Management of psychosis in children and adolescents

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Nuts and Bolts of Pediatric Psychopharmacology and management of Psychosis in children

1st Nov 2022
Conflict of interest: None
We will touch upon

- Presentation of psychosis in children and adolescents
- Differential diagnosis
- Psychosis in children
- Psychosis in adolescents
- Cochrane review: Childhood onset schizophrenia
- Cochrane review: Atypical antipsychotics in adolescents with psychosis
- Cochrane review: Psychological interventions for adolescents with psychosis
- Tying it all together
Presentation of psychosis in youth

- Diagnostic criteria (Positive symp, negative symptoms, disorganized behaviour)
- Misdiagnosis is common (Normal child, OCD, Mania)
- Distinguish formal thought disorder with language disorders
- Children who develop schizophrenia may have premorbid problems with verbal reasoning, memory, attention.
- Cognitive decline typically occurs at the onset and stabilize over time
- **Neurotypical child**
  - Overactive imagination
  - Vivid fantasies

- **High risk state**
  - Family history, recent deterioration in functioning
  - Paranoid thought, social impairment, Substance misuse

- **OCD**
  - Obsessional thinking e.g. symmetry
  - “Something bad will happen”

- **ASD spectrum**
  - Lack of social reciprocity
  - Idiosyncratic beliefs; No acute onset = long standing pattern

- **Mania**
  - Florid delusions and elaborate thoughts
  - Rapid speech as opposed to withdrawal

- **Schizophrenia**
  - Onset (acute or slowly developing)
  - Change in functioning
Conclusion: At 5-year follow-up, 1 in 6 youths diagnosed with an ARMS had transitioned to psychosis, but we did not find evidence that this risk was related to ARMS diagnosis as opposed to sampling/recruitment strategies.

Our findings indicate a need for caution in applying ARMS methodology to children and adolescents and highlight the need for developmentally sensitive approaches when considering psychosis risk.
Psychosis in children and adolescents

- Normal hallucinations that are not part of a psychiatric disorder
- Acute and transient psychosis
- Prodromal symptoms
- Childhood onset schizophrenia (COS)
- Adolescent onset psychosis
  - First episode psychotic bipolar
  - Schizophrenia (1/5\textsuperscript{th} of all patients with schizophrenia)
  - Misdiagnosed psychosis (in OCD, bipolar, developmental disorders etc.)
Childhood onset Schizophrenia

• Less than 13 years of age
• Not adequately studied as its rare (1 in 10,000)
• Diagnostic validity of Schizophrenia below 6 years of age has not been established
• Symptomatology – Positive, Negative symptoms and Cognitive decline
• Course: Prodrome, acute phase, recovery phase and residual phase
• Outcome: Moderate to severe impairment
• All children with suspected schizophrenia should be evaluated for pertinent clinical conditions that may be associated with the presentation
  developmental disorders
  substance misuse
  childhood abuse/psychosocial stressors/ PTSD
  medical conditions
PHYSICAL EXAMINATION OF ALL CHILDREN WITH SUSPECTED SCHIZOPHRENIA
When to be more cautious about medical problems giving rise to psychotic symptoms?

Organic signs e.g. focal neurological deficits, seizures etc.

Past history of a medical illness that can present with psychiatric symptoms

Family history of a medical illness that can present with psychiatric illness (e.g. Wilson’s disease, porphyria etc)
Practice Parameter for the Assessment and Treatment of Children and Adolescents With Schizophrenia
Mainstay of treatment of childhood onset schizophrenia is medications

Psychological and social treatments are complementary and is essential to support a young person and a family
Appendix A: Summary of evidence from surveillance

2022 surveillance of psychosis and schizophrenia in children and young people: recognition and management

(2013 NICE guideline CG155)

Overall surveillance proposal
We will not update the guideline at this time. We will monitor the evidence base for new evidence in the areas indicated below.
Evidence for antipsychotic medications in childhood onset schizophrenia.
Antipsychotic medication for childhood-onset schizophrenia (Review)

