



# Clinical Evidence Handbook

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## Trigeminal Neuralgia

JOANNA M. ZAKRZEWSKA, *Eastman Dental Hospital, London, United Kingdom*

MARK E. LINSKEY, *University of California Irvine, Irvine, California*

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Author disclosure: Joanna M. Zakrzewska and Mark E. Linskey are authors of references cited in this review.

Trigeminal neuralgia is a sudden, unilateral, brief, stabbing, recurrent pain in the distribution of one or more branches of the fifth cranial nerve. The diagnosis is made using the history alone, based on characteristic features of the pain.

- Pain occurs in paroxysms, which can last from a few seconds to several minutes. The frequency of the paroxysms ranges from a few to hundreds of attacks per day.

- Periods of remission can last for months to years, but tend to get shorter over time.

- The condition can impair activities of daily living and lead to depression.

- The annual incidence in the United Kingdom (based on physician practice lists and rather liberal diagnostic criteria) has been reported to be 26.8 per 100,000. However, studies in other countries with stricter definitions, such as the United States and the Netherlands, have reported much lower incidence rates ranging between 5.9 and 12.6 per 100,000.

- Experts find that symptoms worsen

over time and become less responsive to medication, despite dose increases and adding further agents.

Treatment success is defined differently in studies of medical and surgical therapies for trigeminal neuralgia.

- Treatment success in medical studies is usually defined as at least 50% pain relief from baseline. However, complete pain relief is the measure of treatment success in surgical studies.

Carbamazepine is considered the first-line medication for the initial medical treatment of trigeminal neuralgia symptoms.

- Carbamazepine has been shown to increase pain relief compared with placebo, but also increases adverse effects, such as drowsiness, dizziness, rash, liver damage, and ataxia.

- Studies evaluating durability of response with carbamazepine are lacking, but consensus expert opinion suggests that it may have a greater than 50% failure rate for long-term (five to 10 years) pain control.

### What are the effects of ongoing treatments in persons with trigeminal neuralgia?

Likely to be beneficial	Baclofen (in persons with multiple sclerosis who develop trigeminal neuralgia)* Carbamazepine Oxcarbazepine*
Trade-off between benefits and harms	Microvascular decompression* Nonpercutaneous destructive neurosurgical techniques (stereotactic radiosurgery)* Percutaneous destructive neurosurgical techniques (radiofrequency thermocoagulation, glycerol rhizolysis, or balloon compression)*
Unknown effectiveness	Gabapentin Lamotrigine

\*—Categorization based on observational studies and/or consensus.

- Based on the strength of published evidence, carbamazepine remains the best-supported standard medical treatment for trigeminal neuralgia.

There is consensus that oxcarbazepine is an effective treatment in persons with trigeminal neuralgia and may have fewer adverse effects than carbamazepine, although there is a lack of data from randomized controlled trials (RCTs) to confirm this.

- Oxcarbazepine rarely provides complete or long-term pain relief, although studies evaluating durability of response with this drug are lacking.

We found no sufficient evidence to judge the effectiveness of baclofen or lamotrigine.

- Lamotrigine is often used in persons who cannot tolerate carbamazepine, but the dose must be increased slowly to avoid rashes, thus making it unsuitable for acute use.

- There is consensus that baclofen may be useful for persons with multiple sclerosis who develop trigeminal neuralgia.

We found no evidence comparing gabapentin vs. placebo/no treatment or other treatments covered in this review in persons with trigeminal neuralgia.

- Gabapentin does have support for use in treating other neuropathic pain conditions, particularly multiple sclerosis.

Despite a lack of RCT data, observational evidence supports the use of microvascular decompression to relieve symptoms of trigeminal neuralgia.

- Microvascular decompression has been shown in at least two prospective comparative cohort trials to have superiority over stereotactic radiosurgery for complete pain relief, durability of response (up to five years), and preservation of trigeminal sensation.

- However, microvascular decompression requires general anesthesia and is rarely associated with surgical complications, of which a less than 5% risk of ipsilateral hearing loss appears to be the most common.

- Well-conducted observational studies have demonstrated that microvascular decompression has a greater magnitude of therapeutic effect than any medical and surgical therapy for trigeminal neuralgia. As such, this procedure is unlikely to be compared with best medical therapy in an RCT.

