Assessment and treatment of trigeminal neuralgia

Patients with trigeminal neuralgia, a rare facial neuropathic pain, present to both medical and dental specialists. International guidelines on diagnosis and management of trigeminal neuralgia provide a useful framework for this article.

Trigeminal neuralgia is one of the rare forms of facial pain which is initially diagnosed in primary care both by doctors and dentists. Patients are often referred to secondary care where care will vary, depending on the specialty to which the patient is referred. Referrals can vary from neurologists, neurosurgeons and pain specialists through to oral and maxillofacial surgeons. International guidelines on diagnosis and management of trigeminal neuralgia have now been published and this article will review these guidelines in the hope that all patients referred for management of trigeminal neuralgia will receive similar care (Cruccu et al, 2008; Gronseth et al, 2008).

Definitions

The International Association for the Study of Pain defines trigeminal neuralgia as 'a sudden and usually unilateral severe, brief, stabbing, recurrent pain in the distribution of one or more branches of the fifth cranial nerve' (Merskey and Bogduk, 1994). Trigeminal neuralgia therefore is a neuropathic pain. The majority of cases of trigeminal neuralgia are idiopathic, whereas the rarer forms are those of secondary (symptomatic) trigeminal neuralgia as a result of brainstem pathology including neoplasms, benign or malignant, cysts, aneurysms or arteriovenous malformations and multiple sclerosis.

Within the trigeminal neuralgia literature there has been considerable debate about different symptomatology which has led to terminology such as atypical trigeminal neuralgia or type I and II trigeminal neuralgia (Limonadi et al, 2006). In classical trigeminal neuralgia, the terminology used by the International Headache Society, the diagnostic criteria are precise and in theory diagnosis is easy (Anonymous, 2004). Atypical trigeminal neuralgia or type II (Limonadi et al, 2006) occurs in patients who still have fairly classical features of trigeminal neuralgia but also report a background burning, dull type of pain which persists for some time after an attack of pain and is often not as responsive to the usual mainstream medications.

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Epidemiology

Until fairly recently trigeminal neuralgia was regarded as a rare condition occurring more frequently in women, with a peak incidence in the 50–60-year age group (Zakrzewska and Hamlyn, 1999). However, studies of general practice research databases both in the UK and in Holland suggest that trigeminal neuralgia occurs in younger age groups and that it is more frequent, with a prevalence of 26.4 per 100 000, making it more common than phantom limb syndrome and diabetic neuropathy (Hall et al, 2006; Dieleman et al, 2008). This high prevalence, however, could be a result of misdiagnosis.

Risk factors for trigeminal neuralgia include multiple sclerosis and hypertension (Zakrzewska and Hamlyn, 1999).

Prognosis

There are very few studies to date which provide reliable data on prognosis. In the initial phases of the disorder there are often long periods of 6 months or more of pain remission but these periods tend to get shorter and the relapse rate is more frequent. In some patients relapse is also associated with increased intensity of the pain whereas in others it remains at a similar level (Zakrzewska, 2002).

Clinical features

Trigeminal neuralgia can only be diagnosed on clinical features and so it is essential to take time to take a careful history, revisiting it if necessary to ensure that patients have a correct diagnosis.

The classical features of trigeminal neuralgia are summarized in *Figure 1*. However, these features have not been validated by case control studies and are mainly based on features of patients attending the secondary care sector (Zakrzewska, 2002).

The key features which help to distinguish trigeminal neuralgia from other facial pains include:

- Each single burst of pain lasts on average under 2 minutes
- There is no pain between bursts of pain
- Most patients will have complete remission of pain for weeks or months at least initially
- The pain is described as sharp, shooting, electric shock-like

- The pain is provoked by light touch activities but attacks of pain can also be spontaneous
- The pain is always located in the distribution of the trigeminal nerve and first division trigeminal pain is rare
- The severity of the pain can vary, especially if medication is used. However, when the disorder is at its peak the pain is suicidal, grossly impairs quality of life and leads to weight loss
- Sleep disturbance tends to occur if the pain is severe
- Depression is often noted and there are reports of patients committing suicide or feeling suicidal (Zakrzewska, 2006)
- Extremely rare to have any autonomic symptoms or signs.

