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The metabolic syndrome and schizophrenia: the latest evidence and nursing guidelines for management

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The metabolic syndrome and schizophrenia: the latest evidence and nursing guidelines for management

The introduction of second-generation antipsychotic drugs for the treatment of schizophrenia has provided significant benefits for clients experiencing this disorder. While they have been found effective in reducing psychotic symptoms, there is evidence that these drugs are also linked with a group of side effects commonly known as the metabolic syndrome. Mental health nurses are well positioned to prevent, detect and/or manage the development of this problematic constellation of symptoms. Guidelines for practice can be useful in prevention and management of the syndrome and enhance nursing care of clients who are taking second-generation antipsychotics.

Keywords: diabetes, metabolic syndrome, obesity, second-generation antipsychotic drugs, syndrome X

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Introduction

The development of the newer second-generation or atypical antipsychotic drugs has provided benefits to many people with schizophrenia. These are mainly related to their lower risk of extrapyramidal side effects compared with traditional antipsychotics, and their greater efficacy in treating the negative and affective symptoms of psychoses. However, the atypical antipsychotics have been linked to a number of serious side effects, including obesity, hyperlipidaemia, type 2 diabetes mellitus and diabetic ketoacidosis. Together, these comprise the potentially life-threatening syndrome referred to as the metabolic syndrome (Henderson *et al.* 2005).

This review article provides an overview of the metabolic syndrome, its association with schizophrenia, and the underlying mechanisms of the disorder. This article also discusses the clinical implications of this syndrome for mental health nurses and proposes a set of guidelines for use by clinicians managing people with schizophrenia who are prescribed the second-generation antipsychotic drugs.

Antipsychotic drugs and their use in the treatment of schizophrenia

The development of the antipsychotic drugs in the 1950s was a major breakthrough in the treatment of schizophrenia, and these drugs have now become the mainstay of treatment for the disorder. The traditional or first-generation antipsychotics (FGAs) are clearly effective in the treatment of the positive symptoms of psychosis such as hallucinations and delusions. These drugs do not, however, alleviate the negative symptoms of schizophrenia, and are known to produce extrapyramidal side effects such as

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drug-induced Parkinsonism, dystonic reactions and akathisia at clinically effective doses. These side effects can result in distress, stigma, diminished function and failure to take the medications as prescribed (Usher 1997; Therapeutic Guidelines Ltd 2003; Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes 2004). The second-generation antipsychotics (SGAs), on the other hand, have fewer or no extrapyramidal side effects, are more effective at treating the cognitive impairment and negative and affective symptoms of the illness, and are usually better tolerated (Therapeutic Guidelines Ltd 2003; Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes 2004; Masand & Mago 2005). For these and other reasons, the SGAs are increasingly used over the FGAs in the treatment of psychotic disorders, including schizophrenia (Lambert & Castle 2003). Nonetheless, the various SGAs have their own side-effect profiles, and some have been linked to the development of metabolic syndrome in people taking them for the treatment of schizophrenia (Henderson *et al*. 2005). Numerous case reports also indicate a worsening of glycaemic control or new-onset diabetes, including diabetic ketoacidosis (Chen 2005).

The prevalence of metabolic illnesses including diabetes in people with schizophrenia

People with schizophrenia are known to have a reduced life expectancy of as many as 9–12 years less than the general population, reported to be mainly due to factors such as an increased rate of suicide and illness, as well as an increased prevalence of type 2 diabetes and cardiovascular disease (Lambert *et al*. 2003; Holt *et al*. 2004). The recognition of a higher incidence of diabetes in individuals with schizophrenia is not new. Holt *et al*. (2004) claim that diabetes was first linked to people with schizophrenia by Sir Henry Maudsley in 1879, and therefore, people with schizophrenia were known to be affected by insulin resistance, weight gain and type 2 diabetes long before the SGAs were available (Baptista *et al*. 2004).

