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Trigeminal Neuralgia overview, advances in diagnosis & changing trends in its management

[1]Dr Abhishek Mishra, Senior Resident, Department of Oral & Maxillofacial Surgery, M.L.B Government Medical College, Jhansi

[2]Dr Priyanka Puri, Senior Resident (Dental), M.L.B Government Medical College, Jhansi

Corresponding Author: Dr Abhishek Mishra, Senior Resident, Department of Oral & Maxillofacial Surgery, M.L.B Government Medical College Jhansi.

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Abstract

Trigeminal neuralgia is a peripheral neuropathy characterized by intermittent episodes of lancinating pain originating in the sensory root of the trigeminal nerve. The most commonly involved area is the mandibular division with a higher prevalence on the right side. Advances in the field of MRI have play an important role in its diagnosis, especially in case of nerve compression and/or neurovascular conflict. Primary management of trigeminal neuralgia is the use of first line drug that is carbamazepine , although some patients may require surgical or radiotherapeutic intervention, who does not respond to drug therapy. MRI serves as a powerful tool in the segmental evaluation of the trigeminal nerve. A proper diagnosis with a organized treatment protocol is critical for managing cases of trigeminal neuralgia.

Keywords: Trigeminal neuralgia, fifth cranial pair, CN V3

Introduction

Trigeminal neuralgia is the pain experienced along the branches of the trigeminal nerve The pain is sudden and often unilateral. It commonly involved the maxilla and mandibular divisions where patients commonly describe as a recurrent, brief, and stabbing pain. It can last from a few seconds to several minutes. The pain can occur from a few to hundreds of attacks a day (1).The International Association for the Study of Pain (IASP) defines Trigeminal neuralgia (TN) as a sudden, usually unilateral, severe, brief, stabbing recurrent pain in the distribution of one or more branches of the fifth cranial nerve.(2)

Anatomy

The trigeminal nerve is the fifth cranial pair (CN V) consisting of a large sensory root and small motor root. The sensory root transmits sensory information from the unilateral hemiside and is divided into three ophthalmic (V1), maxillary (V2), and mandibular (V3). The motor

root innervates the unilateral masticator muscles. In MRI motor root cant not be distinguished from the sensory root. It has a common extracranial pathway with the common trunk of the nerve and root of CN V3 over the whole pathway. [3]

The gasserian ganglion is located in the trigeminal fossa (Meckel cave) of the petrous bone in the middle cranial fossa. It contains the first-order general somatic sensory fibers that carry pain, temperature, and touch. The peripheral processes of neurons in the ganglion form the 3 divisions of the trigeminal nerve (i.e., ophthalmic, maxillary, and mandibular). The ophthalmic division exits the cranium via the superior orbital fissure; the maxillarydivisions exit via the foramen rotundum and mandibular divisions exit via foramen ovale.

trigeminal nerve are mainly mediate the majority of nociceptive impulses from the orofacial region. The action potentials are transmitted from its peripheral branches, ophthalmic (V1), maxillary (V2), and mandibular (V3), by pseudo-unipolar neurons with the cell bodies located in the trigeminal (gasserian or semilunar) ganglion. [4]

Types of Trigeminal Neuralgia

1. **Possible Trigeminal Neuralgia**
   - paroxysmal nature ,
   - Continuous pain may exist
   - Not triggered by external mechanical stimuli
2. **classical Trigeminal Neuralgia**
   - attacks are paroxysmal and triggered by mechanical stimuli .
   - diagnosis confirmed by MRI. (most common cause is neurovascular compression)
3. **Idiopathic Trigeminal Neuralgia**
   - May be triggered by extraneous stimuli ,
   - MRI does not show any neurovascular compression,
   - associate with cerebellopontine angle lesions

Clinical Characteristic

Trigeminal neuralgia typically manifests as a sudden, unilateral, intermittent paroxysmal, sharp, shooting, lancinating, shock like pain, elicited by slight touching superficial “trigger points” which radiates from that point, across the distribution of one or more branches of the trigeminal nerve. Pain is rarely bilateral (1–4%).

Episodes of severe shooting pain that may feel like an electric shock.

Pain is usually confined to one part of one division of trigeminal nerve—mandibular or maxillary, but may occasionally spread to an adjacent division or rarely involve all three divisions.

Pain rarely crosses the midline: The pain is of short duration and lasts for a few seconds to 2 minutes, but may recur with variable frequency. Even though there is a refractory period (complete lack of pain) between the attacks. The paroxysms occur in cycles, each cycle lasting for weeks or months and with time, the cycle appears closer and closer. (5)

Classical features of trigeminal neuralgia is the Presence of trigger points (intraoral or extraoral). These triggers points can be stimulated while Eating , Drinking , Smiling, Brushing your teeth , Talking , Touching your face, Washing your face, shaving.

The location of the trigger points depends on which division of trigeminal nerve is involved.

