjunctival injections and tears are characteristics that set this illness apart from TN.

*Postherpetic neuralgia:* In senior citizens, the reappearance of herpes zoster virus is prevalent, causing postherpetic neuralgia. Vesicular eruptions over those areas involved in trigeminal nerve terminals indicate its occurrence. It is linked to post-herpetic neuralgia, encephalitis, and eyesight loss. It can occur from aging or a bacteria-related infection. Antiviral drugs are frequently employed to treat this illness.<sup>[7]</sup>

*Post-operative complications:* The Trigeminal nerve, being almost entirely sensory, when undergoing surgeries, often shows hypoesthesia, dysesthesia, or loss of sensation. Invasive, non-ablative procedures have definitive deficits of cranial nerve VIII, VII, and IV in less than 5% of cases. Invasive ablative procedures can offer a degree of damage to the nerve as well, Corneal reflex loss, keratitis, and anesthesia dolorosa, which is quite rare, causing numbness associated with nerve damage and masticatory muscle weakness. In non-invasive ablative procedures, diplopia, hearing loss, mastication muscle weakness can be seen.<sup>[8]</sup>

Therefore, if there are four or more unilateral bouts of face discomfort, such as it involves either all or some trigeminal nerve parts, both the beginning and end of pain are abrupt, whereas there is no pain radiation outside this nerve's dispersion. Pain that exhibits at least three of the following four features: It is intense, recurrent in paroxysmal episodes that can last up to 120 seconds, simulating electrical shockwave, firing, or knifing, and it is brought on by harmless inputs on a portion of the skin on the face that is impacted. Attacks are individual to all affected persons, and neurologic deficits are absent in these individuals.<sup>[9]</sup>

Hence, additional neurological assessments are discussed below that can be used for further examination of certain clinical criteria as novel analytical techniques for trigeminal nerve pain (TN) as follows.

*Computed Tomography (CT):* With the use of digital geometric processing, a sequence of 2D X-ray images recorded around the axis of rotation can be converted into 3D images for use in medical imaging scans like CT. It is used to identify nerve damage brought on by multiple sclerosis, an inflammatory condition that causes nerve inflammation and the destruction of the myelin sheath. TN and multiple

sclerosis can occasionally coexist, and facial nerve tumors, sinusitis, and neurovascular conflicts can also result in nerve injury.

**Magnetic Resonance Imaging (MRI):** Utilizing fields of magnetic attraction and radiofrequency, the technique of MRI produces finely precise pictures that depict the body's inner organs. It is regarded as the gold standard for assessing diseases like TN because it can identify potential trigeminal nerve compression sites in the vasculature. Moreover, it can assist in ruling out any further reasons for TN, such as cysts or tumors that might be pinching the trigeminal nerve root. Individuals who have heart rate monitors or defibrillators are unable to have an MRI because magnetic waves can cause problems with such appliances, even though there is no biological risk involved.

**Magnetic resonance angiography (MRA):** An approach based on MRI principles seeks to identify any neurovascular problems using the foramen ovale. A substance that contrasts, gadolinium therapy or iodine, is injected into Meckel's cave using this technique. While few examples of gadolinium accumulation in the brain have been reported, these investigations have not shown any neurological harm.

**Treating TN can be handled with two sorts of therapies:** Pharmaceuticals and operations, i.e., *in first-line approaches*, medical treatments should be the initial line of care; only if drugs do not work can surgery be considered. Roughly 33–50% of patients can need surgical intervention during some stage. In this article, we will examine the level as well as the duration of pain reduction associated with each course of therapy. As a result, several medications are utilized to relieve pain produced by neural illnesses. For decades, anticonvulsant medicines like Carbamazepine and oxcarbazepine have been effectively practiced as the earliest curative approach for TN, and they can reduce distress by up to 90% in most patients. It interacts strongly with other medicines that patients may be on, and oxcarbazepine causes substantial neural system depression. The medication tolerability determines the progression of the therapy. Carbamazepine dosage spans 200–1200 mg per day, whereas oxcarbazepine dosage spans 600–1800 mg per day. Some of the most often utilized *second-line approaches* include gabapentin, lamotrigine, and baclofen. These medications have fewer undesirable effects and greater potency. These are used when the patient's primary-line medications are not well tolerated. Due to the presence of acute rashes and other harmful reactions, a slow-dose titration protocol is used. These medications work through three major mechanisms, i.e., augmentation of GABA action, inhibition of sodium channel functions, and inhibition of calcium channel functions. Various first-line and second-line drug approaches are mentioned in Table 1.<sup>[10]</sup>

