Stable monotherapy with clozapine or olanzapine increases the incidence of diabetes mellitus in people with schizophrenia


Q Does stable antipsychotic monotherapy increase the risk of diabetes mellitus and diabetic ketoacidosis in people with schizophrenia?

METHODS

Does the introduction of atypical antipsychotics, such as clozapine and olanzapine, lead to an increased risk of developing diabetes mellitus and diabetic ketoacidosis in people with schizophrenia? To answer this question, Leslie and Rosenheck conducted a prospective cohort study involving 56,849 people with schizophrenia who received a stable regimen of clozapine or olanzapine, and compared them to a control group. The study was conducted at the Department of Veterans Affairs Connecticut Mental Illness Research, Education and Clinical Center, USA, and included recruitment between June 1999 and September 2000.

Risk factors for diabetes mellitus were identified among the study participants, with a focus on patients with diabetes mellitus, as hospitalisation for diabetic ketoacidosis was identified from the Department of Veterans Affairs and was predominantly older and male. Time to diagnosis and hospitalisation was modelled using the Cox proportional hazards model, with attributable risks calculated for each outcome associated with different antipsychotics.

Main results:

At 25 months, 4,132 (7.3%) people were diagnosed with diabetes mellitus and 88 (0.2%) were hospitalised with ketoacidosis. Clozapine and olanzapine had the highest risk for diabetes compared with conventional antipsychotics. However, there was no significant difference in the risk for diabetes between both olanzapine and conventional antipsychotics, or quetiapine and conventional antipsychotics. Clozapine and olanzapine also increased the risk of diabetic ketoacidosis (clozapine vs control: HR 3.8, 95% CI 1.4 to 10.1; olanzapine vs control: HR 1.8, 95% CI 1.1 to 3.0). However, when the analysis was restricted to people with diabetes mellitus, the results were no longer statistically significant.

CONCLUSIONS

Diabetes mellitus incidence is increased in people with schizophrenia who are prescribed a stable regimen of clozapine or olanzapine. However, it is unclear whether the medication itself or other confounding factors in these people are responsible for this result (see http://www.ebmentalhealth.com/supplemental for table).

A typical antipsychotic (clozapine, risperidone, olanzapine, quetiapine, and others) has a low efficacy in addressing the negative symptoms of schizophrenia; second, they appear to have a lower propensity than typicals to cause extrapyramidal symptoms such as parkinsonism and tardive dyskinesia. Whereas typical antipsychotics have been available for 50 years, atypicals have only been introduced into clinical practice over the past decade. In this time, evidence has accumulated to suggest that atypicals are associated with a different spectrum of adverse effects. These newly recognised adverse effects include weight gain, dyslipidaemia, and alterations in glucose metabolism including diabetes. The mechanisms that contribute to the development of diabetes in patients taking atypicals are unknown. To complicate matters, people with schizophrenia appear to have a higher risk of diabetes than the general population, regardless of drug treatment.

The study by Leslie and Rosenheck generally supports findings from other studies. The current study suggests that the risk of diabetes attributable to atypical use is relatively small. Several important points should be kept in mind. First, although some studies (including this one) suggest that the risk for diabetes is highest in patients taking clozapine or olanzapine, there is ongoing debate as to whether use of other atypical agents also confers an increased risk of diabetes. Second, it is not clear whether the risk of diabetes with atypical use is generalisable to patients with conditions other than schizophrenia. Further evidence on this important potential adverse drug effect is needed. Pending further study, a consensus group has published guidelines to assist in the monitoring of patients who receive atypical antipsychotic medications.

Sudeep S Gill, MD, MSc, FRCP
Queen’s University, Kingston, Ontario, Canada

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