In atypical trigeminal neuralgia patients report prolonged pain of a lowered intensity and quality, i.e burning, tingling or dull, after the main attack of pain.

On examination pain can often be elicited by touching a relevant trigger point. Most routine neurological examination shows absence of sensory changes but more complex neurophysiological testing may show deficits. These are more likely to occur in the atypical forms.

Differential diagnosis

There are a variety of other unilateral facial pains that need to be considered in the differential diagnosis, especially at the onset when chronicity has not eliminated some of the commoner forms of facial pain. Trigeminal neuralgia can present with principally intra-oral symptoms and so toothache needs to be considered as a differential. Temporomandibular disorders, especially if they are unilateral and the pain is centred in the preauricular area, can also be confused with trigeminal neuralgia (Drangsholt and Truelove, 2001).

Other neuropathic pain to be considered includes post-herpetic neuralgia and traumatic neuropathic trigeminal pain.

If symptoms are predominantly in the first division of the trigeminal nerve then the rarer group of disorders known as the trigeminal autonomic cephalalgias such as cluster headache, paroxysmal hemicranias, SUNCT (short unilateral neuralgiform pain with conjunctival redness and tearing) and SUNA (short unilateral neuralgiform pain with autonomic symptoms) need to be considered (Cohen et al, 2006). Temporal arteritis or giant cell arteritis can cause unilateral or bilateral aching, throbbing pain most frequently around the temples and must be diagnosed rapidly to prevent blindness.

Investigations

Risk factors for symptomatic trigeminal neuralgia are often early presentation, sensory loss and bilateral involvement (Cruccu et al, 2008; Gronseth et al, 2008) and these patients need to be investigated.

The preferred imaging investigation is magnetic resonance imaging, as this will also show up whether there is neurovascular contact between the cerebral vessels and the trigeminal nerve, especially in the root entry zone. Currently magnetic resonance imaging does not have sufficient positive or negative predictive value to assess vascular compression as an aetiological factor for this syndrome (Cruccu et al, 2008; Gronseth et al, 2008). Neurophysiological testing such as quantitative sensory testing and evoked potentials (available only in larger centres) can predict symptomatic cases of trigeminal neuralgia (Cruccu et al, 2008; Gronseth et al, 2008). Haematological and biochemical investigations are useful as baselines when using medical therapies. A psychological assessment which includes quality of life and mood is a useful tool in predicting the need for future neurosurgical interventions.

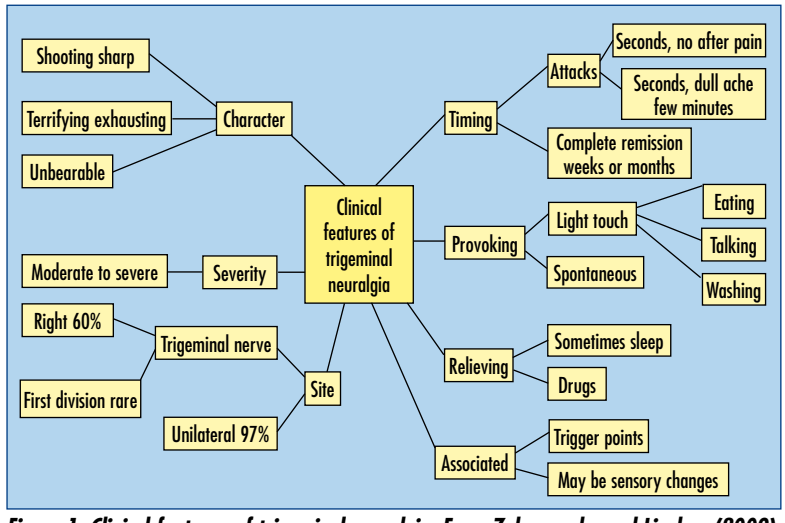

Figure 1. Clinical features of trigeminal neuralgia. From Zakrzewska and Linskey (2009).

Management

There are now a variety of sources from which updated information on management of trigeminal neuralgia can be obtained (*Table 1*) and the international guidelines are summarized below (Cruccu et al, 2008; Gronseth et al, 2008). Some of the tables and figures are from a recently published book (Zakrzewska and Linskey, 2009).

Medical management

The mainstay of medical management is the anticonvulsants, with carbamazepine and oxcarbazepine remaining the drugs of choice (*Table 2*).

