REVIEW ARTICLE

Trigeminal Neuralgia: Current Concepts in the Medical Management

[1]Ceena Denny E, [2]Jeena Priya K, [3]Ravikiran Ongole

[1]Reader, Department of Oral Medicine and Radiology, Manipal College of Dental Sciences, Manipal University, Mangalore, Karnataka India

[2]Senior Lecturer, Department of Oral Medicine and Radiology, Manipal College of Dental Sciences, Manipal University, Mangalore Karnataka, India

[3]Associate Professor, Department of Oral Medicine and Radiology, Manipal College of Dental Sciences, Manipal University, Mangalore Karnataka, India

Correspondence: Ceena Denny E, Reader, Department of Oral Medicine and Radiology, Manipal College of Dental Sciences Manipal University, Mangalore, Karnataka, India, e-mail: ceen226@yahoo.com

Abstract

Trigeminal neuralgia (TN), also known as tic douloureux, is characterized by recurrent attacks of lancinating pain in the trigeminal nerve distribution. Typically, brief attacks are triggered by talking, chewing, teeth brushing, shaving, a light touch, or even a cool breeze. The pain is nearly always unilateral, and it may occur repeatedly throughout the day. The condition is characterized by intermittent one-sided facial pain. Trigeminal neuralgia can be classified based on the symptoms as typical and atypical trigeminal and according to etiology as primary or idiopathic and secondary or symptomatic. An early and accurate diagnosis of TN is important, because therapeutic interventions can reduce or eliminate pain attacks in the large majority of TN patients. Although various drugs have been used in the management of TN such as baclofen, gabapentin, phenytoin sodium, carbamazepine remains the gold standard drug of choice. Surgical approaches to pain management are performed when medication cannot control pain or patients cannot tolerate the adverse effects of the medication.

Keywords: Trigeminal neuralgia, tic douloureux, etiology, management, pharmacotherapy.

INTRODUCTION

Trigeminal neuralgia (TN) is the most common among the neuralgias, is often described as "the most terrible pain known to man." It is also called as Tri facial neuralgia, Fothergill's disease, Tic-douloureux. The etiology of tic douloureux is not known and, though it may occur at any age, it is usually seen in patients over the age of 50 years. Spontaneous recovery is rare, but remission for a variable interval from months to years may take place.

The International Association for the Study of Pain (IASP) defines trigeminal neuralgia as sudden, usually unilateral, severe brief stabbing recurrent pains in the distribution of one or more branches of the 5th cranial nerve.[1]

According to International Headache Society (IHS) it is a painful unilateral affliction of the face, characterized by brief electric shock like pain limited to the distribution of one or more divisions of the trigeminal nerve. Pain is commonly evoked by trivial stimuli such as washing, shaving, smoking, talking, and brushing the teeth, but may also occur spontaneously. The pain is abrupt in onset and termination, and may remit for varying periods.[2] Aretaeus of Cappadocia is credited with the first clinical description of TN.[3] John Locke, in 1677 identified the major clinical features of TN, [4] the name tic douloureux was given by the French physician Nicolaus Andre in 1756 because of the facial spasms that would accompany the attacks.[5] In 1773, John Fothergill an English physician outlined the major clinical features of TN.[6]

Trigeminal neuralgia can be classified into typical which includes paroxysmal pain alone and atypical which is associated with paroxysmal pain and constant pain.[7] The IHS published a criterion for the diagnosis of classical and symptomatic trigeminal neuralgia[8] (Table 1).

Various causes attributed to TN include, chronic stretching or compression of the trigeminal root. Gerhard H. Fromm et. al. suggested that a, chronic irritation of the trigeminal nerve produces failure of segmental inhibition in the trigeminal nucleus, as well as increased activity in the trigeminal nerve due to ectopic-spike initiation. This combination of increased activity in the primary afferent fibers with the impairment of inhibitory mechanisms in the trigeminal nucleus leads to paroxysmal discharges of

Table 1: Diagnostic criteria proposed by IHS

Classic	*Symptomatic*
• Paroxysmal attacks of pain lasting from a fraction of a second to two minutes, affecting one or more divisions of the trigeminal nerve, and fulfilling criteria B and C	• Paroxysmal attacks of pain lasting from a fraction of a second to two minutes, with or without persistence of aching between paroxysms, affecting one or more divisions of the trigeminal nerve, and fulfilling criteria B and C
• Pain has at least one of the following characteristics: – Intense, sharp, superficial, or stabbing – Precipitated from trigger zones or by trigger factors	• Pain has at least one of the following characteristics: – Intense, sharp, superficial, or stabbing – Precipitated from trigger zones or by trigger factors
• Attacks are stereotyped in the individual patient	• Attacks are stereotyped in the individual patient
• There is no clinically evident neurologic deficit	
• Not attributed to another disorder	• A causative lesion, other than vascular compression, has been demonstrated by special investigations and/or posterior fossa exploration

interneuron in the trigeminal nucleus in response to tactile stimulation and an attack of trigeminal neuralgia would occur when these bursts reach the threshold for activating nociceptive neurons in the trigeminal nucleus oralis.[9]

