Galantamine improved cognition and global functioning in vascular dementia or Alzheimer disease with cerebrovascular disease


**Question**
In patients with probable vascular dementia or Alzheimer disease (AD) with cerebrovascular disease, is galantamine more effective than placebo for improving cognitive ability and global functioning?

**Design**
6-month randomized (unclear allocation concealment*), blinded (clinicians and patients), placebo-controlled trial.

**Setting**
Canada, Denmark, Finland, France, Germany, Ireland, Israel, The Netherlands, Poland, and the UK.

**Patients**
592 patients (mean age 75 y, 53% men) who met clinical criteria for probable vascular dementia or possible AD with radiologic evidence of cerebrovascular disease. Additional inclusion criteria included a score of 10 to 25 on the Mini-Mental State Examination and ≥ 12 on the Alzheimer Disease Assessment Scale Cognitive subscale (ADAS-COG). Exclusion criteria included evidence of neurodegenerative disorders other than AD that might cause or contribute to dementia, and cognitive impairment resulting from cerebral trauma. Follow-up was 82% and 77% at 3 and 6 months, respectively.

**Main results**
At 6 months, improvement in cognitive ability was greater in the galantamine group than in the placebo group (Table). More patients in the galantamine group remained stable or had improved global functioning at 6 months (Table). More patients in the galantamine group than in the placebo group withdrew from the study because of adverse effects (20% vs 8%, P < 0.01).

**Conclusion**
In a mixed population of patients with probable vascular dementia or Alzheimer disease and cerebrovascular disease, galantamine was more effective than placebo for improving cognitive ability and global functioning.

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*See Glossary.

**Commentary**
Acetylcholinesterase inhibitors are thought to partially correct the cholinergic deficit characteristic of AD. Benefits from these drugs are described as short-term improvement or lack of decline in cognitive function. In this study by Erkinjuntti and colleagues of older patients with vascular dementia and AD combined with cerebrovascular disease, about one fifth (22.2%) of patients on placebo improved by ≥ 4 points on a scale (ADAS-COG11) commonly used in AD drug trials. Patients with AD were most likely to improve.

Adverse events (predominately nausea and vomiting) caused one fifth (20%) of patients in the galantamine group to discontinue the drug. Erkinjuntti and colleagues recommend a different dose-escalation regimen to minimize this complication, but gastrointestinal toxicity, common to cholinesterase inhibitors, has to be weighed against the potential benefits of galantamine. Interpretation of this study is further complicated because more patients in the galantamine group than in the placebo group were taking antispasmodics and anticholinergics (domperidone 5% vs 1%, and metoclopramide 3% vs 0%) at baseline—a curious difference possibly relevant to the study outcome, which is left unexplained in the published paper.

**References**