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內文：

**Purpose:**
This study undertook a systematic review of the literature on drug treatment of trigeminal neuralgia.

**Methods:**
**January 1960 to February 2005**. The following key words and Boolean operators were used, “Trigeminal neuralgia AND treatment,” “anticonvulsants,” “carbamazepine” “oxcarbazepine” “gabapentin” “phenytoin” “lamotrigen,” “clonazepam” “antidepressants” “amitriptylin” “protriptyline” “nortriptyline” “fluoxetine” “trazodone” “baclofen” “nonsteroidal anti-inflammatory drugs” “opioids” “cafergot” “mexiletine” “misoprostol” “pimozide” “sumatriptan” “valproic acid.”
The literature search was conducted in **February 2005** using the following database:
● **PubMed** (National Library of Medicine; NLM).
PubMed is NLM’s online search interface for MEDLINE and PreMEDLINE (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi);
● **lWebSPIRS (Silverplatter) MEDLINE**: CD-ROM database(1990 to 2000);
● **International Poster Journal of Dentistry and Oral Medicine**: online database (http://ipj.quintessenz.de).
The primary focus of the search was on systematic reviews and meta-analysis of randomized controlled trials that used drug treatment for trigeminal neuralgia(evidence level Ia). Then randomized controlled trials(evidence level Ib), clinical trials without randomization(evidence levels IIa), and other experimental studies (evidence level IIb) were considered. Publications with evidence level III and IV were not included in the evaluation. The levels of evidence of the articles were classified following the guidelines of the Oxford Centre for Evidence-Based Medicine (http://www.cebm.net/levels_of_evidence.asp).

**Results:**
Of 770 publications only **21 publications** showed a high level of evidence (6 randomized controlled trials and 15 clinical trials/controlled clinical trials), with a total of **348 patients**. A total of 749 publications were not included in the review as they showed a low level of evidence.

**Table 1. SUMMARY OF RESULTS OF RANDOMIZED CONTROLLED TRIALS OF DRUG TREATMENT OF TRIGEMINAL NEURALGIA**

| Study | Drugs Used | Comparison | Design | Total No. of Patients | Total No. of Patients Benefited (%) | Adverse Effects |
|---|---|---|---|---|---|---|
| Fromm et al (1993) | Tizanidine | — | Crossover | 10 | 80 | — |
| Kramlinger et al (1994) | CBZ | — | — | 113 | — | Rash in 12% patients |
| Zakrzewska (1997) | Lamotrigine | Placebo | Crossover | 13 | 84.61 | Dose-dependent effects on CNS |
| Simpson (2000) | Lamotrigine | Placebo | — | 42 | — | Rash in 11.9% patients |
| Gilron et al (2001) | Topiramate | Placebo | Crossover | 3 | 100 | — |

Abbreviations: CBZ, carbamazepine; CNS, central nervous system.

*Chole et al. Drug Treatment of Trigeminal Neuralgia. J Oral Maxillofac Surg 2007.*

**Table 2. SUMMARY OF RESULTS OF CLINICAL TRAILS/CONTROLLED CLINICAL TRIALS OF DRUG TREATMENT OF TRIGEMINAL NEURALGIA**

| Study | Drugs Used | Total No. of Patients | Total No. of Patients Benefited (%) |
|---|---|---|---|
| Tomson (1981) | CBZ | 8 | 100 |
| Farago (1987) | CBZ analogues: | | 100 |
| | (i) Dihydroketo | 13 | |
| | (ii) Dihydromono-hydroxy | 11 | |
| Liebel (2001) | Oxcarbazepine and CBZ | 48 | 100 Benefited with oxcarbazepine<br>95 Benefited with CBZ |
| Zakrzewska et al (2002) | Oxcarbazepine | 15 | 100 Benefited initially<br>80 Patients required surgery |
| Lindstrom (1987) | Tocainide and CBZ | 12 | — |
| Lechin et al (1989) | Pimozide and CBZ | 48 | 100 Benefited with pimozide<br>56 Benefited with CBZ |
| Vilming (1986) | Tizanidine | 6 | Effects of tizanidine were inferior to those of CBZ |
| | CBZ | 6 | |
| Merren (1998) | Gabapentin | 60 | 65 |
| Delvaux et al (2001) | Lamotrigen | 25 | 100 |
| Steardo et al (1984) | Baclofen | 25 | All patients were improved by 68.61 |
| Fromm (1984) | Baclofen | 60 | 30 |
| Parmar (1989) | Baclofen | 20 | 65 |
| From et al (1987) | L-Baclofen and racemic baclofen | 9 | 66.6 |

Abbreviation: CBZ, carbamazepine.

