Levetiracetam for neuropathic pain in adults
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Authors' objectives
Background: Antiepileptic drugs have been used in pain management since the 1960s; some have shown efficacy in treating different neuropathic pain conditions. The efficacy of levetiracetam for relief of neuropathic pain has not previously been reviewed.

Objectives: To assess the analgesic efficacy and adverse events of levetiracetam in chronic neuropathic pain conditions in adults.

Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (2014, Issue 6) (via the Cochrane Library), MEDLINE, EMBASE, and two clinical trials databases (ClinicalTrials.gov. and the World Health Organisation Clinical Trials Registry Platform) to 3 July 2014, together with reference lists of retrieved papers and reviews.

Selection criteria: We included randomised, double-blind studies of two weeks duration or longer, comparing levetiracetam with placebo or another active treatment in adults with chronic neuropathic pain conditions. Studies had to have a minimum of 10 participants per treatments arm.

Data collection and analysis: Two review authors independently extracted efficacy and adverse event data, and examined issues of study quality. We performed analysis using three tiers of evidence. First tier evidence derived from data meeting current best standards and subject to minimal risk of bias (outcome equivalent to substantial pain intensity reduction; intention-to-treat analysis without imputation for dropouts; at least 200 participants in the comparison; 8 to 12 weeks duration; parallel design); second tier evidence from data that failed to meet one or more of these criteria and that we considered at some risk of bias but with at least 200 participants in the comparison; and third tier evidence from data involving fewer than 200 participants that was considered very likely to be biased or used outcomes of limited clinical utility, or both.

Main results: We included six studies: five small, cross-over studies with 174 participants, and one parallel group study with 170 participants. Participants were treated with levetiracetam (2000 mg to 3000 mg daily) or placebo for between four and 14 weeks. Each study included participants with a different type of neuropathic pain; central pain due to multiple sclerosis, pain following spinal cord injury, painful polyneuropathy, central post-stroke pain, postherpetic neuralgia, and post-mastectomy pain. None of the included studies provided first or second tier evidence. The evidence was very low quality, downgraded because of the small size of the treatment arms, and because studies reported results using last observation carried forward (LOCF) imputation for withdrawals or using only participants who completed the study according to the protocol, where there were greater than 10% withdrawals. There were insufficient data for a pooled efficacy analysis in particular neuropathic pain conditions, but individual studies did not show any analgesic effect of levetiracetam compared with placebo. We did pool results for any outcome considered substantial pain relief (? 50% pain intensity reduction or ?complete? or ?good? responses on the verbal rating scale) for four studies with dichotomous data; response rates across different types of neuropathic pain was similar with levetiracetam (10%) and placebo (12%), with no statistical difference (risk ratio 0.9; 95% confidence interval (CI) 0.4 to 1.7). We pooled data across different conditions for adverse events and withdrawals. Based on very limited data, significantly more participants experienced an adverse event with levetiracetam than with placebo (number needed to treat for an additional harmful event (NNH) 8.0 (95% CI 4.6 to 32)). There were significantly more adverse event withdrawals with levetiracetam (NNH 9.7 (6.7 to 18)).

Authors' conclusions: The amount of evidence for levetiracetam in neuropathic pain conditions was very small and potentially biased because of the methods of analysis used in the studies. There was no indication that levetiracetam was effective in reducing neuropathic pain, but it was associated with an increase in participants who experienced adverse events and who withdrew due to adverse events.


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