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STREPTOMYCIN AS A THERAPEUTIC OPTION IN REFRACTORY TRIGEMINAL NEURALGIA: A CASE SERIES

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Abstract
Background: Trigeminal neuralgia (TGN) is a chronic facial pain condition often resistant to standard pharmacological treatment. While invasive procedures provide relief in refractory cases, some patients remain reluctant to pursue surgical options. The purpose of this case series was to evaluate the efficacy of perineural streptomycin injections as a non-surgical alternative in such patients. Ten patients with classical TGN unresponsive to at least two antineuralgic medications and unwilling to undergo surgery were selected. Each received a perineural injection of streptomycin targeting either the infraorbital or inferior alveolar nerve. Outcomes were measured by Visual Analog Scale (VAS) and follow-up evaluations over a 6-month period. It has been observed that the all ten patients experienced significant pain relief (VAS reduction >80%) within 7 days post-injection. Duration of relief ranged from 3 to 6 months. Three patients were required repeat injections during the follow-up period. Minor, reversible adverse effects were observed in three cases. It has been concluded that the perineural streptomycin injection may represent a promising low-cost and minimally invasive alternative in patients with refractory TGN who declined surgical treatment. Streptomycin injection seems to be an easy, effective, and a safe method for pain relief in patients with trigeminal neuralgia. Nevertheless, further controlled studies are needed to approve this method as a routine procedure.

Key words: Trigeminal Neuralgia, Streptomycin, Perineural injection, Infraorbital Nerve, Inferior Alveolar Nerve, Neurolysis

Introduction:

Trigeminal neuralgia (TN), also known as tic douloureux, is a disorder that affects the trigeminal nerve and is characterized by the presence of sudden, repetitive waves of pain that last from a few seconds to a few minutes [1]. The pain might be triggered by a sensory stimulus on the face, lips, or oral mucosa, or during certain functional movements of the face, and it is a debilitating chronic condition that occurs following injury or inflammation of the peripheral trigeminal nerve [2]. TN is one of several disorders related to the trigeminal nerve [3].

Background History:

The most common cause of TN:

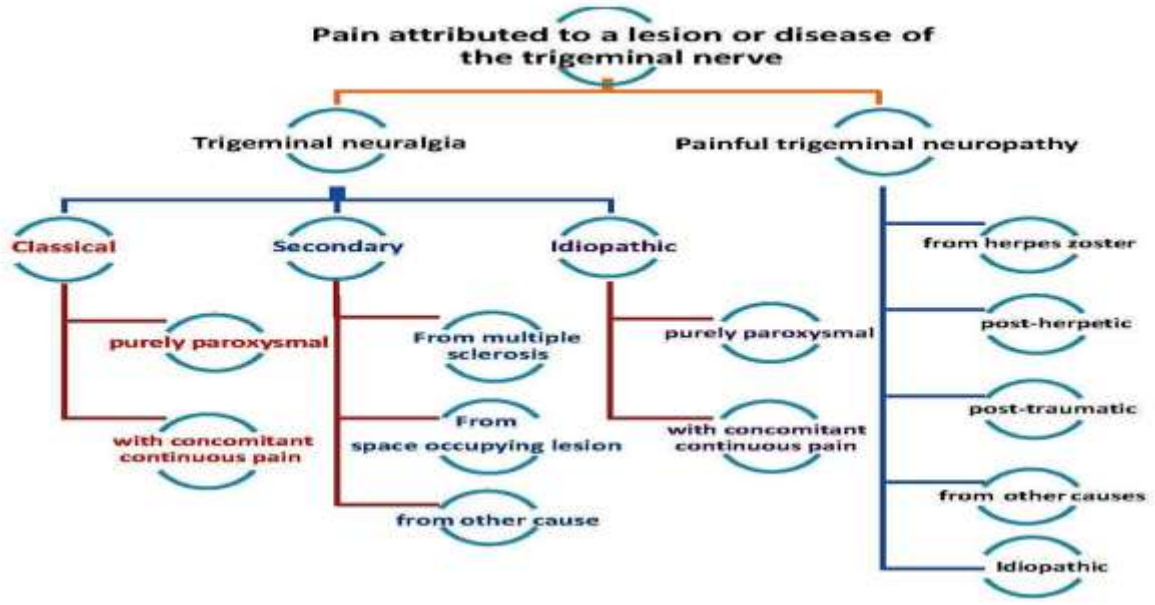
Trigeminal neuralgia (TN) is frequently associated with prolonged suffering and inappropriate treatments before an accurate diagnosis is established. Common misdiagnoses include dental disorders, temporomandibular joint disease, paranasal sinus infections, ophthalmic pain syndromes, temporal arteritis, ice pick-like migraine, facial migraine, myofascial pain, idiopathic facial pain, and psychological disorders [4–6]. As a result, unnecessary interventions such as dental extractions, root canal procedures, nasal and sinus surgeries, biopsies, salivary gland operations, and prolonged courses of antibiotics or narcotics are often undertaken before TN is correctly identified [7,8]. The diagnostic challenge is compounded by the absence of confirmatory clinical, laboratory, or radiological tests, the occurrence of spontaneous remissions that may be mistaken for cure, and the relative rarity of the disorder [9].

