Use of psychostimulants in patients with dementia

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CRD summary
This review concluded that methylphenidate was a possible treatment for apathy in older patients with dementia, but that psychostimulants as a group did not appear to be broadly effective treatments for behavioural or cognitive symptoms of dementia. The poor evidence-base and methodological limitations mean that these conclusions cannot be considered reliable.

Authors' objectives
To review the efficacy and safety of psychostimulants for negative behavioural symptoms and cognition in patients with dementia

Searching
PubMed was searched from inception to June 2010 for articles in English using specified search terms. References of relevant articles were assessed for eligibility.

Study selection
Any studies that measured the cognitive or behavioural effects of any psychostimulant on mostly older adults with dementia were included in the review. Apathy, excessive daytime sedation and cognition were the primary efficacy outcomes.

Study populations comprised inpatients and outpatients with Alzheimer's disease; some patients had vascular dementia and frontotemporal dementia. Psychostimulant treatment consisted of atomoxetine, dextroamphetamine, methylphenidate (10-45mg daily in divided doses), quetiapine or modafinil (100-200mg/day). Study duration ranged from three days to 12 weeks. Mean age of patients ranged from 62 to 82 years; the percentage of men ranged from 44 to 100%, where reported.

The number of reviewers determining study eligibility was not reported.

Assessment of study quality
No formal assessment of study quality was undertaken.

Data extraction
Patient age and sex, study design, drug regimen and a statement about the major outcome were extracted for each study.

The number of reviewers extracting data was not reported.

Methods of synthesis
Outcomes were tabulated and discussed in a narrative synthesis.

Results of the review
Thirteen studies (239 patients) were identified. Sample sizes ranged from one to 92 (mean 18). Study designs included double-blind randomised controlled trials (six RCTs), open label trials (three) and case series/reports (four).

Eight studies (three RCTs, two open label trials and three case series/reports) that measured apathy showed improvement with psychostimulants, but the magnitude of improvement was variable. One RCT showed a statistically significant improvement in apathy with methylphenidate compared with placebo, but the effect was small.

Two studies (one open label trial, one case report) reported on excessive daytime sedation. A single case report found a beneficial effect of methylphenidate in a single patient. Five of eight patients responded to modafinil in an open label trial.
Six studies (four RCTs, two open label trials) of cognition were identified. Two open label non-controlled trials of methylphenidate reported an improvement in cognition, although four RCTs found no significant differences between the psychostimulant and placebo groups.

A range of adverse effects were reported (details in paper).

**Authors' conclusions**
Based on limited studies, methylphenidate was a possible treatment for apathy in older patients with dementia, but psychostimulants as a group did not appear to be broadly effective treatments for behavioural or cognitive symptoms of dementia.

**CRD commentary**
This review addressed a clear question. The inclusion criteria were very broad. The search was limited and may not have identified all relevant material. The methods for selecting studies were unreported, so there may be the potential for reviewer bias in the study selection.

There was no attempt to appraise the quality of the included studies. Given the paucity of the evidence, small size of the studies and the diverse study designs, this was an important shortcoming, although the authors’ discussion and interpretation of results was informed by study design. The lack of quantitative synthesis was consistent with the paucity of evidence and the diversity of interventions and outcomes. However, the synthesis lacked a coherent framework and may suffer from selective reporting as a result. These problems resulted in considerable uncertainty, which was not fully reflected in the authors’ conclusions.

Although the suggestion for further work and the caveat on the review limitations were well founded, the authors’ conclusions cannot be considered reliable.

**Implications of the review for practice and research**

**Practice:** The authors stated that low doses of methylphenidate in patients with Alzheimer's disease and severe apathy may be warranted in conjunction with careful patient selection

**Research:** The authors stated that placebo controlled trials of adequate duration using validated rating scales were needed.

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