Review: Selegiline leads to a small short-term improvement in cognition and activities of daily living in Alzheimer disease

Wilcock GK, Birks J, Whitehead A, Evans JG. **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 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, randomized, double-blind, controlled trials that compared selegiline with placebo in patients with Alzheimer disease. Studies had to have been reported before the end of 1998; patients had to meet the criteria of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Associations or the *Diagnostic and Statistical Manual of Mental Disorders* for Alzheimer disease; and any secondary treatments (e.g., 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/d. Patients' mean age ranged from 65 to 83 years. Selegiline was better than placebo for cognition at 4 to 6 weeks and 8 to 17 weeks (Table), but the groups did not differ at 21 to 30 weeks or 65 to 69 weeks. Selegiline led to an improvement in activities of daily living at 4 to 6 weeks, but the benefit disappeared at later assessments (Table). The groups did not differ for emotional state or global assessment.

CONCLUSIONS

In patients with Alzheimer 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.

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Selegiline vs placebo for Alzheimer disease

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

*Data provided by author; all standardized mean differences favor selegiline.
†Not statistically significant.

COMMENTARY

Wilcock and colleagues did exemplary work using the tools of meta-analysis to combine data from studies that used varying inclusion criteria and outcome measures. This review and the closely related review in the Cochrane Library (1) provide strong evidence that at best the effect of selegiline in Alzheimer disease is of little clinical significance. The magnitude of the improvements in cognition and activities of daily living seen with selegiline treatment were not only small and of no clinical importance; they were also largely dependent on a single study with results that were inconsistent with those of the other included trials. Although few adverse events attributable to selegiline occurred, the lack of clinically important efficacy offers little hope that further studies are warranted.

The review shows 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 therapy was based on sound theoretical grounds, and it is disappointing that the drug turned out to have little utility.

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Reference

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