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Case Report

The effects of antipsychotic switching on diabetes in chronic schizophrenia

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Abstract

Background People with severe mental illness have a 20-year life-expectancy shortfall. The majority of antipsychotic medications are associated with obesity and heightened diabetes risk. People with severe mental illness less frequently achieve benchmarked diabetes care, often attributed to poor adherence, lower clinical attendance and documented medical biases in treatment. This case is presented to highlight the profound effect medication change can have on diabetes control.

Case report A 56-year-old man with a 42-year history of schizophrenia had required clozapine treatment for the preceding 14 years. Type 2 diabetes and obesity occurred within 4 years of clozapine instigation. Glycaemic control had been continuously poor, despite frequent contact with diabetes services and multiple medications, including insulin at a dose exceeding 200 IU daily. Request for consideration of antipsychotic review and close interaction with the psychiatry team was initiated at the diabetes outpatient clinic. A gradual medication switch from clozapine to aripiprazole was associated with a reduction in HbA_{1c} from 80 to 50 mmol/mol (9.5 to 6.7%) over 4 months, associated with a weight loss of 10 kg. Over the ensuing 2 years, the improvement in HbA_{1c} has endured, with total weight loss of 13 kg and halving of insulin requirements.

Conclusion This case illustrates the benefits of engagement between endocrinologists and psychiatrists to achieve the shared goal of improved physical health in severe mental illness. Greater interdisciplinary collaboration will help bridge the life-expectancy gap in severe mental illness and may assist in preventing disabling diabetes complications in this vulnerable patient group.

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Introduction

Severe mental illnesses such as schizophrenia are associated with increased mortality [1] and a 20-year loss of life expectancy [2], the greatest proportion of which is attributable to physical illness, mostly cardiovascular disease [3]. Of concern, this mortality disparity is widening over time [4].

In addition to cardiovascular disease burden, schizophrenia is associated with increased diabetes susceptibility [5–7]. Independently, antipsychotic use is associated with higher rates of diabetes, obesity and the metabolic syndrome [8]. Amongst antipsychotics, clozapine and olanzapine are associated with higher rates of weight gain and hyperglycaemia [9], whilst others (namely, aripiprazole, amisulpride and ziprasaone) appear to be lower risk [10]. Additional risk factors promoting diabetes and cardiovascular disease in this susceptible group are reduced physical activity (a consequence of the illness or medication-induced sedation), poor diet and smoking [11].

This case report illustrates the impact of a change in antipsychotic medication on diabetes control in a man with chronic schizophrenia. It is presented as an example of how endocrinologists might achieve diabetes standards of care targets in this challenging patient group, through increased awareness of the metabolic effects of antipsychotic medications and by working collaboratively with psychiatry colleagues for better patient care and outcomes.

Case report

A 56-year-old man with long-standing schizophrenia is presented. His history of schizophrenia began at age 14 years, with auditory hallucinations and persecutory delusions characterizing his psychosis. He received different

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What's new?

- In a man with chronic schizophrenia, obesity and poorly controlled insulin-requiring diabetes, this case reports marked improvement in glycaemic control and weight following a switch in antipsychotic medication, sustained over 2 years.
- It demonstrates the benefits of collaboration between psychiatrists and diabetologists in facilitating achievement of benchmarked diabetes care in this vulnerable patient group.

antipsychotic medications and in early adulthood led a contained life as an artist, requiring community support and a disability pension. His mental health remained precarious. At age 30 years, a suicide attempt resulted in bilateral below-knee amputations. At age 40 years, his mental health deteriorated again and he received clozapine. At age 44 years, he developed symptomatic hyperglycaemia with polyuria, polydipsia and weight loss. A random glucose level was 16.8 mmol/l with HbA_{1c} 99 mmol/mol (11.2%). There was no family history of diabetes mellitus.

The patient smoked 20 cigarettes/day and consumed no alcohol. He described a lifestyle pattern of being unable to rise before 11.00 h and sedentariness. At first contact with diabetes services, he weighed 94 kg.

