Mental and physical health balance in treatment-resistant schizophrenia

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Treatment-resistant schizophrenia can be very difficult to manage and a significant number of patients go through many different antipsychotic combinations with limited success. Physical health side-effects such as diabetes, raised cholesterol levels and cardiovascular problems secondary associated with some antipsychotics may complicate a patient’s treatment and enforce a difficult but necessary change of antipsychotics. Here, the authors discuss the struggle to balance mental and physical health treatments in a patient who has developed type 2 diabetes, related problems from high HbA1c and cardiac issues.

Diabetes and cardiovascular problems secondary to antipsychotic treatment have been observed on multiple occasions in patients all over the world. The Lester Tool was recently approved by the Royal College of Psychiatrists as the best framework for managing physical health in psychosis and schizophrenia patients. It provides a set of guidelines and algorithms for managing cardiometabolic health and it is a valuable and reliable resource in today’s psychiatric practice. Some antipsychotics such as olanzapine, clozapine and zuclopenthixol have been strongly associated with diabetes and cardiovascular problems more so than others. In this article we discuss the case of a patient who had an acute onset of type 2 diabetes following olanzapine and zuclopenthixol introduction. While this antipsychotic combination greatly benefited him and stabilised his mental state for a sustained two-year period after almost 30 years of unrest, it very adversely affected his physical health. Our discussion is about the difficulty balancing mental and physical health treatments and the importance of physical health monitoring in psychotic and schizophrenic patients.

Presentation
A 45-year-old male patient of Caucasian origin with a 30-year history of treatment-resistant paranoid schizophrenia and polysubstance abuse, presented with acute-onset type 2 diabetes after six months of treatment with oral olanzapine and zuclopenthixol decanoate depot. His previous medical history was hypothyroidism for which he was treated with levothyroxine 150mcg once daily. The patient had been tried on high-dose antipsychotic monotherapy with no success. For many years he had been tried on multiple antipsychotic combinations that included clozapine, olanzapine, haloperidol, flupenthixol, amisulpride, risperidone, aripiprazole, trifluoperazine, chlorpromazine and quetiapine. The patient had multiple hospital admissions due to relapse secondary to non-adherence to his antipsychotic medications. He responded well to clozapine 900mg daily augmented with aripiprazole 30mg daily, but did not comply with clozapine blood tests and clozapine was discontinued.

His psychopathology included grandiose ideas about being God or the Devil, having special powers such as being able to do magic and having telepathic abilities. He was thought disordered with bizarre speech and, on occasion, verbally aggressive. He had delusions of passivity, delusions of control, reflex hallucinations and bizarre beliefs about being a computer. He was sexually disinhibited and wanted to change his sex. He believed that he had had glass pushed into his anal area when he was younger and that he had been raped. He had tried to self-harm on a number of occasions.

In view of his increasing aggression he was started on zuclopenthixol tablets for three days and then switched to decanoate depot (due to non-adherence), which was titrated to a dose of 600mg once weekly. His aggression subsided but his overall mental state remained poor with prominent affective symptoms. Olanzapine was introduced and titrated to a dose of 10mg twice daily. The patient’s mental state started to improve and eventually he became so well that he was able to take escorted leave for six hours every day. He abstained from using illicit substances and his overall behaviour and mental state improved significantly.

Six months after the zuclopenthixol and olanzapine initiation, the patient’s blood tests revealed that his HbA1c was 7.7mmol/L, random blood glucose was 30mmol/L, and postprandial readings were ranging from 25 to 29.8mmol/L. His HbA1c increased to 19.7mmol/L. three months later and post-prandial readings to 39.8mmol/L. His average blood pressure was elevated to 150mmHg systolic and 98mmHg...
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Diastolic. His cholesterol was 3.6mmol/L and triglycerides 3.5mmol/L. The patient lost 10kg in the space of six weeks. His waist circumference decreased by 9cm. The patient started reporting signs of peripheral neuropathy, with sensations of pins and needles on his hands and feet in a sock-like distribution bilaterally. He started having chest pains, headaches, and his ECG showed a QTc interval of 470ms, arrhythmias, tachycardia and conduction abnormalities. His prolactin levels were close to 2000mIU/L and he had developed gynaecomastia.

The GP diagnosed the patient with type 2 diabetes and the recommendation was that he should be started on metformin. The patient did not wish to be treated for diabetes, however, and refused to take any antidiabetic tablets as he was very much afraid of becoming insulin-dependent. In view of the fact that the patient was experiencing significant physical health side-effects and was refusing all diabetic treatment, the reluctant decision was made to stop olanzapine and start aripiprazole instead as this drug has a much better profile in terms of causing diabetes and extrapyramidal side-effects. Olanzapine was titrated down and aripiprazole was introduced at 10mg per day and titrated to 30mg once daily.

