Systematic review of antipsychotics for the treatment of hospital-associated delirium in medically or surgically ill patients

Lacasse H, Perreault M M, Williamson D R

CRD summary
The authors concluded that antipsychotic drugs are an effective and safe treatment of delirium in medically or surgically ill patients. Recommendations for specific agents are limited by the quality and quantity of the available data. The authors’ conclusions reflect the evidence available but the included studies were small and had serious flaws, therefore these conclusions may not be reliable.

Authors' objectives
To evaluate the efficacy and safety of antipsychotic drugs in the treatment of delirium in medically or surgically ill patients.

Searching
MEDLINE (from 1966), Current Contents (from 1993), CINAHL (from 1982), PsycINFO (from 1806), Biological Abstracts (from 1993), the Cochrane CENTRAL Register and EMBASE (from 1980) were searched to July 2006; the search terms were reported. The references from identified studies were checked for additional studies. In addition, the Web of Science database was searched to locate articles citing identified studies.

Study selection
Randomised controlled trials (RCTs) comparing the efficacy of an antipsychotic versus placebo or other treatment options (including antipsychotics) used to treat delirium in medical or surgical patients were eligible for inclusion. Studies involving delirium associated with dementia or Alzheimer’s disease, acute agitation associated with the emergency department, acute brain trauma or agitation secondary to underlying psychiatric illness (such as depression or schizophrenia) were excluded. The antipsychotics included in the review were varying doses of haloperidol, chlorpromazine, lorazepam, risperidone, olanzapine, amisulpride and quetiapine. Where reported, the duration of treatment ranged from 5 to 7 days. Some patients had adjuvant therapy of benzodiazepines and intravenous haloperidol.

In the included studies, cognitive functioning was measured using the Mini-Mental State Examination (MMSE), and delirium was rated using the delirium rating scale (DRS), the revised delirium rating scale (DRS-R-98), the Memorial Delirium Assessment Scale (MDAS) and the delirium index (DI). Rating scales for adverse events were extrapyramidal symptom rating scales (ESRS), a Clinical Global Impression of tardive dyskinesia, and the Angus-Simpson scale.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Study validity was assessed using criteria adapted from established checklists. Three reviewers independently assessed validity, blinded to each others assessments.

Data extraction
Data were extracted on differences in delirium scores from baseline and between groups (when reported), and details of any extrapyramidal symptoms or other adverse events. Three reviewers independently extracted the data, blinded to each others evaluation.

Methods of synthesis
Each study was described in the text, with data presented in the tables. Differences between the studies were discussed in the text and were apparent from inspection of the tables.

Results of the review
Four RCTs (n=158) were included. Two studies were reported to be double-blinded (in an additional study the investigators were blinded). The method of randomisation was described by only one study, but this method was inadequate.

One study (n=30) treating AIDS patients for delirium found statistically significant improvements in the DRS score for haloperidol (p<0.001) and chlorpromazine (p<0.001), but not for lorazepam (p=0.63). Significant improvements were also found in the MMSE score for chlorpromazine (p<0.001), but not for haloperidol (p=0.09) or lorazepam (p=0.40). There were no significant changes in ESRS scores for any of the drugs used. All participants in the lorazepam group experienced treatment-limiting adverse events including oversedation, disinhibition, ataxia and confusion.

One study (n=24) comparing the effects of risperidone and haloperidol for the treatment of delirium in oncology, medical and intensive care unit patients found a significant improvement in the MDAS score in both groups (p=0.05), but showed no statistically significant differences between groups (p=0.51) for treatment effect. One patient developed mild symptoms of akathisia in the haloperidol group; no other adverse events were reported.

One study (n=73) comparing haloperidol and olanzapine for the treatment of delirium in intensive care unit patients found that DI scores improved for both groups (p=0.02), but there were no statistically significant differences between groups for treatment effect (p=0.83). Six participants in the haloperidol group rated low on symptom testing for extrapyramidal symptoms, compared with no extrapyramidal manifestation for the olanzapine group.

One study (n=31) evaluating the treatment of delirium in medical and surgical patients reported an improvement in the DRS-R-98 for treatment with amisulpride (p=0.000) and quetiapine (p=0.001). Again, there were no statistically significant differences between the two groups for treatment effect (p=0.842). One patient in each group developed oversedation.

Authors’ conclusions
The findings suggest that antipsychotic drugs are effective compared with baseline and are a safe treatment for delirium. Haloperidol was the most studied agent. Recommendations for specific agents are limited by the quality and quantity of the available data.

CRD commentary
The review addressed a clear question defined in terms of the participants, interventions, outcomes and study design. Several relevant sources were searched. It was unclear if any language restrictions were applied. Methods were used to minimise reviewer error and bias in the assessment of validity and extraction of data, but it was unclear whether similar steps were taken at the study selection stage. Validity was assessed using established checklists and methodological limitations in the included studies were discussed in the text of the review. The authors described each study individually rather than in a narrative synthesis. As the authors discussed, there were considerable between-study differences in terms of the participants, therapy and dosing, adjuvant therapy and outcome measures. There were also methodological limitations. The authors’ conclusions reflect the evidence available but the included studies were small and had serious flaws, therefore these conclusions may not be reliable.

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

Research: The authors stated that further large, double-blind RCTs in the acute care setting are required, in particular studies evaluating the addition of antipsychotic agents to non-pharmacologic treatments to measure the true effect of pharmacologic treatments.

Funding
Not stated.

Bibliographic details
Lacasse H, Perreault M M, Williamson D R. Systematic review of antipsychotics for the treatment of hospital-

PubMedID
17047137

DOI
10.1345/aph.1H241

Indexing Status
Subject indexing assigned by NLM

MeSH
Antipsychotic Agents /adverse effects /therapeutic use; Delirium /drug therapy /epidemiology /psychology; Haloperidol /therapeutic use; Hospital Departments /trends; Hospitalization /trends; Humans; Surgery Department, Hospital

AccessionNumber
12006009284

Date bibliographic record published
07/02/2008

Date abstract record published
30/09/2008

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.