Because of difficulties in achieving glycaemic control, insulin replacement was instigated with premixed isophane/soluble insulin 56 units in the morning and 58 units in the evening, in addition to metformin 1000 mg twice daily. He ceased smoking and has remained abstinent. HbA_{1c} levels of 45–53 mmol/mol (6.3–7.0%) were achieved, but only short-term. Over the next 8 years, HbA_{1c} levels were consistently 64–80 mmol/mol (8.0–9.5%) and weight gain was progressive (Fig.1). As a result of his poor glycaemic control, he received frequent endocrinologist and diabetes educator reviews (3–7 and 5–20 occasions of service per annum, respectively). Following stabilizations, HbA_{1c} levels would temporarily reach 48–57 mmol/mol (6.5–7.4%) and, then rapidly rise again. There was continual weight gain, paralleling increased insulin doses. At age 54 years, he weighed 112 kg and HbA_{1c} levels consistently exceeded 64 mmol/mol (8.0%) despite insulin therapy of more than 200 units daily. Microalbuminuria developed with borderline hypertension 2 years after diabetes diagnosis and was treated with candesartan 16 mg daily. Blood pressure was subsequently maintained within target range.

He attended the hospital's clozapine services monthly, which supervised adherence and monitored for agranulocytosis as part of the routine national mandatory prescribing requirements for this medication. He also attended his general practitioner intermittently—approximately 6-monthly.

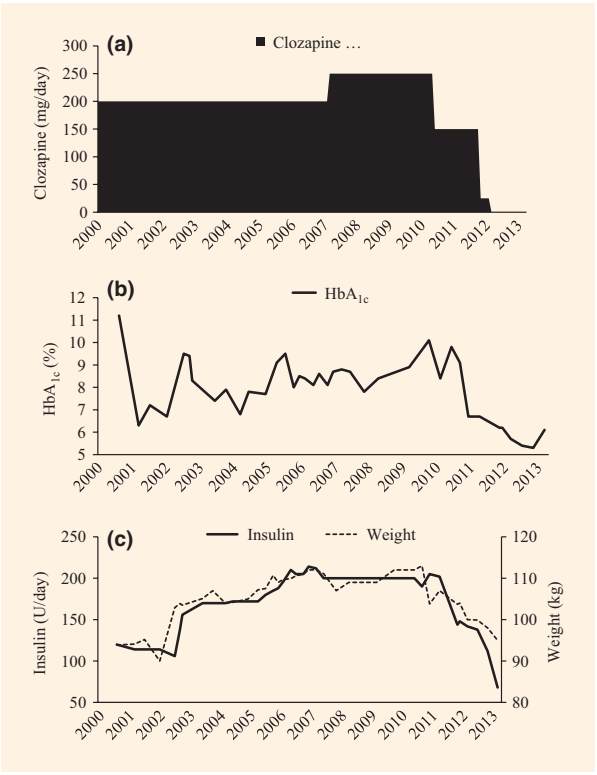

FIGURE 1 Time course of changes in weight and insulin doses and HbA_{1c} (b and c, respectively) in a 56-year-old man with clozapine-treated schizophrenia and diabetes, corresponding to changes in clozapine dose (a) over consecutive diabetes ambulatory care visits between 2000 and 2013.

Because of ongoing challenges in achieving glycaemic targets, referral for formal psychiatry review was requested from diabetes services, asking whether clozapine or its dosage could be altered. Under the careful supervision of a psychiatrist, a very gradual clozapine dose reduction was made, with aripiprazole commenced as a covering antipsychotic. Clozapine was very gradually withdrawn over 18 months under close supervision, eventually switching to aripiprazole as the sole antipsychotic agent. Figure 1 shows the reductions in weight, HbA_{1c} and insulin requirements that followed clozapine dose reduction and withdrawal. Glycaemic improvement was evident within 4 months of clozapine dose reduction, with HbA_{1c} dropping from 84 to 50 mmol/mol (9.8 to 6.7%), paralleling a 10-kg weight loss. Over 2 years, the patient's weight fell by 13 kg and daily insulin doses were more than halved.