Classification:

- Classical TN: It is vascular compression of the trigeminal nerve at the root entry zone. Microvascular decompression (MVD) is the first-line treatment for classical TN.
- Secondary TN: It is caused by tumors or vascular abnormalities in the posterior fossa, or it might be caused by multiple sclerosis.
- Idiopathic TN: When no cause can be found [3,5].

The term paroxysm has been used to describe the sudden, unexpected, and acute nature of the pain. However, some of TN patients experience concomitant continuous pain in the form of a dull ache in the same area as the paroxysmal pain [6]. Although the exact mechanism involved in the development of TN remains poorly understood, the potential mechanisms involve peripheral and central nociceptive circuit dysfunctions, which could lead to cross-excitation of an intact nerve by an injured nerve, neuroglial interactions, alterations in the wirings within the CNS, loss of inhibitory control, disruptions in the functions of ion channels, and sensitization by inflammatory mediators [10].

Figure- 1. Classification of trigeminal nerve disorders



Epidemiology:

The lifetime prevalence of TN is estimated to be 0.16%–0.3%,2 3 while the annual incidence is 4–29 per 100000 people in a year [8-11]. It has a female predilection (F:M ratio 3:2) [5, 7] The incidence increases with age, with a mean age of onset of 53–57 years and range of 24–93 years in adult series [9-11]. Furthermore, a recent pediatric headache clinic of 1040 identified five children in the age range 9.5–16.5 years with TN [8, 10,12].

Etiology and Pathogenesis: [12-16]

- The cause of the majority cases of TN remains controversial, but approximately 10% of cases have detectable underlying pathology such as a tumor of the cerebellar pontine angle, a demyelinating plaque of multiple sclerosis, or a vascular malformation.
- The remainder of cases of TN is classified as idiopathic.
- The most widely accepted theory of TN is that a majority of cases are caused by an atherosclerotic blood vessel pressing on and grooving the root of the trigeminal nerve. This pressure results in focal demyelinization and hyper excitability of nerve fibers, which will then misfire in response to light touch, resulting in brief episodes of intense pain.

Clinical Features

- .
- The majority of individuals with trigeminal neuralgia (TN) present with characteristic clinical features, typically episodes of intense, stabbing or shooting pain lasting only a few seconds and followed by complete remission.
- The pain is usually unilateral characterized by an electric shocklike quality. Pain rarely crosses the midline.
- The maxillary branch is most commonly affected, followed by the mandibular branch and rarely ophthalmic branch. Involvement of more than one branch occurs in some cases. Pain in TN is precipitated by light touch on a “trigger zone” present on the skin or mucosa within the distribution of the involved nerve branch.

- Activities such as shaving, showering, eating, speaking, or even exposure to wind can precipitate painful episodes. Patients often shield the trigger zone with a hand or object, leading to frequent misattribution to dental disorders and, consequently, initial consultation with a dentist.
- During an attack, the patient typically grimaces in pain, clutches the affected side of the face, and ceases all activity. The individual may hold or rub the face, which can become flushed, and the eyes may water until the episode subsides.
- In extreme cases the patient will have a motionless face – the “frozen or masklike face.”
- It is characteristic of the disorder, that attack do not occur during sleep.

Diagnosis:

  - There are few clinical features which are diagnostic of trigeminal neuralgia. Unilateral electric shock kind of pain
  - Presence of trigger points
  - A distinguishing clinical feature of trigeminal neuralgia is the absence of attacks during sleep.
- Diagnosis is made from a well taken history. The classical pattern will lead towards the diagnosis
- In some cases, symptoms may be atypical and mimic conditions such as toothache, sinusitis, stomatitis, or other inflammatory disorders.
- All patients should ideally have MRI scanning or at least a CT scan.

Diagnostic criteria:

The International Classification of Headache Disorders third edition (ICHD-3) criteria for TN require recurrent paroxysms of unilateral facial pain restricted to the trigeminal distribution, lasting from a fraction of a second to severe in intensity with an electric shock-like shooting, stabbing or sharp quality, and precipitated by innocuous stimuli.