Drugs which have been evaluated in randomized controlled trials and shown either to be ineffective or to have severe side-effect profiles include tocainide, tizanidine and pimozide.

It is essential that in the early stages of management patients are encouraged to keep diaries and to monitor their personal response to the drugs used, both in terms of pain relief and side effects. Patients need to learn to take control of their drug management and alter their dosages depending on pain levels. Blood monitoring is essential at the start of therapies and if higher doses are used on a consistent basis.

No studies have been published on polypharmacy for the management of trigeminal neuralgia such as that used in epilepsy.

Patients with multiple sclerosis are often difficult to control with medication as they tend to have a higher incidence of side effects. The only drug that has been reported in use with patients with trigeminal neuralgia and multiple sclerosis has been misoprostol (DMKG study group, 2003). However, this open-labelled trial in 18 patients has not been repeated.

Table 1. Sources of updated information on trigeminal neuralgia

Provider	Internet address	Type of information
The Cochrane Library	www.cochrane.org/reviews, search trigeminal neuralgia in title, abstract, keywords	Several systematic reviews on drugs used in chronic pain and trigeminal neuralgia, and surgical treatments
Clinical Evidence	clinicalevidence.bmj.com/ceweb/index.jsp	Regularly updated topic on trigeminal neuralgia
National electronic Library for Medicines Clinical Knowledge Summaries	www.cks.nhs.uk/trigeminal_neuralgia	Short summaries especially for primary care
American Academy of Neurology	www.aan.com/go/practice/guidelines	Practice guidelines in a variety of formats on trigeminal neuralgia in collaboration with the European Federation of Neurological Societies

Psychological non-medical management

Patients with trigeminal neuralgia have traditionally been treated using a strictly biomedical model. However, data from trigeminal neuralgia support groups and from material that patients have contributed to books on trigeminal neuralgia (Zakrzewska, 2006) have highlighted the fear, loneliness and depression that these patients suffer while trying to manage this condition. Support groups provide useful additional support for patients who want more information and want to meet other patients. Conferences they organize with participation of health-care practitioners show these to be greatly appreciated (Zakrzewska et al, 2009). Some resources available for patients are shown in *Further information*.

Surgical management

In reviewing the literature for the international guidelines, it was impossible to find sufficiently high quality evidence to determine the point at which patients should be offered surgical procedures. A decision analysis study based on hypothetical scenarios given to 156 patients with trigeminal neuralgia showed that they marginally preferred surgical management to medical; however, this study did not determine the timing of the surgical interventions (Spatz et al, 2007).

A Cochrane review in press (Zakrzewska and Akram, 2010) has shown that there are very few randomized controlled trials of the surgical options, and of these

Table 2. Medical management of trigeminal neuralgia

	Drug	Daily dose range	Efficacy NNT	Side effects	Comments
Proven in RCTs and effective	Baclofen	50–80 mg	NNT 1.4 (1–2.6) only 10 patients, possibly effective	Ataxia, lethargy, fatigue, nausea, vomiting beware rapid withdrawal	Useful as add-on therapy
	Carbamazepine	300–1000 mg	NNT 2.6 (2–4), effective	Drowsiness, ataxia, headaches, nausea, vomiting, constipation, blurred vision, rash, introduce slowly, drug interactions NNH 3.4 (2.5–5.2) for side effects, number needed to harm for withdrawal 24 (13–110)	Reduced white cell count, hyponatraemia higher doses, retard form useful in controlled patients
	Lamotrigine	200–400 mg	NNT 2.1 (1.3–6.1) as add-on medication	Dizziness, drowsiness, constipation, ataxia, diplopia, irritability, rapid dose escalation leads to rashes	Slow escalation important
	Oxcarbazepine	300–1200 mg	Effective	Vertigo, fatigue, dizziness, nausea, hyponatraemia in high doses, no major drug interactions	RCT only abstract, cannot calculate NNT
	Gabapentin + topical ropivacaine	1800–3600 mg, in RCT up to 900 mg injection weekly	Good	Ataxia, dizziness, drowsiness, nausea, headache	Ropivacaine reduced need for gabapetin, small trial with newly diagnosed patients
Commonly used but no RCT	Clonazepam	4–8 mg	Low	Severe drowsiness -60%, addictive	
	Phenytoin	200–300 mg	Good	Ataxia, lethargy, nausea, headache, behavioural changes, folate deficiency in prolonged use, gingival hypertrophy	Small margin for dose escalation, used intravenously for immediate effect
	Pregabalin	150–600 mg	Good	Ataxia, dizziness, drowsiness, nausea, headache	Rapid escalation possible
	Valproic acid	600–1200 mg	Poor	Irritability, restlessness, tremor, confusion, nausea, rash, weight gain	

