



Managing the metabolic adverse effects of antipsychotic drugs in patients with psychosis

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Summary

Antipsychotic medications are widely prescribed and carry a variable propensity to cause weight gain and its attendant sequelae – hyperglycaemia, hypertension and hyperlipidaemia. These metabolic risks, along with smoking and poor lifestyle habits, occur between two and five times more often in patients with psychosis than in the general population. Early detection and intervention for cardiometabolic risks, and a judicious tailoring of the use of antipsychotic medications can help to improve long-term outcomes in these patients.

Key words: adverse effects, obesity, psychotic disorders.

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Introduction

Antipsychotic drugs remain the cornerstone of treatment for a number of psychiatric illnesses, including schizophrenia and bipolar disorder, however they have a wide range of adverse effects. A major problem of the older antipsychotics is the neurological effects such as parkinsonism, dystonia, dyskinesia and akathisia. With some of the newer 'atypical' antipsychotics, obesity and other risk factors for cardiovascular and metabolic disease are a problem. Although these metabolic effects can also be caused by the older antipsychotics, they have assumed greater importance as the incidence of premature mortality from preventable cardiovascular disease and diabetes has become increasingly evident.

It is estimated that the life expectancy of patients with schizophrenia will be shortened by up to 25 years compared to the general population, even after controlling for the risk of suicide.¹ At the same time, age-adjusted rates of cardiovascular death in the general population have been falling. For patients with schizophrenia or bipolar disorder as well as diabetes, the chances of premature death are significantly higher compared to matched persons with diabetes alone.² Clearly the illness and its treatment may be contributing to the development of metabolic risk.

Psychosis and cardiometabolic risk factors

Risk factors for cardiovascular disease are over-represented in people with psychosis. In a West Australian study of an adult community psychiatric service, over half of people with severe mental illness had metabolic syndrome.³ This was broadly in agreement with a database of chronic psychiatric patients from Victorian and NSW community and inpatient services (www.ccchip.com.au). Up to 89% of patients had an excess waist circumference. Females had higher rates of obesity.

It is estimated that the risk of diabetes in the people with psychosis is 2–6 times higher than the rest of the population, depending on age (the young have accelerated risk rates). Depending on the sample, impaired fasting glucose was found in up to 41% of those with severe psychiatric illness. People from certain ethnic backgrounds are more likely to develop diabetes than Caucasians. This includes people from Asia, the Middle East and the Indian subcontinent, African Americans and Latinos.*

Hyperlipidaemia is often an early metabolic response to some antipsychotics and is thought to be up to five times higher in those who have received antipsychotics than in the general population. The most common abnormality is a low level of high density lipoprotein cholesterol in up to 58% of patients. Raised triglycerides have been found in up to 53% of people with psychosis.³

High blood pressure (≥ 130 mmHg systolic or ≥ 85 mmHg diastolic in those with diabetes or at risk, as defined by the International Diabetes Federation, www.idf.org) was found in up to two-thirds of patients who are screened.³ This represents a rate at least twice that of the healthy population. Gender differences are common with males being more likely to have elevated blood pressure.

In the West Australian study, 64% of patients with psychosis smoked cigarettes.³ This is compared to 25–30% of the general population. This incidence appears to be similar across western countries over time.

Physical inactivity and unhealthy eating are extremely common in people with psychosis. There are many drivers of inactivity

* www.ahrq.gov/research/diabdisp.htm#HighDiabetes

including sedation and neuroleptic-induced cognitive deficits, negative symptoms, social withdrawal, inadequate social stimuli, lack of opportunity, poverty and severity of persecutory and other positive symptoms. These same clinical drivers as well as the appetite stimulating effects of the patient's psychotropic medication and the inability to plan and carry out meal preparation lead many patients to consume fast foods and sugared fizzy drinks as principal dietary components. Such drinks contribute enormously to obesity and the metabolic syndrome.⁴

Antipsychotics and cardiometabolic risk factors

There remains considerable debate as to the degree that antipsychotics contribute to cardiometabolic risks. In the short term there appears a clear hierarchy of drugs that promote weight gain, but in the longer term (and generally, patients with persistent psychosis are on lifelong maintenance therapy) it is less clear (Table 1).⁵ Clozapine has the highest potential to cause weight gain, followed by olanzapine and then quetiapine. The choice of antipsychotic will depend on many factors relating primarily to the patient's psychopathology. However if there is a family history of diabetes or cardiovascular disease, if the person is from a high-risk ethnic background or is young, the choice of antipsychotic should consider potential metabolic consequences of the prescription. Additionally, many commonly prescribed psychotropics (including valproate, lithium, mirtazepine, tricyclic antidepressants and some selective serotonin reuptake inhibitors) that are used in combination with antipsychotics may themselves lead to considerable weight gain. The weight gain potential of all of the patient's drugs should be considered as a whole.

