Intramuscular olanzapine in the management of acute agitation
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CRD summary
This review assessed the efficacy and safety of intramuscular olanzapine in the management of patients with acute agitation. The authors' overall conclusion that further research is required seems appropriate given the differences between the studies identified and the small data set on which the results were based.

Authors' objectives
To assess the efficacy and safety of intramuscular (IM) olanzapine in the management of patients with acute agitation.

Searching
MEDLINE, EMBASE and PubMed were searched to March 2004 for articles published in English; the search terms were reported. The reference lists of retrieved reports were checked. Abstracts were excluded.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies of IM olanzapine were eligible for inclusion. The included studies compared IM olanzapine (2.5 to 10 mg) with IM haloperidol (7.5 mg), lorazepam (1 and 2 mg) and IM placebo. The studies allowed subsequent injections after more than 2 and 4 hours.

Participants included in the review
Studies of patients with acute agitation and psychosis were eligible for inclusion. Patients with agitation severe enough to require parenteral treatment, with a minimum score of 14 and at least one item score of 4 or more on the Positive and Negative Symptoms Syndrome Scale-Excited Component (PANSS-EC), were included. The primary studies included patients with a variety of diagnoses: patients with schizophrenia, elderly patients with dementia, and patients with bipolar disorder. The review classified the included patients as mildly to moderately agitated according to baseline PANSS-EC scores.

Outcomes assessed in the review
Studies that assessed efficacy or safety outcomes were eligible for inclusion. The primary outcomes measures included change in baseline scores on the PANSS-EC, the Agitation-Calmness Evaluation Scale (ACES), the Agitated Behaviour Scale (ABS) and the Cohen-Mansfield Agitation Inventory (CMAI). Clinical response (defined as 40% or greater reduction in PANSS-EC score from baseline), the number of injections required, and adverse effects were also assessed.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the studies. The authors did not state how any disagreements were resolved.

Assessment of study quality
The validity of the primary studies was not formally assessed, although elements of methodological quality were noted in the individual descriptions of each trial.

Data extraction
Two reviewers independently extracted the data from the primary studies. The authors did not state how any
disagreements were resolved.

Methods of synthesis
How were the studies combined?
A narrative synthesis of the studies was undertaken.

How were differences between studies investigated?
Differences between the studies were discussed in the paper.

Results of the review
Four RCTs (n=1,054) were included.

All of the included studies were double-blind, and the results from 3 of the 4 trials were based on last observation carried forward.

One RCT (270 patients with schizophrenia) found that the response rates for the PANSS-EC at 2 hours demonstrated that all doses of olanzapine and haloperidol were superior to placebo in reducing agitation, and that a greater proportion of participants in the olanzapine and haloperidol groups achieved an improved clinical response. No statistically significant differences in clinical improvement between olanzapine and haloperidol were reported. The RCT also found that olanzapine reduced parkinsonism (0.6% versus 16.7%), akathisia (1.1% versus 7.9%) and acute dystonic reaction (0% versus 5%) compared with haloperidol, but increased hypotension (3.8% versus 0%).

One RCT (311 patients with schizophrenia) found significantly greater mean improvements on the PANSS-EC, ACES and ABS at 2 and 24 hours in the olanzapine 10 mg and haloperidol 7.5 mg groups compared with placebo; no statistically significant differences between olanzapine and haloperidol were found. The study also reported that olanzapine significantly reduced dystonic reactions compared with haloperidol (90% versus 7%, P=0.03).

One RCT (201 patients with bipolar disorder) found greater mean improvement on the PANSS-EC, ABS and ACES in the olanzapine 10 mg group at 2 hours compared with lorazepam 2 mg and placebo (80% versus 34% and 44%, P=0.045 and P<0.001, respectively). The study also found that lorazepam increased adverse effects compared with olanzapine and placebo (51% versus 34% and 26%).

One RCT (272 patients with dementia) found improved response rates on the PANSS-EC, CMAI and ACES for olanzapine 2.5 and 5 mg and lorazepam 1 mg at 2 hours compared with placebo. No statistically significant differences in extrapyramidal symptoms between the treatment groups were found. Lorazepam significantly increased somnolence compared with olanzapine and placebo (10% versus 4% and 3%).

Authors’ conclusions
Differences between the studies with respect to regimens examined and patient characteristics prevented conclusions from being drawn. Further research is required.

CRD commentary
The review question was clear in terms of the study design, intervention, participants and outcomes. Two relevant databases plus references were searched, but no attempts to minimise language or publication bias were made. Two reviewers independently selected studies for inclusion and extracted the data from the primary studies, thus reducing the potential for bias and error. Although only RCTs were included, the validity assessment was limited and the quality of the included studies was therefore uncertain. Given the differences between the studies with respect to patient characteristics and comparators, the narrative synthesis was appropriate. The authors’ conclusions appear appropriate given the evidence presented.

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

Research: The authors stated that further research comparing IM olanzapine with combination antipsychotics/benzodiazepine therapy in more severely agitated patients, including patients with concurrent medical conditions, is required to determine the optimal dose and most appropriate use of additional treatments, and to adequately assess safety.

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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.