CLINICAL FEATURES

TN is characterized by paroxysms of severe, lancinating and electric like bouts of recurrent, unilateral facial pain restricted to the distribution of the trigeminal nerve lasting only for a few seconds. This pain rarely occurs during sleep and the patient maybe totally asymptomatic during the episodes. It may involve one or more branches of the 5th cranial nerve, the maxillary branch is more commonly involved, and the least involved is the ophthalmic branch, and when comparing right with left, the right side of the face was affected more commonly (ratio of 1.5:1), which could be explained that it could be due to the narrower foramens (rotundum and ovale) on the right side.[10,11] TN affects the females more commonly and is seen between 60 to 70 years of age. TN is not usually seen before the age of 40 years.[10]The trigger zones are usually present in the areas like cheekbone, nose, upper lip and upper teeth and in some people, it also extends to the lower lip, teeth, and chin. A detailed history is very important for the diagnosis. Physical examination includes neurologic examination and the finding of typical trigger zones verifies the diagnosis of trigeminal neuralgia. Imaging is performed to rule out other causes of compression of the trigeminal nerve such as mass lesions, or vascular malformations. Imaging modalities include MRI; three-dimensional constructive interference in steady state (3-D-CISS) showed the proximity between the trigeminal nerve and the region of neuralgic manifestation.[12]

Various differential diagnosis include, postherpetic neuralgia, tooth pain, trigeminal neuropathy, post-traumatic neuralgia, glossopharyngeal neuralgia, etc.

TREATMENT

Trigeminal neuralgia is treated mainly by pharmacological methods. Other treatment modalities include surgical, TENS, acupuncture, psychological methods. Medical management of TN is mainly with anticonvulsants and skeletal muscle relaxants. Carbamazepine (Tegretol) is the initial choice for the treatment of TN. Dosages used have ranged from 100 to 1,200 mg per day, with most patients responding to 200 to 800 mg per day in two or three divided doses. Serious side effects have been reported with anticonvulsant drugs, including deaths from hematological reactions. The commonest adverse effects are impaired mental and motor function, which may limit clinical use, particularly in elderly people.[13-15]

Baclofen, a skeletal muscle relaxant has also been shown to be effective. Studies have shown its effectiveness when used alone[16] and also when used with carbamazepine.[17] It is initially given as 5 mg tid for 3 days and then increased to 10 and 20 mg/day every 3 days to a maximum dose of 50 to 60 mg/day.[18] Medications with reported success also include phenytoin (Dilantin), which can be used as monotherapy or as a combination with carbamazepine and baclofen. It can be started with 100 mg twice or thrice daily and dose can be increased as required, sometimes to as much as a total daily dose of 800 mg. Many patients have experienced benefit within 24 to 48 hours.[19]

Lamotrigine is another antiepileptic drug which could be used in trigeminal neuralgia. It is seen to be as potent as carbamazepine in inactivating Na^+ currents, with fewer side

Table 2: Drugs used in the management of trigeminal neuralgia

Drug	*Dosage*	*Side effects*
Carbamazepine	100-1200 mg/day	Impaired mental and motor function, death from hematological reaction, nausea, ataxia, diplopia
Baclofen	Initially 5 mg tid × 3 days, then increase 10-20 mg/day every 3 days to a maximum dose of 50-60 mg/day	Drowsiness, weakness, hypotension, constipation
Phenytoin	Initially 100 mg twice daily can be increased to 800 mg/day	Lethargy, nystagmus
Lamotrigine	25 mg/day × 2 weeks, 25 mg bid × 2 weeks, maximum dose 50-100 mg twice daily	Headache, lethargy, nausea, tremor, insomnia
Clonazepam (Patients in whom Carbamazepine is contraindicated)	4-8 mg/day	Drowsiness, ataxia
Pimozide	2-12 mg/day	Tremor, convulsions hypersensitivity, sedation
Valproic acid	250-500 mg four times daily	Tremors confusion, nausea, weight gain, hepatotoxicity
Sumatriptan (refractory cases)	50-100 mg/day	Nausea, vomiting
Oxycarbazapine	300 mg bid/day upto 1200 mg/day	Dizziness, diplopia, ataxia, nausea, somnolence, headache, hyponatremia
Gabapentin	300 mg 1st day, 2nd day 300 mg bid, 3rd day 300 mg tid and then maintain the dosage. Can be given upto 2400 mg/day	Somnolence, dizziness, tremor, ataxia, fatigue, nystagmus,
Topiramate	50-150 mg/day	Dizziness, somnolence and weight loss

