A systematic review of the use of atypical antipsychotics in autism

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Authors' objectives
To review the efficacy and safety of atypical antipsychotic drugs for patients with autism.

Searching
MEDLINE (from 1966 to June 2000) and ISI Web of Science (from 1981 to June 2000) were searched using the search terms reported in the review. Handsearches of relevant articles were also carried out.

Study selection

Study designs of evaluations included in the review
The authors specifically chose not to restrict the inclusion of studies by design. The included studies were randomised controlled trials (RCTs), case series and non-randomised trials.

Specific interventions included in the review
The authors did not specify any inclusion criteria with regard to the intervention, but it appears that studies examining the use of atypical antipsychotic drugs were eligible for inclusion. The included studies considered the efficacy and safety of risperidone (dosage range: 0.875 to 7.0 mg/day), quetiapine (mean dosage 225 mg/day), olanzapine (dosage range: 7.5 to 15.0 mg/day), clozapine (mean dosage 283 mg/day) and amisulpride (fixed dose 1.5 mg/kg per day). The duration of treatment varied both between the studies and between patients within the studies.

Participants included in the review
The authors did not specify any inclusion criteria with regard to the participants, but it appears that participants with autistic spectrum disorder were eligible for inclusion in the review. The reported ages of the participants ranged from 23 months to 48 years, although most of the included studies focused on children. Some of the participants had learning disabilities.

Outcomes assessed in the review
The inclusion criteria with regard to outcomes were not reported. The authors stated that the review focused on behaviour, cognition and physical well-being. Assessment scales of various designs were employed within individual studies to examine the impact of treatment on overall autistic behaviour (everyday functioning and overall behaviour change), core autistic features (social functioning, repetitive behaviour and language), related psychopathology (agression, hyperactivity and mood), cognition and side-effects.

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

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Patient profiles, treatment details and results of behavioural assessments were extracted from each included study.

Methods of synthesis
How were the studies combined?
The authors undertook a comprehensive narrative synthesis of the studies. This was ordered by outcome and study designs, with the results of the RCTs reported before those of other study designs.

How were differences between studies investigated?
There was some discussion about differences between the studies in the text of the review. Heterogeneity was not formally investigated.

**Results of the review**

Nineteen studies were included in the review: 2 RCTs, 6 open-label non-randomised trials and 11 case series. Overall, 162 patients were included, of which 40 were enrolled in the 2 RCTs.

The 13 studies examining risperidone (including one RCT) indicated that this drug may be effective in treating overall autistic behaviours, specifically hyperactivity, aggression and repetitive behaviour. Fifty-three per cent of the patients treated in the RCT were classed as responders. Risperidone was further found, albeit to a lesser extent, to be beneficial in the improvement of mood states such as depression, irritability and nervousness. 'Affective Exchange' (measured according to the Ritvo-Freeman Real-Life Rating Scale), for example, improved in 71% of the cases.

The authors found evidence (3 studies) that olanzapine may prove to be effective at improving overall autistic features, reducing hyperactivity and aggression, and improving social functioning and language.

The evidence for the benefits of clozapine was weak (based on one prospective case series of 3 patients).

The RCT examining the use of amisulpride found this drug to have a 'moderately positive' effect, although it was unclear to which behavioural domain this applied.

Whilst the quetiapine study indicated positive effects on aggressive behaviour, the drug could only be tolerated by one third of the sample studied.

Overall, with the exception of quetiapine, drug toleration was good. The most common adverse reactions were sedation and weight gain. The latter was reported in 8 of the 13 studies involving risperidone.

**Authors' conclusions**
Atypical antipsychotics have potential in the treatment of autism.

**CRD commentary**
The review lacked explicit inclusion criteria. Instead, the authors appear to have used the presence of particular words in articles to select the papers for inclusion. Thus, the potential for selection bias cannot be ruled out and it is possible that relevant articles may have been missed. The search was adequate, although there was no mention of a search for unpublished material. A validity assessment was not reported; however, the authors clearly emphasised the preliminary and inconclusive nature of the evidence. In addition, the authors did not mention whether steps were taken to minimise the introduction of bias in the review process. Details of the primary studies were described adequately. The data synthesis was comprehensive and ordered sensibly. The authors’ conclusions were cautious, reflecting the inadequacy of the evidence to date.

**Implications of the review for practice and research**
Practise: The authors stated that the evidence to date is inadequate to inform practice reliably.

Research: The authors stated the need for well-designed RCTs (with larger sample sizes), the comparison of patients with varying behavioural and cognitive profiles, and the assessment of cognitive capacities in addition to behavioural and physical outcomes.
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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.