- In V1 —the trigger zone usually lies over the supraorbital ridge of the affected side.
- In V2 —points are located on the skin of the upper lip, ala of nose or cheek or on the upper gums.
- In V3 —this is the most frequently involved branch

Trigger points are seen over the lower lip, teeth or gums of the lower jaw. Usually tongue is not involved (6), (7)

Diagnosis

Trigeminal neuralgia is usually has a characteristic clinical feature. There is a sudden and severe lancinating pain, usually unilateral, aggravated by gently touching triggers points. This pain occurs within the trigeminal nerve distribution; typically involving the maxillary nerve (V2) or mandibular nerve (V3) distribution.[8]

Pain symptoms may be categorized under the following:[9]

- Dysaesthesia (abnormal perception of pain)
- Allodynia (due to a stimulus which does not normally provoke pain)
- Hyperalgesia (an increased sensitivity to pain)

In some patients, these painful bursts can be triggered simply by cutaneous contact with a trigger zone or during movement. Where this trigger zone exists, there is a refractory period at the end of an episode of pain during which the subject can touch the trigger zone without causing pain. Neurological examination of these patients is usually normal. Pain is relieved by sodium channels blockers. Neurovascular compression is the principal cause of trigeminal neuralgia can be ruled out by MRI.[3]

Management

The pharmacological treatment for trigeminal neuralgia includes muscle relaxants, anticonvulsant, and neuroleptic drugs . However, the gold standard method of trigeminal neuralgia treatment is using carbamazepine (10). Patients who does not respond tothese drugs, other techniques are employed such as microvascular decompression, Gasserian ganglion percutaneous techniques, and gamma knife surgery. Both massage and needling (in the form of acupuncture) are commonly used as an alternative treatment to reduce pain in patients who suffered from trigeminal neuralgia.

Carbamazepine (anticonvulsant drug) is the drug of choice in Treatment of trigeminal neuralgia. The second drug of choice is oxcarbazepine (Better tolerability than carbamazepine) (10). Other drugs such as baclofen, lamotrigine, clonazepam, topiramate, phenytoin, gabapentin, pregabalin, and sodium valproate can be used. Polytherapy is useful when patients are unable to tolerate higher doses of carbamazepine.(11) Opioids are not prescribed as it is ineffective against trigeminal neuralgia. A multidisciplinary approach using antidepressants and antianxiety drugs such as amitriptyline and duloxetine is required for emotional imbalance. Acupuncture can be an option in the treatment of idiopathic trigeminal neuralgia and secondary myofascial pain associated with it.[12] Peripheral nerve blocks using local anesthetic along with absolute alcohol or glycerol is also very effective in reducing pain.(11),(13). If nerve blocks are administered appropriately, patient may feel asymptomatic for months to years and may also reduce the number and doses of drugs. Many studies have shown that botulinum toxin type A (BTX-A) injections may reduce pain in people who are not relieved by medications.(14)

Surgery is normally recommended only after drugs has proved ineffective and side effects of drugs are unbearable.

Microvascular decompression is surgical treatment of choice in of trigeminal neuralgia. resistant to medical management, particularly, in young individuals.[15]

Patients with significant medical comorbidities are generally advised to undergo gamma knife radiosurgery, percutaneous balloon compression, glycerol rhizotomy, and radiofrequency thermocoagulation procedures.[16] [17]

Non-Surgical Treatment

Drug	Initial Dose (Mg)	Target Dose (Mg)
1)Carbamazepine (DOC)	100-200	1200
2)Oxcarbazepine	200-400	1200-1400
3)Baclofen	5-15	30-60
4)Clonazepam	0.25-0.5	1-4
5)Gabapentin	300	900-2400
6)Lamotrigine	25	400-600
7)Topiramate	25	100

Percutaneous injections

- 2 days – 1-week Interval
- **Chemical Used:** Local Anesthesia/ Absolute Alcohol/ Phenol glycerin mixture.
- **Injection Site:** Peripheral Nerve/ Trigger Zones/ Gasserian Ganglion
- Intravenous infusion of a **combination of magnesium and lidocaine** can be very effective in some patients.
- **5% lidocaine plaster and 8% capsaicin patch**.
- **Botulinum toxin Type A injections** can be used as alternative treatment in patients who are not responding to drug .
- **Tetracaine nerve block** as an additional treatment after carbamazepine, acupuncture and peripheral nerve stimulation.

Surgical treatment

Peripheral procedures

- Peripheral injections (Local anaesthesia / absolute alcohol)
- Peripheral neurectomy
- Cryotherapy
- Gasserian ganglion procedures (glycerol /thermocoagulation/ percutaneous balloon compression)

Intracranial procedures

- microvascular decompression
- trigeminal root resection

Recent Advances in Treatment Modalities

The continuous search for new drugs have led to the advance of few drugs that reduces the electrical activity of the already excited nerve.

