The use of olanzapine as a first and second choice treatment in schizophrenia

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Authors' objectives
To assess whether olanzapine should be used as a first or second choice neuroleptic, instead of a standard neuroleptic at optimal dose, in the treatment of acute episodes of schizophrenia. The evidence concerning the long-term use of olanzapine was considered, specifically in treatment of acute episodes of schizophrenia as a second choice neuroleptic in cases with poor compliance, non-response or adverse reaction to initial treatment.

Searching
The electronic databases searched included MEDLINE, Science Citation Index, EMBASE, DARE, Cochrane Database of Systematic Reviews, Cochrane Controlled Trials Register, ISI Conference Proceedings and Transcripts, NHS EED; the search dates were not reported. Handsearches were performed in: Drugs and Therapeutic Bulletin (1996 and 1997), British Journal of Psychiatry, American Journal of Psychiatry, Schizophrenia Bulletin (1997), BNF (olanzapine not included in September 1996 edition), MIMMs (March 1997, olanzapine included), Eli Lilly and Co., West Midlands Regional Drugs Information Service.

Study selection
Study designs of evaluations included in the review
Intervention studies and observational studies were searched for. Good quality randomised controlled trials (RCTs) of olanzapine versus placebo or standard neuroleptics were given greatest weight. Only RCTs were included in the analysis.

Specific interventions included in the review
Olanzapine (1, 5 10 or 15 mg/day fixed doses or titrated doses) versus placebo or haloperidol (15 mg/day fixed dose or titrated dose).

Participants included in the review
Patients with schizophrenia, schizophreniform disorder or schizoaffective disorder.

Outcomes assessed in the review
Mean changes in clinical rating scales and response rates. Clinical rating scales included the Brief Psychiatric Rating Scales (BPRS), Positive and Negative Symptom Scale (PANNS), Clinical Global Impression - Severity (CGI-severity), Scale for the Assessment of Negative Symptoms (SANS), and Montgomery-Asberg Depression Rating Scale (MADRS).

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
Quality assessment was based on the Jadad scale (see Other Publications of Related Interest no.1). The authors do not state how the papers were assessed for quality, or how many of the reviewers performed the quality assessment.

Data extraction
Data were extracted on: study design, dose, entry criteria, patient numbers, outcome measures, results, response rates and duration.
Methods of synthesis
How were the studies combined?
A meta-analysis was carried out in the Cochrane Collaboration Review Manager 3.0 and Metaview software. There were no additional details on the methods used. Relative risk estimates and 95% CIs were reported using fixed-effect analysis.

How were differences between studies investigated?
Heterogeneity was assessed using the chi-squared statistic, but although heterogeneity was present the fixed-effect model was used.

Results of the review
Four randomised double-blind clinical trials of olanzapine for treatment of schizophrenia were included (2914 patients). All were published prior to license.

The evidence on the efficacy of olanzapine comes from 4 published double blind randomised clinical trials of only six weeks duration and from 3 extension phases. Higher response rates and fewer side effects have been achieved with olanzapine compared with haloperidol, along with better control of negative symptoms over the six weeks of the trials. Olanzapine was found to have a better reported efficacy and side effects profile than conventional neuroleptics such as haloperidol.

Cost information
Yes, in a simple cost model, neuroleptic treatment of schizophrenia of any sort produced cost savings over no neuroleptic treatment. In all cases, savings associated with olanzapine were greater than those associated with haloperidol. Potential savings are from reduced inpatient and intensive community care and may be absorbed in the general psychiatric budget and not realised. These findings are based on some very significant assumptions: 1-that the short duration of the trials truly represents a longer term period; 2-that the trial patients, particularly those enrolled in extension phases, are representative; 3-potential savings from reduced hospitalisation can be realised.

Authors’ conclusions
[A:In a short term trial with titrated doses of both drugs, olanzapine performed better than haloperidol with respect to mean changes in clinical rating scores and numbers of responders, and this was confirmed in a metaanalysis that included two smaller trials with doses with limited titration. Olanzapine also had a better EPS side effects profile than haloperidol. Further trials are required to address the superiority of olanzapine in the maintenance of relapse.]

CRD commentary
The databases searched seem complete and appropriate. The inclusion criteria seem well chosen. Authors did not report how decisions on inclusion or exclusion of studies were taken, nor did they report the way methodological quality criteria were assessed and how data extraction was done.

The description of the way studies were combined is very limited and although heterogeneity of studies was assessed this seems not to have been taken into account. The evidence was very limited as only studies of up to six weeks duration were found. Therefore the evidence does not support the authors conclusion that ‘olanzapine should be made available as a first and second choice agent for the treatment of all people with schizophrenia’. The authors’ conclusion that ‘definitive proof of the primacy of a particular neuroleptic requires longer-term trials and follow-up’, seems more appropriate.

Implications of the review for practice and research
Practice: According to the authors olanzapine should be made available [A:as a therapeutic option] as a first and second choice agent for the treatment of all people with schizophrenia.
Research: The authors state that definitive proof of the primacy of a particular neuroleptic requires longer-term trials and follow-up.

Bibliographic details

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Other publications of related interest

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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.