The effects of antipsychotics on metabolism and weight gain were additionally identified in the 1960s (Baptista *et al*. 2004). Since this time, there has been increasing interest in the link between antipsychotic medication, weight gain, diabetes and the potential for metabolic syndrome. Recognition of an association between SGAs, obesity and diabetes is also evident (Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes 2004). This is particularly the case with clozapine and olanzapine, and less so with risperidone and quetiapine (Procyshyn *et al*. 2000; Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes 2004). As a result, Sacks (2004) suggests that the term 'metabolic liability' should be considered in relation to the link between antipsychotic drugs and metabolic syndrome, and that a liability assessment should be considered prior to commencing SGAs.

Limited evidence indicates that the prevalence of diabetes among people with schizophrenia is 1.5–2.0 times higher than the general population, but whether this is a result of the illness or the treatment remains unknown. Possible explanations for the higher incidence of diabetes in people with schizophrenia include the higher incidence of obesity, poor diet and the effect of antipsychotic agents (Chen 2005). People's genetic makeup and their environment is also thought to contribute to the development of metabolic syndrome, but it remains unclear as to why some develop it and others do not (Lieberman 2004).

Recent studies suggest that the syndrome is increased in people with schizophrenia (Holt *et al*. 2004; Henderson *et al*. 2005), and in particular in those taking the SGA drugs such as olanzapine and clozapine (Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes 2004). Sacks (2004) reports the prevalence of metabolic syndrome in people with schizophrenia to be as high as 37%; however, Sacks (2004) cites the Ryan *et al*. (2003) study, which suggests there may be metabolic abnormalities present in the person before the commencement of antipsychotic medication and therefore, medication alone may not be responsible for the development of metabolic syndrome.

Drug-induced weight gain, poor diet and a potential association between SGAs and impaired glucose tolerance are all reported in recent literature as potential links between SGAs, schizophrenia and metabolic syndrome (Taylor & McAskill 2000; Chen 2005). Furthermore, antipsychotic drugs are thought to increase appetite and subsequently weight gain, thus inducing metabolic anomalies (Baptista *et al*. 2004).

The metabolic syndrome in schizophrenia

Metabolic syndrome is the presentation of a cluster of metabolic abnormalities associated with an increased risk of cardiovascular disease. This group of abnormalities has been frequently observed in people with schizophrenia, and it appears that a high proportion of patients have the syndrome (Baptista *et al*. 2004). The abnormalities of this complex medical condition include dramatic weight gain, especially abdominal or visceral obesity; diabetes (even the incidence of acute metabolic decompensation such as diabetic ketoacidosis); atherogenic lipid profile [increased low-density lipoprotein (LDL) cholesterol and triglyceride levels, and reduced high-density lipoprotein (HDL) choles-

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terol]; and elevated blood pressure (Antai-Otong 2004; Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes 2004; Holt *et al.* 2004; Sacks 2004). Insulin resistance is known to play a significant role in most components of metabolic syndrome and as a result, carbohydrate metabolism is critically disturbed (Baptista *et al.* 2004). Specifically, abdominal circumference of more than 102 cm in men and 88 cm in women, triglycerides greater than or equal to 150 mg/dL, HDL cholesterol less than 40 mg/dL in men or less than 50 mg/dL in women, a blood pressure greater than or equal to 130/85 mmHg, and a fasting glucose greater than or equal to 100 mg/dL, defines the metabolic syndrome (Wirshing *et al.* 2003; Masand & Mago 2005).

This syndrome, recognized for many years now, has also been called syndrome X or insulin-resistance syndrome (Sacks 2004). Unfortunately, the signs and symptoms of the syndrome often go unrecognized and untreated in people with schizophrenia (Antai-Otong 2004). The causes of metabolic syndrome are not well understood, but involve a number of factors, including the presence of central or visceral obesity and insulin resistance, a sedentary lifestyle, and genetic susceptibility (Sacks 2004).

Obesity

Significant weight gain is often the most obvious sign of metabolic syndrome, and for many patients, is the most distressing (Lieberman 2004). Drug-induced weight gain from antipsychotics has for some time been associated with patients' reluctance to continue taking these medications, which, in many situations, can lead to a higher risk of relapse of psychotic symptoms (Taylor & McAskill 2000). Significant weight gain is also a risk factor for diabetes (Wirshing *et al.* 2003), potentially increasing the risk of metabolic syndrome.