Table-1: International Classification of Headache Disorders edition 3 (ICHD-3) diagnostic criteria for trigeminal neuralgia [19]

A. Recurrent paroxysms of unilateral facial pain in the distribution(s) of one or more divisions of the trigeminal nerve, with no radiation beyond, and fulfilling criteria B and C.
B. Pain has all of the following characteristics:
   1. Lasting from a fraction of a second to 2 min.
   2. Severe intensity.
   3. Electric shock-like shooting, stabbing or sharp in quality.
C. Precipitated by innocuous stimuli within the affected trigeminal distribution.
D. Not better accounted for by another ICHD-3 diagnosis.

Differential diagnosis:

TN is a clinical diagnosis based on detailed history and examination. Though often considered a straightforward diagnosis to make, its differential diagnosis can be challenging, given the considerable overlap with other neuropathic and neuralgiform headache and oro-facial pain disorders. Table 2 outlines the important differential diagnoses of TN. Some selected differential diagnoses in greater detail as they often pose a challenge in neurological clinical practice are discussed below.

Table-2 Differential diagnosis of trigeminal neuralgia

Dental causes	► Dental caries ► Pulpitis ► Dental sensitivity ► Periodontal disorders ► Pericoronitis ► Cracked tooth ► Alveolar osteitis
Sinus causes	► Maxillary sinusitis
Salivary gland causes	► Salivary stone
Temporomandibular joint causes	► Temporomandibular disorders
Neuropathic pain	► Glossopharyngeal neuralgia ► Nervus intermedius neuralgia ► Post-herpetic neuralgia ► Post-traumatic trigeminal neuropathy ► Painful trigeminal neuropathies ► Atypical odontalgia ► Burning mouth syndrome
Trigeminal autonomic cephalalgias	► SUNCT/SUNA ► Paroxysmal hemicrania ► Cluster headache ► Hemicrania continua
Other	► Persistent idiopathic facial pain ► Primary stabbing headache

Laterality and site of pain:

The right side of the face (60%) is affected more than the left side.12 Bilateral simultaneous pain in TN is rare (1.7%–5%) and more often these patients experience side-alternating unilateral pain paroxysms. Rare bilateral trigeminal paroxysmal pains should raise concern about an underlying neurological disorder or a non-neurological disorder affecting the cranium. It therefore warrants careful exclusion of secondary pathology [20] if investigations are normal, then idiopathic cases of chronic bilateral trigeminal pain include: temporomandibular joints dysfunction, persistent idiopathic facial pain and rarely migraine with facial pain. In cases with paroxysmal short-lasting pain episodes, trigeminal autonomic cephalalgias such as short-lasting unilateral neuralgiform headache attacks (SUNHA) should be considered if pain is associated with cranial autonomic symptoms or idiopathic stabbing headache if the pain is predominantly in the ophthalmic (V1) trigeminal distribution. The pain of TN most frequently affects the distribution of the maxillary (V2) and mandibular (V3) divisions of the trigeminal nerve, though approximately a quarter of the cases have ophthalmic (V1) division involvement. [27]

Frequency and duration of attacks:

The frequency and duration of TN attacks are highly variable. While the pain usually lasts from less than a second up to 2min in the majority (74%), a significant minority reports attacks lasting 2–10min. Furthermore, up to 70% of patients occasionally have series of paroxysms lasting up to 1hour, which can cause diagnostic confusion. [28] In patients with long-lasting attacks (>2min) but with a phenotype otherwise consistent with TN, it is imperative to rule out other neuralgiform disorders. The number of attacks is highly variable even in the same patients and ranges from a few attacks to several hundred attacks daily; approximately 40% of patients report more than 10 attacks daily.7 Obtaining a good descriptive history of frequency and duration of attacks in short-lasting trigeminal neuralgic pain conditions is often challenging. Using pain diagrams may help to clarify our definition of a single paroxysm as opposed to a group of paroxysms.[29] TN follows a relapsing–remitting pattern in approximately two-thirds of patients but has a chronic pattern in the remaining one-third. Both the frequency and duration of the remission periods vary greatly, with the remission periods lasting months (37%) or years (63% [30,31].

Triggers and trigger zones:

One of the hallmark clinical features of TN is the triggerability of the attacks by innocuous mechanical stimulation of the face and intraoral mucosa ipsilateral to the side of the pain. Around 91%–99% of patients report triggered attacks and these are often considered to be pathognomonic of TN. [7, 26, 27, 32] Patients usually report a mixture of triggered and spontaneous attacks, with 68%–98% of cases having spontaneous attacks. A complete lack of triggerable attacks should prompt careful assessment to exclude an alternative diagnosis including a trigeminal autonomic cephalalgia or craniofacial pathology. Light tactile stimulation is the most potent trigger and, conversely, painful and thermal stimulation seems ineffective at eliciting pain in TN [33] Common triggers include light touch, talking, chewing, brushing teeth, washing or drying, drinking and shaving[35] Most patients have several trigger factors [34-37]. The location of the pain does not always concord with the site of trigger zone. The most common trigger zones include the nasolabial fold, upper lip, lateral part of the lower lip, chin, cheek and the alveolar gingiva [37-40]

Refractory period:

In most people with TN, a triggered attack is normally followed by a period of seconds or minutes during which further attacks cannot be provoked, a phenomenon called refractory period.[38] This contrasts with the trigeminal autonomic cephalalgia, in which there is mostly no refractory period after exposure to a trigger [30]

Diagnostic Block: [28-41]

- Diagnostic injections of a local anesthetic agent into the patient's trigger zone should temporarily eliminate all pain.

