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Does Rivastigmine Improve Cognitive Functions or Disability in Patients with Alzheimer’s Disease?

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Question

Does rivastigmine improve cognitive functions or disability in patients with Alzheimer’s disease (AD)?

Data Source

We evaluated the Cochrane systematic review of randomised controlled trials [1]. Trials were identified by searching Medline, Embase, Central Cochrane Library, Cochrane Dementia and Cognitive Improvement Group database, abstract from proceedings of the main Dementia Conferences, and by contacting the pharmaceutical company, Novartis, for unpublished and published trials. The search was updated to December 2000.

Patients

Patients with mild to moderate [Mini-Mental State Examination (MMSE) = 10–26] probable AD according to the criteria of DSM-IV and NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer’s Disease and Related Disorders Association). Patients with severe and instable illness were not tested.

Treatment

Rivastigmine 1–12 mg two to three times a day for 6 months. Two treatment groups were identified, rivastigmine 1–4 mg/day (group 1) or 6–12 mg/day (group 2).

Outcome Measures

The primary outcomes chosen were the ratings of cognitive tests [cognitive functions assessed by the Alzheimer’s Disease Assessment Scale (ADAS-Cog) and the MMSE], a functional scale [Progressive Deterioration Scale (PDS)], and a global measure [Clinician’s Interview-Based Impression of Change Scale (CIBIC-Plus)] in comparison with baseline scores, and, as measure of tolerability to the treatment, the number of patients that dropped out due to adverse events.

Quality of the Studies

All trials were randomised with adequate concealment, double-blind, parallel group and all were placebo controlled. There was

approximately a 17% drop-out rate in the placebo group and in the rivastigmine group 1, increasing to 35% in the rivastigmine group 2. Only a third of the patients that dropped out were retrieved and included in an ‘intention to treat’ analysis.

Main Results

Seven trials involving 3,370 patients with mild AD were included. At the 26 weeks’ follow-up, rivastigmine 6–12 mg/day was associated with an improvement in ADAS-Cog, in activities of daily living assessed by PDS, and in the dichotomised CIBIC-Plus Scale. The main adverse events were gastrointestinal (nausea, vomiting, diarrhoea, anorexia, or abdominal pain), severe enough to cause some patients receiving rivastigmine 6–12 mg/day to drop out from the study (table 1).

Table 1. Efficacy and tolerability of rivastigmine in patients with AD

	Rivastigmine 1–4 mg/day	Rivastigmine 6–12 mg/day	Rivastigmine 6–12 mg/day
Patients:	614–650	973–1,054	1,052
Controls:	623–643	839–867	868
<i>ADAS-Cog (score 0–70)</i>			
WMD	–0.8	–2.1	
95% CI	–1.5 to –0.2	–2.6 to –1.5	
<i>PDS (score 0–100)</i>			
WMD	0.4	–2.2	
95% CI	–0.9 to 1.6	–3.2 to –1.1	
<i>CIBIC-Plus (score 1–7)</i>			
OR	0.71	0.68	
95% CI	0.55–0.93	0.55–0.85	
<i>Drop out due to adverse events</i>			
OR			2.97
95% CI			2.33–3.79
ARR			15.3%
NNH			6.5

WMD = Weighted mean difference; OR = odds ratio; CI = confidence interval; Patients = patients treated with rivastigmine; Controls = controls treated with placebo; ARR = absolute risk reduction; NNH = number needed to harm.

Conclusion

Rivastigmine 6–12 mg/day appears to be effective in improving cognitive functions and disability in patients with AD, but it is associated with a significant number of drop-outs due to adverse events. At lower doses, adverse events associated with rivastigmine are less frequent, but benefits are limited to cognitive functions.

Comments

In patients with AD, some beneficial effects on cognition and disability are associated with rivastigmine 6–12 mg/day after 6 months of treatment. Adverse events are responsible for moderate compliance. However, the clinical significance of the results is as yet unknown and longer observation is needed for this chronic, progressive degenerative disorder.

Reference

- 1 Birks JS, Grimley Evans J, Iacovidou V, Tsolaki M: Rivastigmine for Alzheimer's disease; in: Cochrane Library, Issue 2, 2000. Update Software.

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