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Dextromethorphan and memantine in painful diabetic neuropathy and postherpetic neuralgia: efficacy and dose-response trials.

Sang CN[1], Booher S, Gilron I, Parada S, Max MB.

Author information

Abstract

BACKGROUND: There are few repeated dose-controlled trials of N-methyl-d-aspartate glutamate receptor antagonists in patients with neuropathic pain. The authors sought to evaluate two low-affinity N-methyl-d-aspartate antagonists using a novel two-stage design.

METHODS: The authors studied patients with painful diabetic neuropathy (DN) and postherpetic neuralgia (PHN) in two crossover trials: (1) efficacy trial (dextromethorphan vs. memantine vs. active placebo [lorazepam]) and (2) dose-response trial of the preferred active drug in responders from the first study (0% vs. 25% vs. 50% vs. 100% of each patient's maximally tolerated dose). Pain intensity was measured on a 20-point scale.

RESULTS: Nineteen of 23 DN patients and 17 of 21 PHN patients completed the efficacy trial. Median doses for DN and PHN were 400 and 400 mg/day dextromethorphan, 55 and 35 mg/day memantine, and 1.8 and 1.2 mg/day lorazepam. In the efficacy trial, among patients with DN, dextromethorphan reduced pain intensity by a mean of 33% from baseline, memantine reduced pain intensity by a mean of 17%, and lorazepam reduced pain intensity by a mean of 16%; the proportions of subjects achieving greater than moderate pain relief were 68% with dextromethorphan, 47% with memantine, and 37% with lorazepam. Mean reductions in pain intensity in patients with PHN were 6% with dextromethorphan, 2% with memantine, and 0% with lorazepam. No comparison with placebo reached statistical significance in the efficacy trial. In the 10 DN subjects who responded to dextromethorphan, there was a significant dose-response effect on pain intensity (P = 0.035), with the highest dose significantly better than that of lorazepam (P = 0.03).

CONCLUSIONS: Dextromethorphan is effective in a dose-related fashion in selected patients with DN. This was not true of PHN, suggesting a difference in pain mechanisms. Selective approaches to pain-relevant N-methyl-d-aspartate receptors are warranted.

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