Diabetes

Diabetes is a common chronic illness, which currently affects 1.2 million people in Australia (Diabetes Australia 2004a). Diabetes mellitus is classified into four sub-groups, of which drug-induced diabetes is included in the *other types of diabetes* group (Diabetes Australia 2004b). Diabetes has many increased risk factors, including weight gain, age, dyslipidaemia and sedentary lifestyle. More recently, SGA use has been linked to the increasing number of people with schizophrenia and diabetes (Chue 2004; Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes 2004). This link presents a number of challenges for the person with schizophrenia, including coping with another chronic illness, medication compliance and increased risk of metabolic syndrome.

Dyslipidaemia

Impaired glucose tolerance and insulin resistance are closely associated with abnormalities of lipid metabolism (Chue 2004), and weight gain has been shown to be concordant with lipid changes (Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes 2004). Clinical indicators of dyslipidaemia include 'elevated triglycerides, low high-density lipoprotein (LDL) cholesterol, and small, dense low-density lipoprotein (LDL) particles with normal or slightly elevated LDL cholesterol levels' (Ginsberg 2003, p. 31E).

Of the SGAs, clozapine and olanzapine are reported to induce the greatest weight changes along with increases in lipid levels (Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes 2004), while risperidone and quetiapine have a negative relationship to weight gain. Ziprasidone and aripiprazole are considered to have a neutral effect on weight gain (Baptista *et al.* 2004). Phenothiazine treatment has been reported to increase triglycerides and decrease cholesterol levels (Holt *et al.* 2004), while a 52-week open-label extension study comparing aripiprazole and olanzapine found changes in baseline fasting lipid levels, with the researchers concluding that 'symptom improvement was comparable with aripiprazole and olanzapine' (Stock *et al.* 2005).

Clinical implications and guidelines for practice

Given the rising incidence of metabolic syndrome and the high associated morbidity and mortality (Lieberman 2004), efficient strategies are needed to help prevent the development of the condition and/or counteract its effects. Nurses can play an important role in the prevention of metabolic syndrome by increasing their understanding of the syndrome and educating the person who is being treated with SGAs. The incidence of metabolic syndrome related to SGAs in people with schizophrenia can be reduced by client education, assistance with ongoing monitoring and the detection of early indicators of metabolic syndrome (i.e. increased weight circumference and elevated blood pressure). The following discussion provides the nurse with guidelines that can be followed to assist in the early detection and ongoing treatment of metabolic syndrome.

Table 1 provides a summary of the clinical indicators to look for in assessment of metabolic syndrome.

Due to the increased risks for metabolic syndrome in clients with schizophrenia who are prescribed and taking SGAs, there is a need for close monitoring of their physical status. Mental health nurses have a pivotal role to play in implementing this strategy. Baseline assessment should include any personal and/or family history of diabetes, obe-

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sity, hypertension, dyslipidaemia and cardiovascular disease. Weight and height should be recorded and body mass index calculated. Waist circumference should be taken at the level of the umbilicus (Masand & Mago 2005). This in itself may be an effective preventive measure, because measurement of abdominal girth at an outpatient clinic, for instance, has been noted to lead to behaviour change as patients began to enquire about the reason for the measurement and consequently changed their diet in response to the explanation (Gupta 2004).

It is also important to obtain blood chemistries and monitor fasting glucose and lipid levels prior to and at least every 3 months during treatment with SGAs (Wirshing *et al*. 2003; Antai-Otong 2004; Gupta 2004; Lambert & Chapman 2004). Patients should be asked routinely whether they have noticed any weight gain, a change in pants or belt size, or whether they have experienced excessive thirst or increased frequency of urination (Wirshing *et al*. 2003). Information and education about nutrition and physical activity should be provided to all patients on commencement of SGA medication, particularly those who are overweight. If patients gain 5% or more of their initial weight or develop diabetes or dyslipidaemia after commencement of the medication, the SGA may need to be changed to one with a lower-risk profile (Masand & Mago 2005).