Vixotrigine is a novel sodium channel blocker that suppresses seizures or noxious stimuli. In an open-labeled study, vixotrigine 150 mg administered thrice daily in patients with trigeminal neuralgia was compared with placebo and showed successful pain relief in the final week of therapy.22 The drug was administered for 21 days. There was a reduction in the number of paroxysms by 60% compared with only 12% in placebo, and pain severity decreased by 55% compared with placebo. No serious adverse event was noted. [18]

Eslicarbazepine is a third-generation antiepileptic drug. The drug targets the voltage-gated sodium channels and is currently approved as adjunct therapy for focal seizures. In a recent open-labeled trial, 200 to 1200 mg/day eslicarbazepine was administered in a patients suffering from trigeminal neuralgia. About 88.9% patients relieved from Pain, but there was high incidence of side effects to the tune of 71%.[19]

Two randomized controlled trials tested the effectiveness of 3 mg sumatriptan subcutaneous injection and 50 mg twice daily orally. Baseline pain scores decreased 15 minute after injection of sumatriptan.[20],[21]. Dizziness and rebound headaches are the main side effect. Sumatriptan is a 5-hydroxytyptamine receptor receptor blocker agonist. It has been extensively used in migraine and cluster headaches with good pain relief efficacy. This drug effectively inhibits vasodilation and demyelination near the inflamed trigeminal nerve root

In hyperactive neurons CO2 considered as a pain modulator. Recent studies have shown that CO2 is a nociceptive modulator of afferent active trigeminal neurons as it causes a decreased mucosal pH. [22]

Usually, in patients with continuous pain mediated by other pathophysiological mechanisms, a monotherapy with sodium channel blocker is ineffective and other drugs are usually required to control the pain. Calcium channel blockers and antidepressants have been advocated in the treatment of trigeminal neuralgia in patients not relieved by monotherapy with sodium channel blockers.[23]

Recent Advances in Nonpharmacological Therapy

Pulsed radiofrequency uses brief pulses of higher frequency alternate current to produce the same voltage or even higher fluctuations than during conventional radiofrequency (RF) treatment.

Ozone injection around gasserian ganglion (OIAGG): In a retrospective study, under C-arm X-ray guidance the researcher injected an ozone–oxygen mixture gas at a concentration of 30 μg/mL around the gasserian ganglion. The pain relief rates after the treatment, 6 months, 1 year, and 2 years after the procedure were 88.35%, 86.87%, 84.46%, and 83.30%, respectively ($p < 0.05$).[24] The study confirmed that injections in gasserian ganglion is a reliable and effective treatment modality for pain management in Patients who are not responding to the drugs.

Few modifications have been advocated to overcome the shortcomings of conventional cryotherapy in which pain was not subsided and recurrence of pain. These include (a) the use of a curved cryoprobe, (b) maintaining optimal temperature and pressure throughout the surgical procedure, (c) scoring of the epineurium, (d) application of petroleum jelly around the nerve before the introduction of the cryoprobe, and (e) delivery of three cycles of 3-minute freezing and 5-minute thawing to each nerve.[25] In a study, Bansal et al showed that a closed curved cryoprobe tip when used with nitrous oxide at a temperature of–98°C and a pressure of 70 kg/cm2 or 100 psi provided excellent analgesia. Almost 48.97% patients had pain-free interval of 36 to 40 months. The side effect was loss of fine and crude sensation over face for 6 to 24 months. [26]

Neuromodulation is a newer prospect targeting either neural stimulation or inhibition to restore normal neurological function. Various neuromodulation techniques include transcranial magnetic stimulation, motor cortex stimulation, deep brain stimulation, transcutaneous electrical nerve stimulation, and peripheral nerve stimulation. A recent study is establish the feasibility of using transcranial magnetic stimulation (TMS) for chronic orofacial pain in the interim period before surgery. TMS, when applied to the head for a few minutes, has been shown to reduce pain in people with chronic orofacial pain of trigeminal neuralgia.[27], [28].

Low level laser therapy uses a single wavelength light source and works on the principle that irradiation with monochromatic light may affect cell function. This technique involves irradiation of the region of interest followed by laser puncture at predetermined points along the course of the nerve. In a recent systematic study which evaluated the efficacy of Low level laser therapy for the therapeutic management of neuropathic orofacial pain, Pedro et al found a significant reduction in pain intensity in all studies.[29]

Carbon dioxide laser is used to ablate the peripheral nerve in patients with drug refractory trigeminal neuralgia. It reduce the pain scores and persistence of pain relief till 12 months.[30]

Conclusion

For accurate management, a stepwise diagnostic and treatment approach is recommended In most cases the diagnosis can be made clinically, but routine imaging like MRI may be considered.. First-line therapy for the treatment of trigeminal neuralgia is Carbamazepine (6001200 mg/day) or Oxcarbazepine (6001800 mg/day), switching to or adding-on lamotrigine (200400 mg/day), pregabalin (150600 mg/day), gabapentin (18004200 mg/day) or topiramate (100400 mg/day) may also be considered. If the combination therapy fails, a switch to muscle relaxant (baclofen 40-80 mg/day) can be tried. If sufficient and compliant drug therapy failed, Surgical management should be advocated. Some intervention like Gasserian ganglion injections, gamma knife surgery, microvascular decompression should be discussed with the patients with regards to their own individual wishes and overall medical condition. New drugs, such as BTX-A, may be offered to patients before surgery or to patients unwilling to undergo surgery More studies with long-term follow-up will be required to determine the optimal timing for surgical intervention..

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