Assessing cardiometabolic risk factors – how often?

It is important to start monitoring patients immediately after they have started antipsychotics, then every three months during the first year and every six months after that.

Lifestyle interventions

Recommended lifestyle changes are the same for patients taking antipsychotics as they are for the general population. A package of care comprising aerobic exercise, weight loss, smoking cessation, consuming a high soluble fibre diet, reducing alcohol intake and potentially adding omega-3 fish oils may lead to significant improvements in cardiovascular risks. Modifying lifestyle, including diet and exercise, is difficult in any population. However, the response of patients with psychosis may be more vigorous than anticipated and participation rates in structured programs may be high.⁶ Behavioural interventions for weight loss have been shown to reduce weight gain in patients starting antipsychotics. They also lead to weight loss

Table 1

Potential of atypical antipsychotics to cause weight gain

Drug	Metabolic potential
clozapine	high
olanzapine	
quetiapine	
risperidone	mild–moderate
amisulpride	
paliperidone	
aripiprazole	low
ziprasidone	

Prescribers should also be aware of the other common drivers of cardiometabolic risk in this population

and improved lipid and glucose profiles in those who are already receiving treatment.⁷

Using general practice care plans and forming partnerships with patient support organisations will help to offer lifestyle interventions as a routine practice. It is also important to work with families and carers when devising educational and lifestyle changes. Many families play an extensive role in the community care and support of patients with psychosis and may have well-intentioned but medically unhelpful approaches to diet and exercise.

Pharmacotherapeutic interventions

Should lifestyle management fail to provide adequate control of the developing risks, a number of additional strategies should be considered.

Switching antipsychotics

The potential of antipsychotics to cause metabolic effects varies (Table 1). In many cases it is very difficult to find an optimal antipsychotic drug for the individual.⁸ If you are considering switching the patient's antipsychotic, consult a psychiatrist first. A switching protocol can then be worked out. If the patient is becoming increasingly metabolically compromised, but their psychiatric history supports continuing their current medication, it may be wise to enhance the lifestyle modification as much as possible. Patients taking clozapine have probably not responded to other antipsychotics and switching is not advisable. Also, consider the weight gain potential of co-prescribed medications. If these are not absolutely required, they should be either discontinued or substituted for drugs with a lower potential to cause weight gain.

Drugs for metabolic illness

The use of standard pharmaceutical approaches for psychiatric

patients is similar to those for patients without mental illness. Sadly for those with mental illness, the likelihood of receiving adequate and appropriate pharmaceutical therapies, such as statins, is significantly less than for those without mental illness.⁹

Adherence

Up to two-thirds of patients with schizophrenia are non-adherent or partially adherent to their antipsychotic treatments. Adherence is reduced in those who take other medications and adherence rates are lower for hypoglycaemics and antihypertensives than for antipsychotics.¹⁰

Patient counselling to promote adherence should be a mainstay of all interventions offered to patients with metabolic comorbidity, just as it is an essential component of antipsychotic management. The key to success is regular follow-up with the general practitioner, itself an issue of partial adherence. If diabetes has been diagnosed, engaging the patient with appropriate specialist services such as a diabetes nurse educator may help with adherence.

Bariatric surgery

In a small case series, outcomes after bariatric surgery for morbidly obese patients with schizophrenia were similar to controls.¹¹ There are few studies that have carefully considered longer-term outcomes, or formulated consent guidelines for this population. However, it remains an option for those with severe complicated obesity where postoperative medical review is available and patient adherence is adequate.¹²

Conclusion

The rates of metabolic disorder and general cardiovascular risks are high in those receiving antipsychotics. Patients receiving these drugs should be regularly monitored for cardiometabolic risk factors. Prescribing appropriate lifestyle and drug interventions, establishing links with programs that deal with psychosocial aspects of medical and psychiatric illness, being mindful of poor adherence and taking a family-based proactive approach are all important when managing these patients. In some circumstances patients may be switched to an antipsychotic with a lower potential to cause weight gain, after consultation with a psychiatrist.

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Further reading

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Professor Lambert has worked with Janssen Cilag, Pfizer, Hospira, Bristol-Myers Squibb, AstraZeneca and Eli Lilly as a speaker and on advisory boards, and has received education or research support from Janssen Cilag, Hospira, Bristol-Myers Squibb and Eli Lilly.

Self-test questions

The following statements are either true or false (answers on page 123)

1. Patients with psychosis are twice as likely to have high blood pressure than the general population.
2. Ziprasidone has a high potential to cause weight gain.