Antipsychotic treatment of children and adolescents is a double-edged sword

Psychotic disorders are among the most devastating conditions a human being can experience. When the first episode of psychosis occurs in childhood or adolescence, the toll is particularly heavy on the individual and the family. Schizophrenia is extremely rare in prepubertal age, affecting only one in 10,000 children before 12 years of age, but the incidence increases sharply from 13 years of age. Early-onset schizophrenia is related to worse long-term outcomes, more neurocognitive impairment, and higher dropout from school or work compared with adult-onset psychosis. Moreover, treatment options are few and efficacy of antipsychotic medication for children and adolescents has been questioned. Antipsychotic drugs are first-line treatment for schizophrenia, and most patients will need to take medication for substantial parts of their lives. Data indicate frequent use of antipsychotic drugs for non-psychotic mental disorders such as hyperkinetic and anxiety disorders in children and adolescents. Given that most antipsychotic drugs have neurological or cardiometabolic adverse effects, somatic health might be equally important to the effort to relieve psychotic symptoms in early-onset schizophrenia.

Anne Katrine Pagsberg and colleagues' Article published in The Lancet Psychiatry is an important contribution to the establishment of evidence-based pharmacological treatment of broadly defined first-episode early-onset psychosis among children and adolescents. Pagsberg and colleagues compared efficacy and tolerability among 113 children and adolescents recruited at seven Danish university clinics across 4 years. All patients had a first-episode psychosis, mainly schizophrenia or schizoaffective disorder, and were randomly assigned to a 12-week double-blind trial of either quetiapine extended release (target dose 600 mg daily) or aripiprazole (target dose 20 mg daily). The main efficacy measure was change in positive psychotic symptoms as measured by the Positive and Negative Syndrome Scale (PANSS). Main safety measures were weight gain, insulin resistance, akathisia, and sedation.

Both groups had a significant reduction of about 5-6 points on PANSS positive score, but the drugs did not differ with respect to symptom reduction. Children and adolescents receiving quetiapine gained on average 3.33 kg more weight than did those in the aripiprazole group. However, patients receiving aripiprazole had more akathisia and reported more sedation. The latter finding was unexpected, because aripiprazole is generally regarded as a non-sedating antipsychotic given its pharmacological properties as a partial dopamine D2 agonist.

Two ancillary findings from Pagsberg and colleagues' study are worth emphasising. First, only 22 (23%) of patients experienced treatment response, defined as a PANSS total score reduction of at least 30% plus a Clinical Global Impressions-Improvement score of 1 (very much improved) or 2 (much improved). Second, 111 (98%) of patients experienced adverse reactions. Among the 58 patients taking quetiapine, 47 (82%) reported increased duration of sleep and 45 (82%) reported weight gain. Among the 55 patients taking aripiprazole, 52 (91%) reported tremor and 44 (77%) reported failing memory. These findings clearly show that, although efficacious in alleviating psychotic symptoms, first-line pharmacological treatment for paediatric psychotic disorders is no cure for the illness, and it comes with a heavy burden of adverse effects. Pagsberg and colleagues' study shows the importance of head-to-head comparisons in regular clinical patients as an addition to the placebo-controlled registration trials often sponsored by manufacturers of the active drugs. The main message from the study is that aripiprazole and quetiapine are equally efficacious antipsychotic drugs in children and adolescents with psychosis, but they differ in adverse effects profile. A clinical implication of this result is that choice of antipsychotic drug should be based on adverse effect profile rather than efficacy alone.

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Why we need to understand service variation in compulsion

The past decades have seen substantial efforts to move the treatment of patients with mental illness to the community by dramatic reductions in the inpatient capacity of psychiatric hospitals and the scaling up of community services. At the same time, the use of compulsory admission is on the increase. Scott Weich and colleagues have shown that these processes are connected: between 1988 and 2008, the closure of two inpatient spaces was associated with one additional involuntary (compulsory) admission the following year.

Compulsory treatment (treatment against a patient’s will by invoking mental health legislation) has obvious implications for autonomy and liberty. Legislation rightfully sets out stringent criteria and requires that options for voluntary engagement have been exhausted before compulsion is permitted. Compulsion can only be used when clinically indicated in each individual case. This is why the substantial variation in the rates of involuntary admissions across different services and regions, as shown by Weich and colleagues, raises important questions. Such variation is not unique to the UK and is also observed in the use of Community Treatment Orders (CTO, legal regimes for outpatient compulsion) in England at hospital level and between individual psychiatrists. Instead of preventing admissions, the introduction of CTOs in 2008 seems to have increased the overall level of compulsion.

So far, little research has addressed this issue of service variation in compulsory care. Weich and colleagues’ work is therefore breaking new ground. In a previous analysis, Weich and colleagues showed that the rate of involuntary admissions is higher in urban areas with high proportions of young adults, men, and high levels of deprivation. This, they suggest, might explain some of the over-representation of people from ethnic minorities in hospital detention as they tend to be young men from such areas. In their present study, they go one step further by asking what might account for the observed variation in rates of compulsion. Investigating contributing factors at different levels simultaneously, Weich and colleagues find that the characteristics of patients, local areas, and provider trusts explain around 10% of the variance. This finding implies that 90% of the variance is independent of these factors and remain unexplained. This should be a cause for concern: we currently know very little about why some areas have much higher compulsion rates than others or why one patient is compelled while another is not.

Establishing why compulsion is on the increase and why there is variation in its use is important for many reasons. First, it is of relevance for professional conduct. Clinicians must be enabled to fulfill their duty to provide the best care available that is equitable, respectful of patient autonomy and that uses the least restrictive alternative. Second, clinical practice should be evidence-based. While there is scare evidence for patient benefits of inpatient compulsion, the evidence is strong that CTOs, introduced to reduce admissions, fail to do so. Third, compulsion impacts on patient experiences. Some patients have very negative experiences of compulsion that might lead to long-lasting emotional damage and might permeate their relationships with psychiatric services. Fourth, if service variation in compulsion reflects an arbitrary application of the Mental Health Act and not clinical need, it raises questions of the equity and quality of care, potential violations of human rights, and lack of opportunities for appropriate service user involvement. Further research might thus help to facilitate the appropriate use of the law. Fifth, it is a matter of social justice. Unless we can justify


