Letters to the Editor

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SEVERE HYPOGLYCEMIA ASSOCIATED WITH TIAPRIDE IN AN ELDERLY PATIENT WITH DIABETES AND PSYCHOSIS

Dear Editor:

Hyperglycemia is more common in patients being treated with an antipsychotic than in the general population.[1] However, hypoglycemia is also a severe complication of antipsychotic treatment.[2] Moreover, recent research indicates that use of antipsychotic drugs by older patients with diabetes is associated with an increased risk of hypoglycemia.[3] While several cases of antipsychotic-induced hypoglycemia have been reported, its mechanism is not completely understood.[4,5] Here, we report an elderly patient with diabetes and severe hypoglycemia we believe was caused by tiapride, a pure dopamine D_2 receptor antagonist. We discuss the role of D_2 receptors on glucose regulation.

Case presentation. A 75-year-old Japanese woman with a 20-year history of diabetes was transferred to our emergency department for loss of consciousness. According to her attending physician, she recently had an HbA1c of 7.4 percent and was treated with glimepiride (sulfonylurea) 1mg/day. She had never experienced hypoglycemia before. The corroborative history from her family members revealed that she believed her spouse was being unfaithful, which was based on incorrect inferences supported by dubious evidence. As a result, she was diagnosed with delusional psychosis at a mental clinic, and was treated with tiapride 75mg/day for two weeks. On arrival to our emergency department, she was in a deep coma, and her plasma glucose level was 15mg/dL. Fortunately, she was successfully treated with rapid glucose infusion without any neurological deficits. Her insulin/glucose ratio at the time of the deep coma was 0.43 (normal <0.25), indicating the possibility of hyperinsulinemia.[6] After the discontinuation of tiapride, she did not experience another hypoglycemic event.

Discussion. Hypoglycemia in patients with diabetes is the result of a complex interaction between hyperinsulinemia and compromised physiologic and behavioral responses. Several factors can cause hypoglycemia in patients with diabetes, including skipping a meal, exercising harder than usual, alcohol consumption, stress, and infections, none of which were seen in our patient. Hypoglycemia may also result from taking sulfonylurea with some drugs, such as salicylates, beta-blockers, levofloxacin, and antihyperlipidemics.[7]

We believe tiapride may have caused the hypoglycemia in our patient because the attack occurred suddenly after the addition of tiapride to glimepiride. The tiapride did not enhance or diminish the anti-diabetic effect of sulfonylurea.[8]

Plasma concentrations of glucose and insulin are usually tightly linked, and alterations in glucose may result in rapid alteration of insulin in an attempt to bring glucose back to normal. A fall in blood glucose is normally rapidly detected, and counter-regulatory mechanisms are recruited to restore normoglycemia.[9] D_2 receptors are expressed in pancreatic beta-cells and seem to be important for this counter-regulation. Some in-vivo studies have suggested that stimulation of the pancreatic D_2 receptors inhibits insulin release, and the inhibitory effect on insulin secretion is reverted by the addition of D_2 receptor antagonists.[10] Moreover, mutant mice lacking D_2 receptors have been shown to have abnormal insulin secretion.[11] When administering D_2 receptor antagonists, counter-regulatory mechanisms on glucose regulation may not work.

Tiapride has a potent antagonistic effect on D_2 receptors. Therefore, in our patient, these counter-regulatory mechanisms may not have worked, resulting in continuous insulin release even with normal or low glucose levels. Consequently, severe hypoglycemia occurred by mismatch between glucose levels and insulin secretion.

Conclusion. Glucose levels should be monitored closely after the initiation of D_2 receptor antagonists, such as tapride, in patients with diabetes. The importance of D_2 receptors in central nervous system function is well known, but its effects on glucose homeostasis and pancreatic beta-cell function are not well understood. Further studies on the role D_2 receptors play in glucose regulation are needed. Antipsychotics may cause metabolic dysregulation, which can result not only in hyperglycemia but also in hypoglycemia, as was seen in our patient.

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With regard,

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