**Table 1:** Treatment of trigeminal neuralgia (TN) with medicine

	Drugs	Dose	Side effects
First-line drugs	• Carbamazepine	600–1200 mg/day	Headache decreased muscle motor coordination, dizziness, kidney pain, and skin reactions.
	• Oxcarbazepine	600–1800 mg/day	Like carbamazepine, however, without fewer serious adverse reactions reduced adverse effects than using carbamazepine
Second-line drugs	• Gabapentin	12 mg/day	Tiredness, diplopia, vertigo, decreased neuromuscular control, drowsiness, and hand tremor
	• Lamotrigine	400 mg/day	Skin responses, nausea, dizziness, constipation, dysgeusia, and psychological distress
	• Baclofen	40–80 mg/day	Fatigue, nausea, or muscle hypotonia. Errors or convulsions can occur with abrupt pharmaceutical cessation

A surgical procedure is frequently necessary to aid individuals who develop drug resistance or who have intolerable side effects. The present treatments are not lasting, but they can provide temporary pain relief without achieving full remission. The extent and length vary depending on the therapy's option. The several sorts of surgical operations are discussed below.

**Microvascular decompression:** In 1925, Walter Dandy described microvascular decompression as a key factor in treating TN. It is strongly recommended as the treatment of choice due to its long-lasting pain relief, safety, and effectiveness. This procedure aims to target the area where the trigeminal nerve root intersects the nerve pons, requiring surgery on the posterior fossa involving suboccipital craniectomy and nerve combing. It is recommended only for cases of classical TN following a high-resolution contrast-enhanced MRI indicating a neurovascular conflict. CT can also be utilized to pinpoint the compressed region of the trigeminal nerve.<sup>[11]</sup> Sometimes, a division of the basilar artery or the vena petrosa

sparks compaction.<sup>[12]</sup> Over 70% of patients were symptom-free and devoid of pharmacotherapy for 10 years term post-surgery, and 75–80% remained pain-free after 15 years.<sup>[11]</sup> In a previous study, a fatality ratio between 0.2 and 1% was considered an operative deviation. However, recent findings from two large series involving 444<sup>[13]</sup> and 1995<sup>[14]</sup> patients showed no deaths. Even though the MVD's reputation has certainly grown over the last two decades, there is currently a discussion concerning its benefit from the neurodestructive method.

*Percutaneous balloon compression (PBC)* provides an unexplained solution, but it is unknown whether it is the most useful method. Each method has a set number of challenges and occurrences. Its earliest appearance was in 1978 and was issued by Mullan and Lichtor in 1983. The first trial included 50 patients who received gasserian ganglion compaction employing a Fogarty balloon. The operation is carried out upon spinal anesthesia, with a fluoroscopically guided cannula inserted within a foramen ovale and never stretched further. The Fogarty catheter is placed into Meckel's cave until it fills the entire hollow. The catheter tips contain 0.5–1.0 mL of contrast-enhancing substance. The compaction is sufficient, lasting from one to six minutes in total. While this technique causes some little sensory impairment, nearly all patients get immediate pain alleviation.<sup>[15]</sup> The benefits of the percutaneous approach are its ease and speed from a scientific point of view, practical identification that does not require involvement, and its ability to be carried out on a patient throughout only a short time of widespread sedation with minimal pain. It is believed that all precautions should be taken to prevent hypotension and bradycardia during surgery.<sup>[16]</sup>

*Radiofrequency ablation* was discovered to be an efficient and non-intrusive method for managing TN, especially contrasted with balloon compression and microvascular decompression. It is widely acknowledged for its security, potency, and successful percentage of happiness among affected individuals.<sup>[17]</sup> According to a 2016 comprehensive review research, radiofrequency ablation was found to contain an average of 5–10% incidences of reappearance and between 85 and 90 percent rate of survival for treating TN.<sup>[18]</sup> A study done in 2019, including 100 participants that recently appeared in the *Journal of Neurosurgery*, indicated that 98% of procedures were successful following an average monitoring of one year.<sup>[1]</sup> In 2020, research reported that radiofrequency ablation had a more economically viable alternative for TN than microvascular decompression. Furthermore, individuals with hemophilia or specific types of tumors should not undergo radiofrequency ablation.<sup>[19]</sup> This could result in infections, hemorrhagic tendencies, infections, and injuries to the nerves, among possible side

effects. Although these dangers are usually small, they are to be considered when assessing radiofrequency ablation as a substitute for remedy.<sup>[20]</sup> Thus, radiofrequency ablation is a potent alternative to medication overall for persistent TN, but it has drawbacks. While undergoing therapy, it can also be costly, and healthcare may not cover treatment and, therefore, might be a barrier for certain individuals.

