Efficacy and tolerability of antidepressants in the treatment of behavioral and psychological symptoms of dementia: a literature review of evidence

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CRD summary
The review found that antidepressants can be an effective treatment for behavioural and psychological symptoms of dementia in elderly demented patients and were usually well tolerated. Limitations in the review, which included failure to assess study quality, differences between the studies and a lack of predefined outcome measures in the review, mean that the authors’ conclusions require cautious interpretation.

Authors’ objectives
To evaluate the efficacy and tolerability of antidepressants for treating behavioural and psychological symptoms of dementia.

Searching
PubMed, PsycINFO, SCOPUS, Web of Science and The Cochrane Library were searched from 1990 to December 2010. Search terms were reported. Reference lists of published reviews were checked.

Study selection
Double-blinded randomised controlled trials (RCTs) of antidepressants for treating behavioural and psychological symptoms of dementia were eligible for inclusion.

Participants included male and female residents of nursing homes, in-patients, outpatients and community dwellers with Alzheimer’s disease or various types of dementia (such as vascular, frontotemporal). Study interventions included selective serotonin reuptake inhibitors (SSRIs) and trazodone. The most commonly used SSRIs were sertraline and citalopram. Interventions were compared with each other, other active interventions (haloperidol, risperidone, piracetam, behavioural management) or placebo. Drug doses varied. Outcomes reported in the review included behavioural and psychological symptoms measured with a wide variety of tools (depression rating scales, agitation scales, neurobehavioural scales, neuropsychological tests, functional scales) and side effects (measured with rating scales or self-report). Study duration ranged from 17 days to 14 months.

The authors did not state how many reviewers selected the studies.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Descriptive data from primary studies were reported in the text, with p values for between-group or within-group differences.

The authors did not state how many reviewers extracted data.

Methods of synthesis
The studies were combined in a narrative synthesis organised by type of intervention.

Results of the review
Eighteen studies (19 publications) were included in the review (1,122 participants, range 10 to 149).

SSRIs (15 studies): Sertraline (six studies) was of benefit in two out of five studies of sertraline versus placebo and in the one study of sertraline versus haloperidol. In participants with Alzheimer’s disease, citalopram (five studies) was of benefit in all studies of citalopram versus risperidone (two studies) and versus placebo with or without perphenazine (three studies); participants with dementia with Lewy bodies did not benefit from either drug (one study). Fluoxetine
and fluvoxamine were no more effective than haloperidol and/or placebo (one study each). SSRIs were well tolerated in 11 or 12 out of the 13 studies that reported this outcome (text inconsistent).

**Trazodone (three studies):** Trazodone showed benefit in two out of three studies of trazodone versus haloperidol and one of two studies versus placebo. Trazodone was no more effective than either haloperidol or behavioural management techniques in the third study. Trazodone was well tolerated in two of the three studies.

**Authors’ conclusions**
Antidepressants can be an effective treatment for behavioural and psychological symptoms of dementia in elderly demented patients and are usually well tolerated.

**CRD commentary**
The broad objectives of the review were stated, but there was no clear definition of eligible participants, comparisons or outcomes. Relevant sources were searched for studies. It was unclear whether the search was restricted by language or publication status. If so, it was possible that some studies were missed. The potential for publication bias was not discussed. It was unclear whether steps were taken to minimise risks of reviewer bias and error by having more than one reviewer independently select studies and extract data. It appeared that study validity was not assessed.

The review findings were difficult to interpret, partly because there was wide variation in the outcomes measured, types of data reported (within-group change, between-group change) and the samples analysed (completers only, responders only, study subgroups) and also because no confidence intervals were provided. Population characteristics, interventions and comparators varied. Most studies reported a large number of outcomes and it was not always clear which was the primary outcome. Sample sizes were very small in most cases and drop-out rates, where reported, ranged up to more than 40%.

Limitations in the review, which included failure to assess study quality, differences between the studies and a lack of predefined outcome measures in the review, mean that the authors’ conclusions require cautious interpretation.

**Implications of the review for practice and research**
- **Practice:** The authors stated that given current concerns about use of antipsychotics in elderly patients with dementia, antidepressant medications can be an effective alternative.
- **Research:** The authors stated that well designed RCTs and/or meta-analysis of current studies were needed to clarify the efficacy and tolerability of antidepressants for treating the behavioural and psychological symptoms of dementia.

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