Hyperglycemia associated with olanzapine treatment

* Dr. P.N. Suresh Kumar

Abstract

Olanzapine is an atypical antipsychotic clinically very effective in the treatment of schizophrenia and related psychoses with better efficacy and tolerability than older generation antipsychotics. Recently there are flurry of reports that olanzapine is associated with high blood sugar levels in new onset of diabetes mellitus or pre-existing diabetes mellitus. The authors report a series of diabetes associated with olanzapine treatment from Indian context. The clinical implications this emerging side effect is discussed.

Key words : olanzapine, diabetes, hyperglycemia

Introduction

Olanzapine is an atypical antipsychotic that has been widely used because of its better clinical efficacy, superior activity against negative symptoms, lesser extra-pyramidal symptoms and better tolerability profile compare to typical antipsychotics. Recently there are flurry of reports that olanzapine is associated with high blood sugar levels in new onset or pre-existing diabetes mellitus and ketoacidosis which may be reversible after discontinuation of olanzapine. The exact cause of glucose dysregulation by olanzapine is not clear. It has been hypothesized that 5-HT1 antagonism may decrease the responsiveness of the pancreatic beta cells, thus reducing the secretion of insulin and causing hyperglycemia. In-vivo studies suggest that olanzapine impairs glycogen synthesis via inhibition of the classical insulin signaling cascade and this inhibitory effect may lead to the induction of insulin resistance in olanzapine treated patients.

Koller & Doraiswamy reported 188 new-onset diabetes out of 237 cases, which had no previous history of diabetes mellitus. Olanzapine can cause fatal outcome like diabetic ketoacidosis that may lead to death. Same authors reported 23 deaths among 289 cases of hyperglycemia. Similarly Spivak et al reported a case where patient had higher blood sugar level but after discontinuation of olanzapine it became normal. Bechara & Goldman- Levine and Ober et al reported similar cases where treatment with olanzapine had worsened the clinical condition in patients with a history of diabetes mellitus. We report 4 cases of hyperglycaemia in schizophrenic patients after starting olanzapine and sugar values returned to normal after changing the medication.

Case series

A 54-year-old male with no past or family history of diabetes mellitus developed hyperglycemia 10 days after starting treatment with olanzapine with a random blood glucose level 275mg/dl, fasting 118mg/dl, and postprandial 207mg/dl. Same day olanzapine was discontinued and trifluperazine was introduced. 15 weeks later blood sugar level came down to 95mg/dl (fasting) and 129mg/dl (postprandial) and remained well controlled throughout the entire period of follow up of one year.

Another patient a 33-year-old male with no past but family history of diabetes mellitus in father developed hyperglycemia 40 days after starting olanzapine (random glucose level 266 mg/dl, fasting 195mg/dl and postprandial 295 mg/dl). Same day...
olanzapine was stopped and started aripiprazole. Six months later patient’s blood glucose levels were 85 mg/dl (fasting) and 127 mg/dl (postprandial) and remained normal there after.

Third one was a 48-year-old male with no past or family history of diabetes mellitus. Two weeks after starting olanzapine blood glucose levels shouted up to 230mg/dl (random), 120mg/dl (fasting) and 195 mg/dl (post-prandial). Olanzapine was changed to pimozide and one year later patient’s blood sugar levels came down to 74 mg/dl (fasting) and 96mg/dl (postprandial).

Fourth one was a 37-year-old male with positive family history of diabetes mellitus in father who developed hyperglycemia 11 days after starting olanzapine with blood sugar 240mg/dl (random), 118mg/dl (fasting) and 193mg/dl (post-prandial). Olanzapine was changed to quetiapine and two months later blood sugar came down to 100 mg/dl (fasting) and 162 mg/dl (postprandial).

Discussion
Possibility of other risk factors for diabetes like positive family history, obesity etc need to be considered before starting of olanzapine. Regular monitoring of body weight and blood sugar are important in olanzapine treatment especially those having risk factors for diabetes. In this case series for two cases there was no past or family history of diabetes mellitus indicating that these were new-onset diabetes mellitus. But the limitation of a case series is that we do not have base line blood sugar value before starting of olanzapine. However in all these cases blood sugar value became normal after stopping the offending agent and change over to other antipsychotics with lesser propensity to develop hyperglycemia. This clearly shows a link between hyperglycemia and olanzapine.

Since olanzapine is becoming more and more popular as a first line agent in the treatment of psychosis as well as in mood disorders proper guidelines has to be established for monitoring of blood glucose levels and determination of risk factors for diabetes mellitus. Hence it is very important for clinicians that all patients started on olanzapine require regular monitoring of their blood sugar levels. Clinicians should take at most precaution in pre-existing diabetic patients before starting olanzapine. If olanzapine is suspected to being a causal factor for hyperglycemia we can reduce that risk by withdrawal of olanzapine or switching over to some other medicines without worsening the psychiatric condition of patient. India being a diabetics rich country diabetes the author strongly suggests at least a baseline survey on the prevalence of diabetes in Indian population among patients exposed to olanzapine.

References
1. Lindenmayer JP, Patel R. Olazapine-induced ketoacidosis with diabetes mellitus (letter). Am J Psychiatry 1999; 156:1471.
2. Roefaro J, Mukherjee SM. Olanzapine-Induced hyperglycemic nonketonic coma. The Annals of Pharmacother 2001: Vol. 35, No. 3, pp. 300-302
3. Goldstein LE, Sporn J, Brown S, Kim H, Finkelstein J, Gaffey GK, Sachs G, Stern TA. New-onset diabetes mellitus and diabetes ketoacidosis associated with olanzapine treatment. Psychosomatics 1999; 40: 438-443.
4. Seaberg HL, McLendon BM, Doraiswamy PM. Olanzapine-Associated Severe Hyperglycemia, Ketonuria, and Acidosis: Case Report and Review of Literature. Pharmacother 2001; 21(7-8): 865-7.
5. Beettnger TL, Mendelson SC, Dorson PG, Crimson, ML. Olanzapine- induced glucose dysregulation. Ann Pharamacother 2000; 34(7-8): 841-852.
6. Koller EA, Doraiswamy PM. Olanzepine- associated diabetes mellitus. Pharmecotherapy 2002; 22(7): 1599-1606.
7. Bechara CL, Levine JD. Dramatic worsening of diabetes mellitus due to olanzapine after 3 years of therapy. Pharmacotherapy 2001; 21(11): 1444-7.
8. Ober SK, Hudak R, Rusterholtz. Hyperglycemia and olanzapine. Am J Psychiatry 1999: 156(6): 970.