Robust randomised control trials needed for drug treatments for trigeminal neuralgia

What is the efficacy of non-antiepileptic drugs used to treat trigeminal neuralgia?

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Data sources Searches for appropriate studies were made using the following: Cochrane Neuromuscular Disease Group Register, Medline, Embase and LILACS (Latin American and Caribbean Literature on the Health Sciences) together the Chinese Biomedical Retrieval System, the database of the Chinese Cochrane Centre, conference paper databases and checked bibliographies. 10 Chinese journals were searched by hand.
Study selection Randomised controlled trials (RCT) or quasi-randomised controlled trials were included.
Data extraction and synthesis Two authors decided which trials fitted the inclusion criteria and graded methodological quality independently.
Results Nine trials of different non-antiepileptic drugs involving 223 participants were included. Each trial investigated one non-antiepileptic drug.

Two trials tested baclofen. In one, more people achieved 50% reduction from baseline than with placebo [relative risk (RR), 15.00; 95% confidence interval (CI), 0.97–231.84; P 0.05]. In the other, slightly more participants who took baclofen showed a 75% reduction in attacks on the tenth day compared with carbamazepine (RR, 2.38; 95% CI, 0.83–6.85; P 0.11). One trial showed no significant difference in reduction in average daily frequency of attacks with Baclofen compared with Racemic Baclofen.

Tizanidine was investigated in two trials. In one, the proportion of people with a reduction in the mean number of paroxysms per day increased with tizanidine compared with placebo (RR, 8.00; 95% CI, 1.21–52.69; *P* 0.03). In the other, one of five participants improved their visual analogue scale score with tizanidine and four of six did so having taken carbamazepine (RR, 0.30; 95% CI, 0.05–1.89; *P* 0.20).

One study showed that the improvement in mean values of pain scores with tocainide was similar to that of carbamazepine. In a further trial, more participants improved during the pimozide than the carbamazepine period (RR, 1.78; 95% CI, 1.39–2.28). In another, a 0.5% instillation of proparacaine hydrochloride into the eyes did not produce significantly different results from placebo (RR, 1.06; 95% CI, 0.37–2.99; *P* 0.92). Finally, there was moderate or marked improvement in a study in seven of nine participants who took clomipramine and three of nine who took amitriptyline during a 12-week treatment (RR, 2.33; 95% CI, 0.87–6.27).
Conclusions Trials of non-antiepileptic drugs for treating trigeminal neuralgia have all been limited by poor methodological quality or poor reporting. There is insufficient evidence from randomised clinical trials to show significant benefit from non-antiepileptic drugs for trigeminal neuralgia.

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Commentary

This is a systematic review of non-antiepileptic medications used in trigeminal neuralgia, a subject covered already by several systematic reviews.[1–3] Randomised controlled trials for trigeminal neuralgia are in fact very difficult to design. This is for a number of reasons. The condition is rare and its precise natural history is unknown. It is also well-recognised that, especially in the early stages of the disease process, there are long periods of complete pain remission with no need for drug therapy: this can act as a major confounder in clinical trials. When the attacks do occur, however, they are often very severe and therefore it becomes difficult to justify the use of a placebo.

The gold standard of therapy is carbamazepine, but this is a difficult drug to use as an active control. It takes about 3 weeks for it to be totally excreted from the body and, being a liver enzyme inducer, it reacts with many drugs. All non-antiepileptic drugs cause side-effects, especially neurological ones such as drowsiness and ataxia. Therefore there is a need to look at other non-antiepileptic drugs especially if they may provide effective pain control with fewer side effects.

This systematic review shows yet again that the methodology and reporting of trials in medical management of trigeminal neuralgia are of poor quality. Hence, the results are difficult to interpret and no drug can be recommended to be effective. The clinician must thus continue to rely upon carbamazepine as the first-line drug. Baclofen may be useful in people who have multiple sclerosis who are already using this drug to help control their spasticity.

This review also highlights the need to review the design of RCT in trigeminal neuralgia taking into account the factors mentioned above. RCT of trigeminal neuralgia need to state clearly the diagnostic criteria used for inclusion of patients into the studies, and the outcome measures used must be more robust and varied, as suggested by the IMMPACT group (Initiative on Methods, Measurement and Pain Assessment in Clinical Trials) of the International Association for the Study of Pain. That group suggests the use of outcome measures from a wide range of domains, varying from pain severity and intensity through to quality of life and psychological parameters.[4] There are a range of new drugs on the market await evaluation in robust RCT in order to increase the number of drugs available for patients with trigeminal neuralgia.

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