● Always begin injections at surface site of pain and then move proximally. For example, if the pain is perceived in the lower lip, then inject lower lip, then mental nerve and then inferior alveolar nerve.
● Inject 0.5 cc of normal saline at the test site. Wait for 5 minutes. If pain is relieved, then psychogenic pain is likely.
● If the pain persists, then inject 0.5 ml of 2% lignocaine without adrenaline at surface site and wait for 5 minutes. If pain is relieved, then direct therapy at small nociceptor fibers.
● If the pain persist – inject little deeper and wait for 5 minutes. If pain is relieved then consider musculoskeletal origin of pain.
● If pain is not relieved, inject at more proximal portion of nerve – if pain is relieved, direct therapy at site, when relief occurred.

Treatment [9-55]

● First medicinal management is advocated. If the patient dose not respond to it then only surgical management is opted.
● Carbamazepine and phenytoin are the traditional anticonvulsants used primarily. This therapy consists of titration and maintenance with anticonvulsant drug.

Moreover, the therapeutic modalities are based on pharmacological, interventional, and alternative medicine. Pharmaceutical management is minimally invasive, and antiepileptics have mainly been used as first-line treatment [25]. Carbamazepine has been used to treat various types of neuropathic pain since the early 1960s; however, the side effects associated with this drug are a significant cause for concern [26]. Subsequently, several antiepileptic and other types of drugs have been used to treat neuropathic pain, including TN (Table-3A &B)

Table-3A & 3B: The medications available for neuropathic pain.

3A:

Category	Drug	Category	Drug
Antiepileptic	Carbamazepine [6–9]	Anesthetics	Ketamine *, Methadone * [10]
	Clonazepam [11]		Lidocaine [12–15]
	Gabapentin [8,16–21]		
	Lacosamide [22]		
	Lamotrigine [17,24]	Antidepressants	Amitriptyline [23]
	Levetiracetam [25]		Duloxetine [14,26]
	Oxcarbazepine [27]		Milnacipran [28]
	Phenytoin [29]		Nortriptyline [30]
	Pregabalin [14,31–33]		Venlafaxine [34]
	Topiramate [7,17,35]		Desipramine [36]
	Valproic acid [37]	Antipsychotics [38]	
	Zonisamide [39]	Alpha-adrenoceptor stimulants	Clonidine [40]
		Opioids	Tramadol [41]
Herbal [42]			Buprenorphine [43,44]
NSAIDs [45]	Paracetamol [46]		Fentanyl [47]
Miscellaneous	Cannabis [48]		Hydromorphone [33,49]
	Capsaicin [50,51]		Methadone [52]
			Morphine [53]
			Oxycodone [54,55]

3B: Common Medicines with Doses:

Drug	Initial dose	Maintenance dose
Gabapentin	300 mg tid	1800 mg
Baclofen	5 mg bid/tid	80 mg maximum dose
Clonazepam	0.5 mg tid	4 mg, maximum 20 mg
Lamotrigine	50 mg qd	300-500 mg
Oxcarbazepine	300 mg bid	1200 mgbid
Toprimate	50 mg qd	200 mg bid
Carbamazepine	100 mg bid	1200-2400 mg

Interventional Treatments:

A nerve block plays an important role in the diagnosis, prognosis, and treatment of pain by intercepting the vicious cycle of pain, blocking sympathetic nerves, expanding vessels in the lesion area, and improving local blood flow [40]. Peripheral interventions involve blocking or destroying a portion of the trigeminal nerve distal to the Gasserian ganglion [41] (Figure-2). Complications include bleeding, infection, sensory abnormalities, and, rarely, diplopia [42]. Fluoroscopy-guided blocks are standardly performed with an observation of the absence of intravascular contrast spread before injecting local anesthetics [43]. Ultrasound provides real-time images of adjacent tissues, bony structures, and vessels and guides the needle trajectory to the target region without radiation exposure [44, 45]. However, obtaining high-quality ultrasound images may be technically difficult in the deep trigeminal nerves. Nevertheless, in one study, a maxillary nerve block via the pterygopalatine fossa was successfully performed using ultrasound [32].

