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# Citalopram of limited use for dementia-associated agitation

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By Lucy Piper, Senior medwireNews Reporter

The use of citalopram for the treatment of agitation in Alzheimer's disease may be limited to a small group of people with moderate agitation and low levels of cognitive impairment, study findings suggest.

For patients with moderate-to-severe cognitive impairment and more severe agitation, citalopram, at a daily dose of 30 mg, is likely to be ineffective or potentially harmful, the researchers warn.

"[A]long with the established associations of citalopram with delayed cardiac repolarization and with cognitive impairment and given safety concerns of antidepressants for depressed elderly patients and the [Food and Drug Administration's] recommendation to avoid citalopram dosages over 20 mg/day in patients over age 60, citalopram may have limited use for treating agitation in Alzheimer's disease", they write.

Predictors of treatment outcome were assessed in 186 patients with Alzheimer's disease and clinically significant agitation who were randomly assigned to receive citalopram or placebo for 9 weeks. The drug dose was titrated to a maximum of 30 mg/day over the first 3 weeks of treatment.

The researchers, led by Lon Schneider (University of Southern California, Los Angeles, USA), found that the patients' responses to treatment were heterogeneous and there was no one factor that significantly predicted a positive response, other than living at home or with relatives rather than in long-term care.

They therefore adopted a multivariate approach and looked at the effects of covariates. The patients were grouped into decile subgroups according to their age, residency status, current treatment, the presence of psychosis, and performances on the Alzheimer's Disease Cooperative Study-Activities of Daily Living Scale, the Mini-Mental State Examination (MMSE) and the Neurobehavioral Rating Scale agitation subscale and, based on these factors, an index score for their predicted treatment response.

Analysis confirmed that the probability of response on the Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change Scale was greater with citalopram than placebo by an average of 13.6%.

And there were two groups, comprising about 20% of patients, for whom the effect of citalopram was well above the average, with differences in response probabilities of about 60% to 70%. These patients were outpatients, had the least cognitive impairment (MMSE score of 21-28), had mild agitation (Neurobehavioral Rating Scale agitation subscale score of 6-8), were in the middle age range of 76 to 82 years and were not taking lorazepam.

By contrast, there was one group, of about 10% of patients, for whom there was a large negative effect, with a response probability of approximately 70% favouring placebo.

These patients were long-term care residents, had moderate to severe cognitive impairment (MMSE score of 20 or below), had moderately severe to severe agitation (Neurobehavioral Rating Scale agitation subscale score of 9-14), were either in the youngest (47 to 75 years) or oldest (83 to 92 years) age groups and were receiving lorazepam.

"The identification of a subgroup that had markedly better outcomes on placebo suggests that patients with more severe agitation and cognitive impairment may be harmed by citalopram", says the team.

For the remaining patients, the effects of citalopram were "essentially trivial", the researchers write in *The American Journal of Psychiatry*.

They conclude: "The results support heterogeneity of clinical response to citalopram—specifically that outpatients with Alzheimer's disease without severe agitation, who do not have major depression or psychosis for which antipsychotics may be required, may benefit from citalopram compared with placebo."

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