There were additional benefits. First, the patient immediately experienced less sedation following clozapine dose reduction. As a consequence, he woke earlier and exercised more. Social engagement improved, with re-engagement in his art and t'ai chi lessons. In clinic visits, he appeared alert and initiated conversations with his clinicians on various topics, in marked contrast to prior interactions. Second, his

need for diabetes services markedly reduced: only one stabilization was required following clozapine withdrawal (for insulin reduction, in contrast to all prior referrals) and endocrinologist review now occurs routinely, 2–3 times annually. With improved glucose control, the microalbuminuria decreased from 58.7 to 4.8 mM Cr (relative risk < 2.5). Two years after starting the antipsychotic switch from clozapine to aripiprazole, HbA_{1c} remains tightly controlled at 34 mmol/mol (5.3%) on less than half the patient's prior insulin doses.

Discussion

Diabetes in the setting of severe mental illness places an additional burden on individuals who are conceivably the least able to confront the challenges of diabetes self care, such as blood glucose monitoring, complex lifestyle changes and additional medications. The impact of poor diabetes control and its longer-term consequences adds to the burden of poor physical health in this patient group and is likely to contribute to the life-expectancy shortfall. Disparities in healthcare access, utilization and the lesser delivery of standard health care at point of contact, all contribute to the poor physical health of people with severe mental illness [12,13]. For example, despite higher metabolic risk, people with severe mental illness less frequently receive appropriate risk factor assessment, including even rudimentary clinical measures such as weight or blood pressure [8]. There is evidence that people with diabetes and severe mental illness less frequently receive standard diabetes care, including measurement of HbA_{1c} and lipids or eye examinations, despite poorer glycaemic and lipid control [11].

This case reports the impact of antipsychotic change on glucose variables in a man with both chronic schizophrenia and poorly controlled insulin-treated diabetes, with very marked improvements in the latter rapidly observed. The case highlights several important lessons for diabetologists and psychiatrists caring for people with severe mental illness and diabetes. First, antipsychotic treatment with medications such as clozapine can become enduring, particularly where schizophrenia has been severe and life-threatening. Second, as diabetologists we may consider requesting psychiatric review for antipsychotic revision if diabetes or obesity occur or diabetes control deteriorates. This case illustrates that a profound individual improvement in diabetes control and complications risk was effected with coordinated, interdisciplinary collaboration, in arguably one of the most vulnerable patient groups.

Clozapine has a unique place amongst antipsychotics; it is the only antipsychotic with demonstrated efficacy where other antipsychotics are ineffective ('treatment-resistant schizophrenia'). It has a greater side-effect burden compared with other antipsychotics, being the most obesogenic, and it is expensive because of agranulocytosis monitoring. Hence, clozapine is reserved for patients where trials of at least two antipsychotics have failed and the illness is sufficiently severe to justify its significant adverse effects. Many antipsychotics cause weight gain, the metabolic syndrome and increase the risk of diabetes [10], which is of concern as antipsychotics are increasingly in use off-label to treat a variety of mental health issues, including in children. A recent paper highlighted these risks, showing a threefold increase in risk of incident diabetes in children and youth within the first year of use [14]; this risk is likely to be underestimated however [15]. Routine metabolic monitoring for early detection of weight gain and metabolic syndrome co-morbidities is widely recommended and should be considered part of the standard of care for people treated with antipsychotics [16].

Any change in antipsychotic medications requires close supervision by a psychiatrist to monitor progress carefully. Rapid clozapine withdrawal can precipitate rebound psychosis. In this patient, clozapine withdrawal proceeded slowly over 18 months, covered by another antipsychotic and with regular psychiatrist monitoring.

This case illustrates that partnership between endocrinologists and psychiatrists may help achieve our shared goal of improved physical health in severe mental illness. Greater interdisciplinary collaboration will help bridge the life-expectancy gap in severe mental illness.

Funding sources

None.

Competing interests

None declared.

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