

Treating Older Adults With Schizophrenia: Challenges and Opportunities

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Schizophrenia affects people of all age groups. Treatment plans for older adults with schizophrenia must consider the effects of age on the course of the illness as well as on the response to antipsychotics and to psychosocial interventions. Positive symptoms of schizophrenia tend to become less severe, substance abuse becomes less common, and mental health functioning often improves. Hospitalizations are more likely to be due to physical problems rather than psychotic relapses. Physical comorbidity is a rule, however, and older age is a risk factor for most side effects of antipsychotics, including metabolic syndrome and movement disorders. We recently reported high rates of adverse events and medication discontinuation along with limited effectiveness of commonly used atypical antipsychotics in older adults. Psychosocial interventions such as cognitive behavioral social skills training are efficacious in improving functioning in older adults with schizophrenia. In formulating treatment plans for this population, a balanced approach combining cautious antipsychotic medication use with psychosocial interventions is recommended. Antipsychotic medications should generally be used in lower doses in older adults. Close monitoring for side effects and effectiveness of the medications and a watchful eye on their risk:benefit ratio are critical. In a minority of patients it may be possible to discontinue medications. Sustained remission of schizophrenia after decades of illness is not rare, especially in persons who receive appropriate treatment and psychosocial support—there can be light at the end of a long tunnel.

Key words: schizophrenia/aging/antipsychotics/psychosocial treatments/cognition/psychosis

Introduction

The observation that some schizophrenia patients do well while not taking antipsychotic medication has been

previously addressed in the *Schizophrenia Bulletin*,¹ and Harrow and Jobe address the question of whether treatment without antipsychotic drugs is advantageous for some persons with schizophrenia in the present At Issue piece (Harrow and Jobe, this issue). This question has not been directly addressed in older persons with schizophrenia, but there is evidence to suggest that pharmacotherapy is substantially different in later age. Schizophrenia is a serious mental illness across the age spectrum. While the basic considerations for treatment remain similar, specific details vary considerably by age. It is worth repeating that, just as children are not small adults, older people are not merely chronologically older adults. There are several unique characteristics of aging that must be taken into account in considering treatment guidelines for older people with schizophrenia.

Aging in Schizophrenia

The definition of “older” in schizophrenia may differ from how it is defined commonly. Individuals with schizophrenia are reported to have accelerated physical aging, including premature morbidity and mortality compared with the overall population. The mean standardized all-cause mortality rate in schizophrenia is 2.58² and the average life span of a person with schizophrenia is 20–23 years shorter than that of an unaffected person.³ Thus, people with schizophrenia in their 40s and 50s may be comparable medically with those in the 60s and 70s in the general population.

Age-related pharmacokinetic changes relevant to antipsychotics include an increase in the volume of distribution and elimination half-life of the medications⁴ and an increase in the fraction of “free” (biologically active) drug in the blood due to a decrease in hepatic protein synthesis.⁵ Similarly, age-related changes in the permeability

of the blood-brain barrier may result in increased availability of antipsychotic medications in the brain for a given plasma concentration. Relevant pharmacodynamic changes in older adults include decreases in the absolute number of dopaminergic neurons and in the density of D₂ receptors in the brain. In older adults, extrapyramidal symptoms may occur at D₂ receptor occupancies that are lower (33%–79%) than those required in younger patients (80%).⁶ Older age is a risk factor for various antipsychotic-induced side effects including parkinsonism, falls, and metabolic syndrome.

Natural Course of Schizophrenia

Despite the presence of mild baseline cognitive impairment that predates the onset of the psychotic illness, the rate of cognitive aging in community-dwelling patients with schizophrenia appears to be comparable with that in the general population.⁷ Approximately 20% of middle-aged and older adults with schizophrenia have onset of their illness after age 40. This late-onset schizophrenia⁸ has somewhat better prognosis and requires lower daily dosages of antipsychotics than early-onset illness. In older adults with early-onset schizophrenia, outcomes are variable and interestingly aging tends to be associated with improved psychosocial function, less substance use, decreased psychotic symptoms,⁷ reduced risk of psychiatric hospitalization, and improved mental health-related quality of life.⁹ A survivor bias is only a partial explanation for such improvement. A small minority of patients experience a sustained remission of illness. We studied sustained remission over a period of 2–10 years among 155 independently living, middle-aged and older adults (range 40–70 years) with schizophrenia. In this cohort, 8% of patients met research criteria for sustained remission including having been taken off antipsychotic medications or having had their doses decreased by at least 50%.¹⁰

Thus, due to a natural clinical tendency for improvement in the symptoms, as well as increased risk of adverse effects, a reduction in dose or gradual tapering and discontinuation of antipsychotics may be possible in later years in a proportion of aging patients with schizophrenia.