Figure-2: Interventional treatments

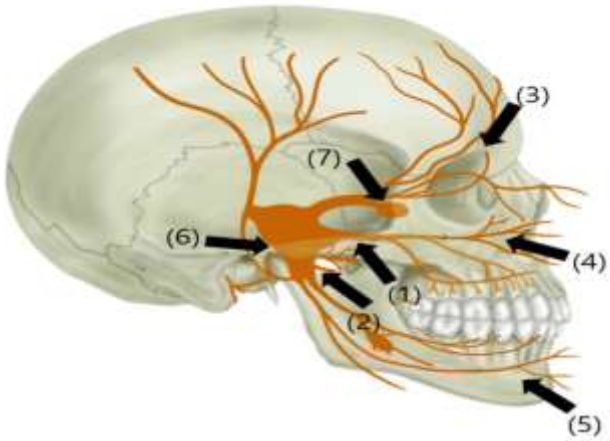


Figure -2, illustrating the (1) Maxillary nerve block; (2) mandibular nerve block; (3) supraorbital nerve block; (4) infraorbital nerve block; (5) mental nerve block; (6) Gasserian

Trigeminal and Peripheral Nerves:

- **Maxillary Nerve**

The trigeminal nerve has three major branches, ophthalmic (V1), maxillary (V2), and mandibular (V3). The maxillary nerve innervates the maxilla, nasal cavity, sinuses, palate, and mid-face [43]. The maxillary nerve exits the skull base through the foramen rotundum and divides into branches to the pterygopalatine ganglion and then across the pterygopalatine fossa. It runs through the infraorbital foramen and terminates into the inferior palpebral, nasal, and superior labial branches [34]. The maxillary nerve block approaches include the intraoral, infrazygomatic, or suprazygomatic routes [44]. In one patient with TN, pulsed radiofrequency (PRF) ablation of the maxillary nerve and subsequent intranasal sphenopalatine ganglion blocks improved pain for 2 years [45].

- **Mandibular Nerve**

The third branch, the mandibular nerve, is the largest of the three divisions of the trigeminal nerve. The mandibular nerve innervates the mandible, lower teeth, oral mucosa, anterior two-thirds of the tongue, lower lip, temporomandibular joint, and skin of the temporal region. The mandibular nerve immediately passes caudally to the foramen ovale at the posterior margin of the lateral pterygoid plate [46]. In 11 patients with TN, 13 procedures of conventional RF (CRF) ablation (70–90 ◦C for 90–180 s) of the mandibular nerve improved pain at 1 and 3 months without complications [47].

- **Supraorbital Nerve**

The supraorbital nerve is a branch of the ophthalmic division of the trigeminal nerve. It emerges from the supraorbital notch, which lies within the medial third of the supraorbital margin, 2–3 cm

lateral to the midline [33]. It innervates the upper eyelid, forehead, and the anterior half of the scalp, except for the innervation area of the supratrochlear nerve, which is close to the midline [48]. The supraorbital foramen has variations, such as holes or notches [37]. A study compared pain and numbness following RF ablation of the supraorbital nerve between the hole and notch types [49]. In the notch type, the supraorbital nerve may have some inner or outer deviation, and an increased risk of shifting the needle point during the procedure induces a lower effective rate owing to incomplete destruction of the nerve [49].

- **Infraorbital Nerve**

The infraorbital nerve is the terminal branch of the maxillary division of the trigeminal nerve and provides sensory innervation to the lower eyelid, nose, and upper lip [33]. It emerges from the infraorbital foramen and is accompanied by infraorbital vessels, approximately at the anterior aspect of the maxillary bone and 1 cm below the midpoint of the infraorbital margin [33]. In three patients with first- or second-division TN, infraorbital nerve blocks with a mixture of 4% tetracaine and 0.5% bupivacaine showed prolonged analgesic effects for more than 3 months [38].

- **Mental Nerve**

The mental nerve is one of the two terminal branches of the inferior alveolar nerve and is rooted in the mandibular division of the trigeminal nerve [33]. It innervates the skin of the chin and lower lip. The mental foramen lies 3 cm lateral to the midline and 1 cm above the lower border of the mandible, between the first and second premolar teeth [33]. In a retrospective case series of nine patients with TN, supraorbital, infraorbital, and mental nerve blocks with local anesthetics showed immediate pain relief of >50%, with seven of nine patients completely pain free or under mild anesthesia, and six of nine patients experiencing lasting pain relief for 1–8 months [49].

Minimally Invasive Procedure: It is consists of

- Alcohol injections
- Glycerol injection
- Streptomycin injection
- Neurectomy and Cryotherapy of peripheral nerves

It has been known that injections of otherwise noxious substances into peripheral branches of the trigeminal nerve, produce anesthesia in the trigger zone or in the area of distribution of spontaneous pain. Generally, these peripheral procedures are easy to perform & are relatively well tolerated by the patients with fewer side effects, only to be limited by shorter duration of action and repeated administrations.

