

DIABETIC KETOACIDOSIS ASSOCIATED WITH QUETIAPINE TREATMENT: A CASE REPORT

Badr Ratnakaran^{1*}, S Sethulakshmi²

¹Consultant Psychiatrist, ²Medical Officer

Holy Cross Hospital and Mental Health Centre, Koovappally, Kottayam Dt.

*Correspondence: Consultant Psychiatrist, Holy Cross Hospital and Mental Health Centre, Koovappally, Kottayam Dt., Kerala, Pin Code: 686518 Email: dr.badrnatnakaran@gmail.com

ABSTRACT

Atypical antipsychotics are known for their metabolic side effects and there have been reports of them precipitating diabetic ketoacidosis which can be even fatal. We present a case of quetiapine induced diabetic ketoacidosis in a case of depression during inpatient treatment, highlighting the need to monitor not only metabolic side effects but also fatal complications like diabetic ketoacidosis.

Keywords: Atypical antipsychotic, diabetic ketoacidosis, quetiapine.

INTRODUCTION

Atypical antipsychotics have been used for, and are effective in, a wide range of psychiatric disorders. However, their side effects of weight gain and metabolic abnormalities like lipid dysregulation and type 2 diabetes mellitus can lead to life-threatening complications like coronary artery disease and diabetic ketoacidosis (DKA).^{1,2} We report a case of DKA precipitated by use of the atypical antipsychotic quetiapine, which progressed rapidly despite the patient being on a low dose of the medicine. Cases like this can pose a challenge in settings with limited laboratory investigation facilities.

CASE REPORT

Mr. A is a 68 year old married male from low socioeconomic status, with no past history of any medical disorders, use of other medications, or substance use disorders. He presented with a first episode of illness characterized by low mood, anhedonia, death wishes, impaired self-care, insomnia and anorexia of one week duration following a personal stressor. He had no family history of mental illness. History of type 2 diabetes mellitus and hypertension was present in first and second degree relatives.

In mental status examination, he was not adequately groomed and had decreased

Please cite this article as: Ratnakaran B, Sethulakshmi S. Diabetic ketoacidosis associated with quetiapine treatment: a case report. Kerala Journal of Psychiatry 2015; 28(1)34 –7.

psychomotor activity. His mood was depressed and he had ideas of guilt, depressive ideas and death wishes. There were no psychotic symptoms. His concentration, immediate memory and abstract ability were impaired, and his insight was grade 3.

Physical examination revealed no abnormalities. He weighed 63 kg, with a body mass index of 23 kg/m². His vitals were stable, and laboratory investigations on the day of admission (hemoglobin, total and differential count, platelet count, erythrocyte sedimentation rate, routine urine examination, renal and liver function tests, lipid profile, serum sodium and potassium) were within the normal limits. A diagnosis of severe depressive disorder was made as per 10th revision of International Statistical Classification of Diseases and Health Related Problems (ICD-10). In view of his death wishes, he was admitted and started on escitalopram 5 mg HS and clonazepam 0.25 mg HS. The next day, doses of both the medications were doubled in view of the persistent and distressing symptoms. His psychomotor activity, self-care and appetite improved by the third day. On that day, as he was still complaining of decreased sleep and anxiety stemming from his feelings of guilt and death wishes, quetiapine 25 mg HS was added.

The next day he was found to be drowsy, with slurred speech and decreased response to questions. Clonazepam was decreased to 0.25 mg in view of his drowsiness. That night he was found to be disoriented and have irrelevant talk and increased psychomotor activity. He was afebrile, his vitals were normal, and neurological examination did not reveal any lateralizing signs. There were no signs of dehydration or any odor in his breath. Abdominal examination did not reveal tenderness or

guarding. His laboratory investigations were repeated: random blood sugar was found to be 363mg/dl, and serum Sodium 130 mEq/L. Other investigations, including serum Potassium and renal function tests, were within normal limits. Trace amounts of urine acetone were found, with urine sugar test showing orange color on testing with urine analysis strips. Analysis of blood pH and serum bicarbonate were not available in our institution. A diagnosis of DKA was made on the basis of raised blood sugar and positive urine sugar and acetone reports.

After consultation with the physician, all psychotropic medications were stopped immediately and the patient was aggressively treated with intravenous 0.9% saline and plain insulin injection. His blood sugar, serum sodium and potassium, urine sugar and urine acetone were assessed every two hours. He was given 6 units of plain insulin as bolus intravenous injection, followed by 6 units of plain insulin in 500 ml of 0.9% saline given intravenously over an hour. His vitals were monitored hourly and fluid input /output chart was maintained. After an hour, his blood sugar became 183 mg/dl. He was later given a total of 36 unit of plain insulin in 1000 ml of 0.9% intravenous saline over 12 hours, upon which his general condition improved. He became oriented, responded to questions appropriately, and was able to eat without assistance. Urine acetone became negative and serum sodium returned to normal. His blood sugar was 155mg/dl and urine sugar test strip was yellow. Subcutaneous plain insulin was started with 6 units in the morning and afternoon and 4 units in the evening for treatment of his diabetes. His fasting and postprandial blood sugar were monitored in the following days, and they became normal on 6th day.

He was restarted on escitalopram 5 mg HS and clonazepam 0.25 mg HS. Subsequently his fasting and postprandial blood sugar, and serum sodium and potassium were monitored daily and they were found to remain normal. On the 8th day, as per his caregiver's request for ease of administration, he was started on oral hypoglycemic medications (glibenclamide 2.5 mg and sustained release metformin 1000 mg both given twice daily) in place of plain insulin injections, after consulting with the physician. His depressive symptoms and sleep gradually improved, and he was discharged on the tenth day on escitalopram 10 mg and clonazepam 1 mg, each once a day, and oral hypoglycemic medications in the dosage mentioned earlier. His blood sugar was normal on the day of discharge.

