Donepezil is more effective than galantamine for mild to moderate Alzheimer’s disease


Q What are the effects of donepezil compared with galantamine in people with mild to moderate Alzheimer’s disease?

Methods

Design Randomised controlled trial.
Allocation Concealed.
Blinding Single blinded (physicians and caregivers not blinded; assessors blinded).
Follow up period Twelve weeks.
Setting Fourteen centres in the UK, Finland, Germany, and Norway.

Patients 120 people with mild to moderate Alzheimer’s disease (minimum age 50 years; MMSE score 10–24), with a caregiver willing to participate in the study. Exclusions: previous cholinesterase inhibitor treatment; hypersensitivity to cholinesterase inhibitors, piperidine, or alkaloids; receiving medication that produces anticholinergic effects; other disease.

Intervention

Donepezil (15 mg/day for 4 weeks increased to 10 mg/day for 8 weeks); galantamine (4 mg twice daily for 4 weeks, increased to 8 mg twice daily for four weeks, then 12 mg twice daily for 4 weeks).

Outcomes Primary outcome: Physician’s and the Caregiver’s Satisfaction Questionnaires; Secondary outcomes: ADAS-cog; MMSE; Disability Assessment for Dementia (DAD) scale.

Patient follow up Donepezil group: 61/64 (95.3%) at 12 weeks; galantamine: 51/56 (91.1%) at 12 weeks.

MAIN RESULTS

At 12 weeks, physicians and caregivers reported significantly greater overall satisfaction and ease of use for donepezil compared with galantamine (physicians p<0.001; caregivers p<0.01). Donepezil significantly improved cognition and activities of daily living compared with galantamine (ADAS-cog: p<0.05; MMSE: p<0.05; DAD: p<0.05). More unscheduled clinic visits occurred with galantamine compared with donepezil (5% donepezil v 23%
galantamine, p<0.001). Adverse events were more common with galantamine compared with donepezil (67% donepezil v 73% galantamine), particularly gastrointestinal problems (46% galantamine v 25% donepezil).

CONCLUSIONS

Compared with galantamine, donepezil is easier to use and may improve cognition and functional ability in people with mild to moderate Alzheimer’s disease.

Commentary

Three cholinesterase inhibitors (donepezil, rivastigmine, and galantamine) are currently available in the UK for treating Alzheimer’s disease (the exact number varies in other countries). Although some concerns remain about the analysis of clinical trials in dementia, evidence for the efficacy of cholinesterase inhibitors in treating Alzheimer’s is based on placebo controlled trials is now quite well established. Evidence is also emerging for the effectiveness of cholinesterase inhibitors in vascular and Lewy body dementia. Because of differences in trial design and study populations, it has not been possible to conclude whether any of these drugs is more effective or better tolerated than the others—until now with the emergence of head-to-head trials as pharmaceutical companies race to find evidence that sets their drug apart.

The finding that donepezil (a once daily drug with a simple titration regimen) was preferred by clinicians and caregivers to galantamine (twice daily dose, more complex titration) is unsurprising. The secondary outcomes in this study are of greater interest; over a relatively short time span for dementia studies, and with very small numbers, donepezil appeared significantly more effective in improving cognition compared with galantamine. This is even more striking as more people dropped out of the galantamine arm of the trial, which would have exaggerated this drugs performance in Last Observation Carried Forward analyses. This is tantalising evidence that donepezil is the more effective drug.

Some caution is needed here. For example, only the raters were blind to treatment allocation, and the study was sponsored by Eisai and Pfizer, which developed and marketed donepezil. Industry sponsored trials with their inherent risk of partisan analysis and reportage may have overemphasised efficacy of other dementia treatments and there remains a compelling need for trials independent of pharmaceutical companies in this area.

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