Kennedy E, Kumar A, Datta SS

Status: New

This record should be cited as:

This version first published online: 18 July 2007 in Issue 3, 2007.
Date of most recent substantive amendment: 21 May 2007

doi:10.1093/schbul/sbm080
Advance Access publication on August 1, 2007

Antipsychotic Medication for Childhood-Onset Schizophrenia
Efficacy data – Limited information on superiority of one medication over another
Evidence for antipsychotic medications in adolescents with psychosis
Atypical antipsychotics for psychosis in adolescents

Ajit Kumar¹, Soumitra S Datta²,³, Stephen D Wright⁴, Vivek A Furtado⁵, Paul S Russell⁶


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Editorial group: Cochrane Schizophrenia Group.
Review content assessed as up-to-date: 18 July 2012.

Citation: Kumar A, Datta SS, Wright SD, Furtado VA, Russell PS. Atypical antipsychotics for psychosis in adolescents. Cochrane Database of Systematic Reviews 2013, Issue 10. Art. No.: CD009582. DOI: 10.1002/14651858.CD009582.pub2.

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### Review: Atypical antipsychotics for psychosis in adolescents

#### Comparison: 2 Atypical vs typical antipsychotics (only short term)

#### Outcome: 5 Mental state 2a. Mean end point scores (various scales, high score = poor)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Atypical antipsychotic</th>
<th>Typical antipsychotic</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>Weight</th>
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<tbody>
<tr>
<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>IVFixed95% CI</td>
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<td>IVFixed95% CI</td>
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<tr>
<td>1 BPRS</td>
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<td></td>
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<tr>
<td>Kumra 1996</td>
<td>10 11.7 (1.3)</td>
<td>11 15.3 (3.8)</td>
<td>-3.60 [-6.64, -0.56]</td>
<td>100.0%</td>
<td>-3.60 [-6.64, -0.56]</td>
<td>100.0%</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>10</td>
<td>11</td>
<td>100.0%</td>
<td>-3.60 [-6.64, -0.56]</td>
<td>100.0%</td>
<td></td>
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<tr>
<td></td>
<td>Heterogeneity: not applicable</td>
<td>Test for overall effect: Z = 2.32 (P = 0.020)</td>
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<tr>
<td>2 BPRS</td>
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<tr>
<td>Huo 2007</td>
<td>20 25.26 (4.46)</td>
<td>20 25.49 (5.36)</td>
<td>-0.23 [-3.29, 2.83]</td>
<td>38.6%</td>
<td>-0.23 [-3.29, 2.83]</td>
<td>38.6%</td>
</tr>
<tr>
<td>Kumra 1996</td>
<td>10 52.5 (12.6)</td>
<td>11 64.7 (18.1)</td>
<td>2.1 [-12.20, 1.04]</td>
<td>100.0%</td>
<td>2.1 [-12.20, 1.04]</td>
<td>100.0%</td>
</tr>
<tr>
<td>Skich 2004 (1)</td>
<td>16 22 (12)</td>
<td>15 33 (19)</td>
<td>11.00 [-22.27, 0.27]</td>
<td>2.8%</td>
<td>11.00 [-22.27, 0.27]</td>
<td>2.8%</td>
</tr>
<tr>
<td>Skich 2004 (2)</td>
<td>19 27 (20)</td>
<td>15 33 (19)</td>
<td>2.1 [-6.00, 1.17]</td>
<td>100.0%</td>
<td>2.1 [-6.00, 1.17]</td>
<td>100.0%</td>
</tr>
<tr>
<td>Skich 2008 (3)</td>
<td>35 24.7 (16)</td>
<td>40 25.5 (14.4)</td>
<td>-7.5 [-10.80, -0.00]</td>
<td>7.5%</td>
<td>-7.5 [-10.80, -0.00]</td>
<td>7.5%</td>
</tr>
<tr>
<td>Skich 2008 (4)</td>
<td>41 29.6 (21.2)</td>
<td>40 25.5 (14.4)</td>
<td>5.1 [4.10 -14.29, 12.49]</td>
<td>5.1%</td>
<td>5.1 [4.10 -14.29, 12.49]</td>
<td>5.1%</td>
</tr>
<tr>
<td>Xiong 2004</td>
<td>30 30.5 (5.8)</td>
<td>30 32.2 (5.8)</td>
<td>-1.7 [-1.70, 1.24]</td>
<td>41.8%</td>
<td>-1.7 [-1.70, 1.24]</td>
<td>41.8%</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>171</td>
<td>171</td>
<td>100.0%</td>
<td>-1.34 [-3.24, 0.56]</td>
<td>100.0%</td>
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</table>

