The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided. The patient described in this column is a composite with characteristics of several real patients.

Collaborative discontinuation of antipsychotics after the first episode of psychosis

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Nine months before presentation, a 29-year-old patient had his university studies interrupted because of a 1-month psychiatric hospital admission for a first episode of psychosis. His auditory hallucinations and grandiose delusions had improved on oral risperidone (4 mg/d), but he had abruptly stopped taking it because of weight gain 3 months later. He had subsequently deteriorated over the next month, with an exacerbation of psychosis, and had agreed to take aripiprazole. He had been on 15 mg of aripiprazole for the 6 months before presentation, had returned to the university and had managed his weight. He had decided to stop all antipsychotics as he felt fully well except for some fatigue.

On examination, he had no features of depression or mania. His scores on the 6 items of the Positive and Negative Syndrome Scale (PANSS) were all less than 3. He was keen to return to his life before antipsychotics. When we highlighted the higher risk of relapse upon discontinuation in the early phases of psychosis, he appreciated the reasoning but pointed out the pervasive lethargy and argued that he was likely to be among the minority who would not relapse. Considering the risk of complete therapeutic disengagement, we prepared a titration and monitoring plan, to which he agreed, and offered to maintain monthly contact with the nurse case manager.

This case raises a widespread therapeutic dilemma faced by clinicians treating patients in the early stages of psychosis. Although several guidelines recommend uninterrupted treatment for the first 2 years of schizophrenia (i.e., 18 months after the resolution of positive symptoms),[1] a firm diagnosis of schizophrenia is often not made in first-episode settings. Even when the diagnostic picture is clear, patients perceive the negative effects of antipsychotics to be more severe when active psychotic symptoms have resolved.[2] Recent evidence in favour of continued use of antipsychotics for up to 5 years after the first episode of schizophrenia to reduce the risk of relapse,[3] symptom exacerbation,[4] death[5] and work disability[6] is robust. Nevertheless, in practice, patients prioritize day-to-day well-being over the risk of future events such as relapse or death.[7] For those in the early phase of illness, a repeated cycle of interruption and reintroduction is the norm rather than the exception. Nearly 50%–60% of patients in some first-episode settings discontinue their antipsychotics within 2 years,[8,9] generally after 6 months of treatment, with more than 45% relapsing in the next 18 months.[9] One study involving a national cohort identified a median of 6 interruptions over 8 years of follow-up.[10] The development and implementation of tools for personalized risk estimations upon discontinuation are important, but given the high prevalence, the most pertinent clinical question is how to guide safe discontinuation within an early intervention setting when patients make such a decision.

Patients who appreciate the ongoing risk of relapse may still wish to test the hypothesis that they no longer need medication, as was the case with our patient. Discussion of the optimal timing and duration of the discontinuation trial and of frequency of monitoring (e.g., measurement of key symptom and functioning domains) is often helpful in such cases. Successful discontinuation is more likely in the absence of schizophrenia and substance use disorders, among patients who achieve premorbid (or satisfactory) levels of functioning and clinical remission (as with our patient) and when a good degree of social support is in place.[11] There are no clear guidelines on when to implement a discontinuation trial, but the presence of more than the minimal burden of psychotic symptoms should prompt a delay or reconsideration. Reinstituting treatment after a relapse appears to be associated with a diminished response that takes longer to occur.[12]

For some patients, discontinuation may induce cholinergic (often gastrointestinal) or dopaminergic (e.g., akathisia, movement disorders) withdrawal symptoms. Although the risk of relapse is highest in the first few months after stopping oral antipsychotics, a gradual worsening of symptoms may occur over longer periods.[4] A recent proposal advocates for hyperbolic tapering over several months;[13] the acceptability of such extended tapering in first-episode settings is yet to be evaluated. Given the lack of data for a firm recommendation, the best approach for tapering is likely to be one of a shared decision between the patient and the prescriber after acknowledging the uncertainties. Some antipsychotics (e.g., partial dopamine agonists, long-acting injections with long half-lives) may have less propensity to cause withdrawal syndromes.

It is risky to discontinue antipsychotics in first-episode settings, but it is a choice often made by patients. Many of the risks can be mitigated by enhanced clinical support, which may not be available in some settings.[14] To reduce concerns of family members of patients undergoing discontinuation trials,[15] it is crucial to develop an inventory of early warning signs of exacerbation (e.g., sleep disturbances, disorganized speech), enhance nonpharmacological support and maintain a positive therapeutic relationship and self-care during the discontinuation trial.[16] The prescribing process (i.e., information exchanged and uncertainties discussed) is a key variable in the overall

outcome, especially among patients who face negative experiences when seeking care.[17] In the absence of reliable, person-specific indicators of an impending relapse, individualized plans of collaborative antipsychotic discontinuation are necessary for optimal early intervention for psychosis.

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