The patient agreed to adopt lifestyle changes to control his diabetes such as healthy eating choices and mild exercise. He further agreed to take metformin if lifestyle changes failed to produce any improvements. The combination of healthy eating, exercise and change of olanzapine to aripiprazole resulted in the patient’s postprandial blood sugar going down from 29.8 to 8mmol/L and his HbA1c reducing to 7mmol/L. The GP agreed to monitor him closely for any adverse signs and blood sugar level increases and gave him six weeks before any diabetic medication was started. The patient successfully managed to control his type 2 diabetes with healthy lifestyle modifications. We are continuing to monitor his blood sugar and HbA1c for any increase.

Discussion

Second-generation antipsychotics are associated with cardiovascular problems, sudden death, strokes, diabetes and dyslipidaemia. There is mounting evidence that such patients can have serious physical health side-effects mainly because of polypharmacy. Patients with treatment-resistant schizophrenia and polysubstance abuse are at even greater risk. These patients can abuse illicit drugs, lead a sedentary lifestyle, smoke tobacco and drink alcohol in addition to their regular medication. Their treatment often includes a combination of one or two antipsychotics, mood stabilisers, antidepressants, benzodiazepines, hypnotics, antimuscarinics, asthma and chronic obstructive pulmonary disease medications, blood pressure and diabetes treatments.

As a result of the greater emphasis being placed on physical health monitoring in psychiatric patients, the Royal College of Psychiatrists implemented the Lester Tool. The Lester Tool is an intervention framework for psychosis and schizophrenia patients that advises a combination of healthy lifestyle choices with balanced nutrition, exercise, smoking cessation and physical health interventions. These decisions are made based on body mass index fluctuations, lifestyle and life skills, blood pressure, blood glucose, HbA1c, lipids and smoking. Psychiatrists need to take into account all these results in their regular patient reviews and refer patients to the GP or other specialists accordingly. The main aim of this framework is to proactively manage physical health conditions in these patients.

Patient compliance in such investigations can, however, be a problem. Long-term schizophrenic patients are sometimes very reluctant to have their blood taken regularly or have an ECG every three to six months as per current NICE guidelines. This can be a problem, and there are many such occasions where psychiatrists, out of necessity, have to treat these patients without knowing if their physical health is compromised. In the past, physical health monitoring was not as important for mental health patients, perhaps because of the way mental illness was understood but in the recent decade many clinicians have become more and more aware about the impact of antipsychotics on physical health.

Mounting evidence from case reports and healthcare audits has shown that it is very important, especially for schizophrenic patients, to closely monitor all physical health aspects as physical health problems can severely impact mental health. Examples include vascular changes and stroke because of diabetes, hyperlipidaemia, high blood pressure or thyroid problems and endocrine disorders. The importance of genetics is not to be underestimated either. In schizophrenia a number of genes have been identified such as COMT, DISC1, DTNBP1, D2R, D3R, etc, and recent research has identified over 108 loci of control that affect, amongst others, calcium channels. Some of those genes and chromosomes are known to be involved in physical health problems. There was a time where augmenting psychiatric treatment
included calcium-channel blockers, which may explain recent confirmed findings about these genes.

The importance of physical health awareness and monitoring should therefore be twofold in our current psychiatric practice. Firstly, proactively monitoring physical health for medication side-effects and secondly, excluding pre-existing genetic or physical health conditions that may adversely affect mental health.

One of the difficulties that may arise is when a particular antipsychotic combination has successfully worked for a patient but harms their physical health. It can potentially be detrimental to the patient’s mental health state to change the antipsychotic treatment and on some occasions alternative options can be limited.

It is becoming very obvious that we need to consider the patient holistically – mental and physical health combined. Patients with schizophrenia should be treated with the appropriate antipsychotic combination tailored to their needs, at the most effective minimum dosage and decisions should be made in proportion to the harm.

Our patient experienced multiple physical health problems, namely acute onset type 2 diabetes, peripheral neuropathy, cardiovascular problems and ECG abnormalities. So, even if his mental state had consistently stabilised after 30 years, we had to ensure that his physical health was not so adversely affected. While still on olanzapine, the patient tried to control his type 2 diabetes with healthy eating with no success. This is why we very carefully changed his antipsychotic. In this case, the combination of aripiprazole with zuclopenthixol did not worsen the patient’s mental state. However, one has to wonder if it was because the patient was mentally stable and well already. On the other hand, his diabetes receded and his physical side-effects did not persist.

Clinicians should treat mental health patients taking into account their physical health, which is equally important. Further work needs to be done to ensure that the physical health of mental health patients is carefully and consistently monitored in psychiatric practice. Clinicians are on the way to achieving this, with the raised awareness of all the work that is being done in this very important direction.

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Declaration of interests
No conflicts of interest were declared.

References