Heterogeneity: Chi² = 8.09, df = 6 (P = 0.23); I² = 26%
Test for overall effect: Z = 1.38 (P = 0.17)
Treatment of Early-Onset Schizophrenia Spectrum (TEOSS) study

- No significant differences were found among treatment groups in response rates (molindone: 50%; olanzapine: 34%; risperidone: 46%) or magnitude of symptom reduction. Olanzapine and risperidone were associated with significantly greater weight gain. (Sikich 2008)

- Follow up: Only 12% adolescents continued in the study.

- No significant differences were found among treatment groups in response rates. All medicines associated with side effects. (Sikich 2010)
Evidence Base for Using Atypical Antipsychotics for Psychosis in Adolescents

Soumitra S. Datta*,1,2, Ajit Kumar3, Stephen D. Wright4, Vivek A. Furtado5, and Paul S. Russell6

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*To whom correspondence should be addressed; Child & Adolescent Psychiatry, Institute of Psychiatry, King’s College London, De Crespigny Park, London SE5 8AF, UK; tel: +91-9830477668, fax: +44-077085800, e-mail: ssdatta2000@yahoo.com
If evidence is so limited, it’s a good idea to see what child psychiatrists actually do?
Antipsychotic prescribing: old wine in new bottles?

Shermin Imran¹, Soumitra Shankar Datta², Elaine Vincent¹, Jade Whitfield¹, & Andrew F. Clark¹

¹Young Persons' Directorate, Greater Manchester West Mental Health NHS Foundation Trust, UK.
E-mail: shermin.imran@gmw.nhs.uk
²Dept. of Paediatric Liaison, Kings College London, South London and Maudsley NHS Foundation Trust, UK

Background: Recent research suggests first generation antipsychotic medications may be no less effective or tolerated than second generation antipsychotics. Aims: To review prescribing practices in UK adolescent mental health settings. Method: A review of literature and a postal survey (structured questionnaire) of clinicians in UK adolescent mental health settings (80 general and specialised in-patient units) were conducted. Results: Second generation antipsychotics remain the drug of first choice for most UK clinicians (based on a survey response rate of 40%). Conclusions: Guidelines for antipsychotic use in adolescents need updating. Clinicians who qualified in the last 10 years may need specific training and experience in use of first generation antipsychotics.
What to do for EOS and Adolescents with psychosis?

- Make sure you have made the correct diagnosis
- There are no tests that can confirm the diagnosis other than a good history and MSE
- Start the young person on atypical antipsychotic medication (start low – go slow)
  - Risperidone, Olanzapine, Quetiapine, Aripiprazole can be used
- Clozapine should be offered for treatment resistant patients
- Depot anti-psychotic medications (no evidence) but can be used in adolescents when indicated
- ECT may be used in severely impaired patients (AACAP).
Lived experience of adolescents on APD is complex – “If I have a problem, I’d rather beat it myself than breaking down and letting something else take care of it.”

Pressure to conform to youth culture – “and I went off my pills ...By choice...Because I had an issue with taking them. I don’t mind taking them now.”

