Do the second-generation "atypical neuroleptics" have analgesic properties: a structured evidence-based review


CRD summary
This review assessed the effectiveness of atypical neuroleptics for treating pain. The authors concluded that the data suggest that atypical neuroleptics may have an analgesic effect on pain, but more research is required. The strongest evidence, which came from generally small, single-dose studies, supports the need for further research but provided very weak evidence of effectiveness.

Authors' objectives
To assess the effectiveness of atypical neuroleptics for treating pain.

Searching
MEDLINE, Psychological Abstracts, the Science Citation Index and PDQ were searched up to 2002 using the reported search terms. Eligible studies were not restricted to English language articles. The references of retrieved reports were checked. Five key pain journals, abstract books of two associations/societies, and references in three textbooks were also searched (details of the sources were given).

Study selection

Study designs of evaluations included in the review
Inclusion criteria for the study design were not specified.

Specific interventions included in the review
Studies of atypical neuroleptics for treating pain were eligible for inclusion. The included studies used tiapride (intravenous and intramuscular formulations), aspirin plus tiapride, olanzapine, risperidone and quetiapine. Control interventions, where present, were placebo and opioid. The duration of the interventions, where reported, ranged from single dose to 2 days; treatment duration was not reported for most studies.

Participants included in the review
Inclusion criteria for the participants were not specified. The included studies were of patients with cancer pain, low back and neck pain, migraine headache and fibromyalgia.

Outcomes assessed in the review
Studies that assessed pain were eligible for inclusion. The included studies assessed pain using a visual analogue scale, a 4-point rating scale and the Migraine Disability Assessment Questionnaire.

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

Assessment of study quality
The authors graded studies using a hierarchy of study design, as described by the Agency for Health Care Policy and Research: type I for a meta-analysis of well-designed controlled studies; type II for at least one well-designed experimental study; type III for well-designed quasi-experimental studies; type IV for well-designed non-experimental studies; and type V for case reports and clinical examples. One author classified the studies.

Data extraction
Methods of synthesis
How were the studies combined?
The level of evidence was graded from I to V using a hierarchy of evidence based on study design and consistency, as described by the Agency for Health Care Policy and Research: level A for evidence of type I or consistent results from studies of type II, III, or IV; level B for evidence of generally consistent results from type II, III or IV studies; other levels were assigned for lower quality or inconsistent studies.

How were differences between studies investigated?
Some differences between the studies were evident from an examination of the data extraction table.

Results of the review
Ten studies (n=209) were included: 4 experimental studies (n=93), 2 quasi-experimental studies (n=58), 2 non-experimental studies (n=54) and 2 case reports (n=4).

In terms of study quality, 3 studies were double-blind and two of these were placebo-controlled. The sample size ranged from 2 to 50.

All but one of the 10 studies reported an analgesic effect with atypical neuroleptics.

Evidence for the analgesic effect of neuroleptics was classified as level B.

Authors' conclusions
The data suggest that atypical neuroleptics may have an analgesic effect on pain, but more research is required.

CRD commentary
The review addressed a clear question but only inclusion criteria for the interventions were specified. The strategy undertaken to identify trials was extensive and attempts were made to minimise language bias. The methods used to select studies were not reported, and only one reviewer extracted the data and assessed validity; this lack of duplication may lead to errors and bias. The quality assessment was generally limited to study design, with no assessment of the validity of methods used to assess the primary review outcome of pain. Some relevant data on the individual studies were tabulated, but actual values for the results were not reported, making it difficult to assess the evidence. Given the differences among the studies, the hierarchy of evidence approach used to combine the studies appeared reasonable. The strongest evidence, which was from generally small, single-dose studies, supports the need for further research but provided very weak evidence on effectiveness.

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 into the effects of neuroleptics on pain is required, and that a comparison between atypical and non atypical neuroleptics would be useful.

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