Hyperglycemia associated with olanzapine treatment

Sir,

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 compared to typical antipsychotics. Recently, a flurry of reports have stated that olanzapine is associated with high blood sugar levels in new onset or pre-existing diabetes mellitus and ketoacidosis,[1-4] 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 hyperglycemia.[5] *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 and Doraiswamy[6] 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*[7] reported a case where patient had higher blood sugar level but after discontinuation of olanzapine it became normal. Bechara and Goldman-Levine[8] and Ober *et al*[9] reported similar cases where treatment with olanzapine had worsened the clinical condition in patients with a history of diabetes mellitus. We report four cases of hyperglycemia in schizophrenic patients after starting olanzepine and sugar values returned to normal after changing the medication.

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 275 mg/dl, fasting 118 mg/dl, and postprandial 207 mg/dl. Same day olanzapine was discontinued and trifluperazine was introduced. Fifteen weeks later blood sugar level came down to 95 mg/dl (fasting) and 129 mg/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 195 mg/dl and postprandial 295 mg/dl). Same day, olanzapine was stopped and aripirazole was started. Six months later patient's blood glucose levels were 85 mg/dl (fasting) and 127 mg/dl (postprandial) and remained normal thereafter.

Third case was a 48-year-old male with no past or family history of diabetes mellitus. Two weeks after starting olanzapine blood glucose levels shooted up to 230 mg/dl (random), 120 mg/dl (fasting), and 195 mg/dl (postprandial). Olanzapine was changed to pimozide and one year later patient's blood sugar levels came down to 74 mg/dl (fasting) and 96 mg/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 240 mg/dl (random), 118 mg/dl (fasting), and 193 mg/dl (postprandial). Olanzepine was changed to quetiapine and two months later blood sugar level came down to 100 mg/dl (fasting) and 162 mg/dl (postprandial).

Possibility of other risk factors for diabetes like positive family history, obesity, etc needs to be considered before starting 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 changing 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 have to be established for monitoring 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; the author strongly suggests at least a baseline survey should be undertaken

on the prevalence of diabetes in Indian population among patients exposed to olanzapine.

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