Functioning – “I battled with drug usage...when you’re on antipsychotics...they don’t make you feel like yourself.”

Relationships - “I have different types of friends now.......”

PSYCHOPHARMACOLOGY

A Qualitative Study of Antipsychotic Medication Experiences of Youth

Andrea L. Murphy BScPharm, PharmD1,2; David M. Gardner MSc, PharmD1,2; Steve Kisely MD, PhD3; Charmaine Cooke BScPharm, MSc4; Stan P. Kutcher MD, FRCP C5; Jean Hughes RN, PhD6
Preventing side effects of antipsychotic medications

Antipsychotic medications are commonly used for several psychiatric conditions. Both first generation antipsychotic (FGA) medications and second generation antipsychotic (SGA) medications are associated with a variety of side effects that often jeopardize treatment and the quality of life of the patients receiving the medications. The side effects often lead to poor treatment adherence and ultimately relapse of the psychiatric illness for which they were prescribed. In the real world, often the potential side effects dictate the choice of medications more than other factors like clinical efficacy. Various risk factors for specific side effects are now known. This article focuses on the strategies that a clinician may use to predict and prevent at least some of the side effects like extra pyramidal symptoms, cardiac side effects, metabolic syndrome, dyslipidaemia and sexual dysfunctions in high risk patients. Primary and secondary preventive measures are discussed in light of current evidence and clinical experience of using antipsychotic medications.

Key words: Antipsychotic agents, adverse effects - Antipsychotic agents, prevention and control - Risk factors.
**Table II.**—*Preventing cardiac toxicities of antipsychotic medications.*

<table>
<thead>
<tr>
<th>Risk factors for increased cardiac adverse effects</th>
<th>Primary prevention strategies</th>
<th>Secondary prevention strategies</th>
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<tbody>
<tr>
<td>Older age</td>
<td>Do a baseline electrocardiogram for patients over 50 years of age and known cardiac problems. Get an opinion from a cardiologist prior to commencement of treatment with antipsychotic medications where cardiac problems are suspected. Avoid typical antipsychotic medications for patients with cardiac problems. Promote healthy lifestyle that includes a good diet and regular exercise. Do regular electrocardiogram for older patients at 3-6 months intervals. For those needing high dose antipsychotic medications (more than 1000 mg of Chlorpromazine equivalent per day), it is important to do regular medical evaluation including a cardiac evaluation.</td>
<td>Identify early any cardiac rhythm problems on commencement of antipsychotic medications. Get inputs from physician and cardiologist as needed. Treat these patients with antipsychotic medications with relatively lesser cardiac toxicities as Aripiprazole if antipsychotic medications are absolutely indicated.</td>
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Follow up

Maintenance dose of APD can be lower than the dose required during the acute episode.

One should be careful about side effects – as this is the key to having good medication adherence (sexual dysfunction in adolescent boys, weight gain in adolescent girls).
Retrospective Review of Clozapine Use in Children and Adolescents

Ardelle Komaryk, NP(F), MSN\textsuperscript{1}, Dean Elbe PharmD, BCPP\textsuperscript{2}, Leah Burgess, PhD, RPsych\textsuperscript{3}

