Prescribing antipsychotics for children and adolescents

POMH-UK Quality Improvement Programme. Topic 10c (baseline audit)

Clinical background
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A recent survey of antipsychotic prescribing practice among child and adolescent psychiatrists in the UK found that well over 95% had prescribed antipsychotics over a 12 month period with the vast majority (almost 90%) choosing second generation antipsychotics (SGAs) (Otasowie et al. 2010). A similar survey conducted in the same region of the UK in the late 1990s found that under 60% of child and adolescent psychiatrists had used antipsychotics over a two year period with only 11% using SGAs (Slaveska et al. 1998). Otasowie et al. also surveyed community paediatricians among whom a third (33%) had prescribed antipsychotics (all used SGAs) over the previous year.

Psychosis, followed by challenging behaviour in autism spectrum disorder (ASD) and Tourette's syndrome are the most common reasons for child and adolescent psychiatrists to prescribe antipsychotics. In contrast, paediatricians most frequently use antipsychotics for non-psychotic developmental disorders including challenging behaviour in ASD and ADHD reflecting the fact that psychosis is treated almost exclusively by psychiatrists. Taking paediatricians and child psychiatrists together, antipsychotics are most commonly prescribed for challenging behaviour in non-psychotic developmental disorders (e.g. learning disability/ASD) followed by psychosis. Risperidone is the antipsychotic favoured by most clinicians treating children and adolescents, followed some way behind by aripiprazole and olanzapine (Otasowie et al. 2010).

The majority of antipsychotics are prescribed ‘off-label’ to children and adolescents, a common situation for drugs used in paediatric populations where clinical trial data are often lacking. However, several antipsychotics are licensed for use in children, for various indications and at different age ranges (see BNF for Children 2010-11 for details). Notably, low-dose risperidone is licensed for the short-term treatment of severe aggression associated with conduct disorder in children (age 5 years and older), short-term treatment of severe aggression in autism (age 5 years and older) and acute and chronic psychoses (age 12 years and older), while aripiprazole is licensed for the treatment of schizophrenia and mania in young people (aged 13 years and older).

Efficacy of antipsychotics in children and adolescents

There is a relatively limited evidence-base of randomised clinical trials to support antipsychotic prescribing in children and adolescents. However, evidence is accumulating to indicate the efficacy of antipsychotic drugs in the treatment of children and adolescents with psychosis/schizophrenia, including clozapine (Kumra et al. 1996), risperidone (Sikich et al. 2004, 2008) and aripiprazole (Findling et al. 2008). Other indications where antipsychotic efficacy in childhood is supported by clinical trial evidence includes management of challenging behaviour in ASD with risperidone (RUPP Autism Network, 2002) and aripiprazole (Owen et al. 2009), treatment of Tourette’s syndrome with risperidone (Scahill et al. 2003) and risperidone for management of aggression with conduct disorder (Findling et al. 2000) and learning disability (Aman et al. 2002).

Recent head-to-head comparisons of SGAs (risperidone and olanzapine) with first generation antipsychotics (FGA: haloperidol) in adolescents with schizophrenia have reported broadly similar efficacy against psychotic symptoms (with a non-significant trend in favor of SGAs) but a differing profile of adverse effects (Gothelf et al. 2003;
Sikich et al. 2008). These findings broadly replicate results from the large NIMH CATIE pragmatic trial that found no overall difference in effectiveness between FGAs and SGAs in adults, whereas there were differences in tolerability and side effect profiles (Lieberman et al. 2005).

**Dosage**

One of the main differences in prescribing between psychotic and non-psychotic disorders is in the dose of antipsychotic used. For example, while the dose of risperidone typically used to treat psychosis in children and adolescents is in the range of 4-6mg/day, considerably lower doses are used to treat challenging behaviour in ASD or tics/Tourette's with a typical dose range of 0.5-2mg/day.

**Adverse effects**

Children and adolescents appear to show greater sensitivity to a range of antipsychotic-related adverse events than adults, including extrapyramidal side effects (EPS) with FGAs (Kumra et al. 1998), and weight gain, obesity, and metabolic syndrome with the newer SGAs (Ratzoni et al. 2002).

Individual drugs differ importantly in terms of tolerability and side effect profiles when prescribed to children and adolescents. In younger patients (children and adolescents), EPS are more common with haloperidol and high-dose risperidone than with olanzapine. Weight gain and obesity are most common with olanzapine then with risperidone, and least with haloperidol. Sedation is greater with olanzapine and haloperidol than with risperidone (Toren et al. 2004). Further evidence is emerging that children and adolescents experience more rapid and serious weight gain on olanzapine and risperidone than do adults (Ratzoni et al. 2002). Morbid obesity [body mass index (BMI) > 90th percentile] is found in up to 50% of adolescents and young people chronically treated with SGAs (Theisen et al. 2001). Complications of obesity include hyperglycaemia (Type 2 diabetes), hyperlipidaemia, and hypercholesterolaemia. It is recommended that dietary advice (reducing carbohydrate intake) combined with regular exercise should be prescribed before initiating SGAs in children and adolescents.

It should be noted that most data relating to tolerability and adverse effects of antipsychotics in children and adolescents are based on the treatment of psychosis in short-term clinical trials over 6 to 12 weeks. There is a lack of adequate information on the adverse effects associated with both longer term prescribing and lower doses typically used in non-psychotic developmental disorders.

**Baseline investigations and monitoring**

Guidelines on appropriate investigations and monitoring of children and adolescents treated with antipsychotics are lacking. In practice, clinicians have to refer to guidelines developed for use in adults with psychosis (NICE Schizophrenia Guideline, 2009). Otasowie et al. (2010) found very little consistency in antipsychotic monitoring practice among child psychiatrists and paediatricians. Most clinicians surveyed said they would only routinely measure height, weight and blood pressure. Reluctance to undertake laboratory investigations among some clinicians may reflect various factors including ethical and practical difficulties in taking blood from children and uncertainty regarding the impact of abnormal results on clinical management (e.g. asymptomatic hyperprolactinaemia). However, most clinicians support the development of clinical prescribing and monitoring guidelines for antipsychotic use in children and adolescents.
Summary

Antipsychotics are prescribed by the vast majority of child and adolescent psychiatrists in the UK and a significant proportion of community pediatricians. The indications and most common uses of antipsychotics in children and adolescents include challenging behaviour/aggression in autism and conduct disorder, psychosis, and tics/Tourette’s syndrome. However, there is a growing awareness of the adverse-effect profiles of different drugs and greater sensitivity to these effects in children and adolescents. Currently in the UK, monitoring practice is inconsistent and most clinicians would welcome antipsychotic prescribing guidelines for children and adolescents covering initiation, dosing and monitoring in both psychotic and non-psychotic disorders.

The present audit focuses on the monitoring of side-effects and the use of antipsychotics in children and adolescents, areas for which there are well-established standards for practice and a large body of comparative data in adult mental health services in the UK (see POMH website: www.rcpsych.ac.uk/pomh). It is the first time that national prescribing practice in child and adolescent mental health services (CAMHS) has been reviewed and benchmarked in this way. In addition, it has taken advantage of what is a unique opportunity to collect data on aspects of psychiatric diagnosis, types of behavioural problem being treated and patterns of co-morbidity.