effects.[19] It is given in the dose of 25 mg/day for 2 weeks then 25 mg bid for 2 weeks with a maximum dose of 50 to100 mg twice daily. Patients in whom carbamazepine is contraindicated clonazepam can be used. It is the treatment of choice and is given in dose of 4 to 8 mg/day. Results are reported of a preliminary trial with clonazepam in 19 patients with trigeminal neuralgia refractory to carbamazepine treatment.[20] Pimozide, 2 to 12 mg/day has also been used in TN. Valproic acid is given in the dose of 250 to 500 mg qid. Careful monitoring is required in these patients due to the side effects like tremors, confusions, nausea, vomiting, weight gain, hepatotoxicity.[21]

In patients who are resistant to carbamazepine, a combination therapy of carbamazepine with phenytoin sodium 100 mg can be advised. Oxcarbazepine 300 mg bid/day up to 1200 mg/day. Gabapentin 300 mg 1st day 300 mg, 2nd day 300 mg bid, 3rd day 300 mg tid and then maintain the dosage. Can be given up to 2400 mg/day.[22]

Topiramate (50-300 mg/day) an antiepileptic drug acts by blocking sodium channels, enhances GABA activity by interacting with a non-benzodiazepine site on GABA A receptors, and selectively blocks AMPA/kainate glutamate receptors.[23] Pregablin 150 to 600 mg daily[24]and amitriptilline 50 to 100 mg/day depending on the frequency of attacks (Table 2).[25]

Botulinum toxin type A (Botox) has been used in some patients. [26]Topical capsaicin was helpful for trigeminal neuralgia in one open-label trial and intramuscular sumatriptan was beneficial in one small, single-dose study. [27] One recent study found that intranasal lidocaine (Xylocaine) significantly decreased second-division trigeminal neuralgia pain for more than four hours. [28]

Topical preparations include drugs like valproate sodium, racemic ketamine, proparacaine hydrochloride, and topical capsaicin cream.[29]

Acupuncture, high-dose dextromethorphan and topical ophthalmic anesthetic have been tried unsuccessfully in small trials. Surgical management is reserved for patients who do not respond or are intolerant to drugs. The treatment modalities include cryotherapy, percutaneous radiofrequency thermal rhizotomy, percutaneous retrogasserian glycerol rhizotomy,[30] microvascular decompression of the trigeminal nerve, Gamma knife therapy,[31] balloon compression[32] other treatment modalities include TENS, acupuncture and psychological approach[33].

CONCLUSION

Trigeminal neuralgia is an uncommon disorder characterized by recurrent attacks of lancinating pain in the trigeminal nerve distribution. Any rational approach to diagnosis and effective treatment in TN should be based on the underlying pathophysiology producing the disorder. Even though various drugs have been used in the treatment of TN carbamazepine is the gold standard in the initial treatment. However, for recalcitrant cases a physician should not hesitate to use adequately tested newer modalities of medical therapy as elevation of patient's suffering is of primary concern in these cases.