DISCUSSION

The American Diabetes Association and the American Psychiatric Association, in their joint consensus guideline on second generation antipsychotics and obesity and diabetes, warn about the increased risk for diabetes in patients on clozapine and olanzapine.³ Antipsychotics associated with DKA are clozapine, olanzapine, risperidone, quetiapine and aripiprazole, with commonest association being for clozapine and olanzapine.² In majority of the cases the initial presentation itself is with DKA, without any prior diagnosis of diabetes, and it can occur at any time in the course of treatment. Risk factors identified for DKA are being male, being overweight prior to starting antipsychotics and having African- American ethnicity.²

In our patient, quetiapine was added considering the evidence for its ability to rapidly alleviate anxiety symptoms in depressed patients on SSRIs.⁵ However, some previous reports have implicated quetiapine in the genesis of DKA. For example, a review of forensic medical

records during a five year period found quetiapine to be associated with majority of cases of fatal antipsychotic induced DKA.⁴ Quetiapine can precipitate hyperglycemia (ranging from mild hyperglycemia to DKA or hyperosmolar coma) in patients with a prior diagnosis of diabetes.⁶ There is also a report of quetiapine precipitating DKA and acute pancreatitis, where quetiapine-associated pancreatitis was hypothesized to be the cause of the DKA.⁷

Our patient developed the symptoms within a day of introduction of quetiapine at a low dose, and deteriorated rapidly. The presentation of DKA can include polyuria, polydipsia, altered mental status, abdominal pain, dehydration, electrolyte abnormalities, etc.⁸ Many hospitals in India similar to ours might not have access to all the laboratory investigation facilities (blood pH, serum bicarbonate, osmolality, anion gap and serum ketones) required to diagnose DKA accurately and interpret its severity. In such a situation, altered mental status of the patient, along with hyperglycemia and positive urine ketone following initiation of atypical antipsychotics should alert the clinician to the possibility of drug induced DKA.

Differential diagnoses in our case would include hyperosmolar hyperglycemic nonketotic syndrome and SSRI induced hyponatremia. But the presence of elevated blood sugar and positive urine ketones favored the diagnosis of DKA. DKA can also be precipitated by infection, pancreatitis, underlying medical illness and drugs like steroids and thiazides, but no such factor was present in our case.⁸ Naranjo Adverse Drug Reaction Probability Scale score of 3 in this case suggests possible association of quetiapine and DKA.

Mechanisms implicated for glucose dysregulation by atypical antipsychotics include antagonism of serotonergic

receptors and muscarinic M₃ receptors on pancreatic beta cells, inhibition of insulin secretion, antagonism of histaminergic H₁ receptor mediated leptin's action on appetite suppression, and inhibition of glucose transporter proteins.^{9,10} Jin et al. proposed that administration of an atypical antipsychotic can be a metabolic stressor to the body, leading to DKA in the absence of other metabolic stressors in the patient.²

Guidelines suggest monitoring of glucose and lipid levels before initiating and during treatment with atypical antipsychotics.³ This is essential not only for monitoring the long term metabolic side effects, but also for promptly recognizing and treating potentially fatal side effects like DKA as highlighted in this report.

Acknowledgement: The authors would like to thank, Dr. Aleykutty Mathai, Physician, Holy Cross Hospital and Mental Health Centre, Kottayam, Kerala, for her valuable inputs in the management of this case.

REFERENCES

1. Newcomer JW. Second-generation (atypical) antipsychotics and metabolic effects: a comprehensive literature review. *CNS Drugs* 2005; 19 Suppl 1:1–93.
2. Jin H, Meyer JM, Jeste DV. Phenomenology of and Risk Factors for New-Onset Diabetes Mellitus and Diabetic Ketoacidosis Associated with Atypical Antipsychotics: An Analysis of 45 Published Cases. *Ann Clin Psychiatry* 2002; 14:59–64.
3. American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, North American Association for the Study of Obesity. Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. *Diabetes Care* 2004; 27:596–601.
4. Ely SF, Neitzel AR, Gill JR. Fatal diabetic ketoacidosis and antipsychotic medication. *J Forensic Sci* 2013; 58:398–403.
5. McIntyre A, Gendron A, McIntyre A. Quetiapine adjunct to selective serotonin reuptake inhibitors or venlafaxine in patients with major depression, comorbid anxiety, and residual depressive symptoms: a randomized, placebo-controlled pilot study. *Depress Anxiety* 2007; 24:487–94.
6. Koller EA, Weber J, Doraiswamy PM, Schneider BS. A survey of reports of quetiapine-associated hyperglycemia and diabetes mellitus. *J Clin Psychiatry* 2004; 65:857–63.
7. Rashid J, Starer PJ, Javaid S. Pancreatitis and Diabetic Ketoacidosis with Quetiapine Use. *Psychiatry Edgmont* 2009; 6:34–7.
8. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic Crises in Adult Patients With Diabetes. *Diabetes Care* 2009;32: 1335–43.
9. Nasrallah HA. Atypical antipsychotic-induced metabolic side effects: insights from receptor-binding profiles. *Mol Psychiatry* 2007; 13:27–35.
10. Ardizzone TD, Bradley RJ, Freeman AM, Dwyer DS. Inhibition of glucose transport in PC12 cells by the atypical antipsychotic drugs risperidone and clozapine, and structural analogs of clozapine. *Brain Res* 2001; 923:82–90.

Source of support: None *Conflict of interest:* None declared *Consent:* Informed Consent was taken from the patient