Long-Term Safety and Effectiveness of Antipsychotic Medication Treatment in Older Adults

Although the long-term safety and effectiveness of antipsychotic medications in middle-aged and older adults with schizophrenia have been inadequately investigated, emerging data raise concerns. Using a study design that closely mimicked clinical practice (including equipoise-stratified randomization), we recently compared the safety and effectiveness of 4 atypical antipsychotics (aripiprazole, olanzapine, quetiapine, and risperidone) in

a group of 332 middle-aged and older outpatients with psychotic symptoms related to schizophrenia, mood disorders, posttraumatic stress disorder, or dementia, over a 2-year period.¹¹ Over half the patients discontinued their assigned antipsychotic medication within 6 months (median time to discontinuation was 26 weeks). Furthermore, there was a high 1-year cumulative incidence of metabolic syndrome (36% in 1 year). Serious (23.7%) and nonserious (50.8%) adverse events were common, while there was no significant improvement in psychopathology as measured with the Brief Psychiatric Rating Scale. There were relatively few significant differences in findings across disorders and among the 4 antipsychotics.

Effective Psychosocial Interventions to Improve Functioning

Several manualized psychosocial interventions have been found to be efficacious in improving functioning in middle-aged and older adults with schizophrenia in randomized controlled trials. For example, Cognitive Behavioral Social Skills Training, a group therapy that combines cognitive behavior therapy with social skills training and problem solving training, resulted in improvement in insight, frequency of social activities, and overall functioning in adults with schizophrenia over age 45, and participants reported maintenance of improvement in functioning 1 year after the end of treatment.¹² Functional Adaptation Skills Training, a 24-week manualized behavioral intervention targeting 6 areas of everyday functioning (medication management, social skills, communication skills, organization and planning, transportation, and financial management) enhanced everyday living skills and social skills in adults over age 40, with schizophrenia; the benefits were maintained at a 3-month follow-up.¹³ A social rehabilitation and integrated health care program (Helping Older People Experience Success) resulted in improvement in measures of social skills, psychosocial and community functioning, negative symptoms, and self-efficacy compared with treatment as usual in 183 older adults with serious mental illness, more than half of whom had a diagnosis in the schizophrenia spectrum.¹⁴ Use of mobile devices to facilitate psychosocial interventions may be a promising avenue to enhance dissemination of psychosocial treatments in community settings.¹⁵

Therapeutic Strategies for Middle-Aged and Older Adults With Schizophrenia

Sharing information with patients and their caregivers about a need for reducing dosages and increased risk of side effects of antipsychotics in older adults is important. The treatment decision-making process should involve

partnership with the recipients of treatment. It is generally advisable to start with a low initial dose (25%–50% of that used in a younger adult) of an antipsychotic and titrate slowly, depending on the response. In patients who have been stably maintained on antipsychotic medications, consideration should be given to gradual and incremental dose decreases in order to determine the lowest effective dose, and occasionally, eventual discontinuation. Patients should be vigilantly monitored for side effects and to determine whether the prescribed medication is effectively treating their symptoms. Importantly, there are psychosocial interventions that can be used to improve functioning, usually in combination with antipsychotic medication.

Future Directions

There are several critical gaps in the current knowledge regarding schizophrenia in late life that represent research opportunities. Elucidating the neurobiology underlying the variability in the clinical course of early-onset schizophrenia could help guide treatment decisions, inform prognosis, and potentially yield information to direct the development of novel treatment strategies. A better understanding of the pathophysiology of late-onset schizophrenia including the mechanisms underlying the preponderance of women compared with men is required. Finally, determination of the biological pathways underlying cognitive impairment in schizophrenia and development of treatments to improve these deficits in older adults should also be priority areas.

The data supporting the above comments do not directly address the issue raised by Harrow and Jobe. However, they do reinforce the notion that maintaining a sense of optimism in treating older persons with schizophrenia is vital because remission can occur even after decades of illness; there is often a light at the end of a long tunnel.

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