Abstract

**Objective:** Literature describing use of clozapine by children and adolescents is limited. The primary study objective was to assess the patterns of clozapine use in an inpatient child and adolescent population. **Methods:** A retrospective review of child and adolescent inpatients receiving clozapine at a Canadian children’s hospital from January 2000 through December 2014 was conducted. Interdisciplinary comprehensive data collection was conducted by experienced clinicians. Baseline population characteristics and psychiatric illness risk factors were captured. Illness symptoms and severity were assessed retrospectively using validated measures including the Brief Psychiatric Rating Scale (BPRS), Children’s Global Assessment Scale (CGAS) and Clinical Global Impressions (CGI) scales. Estimated clozapine dosing requirements for each patient to achieve a serum level associated with response was calculated. Clozapine-related adverse events were captured. **Results:** Twenty-eight inpatients (64% female) receiving clozapine during the study period were identified. Mean age at clozapine initiation was 15.8 years. Twenty-three patients (82%) were taking clozapine at discharge, and of these 22 patients (96%) experienced at least minimal improvement in BPRS and CGAS scores. Patients took a mean of 33.1 days from clozapine start to reach their maximum clozapine dosage, a mean maximum of 57% of their estimated clozapine dose requirement. Mean length of stay following clozapine initiation was 60.7 days. We observed a high rate of benign hematological adverse events, but no episodes of severe neutropenia. The majority of patients were of ethnicity associated with high risk for metabolic adverse events. **Conclusion:** Most hospitalized, treatment-refractory children requiring clozapine clinically improve despite experiencing high, but largely manageable, adverse event rates.

**Key Words:** clozapine, child, adolescent, early-onset, schizophrenia spectrum disorders
Psychological interventions: Adolescents with psychosis
Psychological interventions for psychosis in adolescents (Review)

Datta SS, Daruvala R, Kumar A

Datta et al 2020
Do Psychological Interventions Work for Psychosis in Adolescents?

Rhea Daruvala¹, Ajit Kumar², and Soumitra Shankar Datta*¹,³

¹Department of Palliative Care and Psycho-oncology, Tata Medical Centre, Kolkata, India; ²Child and Youth Mental Health Service, Latrobe Regional Hospital, Victoria, Australia; ³MRC Clinical Trials Unit, Institute of Clinical Trials & Methodology, University College London, London, UK

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Types of psychological therapies tested for adolescents with psychosis

<table>
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<tr>
<th>Psycho-education</th>
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<tbody>
<tr>
<td>Cognitive Remediation therapy</td>
</tr>
<tr>
<td>Computer assisted cognitive remediation therapy</td>
</tr>
<tr>
<td>Non structured group therapy</td>
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<tr>
<td>Family therapy</td>
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</tbody>
</table>

All patients were also on medications, but details were mostly not reported by the authors.
Cognitive remediation therapy vs TAU

- 2 STUDIES
- No difference in Global State
- PANNS (TAU was better as reported by one study)
- Short term memory improved in CRT group ((1 study, n = 31, RR 0.58, 95% CI 0.37 to 0.89; very low certainty evidence)}
Group therapy vs TAU

- **Global state improved slightly** (1 study, n = 31, RR 0.58, 95% CI 0.37 to 0.89; very low certainty evidence)
- Mental State (No difference)
Cognitive Remediation Programme (CRP) + Psychoeducational Treatment Programme (PE) vs PE

- No difference in
  - Global state
  - Mental State
  - Cognitive functioning
  - Global functioning
Psychoeducational (PE) + Multifamily Treatment (MFT) Versus Nonstructured Group Therapy (NSGT, all long-term)

• No difference in
  • Global state
  • Mental State
  • Global functioning
  • Hospital admissions
Some evidence for group therapy (POOR QUALITY)
Some evidence for CRT (POOR QUALITY)
Impact of a review: Lay literature

Psychosis

From Wikipedia, the free encyclopedia

For other uses, see Psychosis (disambiguation).
Not to be confused with Psychopathy.

Psychosis in adolescents  [ edit ]

Psychosis is rare in adolescents.[26] Young people who have psychosis may have trouble connecting with the world around them and may experience hallucinations and/or delusions.[26] Adolescents with psychosis may also have cognitive deficits that may make it harder for the youth to socialize and work.[26] Potential impairments include the speed of mental processing, ability to focus without getting distracted (limited attention span), and deficits in verbal memory.[26]
Conclusions

Medications remain important in treatment of children and adolescents with psychosis.

There is almost no evidence in showing one medicine superior to other. Practice follows starting atypical APD and titrate slowly.

Psychological care includes educational, supportive and psychotherapeutic interventions.

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