Update and recommendations for the use of antipsychotics in early-onset psychoses

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Authors' objectives
To evaluate the efficacy and tolerability of antipsychotic medications for the management of child and adolescent onset psychosis.

Searching
It should be noted that although this review article dates from 2001, the searches covered the time period from January 1996 to October 1998. MEDLINE was searched using the MeSH terms 'haloperidol', 'clozapine', 'risperidone', 'olanzapine', 'quetiapine', 'ziprasidone' and 'sertindole' for studies of patients aged less than 18 years. The authors also contacted the Cochrane Schizophrenia Group for relevant reviews. Additional material was identified by examining the reference lists of relevant studies and review articles, by contacting the manufacturers of three of the drugs (risperidone, olanzapine and quetiapine), and by manually searching selected journals and abstracts.

Study selection
Study designs of evaluations included in the review
All types of study were eligible for inclusion in the review. The included studies were randomised controlled trials (RCTs), open-label trials, retrospective chart reviews and case reports. The duration of the studies ranged from 25 days to 36 weeks.

Specific interventions included in the review
Interventions were antipsychotic drugs used in the treatment of patients aged 18 years or younger. The included studies assessed the use of the following drugs: haloperidol (16 plus or minus 8 mg/day), clozapine (from 176 plus or minus 149 mg/day, to 325 mg/day), risperidone (0.25 to 10 mg/day), olanzapine (2.5 to 10 mg/day) and quetiapine (25 to 400 mg/day).

Participants included in the review
The stated participants were child and adolescents patients with psychosis, aged 18 years or younger. The studies included a variety of age bands, one of which included patients aged up to 22 years.

Outcomes assessed in the review
Studies were included if they provided some assessment of the safety and efficacy of antipsychotics in the treatment of psychosis in this patient population. Reports of antipsychotic efficacy or adverse events in patients with nonpsychotic diagnoses were excluded.

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
No formal assessment of validity was undertaken.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

The data presented for each study included details of the participants, study design, drug dosage, clinical efficacy, and notable adverse effects.
Methods of synthesis

How were the studies combined?
A narrative synthesis was undertaken. The studies did not appear to have been weighted. The authors do not report any methods for assessing publication bias.

How were differences between studies investigated?
The authors do not state a method for assessing the impact of any differences between studies. Studies of the same drug were found to differ in terms of the numbers and ages of participants, study design, dosages and outcome measures.

Results of the review

Twenty-three studies were included in this review: 1 RCT (N=21), 7 open-label trials (N unavailable), 6 retrospective chart reviews (N=241) and 9 case reports (N=11).

Clozapine: overall, the therapeutic efficacy of clozapine in youth with schizophrenia seemed clear. However, its use was complicated by the significant profile of side-effects, which included sedation, sialorrhoea and weight gain.

Risperidone: there was evidence of the therapeutic efficacy and tolerability of risperidone in youth with psychosis. A similar profile of adverse events to that noted in adults was found in young people, including extrapyramidal side-effects and weight gain. Case reports of hepatotoxicity highlighted the importance of careful monitoring of liver function, particularly in youth who are obese.

Olanzapine: there were insufficient data to provide information on its use in younger populations. The limited evidence available suggested modest therapeutic efficacy and tolerability. Side-effects may include sedation, cognitive impairment and weight gain.

Quetiapine: with the limited evidence of an open-label trial and a case report, it was found that psychotic symptomatology improved and that the pharmacokinetic profile of quetiapine was similar to that reported for adults.

No studies of the use of sertindole or ziprasidone in the treatment of children and adolescents with psychoses were identified. However, there was one RCT that described the use of ziprasidone in the management of Tourette's syndrome in children and adolescents.

Authors' conclusions

Most of the studies reported a reasonable treatment response. However, extrapyramidal side-effects, sedation and weight gain were of concern. In the use of antipsychotics in children and adolescents, there is a need to consider baseline assessments, drug choice and dosage, monitoring for clinical response, and the treatment of adverse effects.

The heterogeneous nature of patients with psychosis points to a need to establish individual treatment regimens, based on the patient’s initial symptom profile. The authors emphasise the importance of a slow upward titration of the dosage for minimising side-effects and improving medication tolerability.

CRD commentary

A clear review question was addressed by the stated inclusion criteria. The literature search was comprehensive, although it relates only to the time period January 1996 to October 1998. Some efforts were made to find unpublished studies. No formal validity assessment was performed and all types of study designs were accepted for inclusion. The authors' conclusions appeared sound but, particularly in the case of quetiapine and olanzapine, were based on limited evidence. The authors provided an appropriate narrative summary of the evidence, comparing it with the literature on antipsychotics in the adult population. Studies were grouped and analysed according to drug treatment, with extra discussion of developmental issues in the use of antipsychotics. Guidelines for the use of antipsychotics and the management of adverse effects were provided.

This review highlights the need for further controlled studies of the use of antipsychotic medications in children and adolescents, not only to seek to minimise the side-effects of therapy but also to lessen the long-term morbidity of the
Implications of the review for practice and research
Practice: The authors state that clinicians need to be aware of how developmental tasks and body image may have an impact on the compliance and acceptance of diagnosis and treatment, including adherence to treatment regimens. Prior to initiating treatment with antipsychotic agents, appropriate baseline assessments should be made; these should give particular attention to the extrapyramidal system, baseline weight, lipid profile and blood glucose levels. It is important to institute effective early treatment in youth with psychoses, which may lessen the long-term morbidity of the illness.

Research: The authors state that further study is needed to refine the use of antipsychotic medications in children and adolescents, in order to minimise adverse effects while conferring an optimum therapeutic response.

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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.