

Review: Galantamine improves most outcomes in suspected Alzheimer disease

Olin J, Schneider L. Galantamine for Alzheimer's disease. *Cochrane Database Syst Rev.* 2001;(2):CD001747 (latest version 01 Nov 2000).

QUESTION

In elderly persons with suspected Alzheimer disease (AD), does galantamine improve clinical global ratings, cognition, behavior, and activities of daily living?

DATA SOURCES

Studies were identified by searching with the terms galantamine and galanthamine in 14 databases and trial registers. The manufacturer of galantamine (Janssen) was also contacted.

STUDY SELECTION

Randomized, unconfounded, double-blind, placebo-controlled trials were selected if participants were elderly persons with suspected AD, if oral galantamine was studied, and if outcomes were assessed using standardized measurement tools (Clinician's Interview-Based Impression of Change plus Caregiver Input [CIBIC-plus], Alzheimer's Disease Assessment Scale—Cognitive Subscale [ADAS-cog], Alzheimer's Disease Cooperative Study—Activities of Daily Living [ADCS-ADL] scale, Disability Assessment for Dementia [DAD] scale, and Neuro-psychiatric Inventory [NPI]).

DATA EXTRACTION

Data were extracted on study quality, patient characteristics, drug dosage and duration, and outcomes.

MAIN RESULTS

6 trials met the inclusion criteria and had data suitable for analysis. 6 trials evaluated CIBIC-plus. At 6 months, galantamine in doses of 16, 24, and 32 mg/d showed improvements (Table), but a dose of 8 mg/d did not. All 3 trials evaluating ADAS-cog showed improvements of ≥ 4 points at 6 months with galantamine in doses of 16, 24, and 32 mg/d (Table) but not with a dose of 8 mg/d. 1 trial each evaluated ADCS-ADL and NPI scores: Each showed improvements with galantamine, 16 and 24 mg/d, but not with 8 mg/d. 1 trial evaluated DAD scores: Galantamine, 32 mg/d, but not 24 mg/d showed improvements. Galantamine, at least in higher doses, increased the frequency of adverse events, including tremor, anorexia, vomiting, nausea, weight

loss, headache, abdominal pain, diarrhea, dizziness, and agitation. More patients receiving galantamine stopped taking their medication because of adverse events.

CONCLUSION

In patients with suspected Alzheimer disease, galantamine, in doses between 16 and 32 mg/d, improves global clinical status, cognition, activities of daily living, and behavior but also causes more adverse events than does placebo.

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Galantamine (Gala) vs placebo for suspected Alzheimer disease*

Outcomes at 6 mo	Gala dose	Gala	Placebo	RBI (95% CI)	NNT (CI)
CIBIC-plus	16 mg/d	68%	48%	42% (21 to 67)	6 (4 to 10)
	24 mg/d†	67%	50%	32% (20 to 47)	7 (5 to 10)
	32 mg/d†	51%	37%	35% (19 to 54)	8 (6 to 14)
ADAS-cog	16 mg/d	36%	20%	82% (32 to 151)	6 (5 to 13)
	24 mg/d†	34%	18%	82% (3 to 151)	7 (5 to 13)
	32 mg/d	35%	15%	129% (52 to 248)	6 (4 to 10)

*CIBIC-plus = Clinician's Interview-Based Impression of Change plus Caregiver Input showing no change or improvement; ADAS-cog = Alzheimer's Disease Assessment Scale—Cognitive Subscale ≥ 4 points improvement. Other abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article. †Weighted events rates (≥ 1 study).

COMMENTARY

The meta-analysis by Olin and Schneider shows that galantamine has efficacy similar to tacrine, donepezil, and rivastigmine, the 3 acetylcholinesterase inhibitors (AChE-Is) currently marketed in the United States for treatment of AD. Their comparable efficacy suggests that touted unique properties, such as the allosteric modulation of nicotinic receptors with galantamine, may not confer a measurable added benefit; however, head-to-head trials of galantamine and its competitors are needed to definitively determine this. In the meantime, clinicians should continue to select an AChE-I on the basis of adverse-effect profile, patient tolerance, convenience of dosing, and cost. Although anecdotal reports show clinical improvement after switching nonresponders to a different AChE-I, no published data support this practice.

The functional dependence, behavioral disturbances, and memory loss that are part of Alzheimer disease contribute to institutionalization and caregiver stress. Because of the uncertain clinical relevance of the ADAS-cog, recent clinical trials of AD treatments have incorporated instruments to assess their effect on activities of daily living

and behavioral complications (1, 2). The slowing of decline in activities of daily living by galantamine and other AChE-Is, as well as these agents' potential to mitigate behavioral disturbances, are important reasons to recommend AChE-Is for patients with AD. Although the major clinical trials have not included patients with advanced AD, long-term, open-label studies suggest that AChE-Is may delay institutionalization (3).

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