Schizophrenia, drugs and diabetes

Helen Rodenburg is a general practitioner in Wellington and the President of the RNZCGP

This article is a summary of recent literature about the problem of diabetes for those with schizophrenia, particularly in relationship to certain medication. This is an evolving area with knowledge being regularly updated.

Type 2 diabetes mellitus and impaired glucose tolerance are associated with antipsychotic treatment. Risk factors for Type 2 diabetes and impaired glucose tolerance include abdominal adiposity, age, ethnic status, and certain neuropsychiatric conditions. While impaired glucose metabolism was first described in psychotic patients prior to the introduction of antipsychotic medications (there is probably a two- to three-fold increased risk,[1] treatment with antipsychotic medications is associated with impaired glucose metabolism, exacerbation of existing Type 1 and 2 diabetes, new-onset Type 2 diabetes mellitus, and diabetic ketoacidosis.[2]

The strength of the association between antipsychotics and diabetes varies across individual medications, with the largest number of reports for chlorpromazine, clozapine, and olanzapine.

Recent controlled studies suggest that antipsychotics can impair glucose regulation by decreasing insulin action, although effects on insulin secretion, glucose transport or other mechanisms are possible.[1] Antipsychotic medications induce weight gain, and the potential for weight gain varies across individual agents with larger effects observed again for agents like chlorpromazine, clozapine, and olanzapine. Increased abdominal adiposity may explain some treatment-related changes in glucose metabolism. However, case reports and recent controlled studies suggest that clozapine and olanzapine treatment may also be associated with adverse effects on glucose metabolism independent of weight gain.[1] Dyslipidemia is a feature of Type 2 diabetes, and antipsychotics such as clozapine and olanzapine have also been associated with hypertriglyceridemia, with agents such as haloperidol and risperidone associated with reductions in plasma triglycerides.[2]

Clozapine appears to be a substantial problem. Investigators found no significant differences in overall incidence rates for diabetes, hyperlipidaemia or hypertension in patients receiving clozapine when compared with conventional antipsychotics BUT among younger patients (aged 20–34 years) clozapine administration was associated with a significantly increased relative risk of diabetes (2.5 [95% confidence interval, 1.2–5.4]) and hyperlipidemia (2.4 [95% confidence interval, 1.1–5.2]), but not hypertension (0.9 [95% confidence interval, 0.4–2.0]).[3] While in a further study[4] most cases of diabetes appeared within six months of initiating clozapine therapy and there were several cases of metabolic acidosis or ketosis, it is possible for diabetes to develop at any time and therefore screening six monthly has been suggested.[5] Baseline screening is obviously important. There is a prompt reversibility on withdrawal of the drug in some patients.[3]

Other points to be aware of are that people with schizophrenia:

- who have abnormal glucose metabolism have a higher prevalence of drug-induced tardive dyskinesia than patients with a normal glucose profile.[1]
- are also at risk of increased mortality due to cardiovascular disease, with presumed contributions from a number of modifiable risk factors (e.g. smoking, sedentary lifestyle, poor diet, obesity, hyperglycemia, and dyslipidemia).

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