

Comparison of antipsychotic treatments in adolescents with schizophrenia

There is a wealth of scientific literature available on the treatment of adults diagnosed with schizophrenia. However, there is a paucity of data to guide the treatment of children and adolescents with schizophrenia.

“Although the U.S. Food and Drug Administration (FDA) has recently approved the use of aripiprazole and risperidone for adolescents with schizophrenia, few controlled data are available to help guide clinicians regarding the management of children and adolescents with schizophrenia who fail to respond to these standard 'first-line' antipsychotic treatments,” according to Dr. Sanjiv Kumra. Dr. Kumra is one of the authors of a new study to be published in the March 1st issue of *Biological Psychiatry*, which was undertaken to help fill this gap in knowledge.

The authors recruited 39 children, 10-18 years of age, who had already failed to respond to at least two antipsychotic treatments, to participate in a 12-week, double-blind, randomized study – the most rigorous of clinical trial designs. After initial assessments, the patients received treatment with either clozapine or “high-dose” olanzapine (doses that exceed the package insert recommendations) and were monitored for improvement in their symptoms.

The researchers discovered that clozapine was approximately twice as likely to produce a treatment response as olanzapine. Both positive symptoms (psychosis) and negative symptoms (blunted emotional response, reduced motivation) responded better to clozapine. John H. Krystal, M.D., Editor of *Biological Psychiatry* and affiliated with both Yale University School of Medicine and the VA Connecticut Healthcare System, comments on the findings: “Olanzapine is among the most effective antipsychotic medications, so the distinctive effectiveness of clozapine in this study could be very important.”

Dr. Kumra discusses this patient population: “The majority of these youth had histories of multiple hospitalizations, extreme violence, suicidality and trauma prior to study enrollment. Without appropriate intervention it is likely that many would have ended up in long-term care institutions, psychiatric prison settings, and/or experienced early death from drug use, violence, or suicide.” So, this preliminary data is hopeful, indicating that proper and effective treatment may be available for these adolescents, although there are also concerns.

Both medications produced significant weight gain and associated metabolic abnormalities. Dr. Krystal also adds that “clozapine has important side effects that have discouraged its prescription to children.” Dr. Kumra agrees, stating that “although clozapine is often considered as a treatment of ‘last resort’ because of its associated risk of agranulocytosis [a severe reduction in the number of white blood cells in the body], the striking symptom reduction observed in this clinical trial make apparent that clozapine has truly revolutionized the care of youth with treatment-refractory schizophrenia.”

Dr. Krystal concludes: “The long-term risks of medications, such as clozapine and olanzapine, will need to be weighed against their potential benefits. Thus, additional research will be needed to follow-up on this exciting but very preliminary finding.”

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