Review: selegiline leads to a small short term improvement in cognition and activities of daily living in Alzheimer's disease

Wilcock GK, Birks J, Whitehead A, et al. *The effect of selegiline in the treatment of people with Alzheimer's disease: a meta-analysis of published trials. Int J Geriatr Psychiatry* 2002 Feb;17:175-83.

QUESTION: In patients with Alzheimer's disease, does selegiline improve cognitive performance, functional ability, emotional state, and global response?

Data sources

Studies were identified by searching Medline, EMBASE/Excerpta Medica, PsycLIT, the Cochrane Controlled Trials Register, reference lists of retrieved articles, and conference proceedings; and by contacting pharmaceutical companies and authors.

Study selection

Studies were selected if they were unconfounded, double blind, randomised controlled trials that compared selegiline with placebo in patients with Alzheimer's disease. Studies had to have been reported before the end of 1998; patients had to meet NINCDS-ADRDA or DSM criteria for Alzheimer's disease; and any secondary treatments (eg, physostigmine and lecithin) had to be given to both the selegiline and placebo groups.

Data extraction

Individual patient data were requested. When these data were not provided, summary data were extracted from the published reports for patient characteristics, treatment completion, and outcomes.

Main results

14 studies (1073 patients) met the selection criteria, and individual patient data were available for 8 studies (821 patients). 5 studies used a crossover design. Study duration ranged from 3 weeks to 2 years, and the selegiline dose was 10 mg/day. Patients' mean age ranged from 65-83 years. Selegiline was better than placebo for cognition at 4-6 weeks and 8-17 weeks (table), but the groups did not differ at 21-30 weeks or 76-69 weeks. Selegiline led to a benefit for activities of daily living at 4-6 weeks, but the benefit disappeared at later assessments (table). The groups did not differ for emotional state or global assessment.

Selegiline v placebo for Alzheimer's disease

Outcomes	Number of studies	Standardised mean difference (95% CI)
Cognition at 4-6 weeks	8	0.39 (0.07 to 0.72)*
Cognition at 8-17 weeks	10	0.45 (0.03 to 0.88)
Activities of daily living at 4-6 weeks	6*	0.27 (0.12 to 0.40)*
Activities of daily living at 8-17 weeks	7	0.33 (-0.33 to 0.69)†

*Data provided by author; all standardized mean differences favour selegiline.

†Not statistically significant.

Conclusions

In patients with Alzheimer's disease, selegiline leads to a small short term improvement in cognition and activities of daily living. Selegiline does not improve emotional state or global response.

COMMENTARY

Wilcock *et al* did an exemplary job using the tools of meta-analysis to combine data from studies that used varying inclusion criteria and outcome measures. This article and the closely related review in the *Cochrane Library*¹ provide strong evidence that, at best, the effect of selegiline in Alzheimer's disease is of little clinical significance. Not only were the magnitudes of the improvements in cognition and activities of daily living seen with selegiline treatment small and of no clinical significance, they were both largely dependent on a single study that was inconsistent with the results of the other included trials. Although few adverse events attributable to selegiline occurred, the lack of clinically significant efficacy offers little hope that further studies are warranted.

This article illustrates the value of using meta-analysis to allow relatively confident conclusions to be drawn from studies that are individually small and that use varying outcome measures. Selegiline treatment was based on sound theoretical grounds, and it is disappointing that it turned out to have little utility.

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1 Birks J, Flicker L. Selegiline for Alzheimer's disease *Cochrane Database Syst Rev* 2002;(1):CD000442.

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