Lifestyle modification is considered first-line treatment for metabolic anomalies and has been found to be effective in halting the progression of metabolic syndrome (Ginsberg 2003; Sacks 2004). Lifestyle modification involves assessing the person's diet and nutritional status and exercise regime, and making changes to influence weight reduction and increase physical activity (Nutrition Australia 2002; Ginsberg 2003; Diabetes Australia 2004b; Sacks 2004). There are many weight loss programmes available, and nurses can help guide the client to choose a reputable group, for example, Diabetes Australia, the National Heart Foundation, Nutrition Australia or local dieticians (Evans *et al*. 2005). A recent study found that individual nutrition education from a dietician alone can minimize weight gain for the person commenced on olanzapine (Evans *et al*. 2005). Table 2 outlines steps that the client can take to assist in reducing the development of metabolic syndrome.

Table 1
Clinical indicators of metabolic syndrome

Waist circumference	
Women	>88 cm
Men	>102 cm
Serum triglycerides	≥150 mg/dL
HDL cholesterol	
Women	<50 mg/dL
Men	<40 mg/dL
Blood pressure	≥130/≥85 mmHg
Fasting glucose	≥100 mg/dL

Masand & Mago (2005).
HDL, high-density lipoprotein.

Table 2
Steps to reduce the development of metabolic syndrome

Six steps to reduce metabolic syndrome
Increase activity level
Improve health through better eating habits
Lose weight
Quit smoking
Reduce stress levels
Take any medication prescribed

Nutrition Australia (2002).

Table 3
Guidelines for practice

Guidelines for practice for the person who is taking second generation antipsychotics

Comprehensive baseline assessment, including:

- Physical examination
- Cardiac investigations
- Blood chemistries
- Weight
- Height
- Waist measurement
- Body mass index (BMI)
- Family history
- Personal history
- Monitoring of BP, BMI and waist circumference at 4, 8 and 12 weeks after commencing treatment is recommended then 3 monthly (Baptista *et al*. 2004; Masand & Mago 2005)
- If there are no signs or current risk factors for metabolic syndrome indicated that the nurse needs to continue regular monitoring of BP, waist circumference and educate the person re: diet and exercise (Wirshing *et al*. 2003; Antai-Otong 2004; Gupta 2004; Lambert & Chapman 2004)

If there is evidence of early indicators (increased waist circumference and elevated blood pressure), there is a need to monitor:

- waist circumference every 3 months
- BP every 3 months
- BMI every 3 months (Wirshing *et al*. 2003; Antai-Otong 2004; Gupta 2004; Lambert & Chapman 2004)
- Commence treatment, e.g. reduction of weight and an increase in physical activity (Wirshing *et al*. 2003; Antai-Otong 2004)
- If there are three or more symptoms of metabolic syndrome need to commence treatment (e.g. reduction of weight, and an increase in physical activity and medications Wirshing *et al*. 2003; Antai-Otong 2004), ongoing monitoring and referral to a specialist

BP, blood pressure.

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Good early clinical indicators of metabolic syndrome include an increase in waist circumference and elevated blood pressure (Gupta 2004). When three or more of the components of metabolic syndrome are present (i.e. weight gain, increased blood pressure, raised triglycerides, lowered HDL, and raised fasting glucose levels), there is a need for active intervention (Wirshing *et al*. 2003). First-line therapy involves reduction of weight and an increase in physical activity (Wirshing *et al*. 2003; Antai-Otong 2004). Table 3 summarizes the guidelines for practice for mental health nurses working with the person taking SGAs.

Conclusion

Metabolic syndrome is becoming increasingly prevalent in at-risk populations, including clients treated with SGA medication. Several explanations for the increase of this syndrome in people with schizophrenia include hereditary factors, the environment, lifestyle and drugs. Mental health nurses need to consider their important role in the prevention and ongoing management of people with this syndrome. To begin, mental health nurses must become aware of the syndrome, its link to SGAs and its implications. The benefits of increased awareness of metabolic syndrome for mental health nurses are the early detection of symptoms for clients and increased understanding of the need for ongoing monitoring and treatment. Careful monitoring of at-risk clients may help prevent the onset of metabolic syndrome or help prevent further deterioration of the client's physical health status. Nurses also have an important role to play in educating clients about the potential for metabolic syndrome and its link to SGAs. As a group with a higher than average risk for diabetes, the client needs assistance to weigh up the advantages and disadvantages of taking antipsychotic drugs, particularly the SGAs.

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