*Glycerol Rhizotomy (GR)*: In 1904, Schloesser gave some of the earliest described administrations of alcohol through the trigeminal neurons. It has been found by coincidence that glycerol has been utilized as an agent for injecting tantalum particles through the trigeminal canal.<sup>[21]</sup> The precise process underlying glycerol injection-induced injury to big myelinated fibers is believed to be caused by a rapid shift in intracellular osmolarity and axonal degeneration with shattering. In a study, it was found that the treatment provided mild-to-moderate pain relief, which usually lasted between 3 and 6 months with an average span of 11 months.<sup>[22]</sup> Over one year, around 70% of the patients stated that they were able to manage their pain.<sup>[23]</sup> In some patients, post-procedure symptoms such as reduced sensation and temporary facial paralysis were observed, usually from hours to days after the procedure.<sup>[23,24]</sup> While severe reductions in sensitivity and pain relief are rare, individuals who undergo ongoing treatments may be more vulnerable.<sup>[25]</sup> However, the percentages of oral hemorrhage and epithelial penetration are reported following the carotid stab rate.<sup>[25,26]</sup>

*Gamma knife radiosurgery*: This protocol, invented by Lars Leksell<sup>[27]</sup> over half a century ago, is a radiosurgical tool that replaces open intracranial procedures in the treatment of cognitive neurological disorders. Nonetheless, the proximal trigeminal root close to the pons has been the goal in recent years, with substantially better results.<sup>[28]</sup> In this method, the individual receiving treatment lies down, and their forehead is protected by an electromagnetic collimator mask. Securing the frame is done under local anesthesia, and irradiation is often done under intravenous or moderate mouth sedation.<sup>[29]</sup> Usually, relief from discomfort takes time to manifest. There was evidence of localized axonal degeneration for six months afterwards following 80 Gy to 100 Gy of recommended radiation. This seems to be associated with MRI enhancement of contrast observed several months following radiosurgery with no visible ganglion alterations.<sup>[30]</sup> As a result, it is now recognized as one of the main therapeutic methods for TN for individuals whose alternative therapies have failed. Among the other neurosurgical treatment techniques, it has the best level of security and is the least invasive. It has drawbacks, a delay until pain alleviation and an elevated probability of recurrence at prolonged examination. It is anticipated that current advances in neuroscience will enhance these methods and clinical results for TN individuals.<sup>[31]</sup>



*Peripheral nerve resection*: Straightforward, relatively secure treatment for any terminating branch of all three trigeminal divisions. This operation can be performed without general anesthesia in an outpatient environment. This type of surgery is known as postganglionic surgery and involves severing the nerve after it exits the skull. Peripheral nerve regeneration is the secondary cause of pain recurrence. Ali *et al.* carried out a study in rural India where 14 individuals affected with TN who were medically unfit for major surgeries and who could not afford the other treatments or patients who were unresponsive to conservative therapy were selected. Throughout 12 to 24 months beyond the operation, many patients experience pain recurrence. A second neurectomy may be used to address recurrent pain; however, these operations frequently result in less long-lasting pain relief.<sup>[32]</sup>

*Cryotherapy*: Lloyd, in 1976, published the first description of cryotherapy for inhibiting peripheral nerves. Pradel *et al.* invented a cryoprobe with a radius of 1.3 mm, which harnesses liquid nitrogen to cool the tip of the probe. It can reach up to a maximum of 158°C. The temperature reached at the nerve determines the duration of numbness and the speed of pain relief. The guidance structures for nerve fibre regeneration are critical to the healing phase with the resulting repair of perception. The probe's tip is placed transmucosal over the nerve with extreme accuracy. The ablated nerve stands anesthetized and begins to regain its sensory output in the first 3 months. Few physicians use this to be a primary management protocol for TN-affected individuals since the results are generally less favorable in terms of pain-free longevity when compared to other percutaneous methods.<sup>[33]</sup>

*Alcohol block*: When treating TN, alcohol nerve block was often administered; however, these days, percutaneous techniques or microvascular decompression are more frequently utilized. While frequent administration of peripheral phenol or alcohol-based injections may induce adjacent membranous damage to the site of administration, such as tenderness along with fibrotic scarring, there is a continuous discussion on the injection's suitability for managing TN, even though it offers moderate pain relief.<sup>[34,35]</sup> The principal adverse impact caused by alcohol doses is the transient weakening of the masticatory apparatus, as the motor root is near the inferior alveolar nerve.<sup>[36]</sup>

