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The Role of Levetiracetam in Treating Chronic Neuropathic Pain Symptoms

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Clinical Question

In patients with chronic neuropathic pain, does levetiracetam (Keppra) effectively treat pain symptoms?

Evidence-Based Answer

Based on low-quality evidence, levetiracetam was found to be ineffective for the treatment of chronic neuropathic pain symptoms. Moreover, patients who were taking levetiracetam experienced adverse effects at a significantly higher rate than those who were taking placebo. (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

Chronic neuropathic pain is commonly encountered in primary care, with a prevalence between 7% and 10% in one systematic review.[1] By some estimates, the prevalence of such conditions as diabetic neuropathy and postsurgical chronic pain is increasing.[2] Chronic pain reduces quality of life, hinders employment, and increases costs and utilization of health care.[3] Less than 30% of patients with diabetic neuropathy and less than 13% of patients with fibromyalgia achieve a 50% reduction in pain intensity with available treatments.[4] Therefore, interest is high in exploring novel agents that may prove more effective. Levetiracetam is an anticonvulsant with a unique (and not yet fully understood) mode of action that has been investigated as a possible treatment for chronic neuropathic pain.

In this Cochrane review, the authors analyzed the effectiveness and relative safety of levetiracetam in the treatment of chronic neuropathic pain in adults. They included only published, high-quality, peer-reviewed randomized controlled trials that compared levetiracetam at any dose with placebo for several different neuropathic pain conditions. The authors used the standardized definitions of moderate and substantial benefit in chronic pain studies from the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT).[5] Moderate benefit is defined as at least 30% pain relief over baseline, and substantial benefit is defined as at least 50% pain relief over baseline.

The review included six studies of 344 patients with six different types of neuropathic pain (i.e., central pain caused by multiple sclerosis, pain following spinal cord injury, painful polyneuropathy, central poststroke pain, postherpetic neuralgia, and postmastectomy pain). None of the studies found a significant benefit to pharmacotherapy with levetiracetam for chronic neuropathic pain, although the pooling of data across studies was not possible.

Moreover, 67% of participants experienced adverse effects from levetiracetam therapy compared with 54% of the participants who were taking placebo (number needed to treat to harm = 8). The most commonly reported adverse effects of levetiracetam therapy included fatigue or tiredness, dizziness, headache, constipation, and nausea. Participants in the treatment arm were nearly five times as likely to withdraw from the study because of adverse effects compared with those who were randomized to placebo. Given the lack of benefit, the likelihood of increased adverse effects, and the findings of other research studies suggesting the benefit of alternative agents in chronic neuropathic pain, the authors recommend against using levetiracetam for this indication.

In a review from 2010, the Neuropathic Pain Special Interest Group of the International Association for the Study of Pain

released evidence-based guidelines for the pharmacologic treatment of neuropathic pain.[6] These guidelines recommend the use of tricyclic antidepressants, dual reuptake inhibitors of serotonin and norepinephrine, calcium channel alpha-2-delta ligands (e.g., gabapentin [Neurontin], pregabalin [Lyrica]), and topical lidocaine as first-line therapies. According to the guidelines, opioid analgesics and tramadol were considered second-line agents for the treatment of neuropathic pain symptoms.

SOURCE: Wiffen PJ, Derry S, Moore RA, Lunn MP. Levetiracetam for neuropathic pain in adults. *Cochrane Database Syst Rev.* 2014;(7):CD010943.

The practice recommendations in this activity are available at http://summaries.cochrane.org/CD010943.

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