We found no RCT evidence comparing percutaneous destructive neurosurgical techniques (radiofrequency thermocoagulation, glycerol rhizolysis, balloon compression) or nonpercutaneous destructive neurosurgical techniques (stereotactic radiosurgery) vs. placebo/no treatment or other treatments covered in this review in persons with trigeminal neuralgia.

- Observational data suggest that radiofrequency thermocoagulation may offer higher rates of complete pain relief than glycerol rhizolysis and stereotactic radiosurgery, but may also be associated with higher rates of complications (e.g., facial numbness, corneal insensitivity).

- In contrast with stereotactic radiosurgery, pain relief with microvascular decompression and percutaneous destructive neurosurgical techniques is immediate, but they require sedation and/or anesthesia to perform, which are not required for stereotactic radiosurgery.

### Definition

Trigeminal neuralgia is a characteristic pain in the distribution of one or more branches of the fifth cranial nerve. The diagnosis is made on the history alone, based on characteristic features of the pain. It occurs in paroxysms, with each lasting from a few seconds to several minutes. The frequency of paroxysms is highly variable, ranging from hundreds of attacks per day to long periods of remission that can last years. Between paroxysms, the person is asymptomatic. The pain is severe and described as intense, sharp, superficial, stabbing, or shooting, often like an electric shock. It can be triggered by light touch in any area innervated by the trigeminal nerve, including from eating, talking, washing the face, or brushing the teeth. The condition can impair activities of daily living and lead to depression.

In some persons, there remains a background pain of lower intensity for 50% of the time. This has been termed atypical trigeminal neuralgia or type 2 trigeminal neuralgia. The International Classification for Headache Disorders refers to this condition as trigeminal neuralgia with concomitant pain. Other causes of facial pain may need to be excluded. In trigeminal neuralgia, the

neurologic examination is usually normal but sensory and autonomic symptoms may be reported, and persons with longer histories may demonstrate subtle sensory loss on careful examination.

### Incidence and Prevalence

Most evidence about the incidence and prevalence of trigeminal neuralgia is from the United States. The annual incidence (age adjusted to the 1980 age distribution of the United States) is 5.9 per 100,000 women and 3.4 per 100,000 men. The incidence tends to be slightly higher in women at all ages, and increases with age. In men older than 80 years, the incidence is 45.2 per 100,000. One questionnaire survey of neurologic disease in a French village found one out of 993 persons had trigeminal neuralgia. A retrospective cohort study in UK primary care, which examined the histories of 6.8 million persons, found that 8,268 persons had trigeminal neuralgia, giving it an incidence of 26.8 per 100,000 person-years. A similar primary care study carried out in the Netherlands reported an incidence of 12.6 per 100,000 person-years when trained neurologists reviewed the data. A population-based study in Germany reported a lifetime prevalence of 0.3%.

### Etiology and Risk Factors

The cause of trigeminal neuralgia remains unclear, but the most common hypothesis is that of the ignition theory. More peripheral and central mechanisms may be involved, and trigeminal nerve microstructure may be altered. It is more common in persons with multiple sclerosis (relative risk = 20.0; 95% confidence interval, 4.1 to 59.0) and stroke. Hypertension is a risk factor in women (relative risk = 2.1; 95% confidence interval, 1.2 to 3.4), but the evidence is less clear for men

(relative risk = 1.53; 95% confidence interval, 0.30 to 4.50).

### Prognosis

One retrospective cohort study found no reduction in 10-year survival in persons with trigeminal neuralgia. We found no evidence about the natural history of trigeminal neuralgia. However, the TNA Facial Pain Association continues to periodically receive individual isolated reports of persons with trigeminal neuralgia who either die from overdose of medications, take their own life, or both. The illness is characterized by recurrences and remissions. Many persons have periods of remission with no pain lasting months or years. At least 50% of persons with trigeminal neuralgia will have remissions lasting at least six months.

Collective expert experience suggests that, in many persons, trigeminal neuralgia becomes more severe and less responsive to treatment over time, despite increasing medication doses and adding additional agents. Most persons with trigeminal neuralgia are initially managed medically, and some eventually have a surgical procedure. We found no good evidence about the proportion of persons who require surgical treatment for pain control. Anecdotal evidence indicates that pain relief is better after surgery than with medical treatment. Furthermore, responses from a questionnaire taken by persons who had surgery for trigeminal neuralgia indicated that the majority of respondents wished they had surgery earlier.

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