NNT = number needed to treat; RCT = randomized controlled trials. Check dosages in British National Formulary. Adapted from Zakrewska and Linskey (2009)

only three fulfil the quality criteria for inclusion in a systematic review. Thus, the evidence for surgical treatment is based on case studies and rare cohort studies. *Table 3* summarizes the major surgical procedures and their outcomes.

Apart from microvascular decompression, all the other surgical procedures rely on destruction of the sensory fibres of the trigeminal nerve and hence result in varying degrees of sensory change postoperatively.

Treatments can be at three levels:

1. Posterior fossa procedures. Most frequently performed is the non-destructive microvascular decompression. Other procedures carried out at this level include stereotactic radiosurgery (gamma knife most frequently) and in cases of no compression partial sensory rhizotomy.
2. Gasserian ganglion level. Once access to the Gasserian ganglion is obtained by passing a needle through the foramen ovale under radiographic control, a variety of ablative procedures can be done. These include radiofrequency thermocoagulation using temperatures between 60°C and 90°C, percutaneous glycerol rhizotomy where the nerve is bathed in glycerol or balloon compression where a Foley catheter balloon is used to compress the nerve.
3. Peripheral procedures. These are carried out for the most part in outpatients under local anaesthesia and include application at identified trigger points of agents such as cryotherapy, laser, alcohol, adriamycin, glycerol, streptomycin or even the performance of a neurectomy.

Pain relief outcomes

Peripheral treatments give the shortest pain relief outcomes, a maximum of 10 months, whereas all the ablative procedures are similar – 4 years for 50% of patients. Up to 70% of patients are likely to be pain free at 10 years after a microvascular decompression with the highest recurrence rate being in the first 2 years.

Complications and side effects

These are summarized in *Table 3*. Ablative procedures result in sensory loss which can be variable both in extent and severity. The most severe form is that of anaesthesia dolorosa. Stereotactic radiosurgery is the least invasive of all the procedures but up to 7% of patients may report some form of sensory loss and this can extend to anaesthesia dolorosa. Microvascular decompression, being a major neurosurgical procedure, does carry with it a risk of mortality which ranges from 0.2–0.4%. Other complications include CSF leak (around 5%) which can require further surgery, meningitis (both bacterial and aseptic; less that 5%), cerebral infarcts and haemorrhage resulting in strokes (less than 2%), pulmonary emboli (less than 1%), and gastrointestinal bleeds (less than 1%). The major long-term neurological deficit is that of ipsilateral hearing loss which can be reduced by intraoperative auditory brainstem evoked response monitoring.

Recurrences

There is relatively little literature on management of recurrences. Some patients will opt to have repeat surgery, others will continue with medication.

Conclusions

Classical trigeminal neuralgia has distinctive clinical features and it is essential to differentiate the idiopathic forms from symptomatic trigeminal neuralgias, including those related to tumours or multiple sclerosis. International guidelines provide a rationale for managing patients with trigeminal neuralgia. There are a number of randomized controlled trials on drug management of trigeminal neuralgia but there is a complete lack of high quality evidence on the surgical management of this condition.

