PubMed Search term

↓ Full text

Effect of Dextromethorphan-Quinidine on Agitation in Patients With Alzheimer Disease Dementia: A Randomized Clinical Trial.

Randomized controlled trial

Cummings JL, et al. JAMA. 2015 Sep 22-29.
Show full citation

Abstract

IMPORTANCE: Agitation is common among patients with Alzheimer disease; safe, effective treatments are lacking.

OBJECTIVE: To assess the efficacy, safety, and tolerability of dextromethorphan hydrobromide-quinidine sulfate for Alzheimer disease-related agitation.

DESIGN, SETTING, AND PARTICIPANTS: Phase 2 randomized, multicenter, double-blind, placebo-controlled trial using a sequential parallel comparison design with 2 consecutive 5-week treatment stages conducted August 2012-August 2014. Patients with probable Alzheimer disease, clinically significant agitation (Clinical Global Impressions-Severity agitation score ≥4), and a Mini-Mental State Examination score of 8 to 28 participated at 42 US study sites. Stable dosages of antidepressants, antipsychotics, hypnotics, and antidementia medications were allowed.

INTERVENTIONS: In stage 1, 220 patients were randomized in a 3:4 ratio to receive dextromethorphan-quinidine (n = 93) or placebo (n = 127). In stage 2, patients receiving dextromethorphan-quinidine continued; those receiving placebo were stratified by response and rerandomized in a 1:1 ratio to dextromethorphan-quinidine (n = 59) or placebo (n = 60).

MAIN OUTCOMES AND MEASURES: The primary end

Similar articles

Effect of citalopram on agitation in Alzheimer disease: the CitAD randomized clinical trial.
Randomized controlled trial
Porsteinsson AP, et al. JAMA. 2014.

Management of agitation, aggression, and psychosis associated with dementia: a pooled analysis including three randomized, placebo-controlled double-blind trials in nursing home residents treated with risperidone.
De Deyn PP, et al. Clin Neurol Neurosurg. 2005.

A randomized, double-blind, placebo-controlled trial of memantine in a behaviorally enriched sample of patients with moderate-to-severe Alzheimer's disease.
Randomized controlled trial
Herrmann N, et al. Int Psychogeriatr. 2013.

Antidepressants for agitation and psychosis in dementia.
Review article
Seitz DP, et al. Cochrane Database Syst Rev. 2011.

Dextromethorphan/quinidine: in pseudobulbar affect.
Review article
Garnock-Jones KP, et al. CNS Drugs. 2011.

See all

point was change from baseline on the Neuropsychiatric Inventory (NPI) Agitation/Aggression domain (scale range, 0 [absence of symptoms] to 12 [symptoms occur daily and with marked severity]).

RESULTS: A total of 194 patients (88.2%) completed the study. With the sequential parallel comparison design, 152 patients received dextromethorphan-quinidine and 127 received placebo during the study. Analysis combining stages 1 (all patients) and 2 (rerandomized placebo nonresponders) showed significantly reduced NPI Agitation/Aggression scores for dextromethorphan-quinidine vs placebo (ordinary least squares z statistic, -3.95; P < .001). In stage 1, mean NPI Agitation/Aggression scores were reduced from 7.1 to 3.8 with dextromethorphan-quinidine and from 7.0 to 5.3 with placebo. Between-group treatment differences were significant in stage 1 (least squares mean, -1.5; 95% CI, -2.3 to -0.7; P<.001). In stage 2, NPI Agitation/Aggression scores were reduced from 5.8 to 3.8 with dextromethorphan-quinidine and from 6.7 to 5.8 with placebo. Between-group treatment differences were also significant in stage 2 (least squares mean, -1.6; 95% CI, -2.9 to -0.3; P=.02). Adverse events included falls (8.6% for dextromethorphan-quinidine vs 3.9% for placebo), diarrhea (5.9% vs 3.1% respectively), and urinary tract infection (5.3% vs 3.9% respectively). Serious adverse events occurred in 7.9% with dextromethorphan-quinidine vs 4.7% with placebo. Dextromethorphan-quinidine was not associated with cognitive impairment, sedation, or clinically significant QTc prolongation.

CONCLUSIONS AND RELEVANCE: In this preliminary 10-week phase 2 randomized clinical trial of patients with probable Alzheimer disease, combination dextromethorphan-quinidine demonstrated clinically relevant efficacy for agitation and was generally well tolerated.

TRIAL REGISTRATION: clinicaltrials.gov Identifier: