

Hyperglycemia associated with olanzapine treatment

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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^{1,2,3,4} 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 hyperglycemia⁵. 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 & Doraiswamy⁶ 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 al⁷ reported a case where patient had higher blood sugar level but after discontinuation of olanzapine it became normal. Bechara & Goldman-Levine⁸ and Ober et al⁹ 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 trifluoperazine 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

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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 thereafter.

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 shot 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 of 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 diabetes 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.

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