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1: 2005 Jan-Mar;19(1):23-8.

Propranolol for disruptive behaviors in nursing home residents with probable or possible Alzheimer disease: a placebo-controlled study.

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OBJECTIVE: Enhanced behavioral responsiveness to central nervous system (CNS) norepinephrine (NE) in Alzheimer disease (AD) may contribute to the pathophysiology of disruptive behaviors such as aggression, uncooperativeness with necessary care, irritability, and pressured pacing. We evaluated the efficacy of the beta-adrenergic antagonist propranolol for treatment-resistant disruptive behaviors and overall behavioral status in nursing home residents with probable or possible AD. METHODS: Thirty-one subjects (age 85 +/- 8 [SD]) with probable or possible AD and persistent disruptive behaviors that interfered with necessary care were randomized to propranolol (n = 17) or placebo (n = 14) in a double-blind study. Stable doses of previously prescribed psychotropics were maintained at pre-study dose during the study. Following a propranolol or placebo dose titration period of up to 9 days (per a dosing algorithm), subjects were maintained on maximum achieved dose for 6 weeks. Primary outcome measures were the Neuropsychiatric Inventory (NPI) and the Clinical Global Impression of Change (CGIC). RESULTS: Propranolol augmentation (mean achieved dose 106 +/- 38 mg/d) was significantly more effective than placebo for improving overall behavioral status on the total NPI score and CGIC. Improvement in individual NPI items within propranolol subjects was significant only for "agitation/aggression" and "anxiety," and reached borderline statistical significance favoring propranolol over placebo only for "agitation/aggression." Pressured pacing and irritability did not appear responsive to propranolol. In propranolol subjects rated "moderately improved" or "markedly improved" on the CGIC at the end of the double-blind study phase, improvement of overall behavioral status had diminished substantially after 6 months of open-label propranolol treatment. CONCLUSION: Short-term propranolol augmentation treatment appeared modestly effective and well tolerated for overall behavioral status in nursing home residents with probable or possible AD complicated by disruptive behaviors. Propranolol may be helpful specifically for aggression and uncooperativeness (the behaviors assessed by the NPI "agitation/aggressiveness" item). However, the usefulness of propranolol in this very old and frail population was limited by the high frequency of relative contraindications to beta-adrenergic antagonist treatment and diminution of initial behavioral improvements over time.

PMID: 15764868 [PubMed - indexed for MEDLINE]