There are no clear guidelines on how to manage patients with multiple sclerosis. *Figure 2* provides a possible evidence-based approach to the management of trigeminal neuralgia. **BJHM**

Tables 2 *and* 3 *and* Figures 1 *and* 2 *are based on tables and figures from Zakrzewska and Linskey (2009) by kind permission of Oxford University Press. This work was undertaken at UCL/UCLHT who received a proportion of funding from the Department of Health's NIHR Biomedical Research Centre funding scheme.*

Table 3. Surgical management of trigeminal neuralgia, data on 5 years not available for some procedures

Procedure	% probability of being pain free	Mortality	Morbidity
Peripheral: neurectomy, cryotherapy, alcohol, injections, acupuncture	Two years – 22	Nil	Low, sensory loss, transient haematoma, oedema
Radiofrequency thermorhizotomy (RFT)	Two years – 68 Five years – 48	Low	Complications mainly relating to trigeminal nerve, dysaesthesia, anaesthesia dolorosa, eye problems, masticatory problems, sensory loss over 50%
Percutaneous glycerol rhizotomy	Two years – 63 Five years – 45	Low	Complications as for RFT but fewer cases of sensory loss
Balloon microcompression	Two years – 79	Low	Complications as for RFT, fewer with sensory loss but temporary masticatory problems common
Microvascular decompression	Two years – 81 Five years – 76 Ten years – 70	0.4%	Overall 75% no complications, 16% perioperative complications, 2% transient cranial nerve 4th, 6th, 4% 8th dysfunction with 2% permanent deafness
Gamma knife surgery	Two years – 58	Nil	Late onset of relief, may only be partial, 7% sensory loss up to 2 years post treatment

Adapted from Zakrzewska and Linskey (2009)

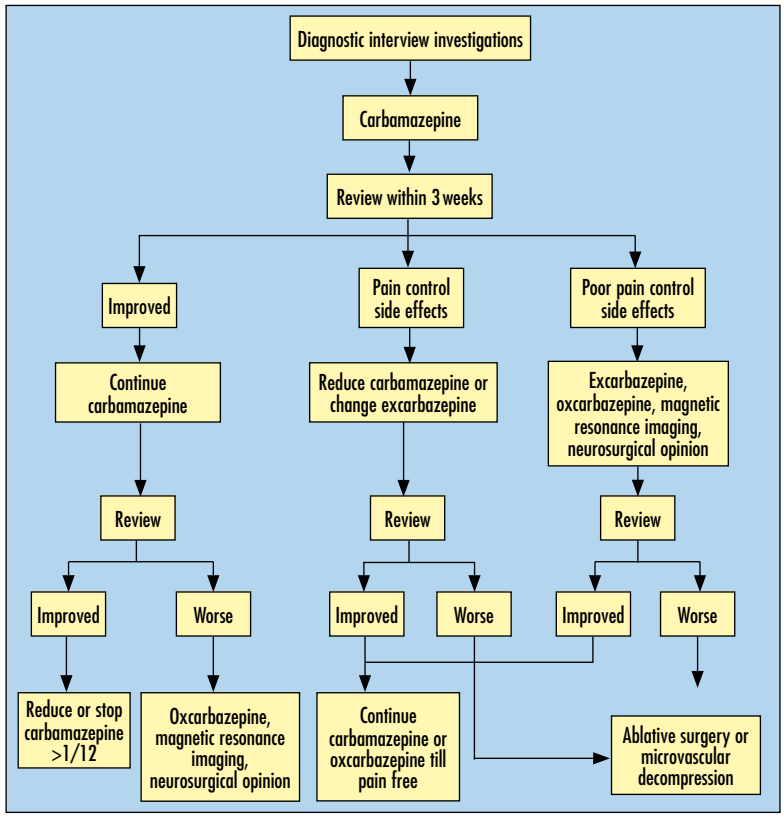

Figure 2. Algorithm for managing trigeminal neuralgia. From Zakrzewska and Linskey (2009).

KEY POINTS

- The key diagnostic features of trigeminal neuralgia are a unilateral pain in the distribution of the trigeminal nerve of a shooting, electric shock-like quality that can be spontaneous but is most frequently evoked by light touch. There is no pain between attacks (which last up to 2 minutes) and patients can have months of remission.
- Rarely trigeminal neuralgia is secondary to tumours or multiple sclerosis, which can be ruled out through imaging.
- National and international guidelines on management are now available.
- First line drugs are carbamazepine and oxcarbazepine. If neurovascular contact has been detected then surgical options can provide long-term pain relief especially microvascular decompression.
- Specific patient support groups are very valuable.

Conflict of interest: none.

