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Abstract

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High-dose oral dextromethorphan versus placebo in painful diabetic neuropathy and postherpetic neuralgia.

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Abstract

N-methyl-D-aspartate (NMDA) receptor antagonists relieve neuropathic pain in animal models, but side effects of dissociative anesthetic channel blockers, such as ketamine, have discouraged clinical application. Based on the hypothesis that low-affinity NMDA channel blockers might have a better therapeutic ratio, we carried out two randomized, double-blind, crossover trials comparing six weeks of oral dextromethorphan to placebo in two groups, made up of 14 patients with painful distal symmetrical diabetic neuropathy and 18 with postherpetic neuralgia. Thirteen patients with each diagnosis completed the comparison. Dosage was titrated in each patient to the highest level reached without disrupting normal activities; mean doses were 381 mg/day in diabetics and 439 mg/day in postherpetic neuralgia patients. In diabetic neuropathy, dextromethorphan decreased pain by a mean of 24% (95% CI: 6% to 42%, p = 0.01), relative to placebo. In postherpetic neuralgia, dextromethorphan did not reduce pain (95% CI: 10% decrease in pain to 14% increase in pain, p = 0.72). Five of 31 patients who took dextromethorphan dropped out due to sedation or ataxia during dose escalation, but the remaining patients all reached a reasonably well-tolerated maintenance dose. We conclude that dextromethorphan or other low-affinity NMDA channel blockers may have promise in the treatment of painful diabetic neuropathy.

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