REFERENCES

1. Merskey H, Bogduk N. Classification of chronic pain: Description of chronic pain syndromes and definition of pain terms (2nd ed). IASP Press, Seattle, 1994.
2. Olesen J. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain (1st ed). Cephalalgia 1988;8 suppl:1-96.
3. Adams F. The extent works of Aretaeus, the Cappadocian. London: Sydenham Society, 1856.
4. Ameli NO. Avicenna and trigeminal neuralgia. J Neurol Sci 1965;2:105-07.
5. Andre NA. Observations. College et. de l' Academie Royale de Chururgie. Paris: Delaguette; 1756.
6. Fothergill J. Of a painful affection of the face. London: Medical Society of London, 1776.
7. Toda K. Etiology of trigeminal neuralgia. Oral Science International 2007;4.
8. Headache Classification Subcommittee of the International Headache Society. The international classification of headache disorders (2nd ed). Cephalalgia 2004;24(Suppl 1):9-160.
9. Gerhard H Fromm, Christopher F Terrence, Joseph C Maroon. Trigeminal Neuralgia; Current Concepts Regarding Etiology and Pathogenesis. Arch neurol Nov 1984;41:1204-07.
10. Katusic S, Beard CM, Bergstralh E, Kurland LT. Incidence and clinical features of trigeminal neuralgia, Rochester, Minnesota, 1945-1984. Ann Neurol 1990;27(1):89-95.
11. Cruccu G, Biasiotta A, Galeotti F, et al. Diagnosis of trigeminal neuralgia: A new appraisal based on clinical and neurophysiological findings. In: Cruccu G, Hallett M (Eds). Brainstem Function and Dysfunction. Amsterdam, the Netherlands: Elsevier, 2006;171-86.
12. Katsuhiro Toda. Trigeminal Neuralgia: Symptoms, Diagnosis, Classification and Related disorders. Oral Science International: May 2009:9.
13. Wiffen PJ, mcquay HJ, Moore RA. Carbamazepine for acute and chronic pain. Cochrane Database Syst Rev 2005;(3): CD005451.
14. Henry Mcquay, Dawn Carroll, Alejandro R Jadad, et al. Anticonvulsant drugs for management of pain: A systematic review. BMJ 1995;311:1047-52.
15. Grahame-Smith DG, Aronson JK. Oxford textbook of clinical pharmacology and drug therapy (2nd ed). Oxford: Oxford University Press 1992:433-36, 443-44, 529-717.
16. Fromm GH, Terrence CF, Chattha AS. Baclofen in the treatment of trigeminal neuralgia: Double-blind study and long-term follow-up, Ann Neurol Mar 1984;15(3):240-44.
17. Baker KA, Taylor JW, Lilly GE, Treatment of trigeminal neuralgia: Use of baclofen in combination with carbamazepine, Clin Pharm Jan-Feb 1985;4(1):93-96.
18. Bennetto L, Patel NK, Fuller G. Trigeminal neuralgia and its management. BMJ Jan 27, 2007;334 (7586):201-05.
19. Treatment of Trigeminal Neuralgia, British Medical Journal, 1972;2:583-84.
20. Canavero S, Bonicalzi V, Ferrules P, et al. Lamotrigine control of idiopathic trigeminal neuralgia. J Neurol Neurosurg Psychiatry Dec 1995;59(6):646.
21. Chandra B. The use of clonazepam in the treatment of tic douloureux a preliminary report. Proc Aust Assoc Neurol 1976;13:119-22.
22. Ajay Nayak, Joanna Baptist, Sumanth KN. Orofacial pain. Chapter 7, In Text book of Oral Medicine, Oral Diagnosis and Oral Radiology. Dr. Ravikiran, Dr. Praveen B.N (Eds). Elsevier Science Publication, New Delhi (1st ed), 2010;144-45.
23. Renan Barros Domingues, Gustavo Wruck Kuster; Camila Catherine Henriques Aquino. Treatment of trigeminal neuralgia with low doses of topiramate. Arq. Neuro-Psiquiatr. Sept 2007;65(3).
24. Obermann M, Yoon MS, Sensen K, Maschke M, Diener HC, Katsarava Z. Efficacy of pregabalin in the treatment of trigeminal neuralgia Cephalalgia. Feb 2008;28(2):174-81.
25. Bou Hassira, et al. SUNCT Syndrome. A case of transformation from trigeminal neuralgia? Cephalgia 1994;14;168-70.
26. Goodman LS, Gilman A, Rall TW, Nies AS, Taylor P (Eds). Drugs effective in the therapy of the epilepsies. The pharmacological basis of therapeutics (8th ed). Toronto: Mcgraw-Hill, 1992:436-62.
27. Kanai A, Saito M, Hoka S. Subcutaneous sumatriptan for refractory trigeminal neuralgia. Headache. 2006; 46(4):577-582.
28. Kanai A, Suzuki A, Kobayashi M, Hoka S. Intranasal lidocaine 8% spray for second-division trigeminal neuralgia. Br J Anaesth. 2006;97(4):559-63. Epub 1 Aug, 2006 .
29. John E Delzell (Jr), Amy R Grelle. Trigeminal Neuralgia New Treatment Options for a well-known Cause of Facial Pain Arch Fam Med. 1999;8:264-68.
30. Piovesan EJ, Teive HG, Kowacs PA, et al. An open study of botulinum: A toxin treatment of trigeminal neuralgia. Neurology 2005;65(8):1306-08.
31. Lunsford LD, Bennett MH. Percutaneous retrogasserian glycerol rhizotomy for tic douloureux, part I: Technique and results in 112 patients. Neurosurgery 1984;14:424-30.
32. Belber CJ, Rak RA. Balloon compression rhizolysis in the surgical management of trigeminal neuralgia. Neurosurgery 1987;20:908.
33. Prasad S, Galetta S. Trigeminal neuralgia: Historical notes and current concepts Neurologist. Mar 2009;15(2):87-94.