

Diabetic ketoacidosis and prolonged hyperchloraemic acidosis in a patient treated with risperidone

Steven Fong, Alex Bazeos, Julia Thomas and Tahseen A. Chowdhury

Department of Diabetes and Metabolism, The Royal London Hospital, London, UK

Corresponding address: Dr T.A. Chowdhury, Department of Diabetes and Metabolism, 7th Floor, John Harrison House, The Royal London Hospital, Whitechapel, London, E1 1BB, UK.

E-mail: tahseen.chowdhury@bartsandthelondon.nhs.uk

Date accepted for publication 21 May 2008

Abstract

Diabetic ketoacidosis (DKA) is a life-threatening complication of diabetes. The development of metabolic syndrome is widely recognised with the use of atypical antipsychotic agents, and not infrequently DKA has been described with some of these drugs. We describe a complex patient with HIV who presented with severe DKA and prolonged hyperchloraemic acidosis, which we postulate was associated with risperidone therapy.

Keywords

Diabetic ketoacidosis; atypical anti-psychotics; hyperchloraemic acidosis; risperidone.

Case history

A 35-year-old Ethiopian lady living in the UK for 12 years, presented acutely to the emergency unit with a 1-day history of vomiting and 4-h history of reduced conscious level. She had a past history of schizoaffective disorder, treated with bi-monthly intra-muscular risperidone 50 mg, the previous dose having been given 8 days prior to admission. She had HIV diagnosed 5 years previously, initially treated with anti-retroviral therapy, although she had not complied with anti-retroviral therapy for over a year.

On admission, she had a Glasgow Coma Score of 6, blood pressure of 73/43, pulse 120 regular, respiratory rate 40, with ketotic odour on her breath and severe dehydration. Random plasma glucose was 40.2 mmol/l, with +++ ketonuria. Arterial pH was 6.97, bicarbonate 3 mmol/l (22–29 mmol/l), base excess –27.0. Creatinine was 148 µmol/l (44–80 µmol/l), sodium 152 mmol/l (136–146 mmol/l), potassium 4.1 mmol/l (3.6–4.6 mmol/l), chloride 126 mmol/l (100–110 mmol/l), haemoglobin 14.5 g/dl (11.5–17.5 g/dl) and white cell count $21.0 \times 10^9/l$ ($4-11 \times 10^9/l$). Serum lactate was 1.5 mmol/l (1–4 mmol/l).

She was admitted to the intensive therapy unit and treated for severe DKA with intravenous 0.9% saline and insulin infusion. Chest radiograph showed right mid-zone consolidation, and blood culture grew pneumococcus, treated with broad spectrum antibiotics. Despite fluid resuscitation, her renal function deteriorated, with serum creatinine reaching a peak of 371 µmol/l. Nephrological review suggested that this deterioration was compatible with acute

tubular necrosis due to hypotension, possibly with a background of HIV-associated nephropathy. CD4 count was 8 (800–1500), with an HIV viral load of 148,965 copies.

Her progress was complicated by prolonged hyperchloraemic acidosis, with serum bicarbonate persistently less than 8 mmol/l, and chloride persistently above 130 mmol/l, despite high dose insulin and 10% dextrose therapy. The anion gap was normal. Sodium initially rose to 160 mmol/l, but settled within 3 days to the normal range. Despite the marked acidosis, urinary pH was 6.0, suggesting a degree of renal tubular acidosis (RTA). Urine ketones were negative after the first day. The hyperchloraemic acidosis eventually settled over 10 days, without the need for bicarbonate therapy. Renal function improved, and she was converted to low dose subcutaneous Novomix 30 insulin, at a total daily dose of 28 units, achieving excellent glycaemic control. Taking advice from the psychiatrists, risperidone was stopped, with a view to using older anti-psychotic agents should the need arise. She commenced on anti-retroviral therapy, and was transferred to the care of her local mental health team for ongoing management.

Diagnosis

Severe diabetic ketoacidosis and prolonged hyperchloraemic acidosis due to atypical-antipsychotic therapy in a patient with HIV.

Discussion

We present a complex case of DKA in a patient with HIV infection and schizoaffective disorder treated with risperidone. We postulate that her DKA and prolonged hyperchloraemic acidosis may be related to her risperidone therapy.

Patients with schizophrenia are more prone to developing type 2 diabetes, possibly due to poor dietary habits, tobacco use and lower levels of physical activity^[1]. Newer anti-psychotic drugs appear to augment this increased risk for the development of type 2 diabetes. In addition, there appears to be a small, but significant risk for the development of DKA using atypical antipsychotics, although the increased frequency of DKA in this population is not explained by the increased risk of type 2 diabetes^[2]. DKA appears to develop rapidly after commencement of the medication, and insulin requirement frequently reverses on cessation of the atypical anti-psychotic agent. The prolonged acidosis in our patient may be attributable to the intramuscular risperidone, given as a depot injection. To our knowledge, this is the first report of DKA in a patient treated with intramuscular risperidone. It seems probable that the severity of illness was in part due to the ongoing metabolic effects of this drug given as a depot injection.

The mechanism behind the development of DKA in patients treated with atypical anti-psychotic agents is not clear^[3]. Excessive weight gain may be a factor, although the rapid onset of DKA shortly after commencing these agents is unlikely to be solely due to weight gain. A direct effect on glucose metabolism and insulin release has been postulated, particularly impaired insulin action on adipocytes. Other potential mechanisms postulated include a direct effect on fatty acid metabolism leading to increased ketone body formation, increased plasma leptin levels, a direct inhibitory effect on pancreatic beta cells and serotonin receptor blockade.

A number of guidelines suggest that careful monitoring of metabolic parameters are required when commencing atypical anti-psychotic therapy, including monitoring of plasma glucose, lipids and weight^[4]. It is generally agreed that, although monitoring for diabetes is essential and should be interpreted in light of the patients pre-existing risk factors for diabetes such as family history, patients should not be denied the best symptom control possible from their anti-psychotics. Following an episode of DKA, however, it seems prudent to stop the atypical anti-psychotic and convert to an older anti-psychotic agent.

A final point of note is that it is possible that this patient's HIV status may have contributed to her mild RTA and prolonged hyperchloraemic acidosis. HIV has been reported as associated with distal RTA^[5], although the resolution of her acidosis despite lack of therapy for her HIV seems to make this possibility unlikely.

Teaching points

DKA is an unusual, but severe and potentially life-threatening complication of atypical anti-psychotic therapy. Depot injection may lead to a prolonged acidosis that is slow to resolve.

HIV can also cause a metabolic acidosis due to distal RTA. All patients treated with atypical anti-psychotics should have careful metabolic monitoring after commencement of such therapy, and advice to seek medical attention should they develop symptoms suggestive of diabetes.

References

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