Anonymous (2004) The International Classification of Headache Disorders 2nd edn. *Cephalalgia* **24**(Suppl 1): 9–160

Cohen AS, Matharu MS, Goadsby PJ (2006) Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) or cranial autonomic features (SUNA)--a prospective clinical study of SUNCT and SUNA. *Brain* **129:** 2746–60

Cruccu G, Gronseth G, Alksne J et al JM (2008) AAN-EFNS guidelines on trigeminal neuralgia management. *Eur J Neurol* **15:** 1013–28

Dieleman JP, Kerklaan J, Huygen FJ, Bouma PA, Sturkenboom MC (2008) Incidence rates and treatment of neuropathic pain conditions in the general population. *Pain* **137:** 681–8

DMKG study group (2003) Misoprostol in the treatment of trigeminal neuralgia associated with multiple sclerosis. *J Neurol* **250:** 542–5

Drangsholt M, Truelove E (2001) Trigeminal neuralgia mistaken as temporomandibular disorder. *J Evid Base Dent Pract* **1:** 41–50

Gronseth G, Cruccu G, Alksne J et al (2008) Practice parameter: the diagnostic evaluation and treatment of trigeminal neuralgia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the European Federation of Neurological Societies. *Neurology* **71:** 1183–90

Hall GC, Carroll D, Parry D, McQuay HJ (2006) Epidemiology and treatment of neuropathic pain: The UK primary care perspective. *Pain* **122:** 156–62

Limonadi FM, McCartney S, Burchiel KJ (2006) Design of an artificial neural network for diagnosis of facial pain syndromes. *Stereotact Funct Neurosurg* **84:** 212–20

Merskey H, Bogduk N (1994) *Classification of Chronic Pain. Descriptors of Chronic Pain Syndromes and Definitions of Pain Terms.* 2nd edn. IASP Press, Seattle

Spatz AL, Zakrzewska JM, Kay EJ (2007) Decision analysis of medical and surgical treatments for trigeminal neuralgia: how patient evaluations of benefits and risks affect the utility of treatment decisions. *Pain* **131:** 302–10

Zakrzewska JM (2002) Diagnosis and differential diagnosis of trigeminal neuralgia. *Clin J Pain* **18:** 14–21

Zakrzewska JM (2006) *Insights: facts and stories behind trigeminal neuralgia.* Trigeminal neuralgia association, Gainesville

Zakrzewska JM, Akram H (2010) Neurosurgical interventions for classical trigeminal neuralgia. *Cochrane Database Syst Rev* (in press)

Zakrzewska JM, Hamlyn PJ (1999) Facial pain. In: Crombie IKCPR, Linton SJ, LeResche L, Von Korff M, eds. *Epidemiology of Pain.* IASP, Seattle: 171–202

Zakrzewska JM, Linskey ME (2009) Trigeminal neuralgia. In: Zakrzewska JM, ed. *Orofacial Pain.* Oxford University Press,Oxford: 119–34

Zakrzewska JM, Jorns TP, Spatz A (2009) Patient led conferences--who attends, are their expectations met and do they vary in three different countries? *Eur J Pain* **13:** 486–91

Further information

Organization	Contact details	Type of help
Trigeminal Neuralgia Association UK	PO Box 234, Oxted, Surrey RH8 8BE, UK Tel: 01883 370214 www.tna.org.uk	Email and telephone help lines, newsletters, conferences, books
The Facial Pain Association (formerly The Trigeminal Neuralgia Association)	925 NW 56th Terrace, Suite C, Gainesville, FL 32605-6402 USA www.fpa-support.org/	Email and telephone help lines, newsletters, conferences, books
Trigeminal Neuralgia Association Australia	Irene Wood, PO Box 1611, Castle Hill NSW 1765 Australia www.tnaaustralia.org.au	Email and telephone help lines, newsletters, conferences
American Academy of Neurologists	www.aan.com/go/practice/guidelines	Patient information leaflet on guidelines for trigeminal neuralgia
Brain and Spine Foundation	3.36 Canterbury Court, 1-3 Brixton Road, London SW9 6DE Tel: 020 7793 5900 www.brainandspine.org.uk/	Booklet on facial pain, helpline but not specific to trigeminal neuralgia
The Cochrane Library	www.cochrane.org/reviews, search trigeminal neuralgia in title, abstract, keywords	Lay summaries of reviews on drugs used in chronic pain, trigeminal neuralgia