

Olanzapine-induced diabetic ketoacidosis in a Chinese man

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We present a case report of a 22-year-old Chinese man with schizophrenia and dissociative personality disorder who was normoglycaemic before taking olanzapine. After commencing olanzapine he developed diabetic ketoacidosis and was managed in the intensive care unit of a general hospital. Olanzapine was stopped and replaced by haloperidol 5 mg/day. He was put on a strict 1500 kcal diabetic diet and required insulin injections to maintain a normal blood sugar level despite cessation of olanzapine for 4 months. Doctors prescribing olanzapine should be aware of the risk of diabetes mellitus. Baseline and regular monitoring of body weight, body mass index, and fasting blood glucose are essential to prevent serious consequences.

Introduction

Patients with schizophrenia are 2 to 4 times more likely to develop diabetes mellitus than the general population.^{1,2} Atypical antipsychotics, in particular clozapine and olanzapine, have been shown to be more likely to cause diabetes mellitus²⁻⁷ and even diabetic ketoacidosis⁸⁻¹⁴ than conventional antipsychotics. We report a case of possible olanzapine-induced diabetic ketoacidosis in a young man diagnosed with paranoid schizophrenia.

Case report

The patient is a 22-year-old Chinese male with no personal or family history of diabetes mellitus. He was admitted to our hospital on 1 November 2004 after attempting suicide. He had been treated with haloperidol 1.5 mg/day (from June to August 2001) and risperidone up to 4.5 mg/day (from September 2001 to May 2002) for his schizophrenic illness. He developed galactorrhoea so the risperidone was stopped and he was given olanzapine 10 mg/day from June 2002 onwards. Concomitant medications included controlled-release sodium valproate 900 mg/day from August 2003 onwards. Controlled-release carbamazepine 200 mg/day was given for a brief period (8 to 15 September 2005), but was stopped due to mild liver function abnormality. Both anticonvulsants were given for impulse control.

His fasting blood glucose samples were normal before and during treatment with risperidone. His fasting blood glucose prior to treatment with olanzapine was also normal. A fasting lipid profile was not performed before he commenced both risperidone and olanzapine.

On admission in November 2004, his body weight was 63 kg, and his body mass index (BMI) was 24.6 kg/m². He gained weight steadily to reach 73 kg and a BMI of 28.5 kg/m² by August 2005. An increased appetite was reported. On a typical day, he consumed a bowl of noodles and one litre of sugary fluids in addition to regular hospital meals. He did not do any physical exercise.

From 8 to 24 September 2005, he reported generalised discomfort and fatigue. He attributed this to the controlled-release carbamazepine, which was given from 8 to 15 September but was stopped due to mild liver function abnormality. He reported chest discomfort for 2 days, with no biochemical or electrocardiographic evidence of myocardial ischaemia. He had one episode of tachycardia that resolved spontaneously and vomited once on 24 September 2005. On 25 September 2005, he complained of nausea and vomiting. He refused food and only drank a litre of sugary fluid. On examination, he was dehydrated and his breath smelled of ketones. He was conscious and alert. His body weight was 65 kg, a loss of 8 kg over 1 month. His finger-prick blood glucose was 25.4 mmol/L and the urine dipstick was strongly positive for glucose, ketones, and protein. He was diagnosed as being in diabetic ketoacidosis and was transferred to a general hospital for further management, where he was admitted to the intensive care unit.

On admission to the intensive care unit his laboratory results were: sodium 127 mmol/L, potassium 4.5 mmol/L, blood pH 7.15, base excess -20.9 mmol/L, bicarbonate 5.8 mmol/L, urea 5.3 mmol/L, creatinine 146 µmol/L, glucose 40.1 mmol/L, white cell count 11.29 x 10⁹ /L, and

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一名華籍男子因奧氮平引致糖尿病酮症酸中毒

本文報告一名22歲患有精神分裂及社交性格失調的華籍男子，在使用奧氮平（olanzapine）前血糖正常，但使用後出現糖尿病酮症酸中毒，被送入一間普通科醫院深切治療部，停用奧氮平代之以氟派啶醇（每日5毫克）。為了維持正常血糖水平，病人在停用奧氮平4個月後仍須嚴格執行每日1500卡路里的糖尿病飲食餐單和注射胰島素。醫生在處方奧氮平時，應留意糖尿病的風險，開始用藥時和以後必須定期監察病人體重、體重指數和空腹血糖度，避免引致嚴重後果。

haemoglobin A_{1c} 11.9%. His fasting triglycerides were 2.86 mmol/L while his fasting cholesterol level was normal. Olanzapine was stopped and replaced with haloperidol 5 mg/day. He was started on intravenous insulin, fluids, and electrolyte replenishment. His nausea and vomiting resolved and, initially, he required 60 to 70 units of insulin intravenously per day to attain glycaemic control. His blood glucose dropped to 7.4 mmol/L after 4 days of intensive care. He was transferred from the intensive care unit and returned to the psychiatric unit 2 weeks later. Initially he required four insulin injections per day (total 42 units of Actrapid HM [Novo Nordisk, Copenhagen, Denmark] thrice a day and 24 units of Protaphane HM [Novo Nordisk, Copenhagen, Denmark] at night) to maintain normal blood sugar levels. His medication was subsequently changed to Protaphane HM 20 units in the morning and 16 units at 5

pm. His most recent haemoglobin A_{1c} in January 2006 was 5.7%, while his fasting glucose was 4.2 mmol/L.

Discussion

Olanzapine may have been responsible for the development of diabetes mellitus and diabetic ketoacidosis in this man. Other contributing factors were his weight gain and sedentary life style. Even after cessation of olanzapine for 4 months, this patient still needed dietary restriction and insulin injections to maintain a normal blood glucose level. The question of whether diabetes mellitus will resolve after cessation of olanzapine has not been conclusively answered.^{8,9,14}

Various mechanisms are thought to be responsible for this effect, including antagonising histaminic and possibly serotonergic systems to induce weight gain and subsequent alterations in glucose metabolism,¹ an increase in serum insulin, lipid and leptin,¹⁵ disruption of the sympathetic nervous system, and serotonin_{1A} antagonism blunting pancreatic beta-cell responsiveness, resulting in an inappropriately low level of insulin secretion.^{3,9}

This case illustrates the importance of being alert to the possibility of olanzapine-induced diabetes mellitus. One should consider the risk factors before prescribing atypical antipsychotics and monitor patients regularly, including checking their body weight, fasting glucose, and fasting lipids once they have started on the medication.

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