*Transcutaneous electric nerve stimulation [TENS]*: It is a treatment that essentially includes running an electronic impulse beneath the upper dermis area to stimulate receptors more thoroughly, decreasing discomfort. Patients have the potential to alleviate both severe and persistent pain with TENS therapy.<sup>[37]</sup> Several research studies compared the effects of two different TENS modes, constant mode, and burst mode, over three weeks. A constant mode of TENS was shown to considerably reduce the Visual Analogue Score from

a mean value of 9 to 20 in 26 out of 31 patients, indicating considerable improvement. Both burst and steady modes of TENS were helpful; however, some studies of 30 to 40 patients using only the burst mode showed a noticeable rise in the degree of alleviating discomfort.<sup>[38]</sup> It, therefore, serves as an appropriate care option for the condition attributable to its non-invasiveness, affordability, security, and low adverse effects.<sup>[39]</sup> It can also be utilized for individuals who have intolerable side effects, are unable to tolerate medicine, or are not responding effectively to past therapy approaches.

*Botulinum toxins (BNT)*: In 2010, a whole new application for BT arose with the approval of BT medications for the therapy of severe vertigo. This condition can be safely and effectively controlled with an injectable botulinum toxin A; once the procedure terminated, the highest potency was observed between three and six weeks; most side effects disappeared in a week, and headaches in the symmetry of the face were relieved immediately after the dose. More research is needed to determine the longest time a patient can be pain-free, the most effective injection method, the optimal dosage of BT-A, any drug interactions with potential consequences, and to design the best course of care.<sup>[40]</sup> The studies reported significantly less discomfort, although additional double-masked trials will be essentially needed to verify the positive effects of the approach despite its drawbacks.<sup>[41]</sup>

*Transcranial magnetic stimulation (TMS)*: A developing innovative management for psychological distress and valuable in managing neurologic situations.<sup>[42]</sup> Based on this single-case investigation, persons with refractory TN may benefit from 10 hz TMS as adjuvant care. Long-term recurrent exposure to 10 hz is not linked to major problems. These findings offer promising new perspectives for creating neurological treatments that are customized for every individual to produce durable pain alleviation; however, these initial findings highlight the necessity for additional patient trials to look at the prospective medical advantages of long-term TMS use in TN.

*Low-level laser therapy (LLLT)*: Many physicians employ lower-level wavelength laser therapy, a type of electromagnetic radiation treatment, to treat an array of illnesses. It is applied by professionals to treat acute as well as persistent pain, by dentists to treat ulcerations and inflamed oral tissues, by dermatologists to treat burns, dermatitis, and edema, and by rheumatologists to manage autoimmune medical conditions with prolonged inflammation. According to multiple authors, ectopic action potentials in this nerve and a lack of segmental inhibition of the craniofacial nucleus have been attributed to persistent discomfort of the trigeminal nerve.<sup>[43]</sup> Certain study findings aligned with those of earlier studies. Eckedral conducted a randomized, placebo-controlled, double-masked trial to examine the beneficial effects of LLLT in treating TN.

For five weeks, 16 TN-affected individuals (830 nm, 30 mW) received laser radiation, and they were compared to fourteen patients in the control group. Post-assessment for a year, they concluded that LLLT is a great way to complement traditional TN therapy techniques while still being an effective treatment. Additionally, lasers can eliminate accumulated waste materials while simultaneously enhancing local microcirculation and the oxygen delivered to hypoxic cells in trigger point (TP) regions.<sup>[44,45]</sup> As for side effects, no occurrences were identified. The outcome derived from both current studies and earlier investigations concluded overall LLLT had been equivalent to a placebo in addition to laser application for activating sites that seemed preferable in brain pathway administration.

## CONCLUSION

We would like to conclude that no single treatment is best for all TN patients. Every technique has benefits, drawbacks, uses, and contraindications. Thus, the course of treatment is solely determined by what the patient responds to. An early diagnosis makes a favorable prognosis for the possible treatment plan. Dentists are essential in diagnosing TN and referring patients to neurosurgeons since the condition frequently resembles dental pain. The effects of chronic pain on one's physical and mental well-being can be negative. Professional guidance, comfort, and assistance groups, particularly for individuals with TN, may offer insights, advice, and coping mechanisms to alleviate isolation. Additional investigations into the molecular mechanisms beneath TN will open pathways for innovative, profitable therapies with fewer invasive therapeutics.

## Ethical approval

Institutional Review Board approval is not required.

## Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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## Conflicts of interest

There are no conflicts of interest.

## Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the

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