Peripheral Streptomycin Injections: [32, 37]

This procedure can be done under local anesthesia without sedation. After the identification of involved nerve, the nerve is carefully anesthetized. Once the nerve block is deemed effective, streptomycin sulphate solution is deposited adjacent to peripheral branches of maxillary or mandibular nerves. The patients are given five injections at approximately one-week intervals.

Streptomycin Action on Nerves:

The mechanism of action of the streptomycin nerve block , is not clear. A researcher has studied the effects of streptomycin on frog nerve in vitro [32]. The effects of streptomycin on intact frog nerve were examined by bathing the nerve in increasing concentrations of streptomycin. It was concluded from this experiment that streptomycin produces a repolarization of depolarized nerves due to a membrane stabilizing effect. In 1972, a few researchers have studied the effects of streptomycin on rabbit and rat superior sympathetic cervical ganglia. The ganglia were exposed to streptomycin (1 mg/ml) in successive bathing solutions, which resulted in a decreased release of acetylcholine [37].

A study explored the adverse reactions to a once weekly regimen of streptomycin (1 g) plus a slow-release preparation of isoniazid in high dosage for six months. This regimen was very well tolerated by most of the patients and there were no cases of peripheral neurotoxicity after the trial had been

completed [32]. Because of the above physiological information that antibiotics, including streptomycin, may affect nerve conduction and nociception, and also because of other uncontrolled trials on the effect of streptomycin injections in patients with trigeminal neuralgia we decided to conduct the current study**.**

A double-blind placebo controlled randomized design was used to assess the long-term analgesic effect of a peripheral block containing streptomycin applied at selected peripheral sites in the trigeminal nerve distribution [38].

A study was conducted to evaluate Streptomycin, considering its neurolytic property, in the treatment of trigeminal neuralgia and concluded that peripheral injections of streptomycin were effective in management of trigeminal neuralgia [39]. In their retrospective study they injected streptomycin sulphate dissolved in 2% lidocaine solution adjacent to peripheral branches of maxillary and mandibular nerves in 20 patients with ITN. The patients were given five injections at approximately one-week intervals. In the post-injection period once the local anesthetic wore off, apparently normal sensation returned. All patients obtained relief, only four having a recurrence of symptoms. The remaining 16 patients remained free of pain for periods of up to 30 months [57]

A similar study was also conducted to investigate the long-term effect of a peripheral sensory block using streptomycin sulphate on trigeminal neuralgia and concluded that streptomycin has no beneficial effects for idiopathic and traumatic trigeminal neuralgia [53].

Another study which evaluated the effect of streptomycin in the management of trigeminal neuralgia. Seventeen patients with long-lasting idiopathic trigeminal neuralgia (ITN) were treated with either five, weekly peripheral streptomycin/lidocaine (S/L) or lidocaine alone injections, in a double-blind controlled study and concluded that S/L injections were initially effective in the treatment of ITN. In the long term, however, their effects were similar to the effects of lidocaine alone [53].

A study reported the case of a 47-year-old female with secondary progressive multiple sclerosis (MS) and refractory trigeminal neuralgia (TN), initially diagnosed in 2008. After unsuccessful pharmacological and surgical interventions, including microvascular decompression and gamma knife surgery, she was admitted to a rehabilitation center for motor, cognitive, and functional recovery. Severe pain unresponsive to conventional medication impaired her participation in rehabilitation, prompting the use of botulinum toxin type A (BoNT-A) as an adjunctive therapy. A total of 100 U of BoNT-A was injected subcutaneously at 1 cm intervals across the most painful facial regions. Following treatment, the patient reported substantial pain reduction (VAS score decreased from 8–9/10 to 1/10), less frequent exacerbations, and decreased reliance on emergency analgesics. The only adverse effect was transient ipsilateral facial paresis (House–Brackmann grade II). This case highlights the potential role of BoNT-A as a safe and effective adjunctive option for refractory TN, particularly in complex patients where conventional therapies have failed. Despite the lack of standardized guidelines, BoNT-A demonstrated good tolerability, significant pain relief, and minimal side effects,underscoring the need for further research to optimize dosing and administration techniques [58].

Materials and Methods:

This Prospective-experimental study was conducted in the Dental Department by the Oral and Maxillofacial surgeons, Hind Institute of Medical Science, Sitapur, UP, India from 1st Jun 2024-31st July 2025.

Ten patients (aged 30–70 years, both genders) suffering from refractory trigeminal neuralgia (RTN) were included in the study. Approval to conduct the study was obtained from the institutional ethics committee, and informed written consent was secured from all participants after explaining the possible postoperative complications.

