Antipsychotics for behavioural and psychological problems in elderly people with dementia: a systematic review of adverse events
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CRD summary
This review concluded that there was a need for better reporting of harms in randomised controlled trials of antipsychotics for behavioural and psychological symptoms of dementia. This conclusion appears appropriate given the evidence presented.

Authors' objectives
To evaluate adverse events in relation to antipsychotic medications for behavioural and psychological symptoms of dementia

Searching
MEDLINE, EMBASE, PsycINFO and Cochrane Central Register of Controlled Trials (CENTRAL) were searched up to 2005. Search terms were reported. No language restrictions were imposed. Reference lists of retrieved articles were searched and a search was conducted in SumSearch (University of Texas search tool). Only studies published in full were eligible.

Study selection
Eligible studies were randomised, double-blind, placebo-controlled trials that used an intention-to-treat analysis. Articles published before 1984 were excluded if they had fewer than 100 patients. Trials needed to compare two antipsychotics or an antipsychotic with placebo. All drugs were to be administered orally. Trials needed to assess, as a primary outcome, the effect of treatment on behavioural and psychological symptoms of dementia (diagnosed according to international criteria) or on adverse events.

Mean age of participants was 80 years. Most had moderate to severe dementia; mean scores on Mini-Mental State Examination ranged from 5.5 to 15.2. Nine per cent lived in the community. Trials evaluated the antipsychotics haloperidol, tiapride, risperidone, loxapine, perphenazine, quetiapine and olanzapine. Trial duration was three to 16 weeks. Adverse events were assessed using questionnaires and physical performance tests; in some trials spontaneous reporting was used.

One researcher screened titles and abstracts of potentially eligible studies. Two reviewers were involved in the screening of full papers and resolved disagreements through discussion.

Assessment of study quality
Two reviewers independently appraised study methodological quality according to Cochrane Collaboration criteria. They also assessed the quality of reporting of harms using the Consolidated Standards of Reporting Trials (CONSORT) tool.

Data extraction
The authors calculated, where possible, numbers needed to harm with 95% confidence intervals (CI) for adverse events reported in the included trials. Two reviewers independently extracted data.

Methods of synthesis
The authors conducted a narrative synthesis.

Results of the review
Twelve randomised controlled trials (RCTs) were included in the review (n=2,809). Methodological quality was rated moderate to good. None of the trials fulfilled all standards for reporting of harms.
Based on 11 studies, the percentage of patients who experienced adverse events ranged from 49% to 100%. The overall percentage of withdrawals caused by adverse events ranged from 25% to 100% in the active treatment groups compared to 13% to 100% in placebo groups. Higher doses of antipsychotics did not cause higher percentages of withdrawals. Atypical antipsychotics caused fewer extrapyramidal symptoms and less somnolence than typical antipsychotics; these differences disappeared when dosages increased. Only one trial reported cerebrovascular events with a number needed to harm of 14 (95% CI 8 to 41).

Authors' conclusions
The authors concluded that better reporting of harms in RCTs was needed to enable rational treatment decisions in relation to antipsychotics for behavioural and psychological symptoms of dementia.

CRD commentary
The review question was underpinned by broad inclusion criteria on study design, population, intervention and outcomes. Searching encompassed a range of databases and other sources. There were no language restrictions. The restriction to studies published in full raised the possibility of publication bias. Study quality was assessed, but results were presented only for the quality of reporting. A narrative synthesis was appropriate given the heterogeneity between trials. Attempts were made to avoid bias and error in the selection, extraction and validity assessment processes. The authors' conclusion on the need for better reporting of harms appears appropriate given the evidence presented.

Implications of the review for practice and research
The authors did not state any implications for practice.

Research: Future studies should include a clearer description of the study population, better reporting of the harms of treatments and include numbers needed to harm.

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