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Antiepileptic drugs for neuropathic pain and fibromyalgia - an overview of Cochrane reviews.

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Abstract

BACKGROUND: Antiepileptic drugs have been used for treating different types of neuropathic pain, and sometimes fibromyalgia. Our understanding of quality standards in chronic pain trials has improved to include new sources of potential bias. Individual Cochrane reviews using these new standards have assessed individual antiepileptic drugs. An early review from this group, originally published in 1998, was titled 'Anticonvulsants for acute and chronic pain'. This overview now covers the neuropathic pain aspect of that original review, which was withdrawn in 2009.

OBJECTIVES: To provide an overview of the relative analgesic efficacy of antiepileptic drugs that have been compared with placebo in neuropathic pain and fibromyalgia, and to report on adverse events associated with their use.

METHODS: We included reviews published in theCochrane Database of Systematic Reviews up to August 2013 (Issue 7). We extracted information from each review on measures of efficacy and harm, and methodological details concerning the number of participants, the duration of studies, and the imputation methods used, in order to judge potential biases in available data.We analysed efficacy data for each painful condition in three tiers, according to outcome and freedom from known sources of bias. The first tier met current best standards - at least 50% pain intensity reduction over baseline (or its equivalent), without the use of last observation carried forward (LOCF) for dropouts, an intention-to-treat (ITT) analysis, in parallel group studies with at least 200 participants lasting eight weeks or more. The second tier used data from at least 200 participants where one or more of the above conditions were not met. The third tier of evidence related to data from fewer than 200 participants, or with several important methodological problems that limited interpretation.

MAIN RESULTS: No studies reported top tier results.For gabapentin and pregabalin only we found reasonably good second tier evidence for efficacy in painful diabetic neuropathy and postherpetic neuralgia. In addition, for pregabalin, we found evidence of efficacy in central neuropathic pain and fibromyalgia. Point estimates of numbers needed to treat for an additional beneficial effect (NNTs) were in the range of 4 to 10 for the important outcome of pain intensity reduction over baseline of 50% or more.For other antiepileptic drugs there was no evidence (clonazepam, phenytoin), so little evidence that no sensible judgement could be made about efficacy (valproic acid), low quality evidence likely to be subject to a number of biases overestimating efficacy (carbamazepine), or reasonable quality evidence indicating little or no effect (lamotrigine, oxcarbazepine, topiramate). Lacosamide recorded such a trivial statistical superiority over placebo that it was unreliable to conclude that it had any efficacy where there was possible substantial bias.Any benefits of treatment came with a high risk of adverse events and withdrawal because of adverse events, but serious adverse events were not significantly raised, except with oxcarbazepine.

AUTHORS' CONCLUSIONS: Clinical trial evidence supported the use of only gabapentin and pregabalin in

some neuropathic pain conditions (painful diabetic neuropathy, postherpetic neuralgia, and central neuropathic pain) and fibromyalgia. Only a minority of people achieved acceptably good pain relief with either drug, but it is known that quality of life and function improved markedly with the outcome of at least 50% pain intensity reduction. For other antiepileptic drugs there was no evidence, insufficient evidence, or evidence of a lack of effect; this included carbamazepine. Evidence from clinical practice and experience is that some patients can achieve good results with antiepileptics other than gabapentin or pregabalin.There is no firm evidence to answer the important pragmatic questions about which patients should have which drug, and in which order the drugs should be used. There is a clinical effectiveness research agenda to provide evidence about strategies rather than interventions, to produce the overall best results in a population, in the shortest time, and at the lowest cost to healthcare providers.

Comment in

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