For newly diagnosed patients, the diagnosis of RTN was established on the basis of history and clinical examination, and further confirmed by administering carbamazepine 200 mg every eight hours for five days. For patients with a prior confirmed diagnosis, this step was not repeated. The affected branch of the trigeminal nerve was identified by infiltrating 2 ml of 2% lignocaine with 1:100,000 adrenaline. Three successive infiltrations were administered on alternate days to confirm the involved branch.

Once the diagnosis and nerve branch involvement were confirmed, various medical and surgical treatment options were discussed with patients. Only those who voluntarily opted to participate in the research were included. Exclusion criteria comprised a history of surgical intervention for TN, renal disease, hearing impairment, medical conditions contraindicating streptomycin use, and known allergy to streptomycin.

For included patients, the injection was prepared by mixing 1 g streptomycin sulphate with 3 ml of 2% lignocaine containing 1:100,000 adrenaline (Septodent). The solution was administered at the site of the involved branch using a 5 ml disposable syringe after careful aspiration. Injections were given once weekly for five consecutive weeks. Following completion of treatment, patients were advised to attend follow-up visits at one, two, and six months.

Maxillary Nerve blocks:

Patients were positioned in a partially reclined posture in a dental chair, with the occlusal plane maintained at approximately a 45° angle to the floor. The operator palpated the mucobuccal fold distal to the maxillary second molar to identify the concavity serving as the landmark. Using a dental aspirating syringe fitted with a 1 5/8-inch, 22-gauge needle, the needle was directed inward, upward, and backward toward the maxillary tuberosity. Advancement was performed slowly with intermittent aspiration to avoid intravascular placement. At the desired position, 2 ml of the prepared solution was deposited.

Mandibular Nerve blocks: An inferior alveolar nerve block was carried out. The nerve was approached intraorally, with the operator positioned in front and slightly to the side of the patient.

The thumb of one hand was placed buccal to the teeth on the external oblique ridge with the tip touching the anterior border of the ramus. With gentle pressure against the buccal mucosa the thumb provided clearer exposure to the internal oblique ridge and the pterygomandibular raphe. With a dental aspirating syringe and a I and 5/8" 22-gauge needle directed from the opposite bicuspid tooth, the needle was inserted at the level of the middle of the thumb nail, and lateral to the pterygomandibular raphe. The needle was advanced posteriorly and laterally while held horizontal to the occlusal plane. When the needle came into contact with the mandible it was withdrawn slightly and 2 ml of the solution was slowly deposited. The washout period for the crossover was seven days. Typically, the patients received five blocks of streptomycin-lidocaine for a period of five consecutive weeks.

In the subsequent visits, the patients were assessed regarding their level of pain and sensory function of the involved branch. The pain was categorized into five levels,

- no pain (level 1),
- occasional pain (level 2),
- mild pain controlled by medication (level 3),
- moderate pain not controlled by medication (level 4),
- severe pain not controlled by medication (level 5).

Measures of pain intensity and pain frequency were used to assess treatment outcome. At every appointment patients were required to score their pain intensity on a visual analogue scale (VAS). They also scored the frequency of pain (idiopathic cases) in comparison to the previous week using a VAS scale. Patients were asked to keep a daily record of pain severity (0-10) and frequency of attacks (idiopathic cases). They also recorded the possible side effects of the blocks. Patients were allowed to call the investigators if any problem arose. Sensory function of the affected trigeminal

branch was assessed at every visit, by pin-prick and light touch tests. Patients were allowed to take any medication they were on prior to the study but alteration in dosage was not allowed.
Data had been analyzed using SPSS version 26.1. Mean and standard deviation (SD) were calculated for quantitative variables while frequency and percentages for qualitative variables. Six variables were analyzed: VAS pain, VAS frequency, observed (diary) frequency, observed (diary) severity, pin-prick difference and light touch difference. All cases were analyzed for the level of pain relief and sensory function of the involved branch after one, two and six months.

Results

A total of 10 patients of RTN were included in the study. The age ranged from 30- 70 years with an average age of 43.67 years (SD ± 12.26). Four (40%) patients were males and 6 (60%) were females with an overall male to female ratio of 1: 1.15. Right side of the face was involved in 7 (70%) patients and only 3 (30%) showed involvement of left side. The distribution of nerves involved was shown in Table-4

Table-4: Description of nerves involved in patients with RTN.

Variables	N (%). N=10
Infra-Orbital Nerve	4 (40%)
Inferior Alveolar Nerve	3(30%)
Inferior Alveolar Nerve	1 (10%)
Infra-Orbital and Inferior Alveolar Nerve	2(20%)

The results of follow up at 1-, 2- and 6-months regarding level of pain were also shown in table-5.

Table-5: Follow up of the patients with varying levels of pain relief.