*Chole et al. Drug Treatment of Trigeminal Neuralgia. J Oral Maxillofac Surg 2007.*

**Discussion:**

1. Anticonvulsants are usually most effective for treating classical trigeminal neuralgia pain
2. Tomson et al3 studied diurnal pain distribution, its relation to carbamazepine dosing and plasma concentration, and the effect of decreasing the dose. The diurnal pain distribution showed marked intraindividual similarities with pain-free nights and a significant
   drop in pain during mid-day hours. The latter coincided in time with the peak plasma concentration of CBZ, thus indicating an effect of plasma concentration fluctuations on pain relief.
3. Farago tested the dihydroketo and dihydromonohydroxy analogues of carbamazepine against carbamazepine for efficacy and tolerability in trigeminal neuralgia. Doses almost twice as high as those of carbamazepine are needed to achieve freedom from symptoms with the carbamazepine analogues. Because unwanted effects, in the form of dizziness and ataxia, occur much less frequently than with carbamazepine,the analogues can be administered in higher doses.
4. Gabapentin offers an effective, safe, alternative therapy or cotherapy for trigeminal neuralgia. Well-tolerated. Best responses occur in patients with peripherally mediated neuropathic pain.
5. Lamotrigine is a chemically novel antiepileptic drug. Blocks voltage sensitive sodium channels and inhibits release of glutamate and aspartate.

6. Clonazepam seems to be an effective drug in idiopathic trigeminal neuralgia
7. Oxcarbazepine is a potent antineuralgic drug with very good acceptability and tolerability
8. Tizanidine partly resembled carbamazepine and baclofen in that it depressed excitatory transmission and facilitated segmental inhibition of neurons in the spinal trigeminal nucleus oralis.
   The limited efficacy of tizanidine in the treatment of trigeminal neuralgia may be related to the fact that it has no effect on neuronal responses to low-threshold mechanoceptive stimuli, suggesting that low-threshold mechanoceptive neurons play an important role in the pathogenesis of trigeminal neuralgia.
9. Pimozide produced greater reduction in symptoms than carbamazepine
10. Baclofen is a new antineuralgic drug. Resembles carbamazepine and phenytoin in its effects on the spinal trigeminal nucleus of cats; however baclofen gives less undesirable side effects.
11. Antidepressants tend to be particularly effective for atypical forms of trigeminal neuralgia.
    Clomipramine is the most potent 5-HT reuptake blockade agent among antidepressants. Clomipramine was better tolerated than amitriptyline . The results support the hypothesis that in certain pain situations, clomipramine exerts a beneficial effect, not only because of its effect on the depression and anxiety level of the patient, but also via its effects on the 5-HT brain system.
12. Epstein et al studied the efficacy of topical capsaicin in neuropathic and neuralgic pain and the effect of differing dosages and frequency of application. On the basis of the findings in this open-label clinical trial, controlled clinical study of capsaicin in neuropathic oral pain states seems warranted.

**Conclusion:**

1. Anticonvulsants are effective in treating trigeminal neuralgia.
2. Carbamazepine and its analogues were effective in trigeminal neuralgia in one study each.
3. Phenytoin is considered the second drug of choice in trigeminal neuralgia after the failure of carbamazepine but our research did not show a single study with high level of evidence on phenytoin.
4. Lamotrigine is effective in refractory trigeminal neuralgia; however, adverse effect may occur.
5. Only 1 study showed the effectiveness of gabapentin, clonazepam, and topiramate each and further research is needed to prove their efficacy.
6. The effects of tizanidine are inferior to that of carbamazepine and recurrence may occur.
7. Oxcarbazepine, lamotrigine, and pimozide offer satisfactory treatment in refractory trigeminal neuralgia.
8. Baclofen, a skeletal muscle relaxant, also provides promising results mainly in refractory trigeminal neuralgia.
9. Common side effects associated with these agents typically involve the central nervous system and include sedation, dizziness, ataxia, and nausea.
10. In addition, hematologic toxicity and skin rash can be induced by the older anticonvulsants like carbamazepine. No drug has shown superiority over carbamazepine at acceptable toxicities.
11. An antidepressant like clomipramine is better than amitriptyline in treating trigeminal neuralgia.
12. Anticonvulsants are effective in treating trigeminal neuralgia; however, few

studies with high levels of evidence were found. It is quite difficult to compare or even combine their outcomes in a scientifically meaningful manner. Due to insufficient research data, there is a need for high-quality randomized controlled trials in this area of medicine.

| 題號 | 題目 |
|---|---|
| 1 | 下列疾病何者和Trigeminal neuralgia有關?<br>(A) Gradenigo syndrome<br>(B) Neuralgia-inducing cavitational osteonecrosis<br>(C) Chronic paroxysmal hemicrania-tic syndrome<br>(D) Multiple sclerosis |
| 答案(D) | 出處：Oral & Maxillofacial Pathology, second edition,P.743 |
| 題號 | 題目 |
| 2 | Trigeminal neuralgia的Trigger point最少出現在下列何處? |
| | (A) Alveolus<br>(B) Nasolabial fold<br>(C) Vermilion border of lip<br>(D) Midfacial and periorbital skin |
| 答案(A) | 出處：Oral & Maxillofacial Pathology, second edition,P.743 |