Pain levels	Baseline N=10	1 Month N=10	2 Month N=10	6 Months N=10	P value
No Pain (Level 1)	0 (0%)	3 (30%)	3 (30%)	5 (50%)	0.01
Occasional Pain (Level 2)	0 (0%)	3 (30%)	2 (20%)	3 (30%)	0.01
Mild pain controlled by medication (Level 3)	0(0%)	2(20%)	2(20%)	1(10%)	0.05
Moderate pain not controlled by medication (Level 4)	3 (30%)	2 (20%)	2 (20%)	1(10%)	0.05
Severe pain not	7 (70%)	0(0%)	1 (10%)	0 (0%)	0.001

controlled by medication (Level 5)					

Pain was significantly decreased from baseline to 1 month ($p< 0.001$). The level of pain was increased a bit but the increase was significant at two months ($p = 0.001$) and at 6 months ($p = 0.01$). After two months, 2 (20%) and after six months 1 (10%) patient showed moderate to severe pain which could not be controlled by medication. For these patients, other treatment options had to be considered. Six (60%) patients reported with post injection swelling at the site of injection, which persisted for 3-4 days. Two (20%) patients complained of pain at injection site which was subsided within one week with the use of simple analgesics. One (10%) patient complained of trismus which improved by physiotherapy. No other significant side effects were noted.

Discussion:

Peripheral injections of streptomycin sulphate have been tried in various neuropathic pains. Different proposed mechanisms of action include, membrane stabilization effects, decreased release of acetylcholine at the ganglion level, reduction in conduction velocity of nerves and antagonization of physiological effects of calcium in neural tissues [11,33,36]. It affects protein synthesis, cellular respiration in mitochondria and phosphoinositide system [41]. Streptomycin in available in India as a sulphate and is soluble in water. It is stable at pH 2-11 with optimum pH in the alkaline range. It is slowly released with a tissue half-life varying between 40-700 hours [32]. When we analyzed age in our study, it ranged between 30-70 years with a mean age of 43.67 years (SD ± 12.26) [37, 51, 53-54]. A Study showed a mean age of 54.9 years while another study has reported mean age to be 52 years [32, 37, 38]. On the other hand, a similar study has showed mean age of 43.3 years [39]. Regarding gender, various authors have observed a female preponderance [33-42]. In our study male to female ratio of 1:1.15 was observed. A study has also reported female predilection with a ratio of 5.9:3.4. On the contrary, a study has observed equal involvement of both genders [53]. For involvement of side, results of our study coincide with other studies [18,19,20,23, 58] in which frequent involvement of the right side is observed.

No cases of bilateral trigeminal neuralgia were observed in our study, although previous authors have reported bilateral involvement in a small proportion of patients [23].

The mandibular division was more frequently affected than the maxillary division in our study [30]. The ophthalmic division was not involved in any case, while 10% of patients demonstrated combined maxillary and mandibular involvement. A study evaluating the effects of streptomycin in idiopathic TN reported that the treatment was initially effective [39]. This finding is consistent with our study, in which 80% of patients initially responded effectively to treatment. A similar study observed that approximately 80% of patients remained pain-free for up to 30 months, whereas in our cohort, nearly 80% remained pain-free for up to six months.

Pain levels in the present study were monitored and recorded throughout the follow-up period. Approximately 80% of patients either remained pain-free or experienced only mild pain. Peripheral streptomycin injections did not cause any statistically significant alteration in the perception of light touch or pinprick, a finding that is consistent with previous reports [33–39]. Post-injection swelling at the site of administration has also been described by other authors [33,35]. In our series, 20% of patients experienced recurrence of pain, a rate similar to that reported by one study \[33], although slightly lower than that observed in another [32]. Two patients reported swelling around the injected nerve, which may have temporarily affected nerve conduction.

Other treatment modalities have been reported to carry a higher risk of complications. For example, peripheral injections of alcohol and glycerol have been associated with trismus and transient or even permanent paresthesia within the nerve distribution [33–38]. In contrast, streptomycin did not

demonstrate such post-injection complications in the present study. Therefore, further studies with larger sample sizes and longer follow-up periods are warranted to better document the benefits of streptomycin in the rural population of Northern India and to strengthen the evidence supporting the reliability of streptomycin sulfate in the treatment of idiopathic TN.

Conclusion:

Repeated peripheral streptomycin injections were found to be effective in reducing pain in patients with either idiopathic or traumatic trigeminal neuralgia. Streptomycin did not appear to cause permanent alteration of sensory function in the treated nerves. Although all patients reported temporary swelling and hyperesthesia at the injection site, the treatment was generally well tolerated. Streptomycin may therefore be considered a useful option for managing intolerable pain in TN, particularly in cases where other modalities have failed to provide satisfactory relief or were associated with adverse effects. It is inexpensive, widely available, and associated with minimal complications, making it a practical alternative in resource-limited settings.

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