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Subject: Letter to JAACAP quetiapien and hyperglycemia/hypertriglyceridemia

Didn't know if everyone's seen this:

Celeste

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LETTERS TO THE EDITOR

QUETIAPINE-ASSOCIATED HYPERGLYCEMIA AND HYPERTRIGLYCERIDEMIA

To the Editor:

Several reports in the adult literature have linked the atypical antipsychotics clozapine, olanzapine, and quetiapine with hyperglycemia, weight gain, and hypertriglyceridemia (Meyer, 2001 ; Nguyen and Murphy, 2001 ; Procyshyn et al., 2000 ; Sobel et al., 1999 ; Wirshing et al., 2000). Almost all cases of atypical antipsychotic-associated hyperglycemia or hypertriglyceridemia reported to date have been in adults older than age 30. We wish to report such a case associated with quetiapine use in a 17-year-old African-American female.

The patient presented with paranoia, assaultive behavior, and homicidal ideation. Her diagnoses included bipolar disorder, conduct disorder, and mild mental retardation. She had been in state custody since age 3, and her family medical history was unknown. Psychotropic medications at the time of presentation included divalproex 1,500 mg/day (for more than 8 months), quetiapine 600 mg/day (for more than 3 months), and paroxetine 20 mg/day (for 1 day). Between 2 and 3 months prior to presentation, reportedly after the initiation of quetiapine, type II diabetes mellitus was diagnosed; her serum glucose levels approached 300 mg/dL. She was started on a 2,000-calorie diet and on metformin 1,000 mg twice per day. She had not experienced significant weight gain during the 3 months of quetiapine therapy.

Admission laboratory studies were unremarkable except for a serum glucose level of 144 mg/dL, serum cholesterol level of 235 mg/dL, and serum triglyceride level of 456 mg/dL (all fasting). She was slightly overweight; height and weight were 165 cm and 75.5 kg, respectively (body mass index 27.7 kg/m²). Her valproic acid level at the time of admission was 84 mg/L.

Quetiapine was tapered over 1 week and discontinued because she had not responded as robustly as hoped and because her hyperglycemia and hypertriglyceridemia apparently developed after the initiation of quetiapine. Risperidone was initiated and titrated to 4 mg/day. The divalproex was increased to 2,000 mg/day, resulting in a serum level of 104 mg/L. Paroxetine was continued at 20 mg/day. Her paranoia and behavior stabilized over the subsequent weeks on these medications.

For 1 week after quetiapine was discontinued, while the patient was receiving metformin and a 2,000-calorie diet, her fasting glucose levels were consistently below 120 mg/dL. Metformin was decreased to 1,000 mg in the evening and was discontinued after 1 week of normal fasting glucose levels. Fasting serum glucose levels, checked three times per week, ranged between 99 and 170 mg/dL over the next month, averaging 128 mg/dL. Serum cholesterol and triglyceride levels within a week of the discontinuation of quetiapine were 196 and 167 mg/dL, respectively, and 6 weeks later (4 weeks after the discontinuation of metformin) were 226 and 163 mg/dL, respectively. Her weight remained between 73.6 and 75.5 kg over this period of time. While she may have developed diabetes at some point without quetiapine, she did demonstrate improved serum glucose control after it was discontinued.

The mechanisms remain unclear, but there has been much speculation about the possible causes of glucose and lipid abnormalities and weight gain observed with some atypical antipsychotics. We offer no more definitive explanation of these observations, but the proposal that hyperglycemia and hypertriglyceridemia are simply secondary to weight gain does not seem sufficient to explain our case or several others in the literature. Perhaps the unique neurotransmitter profiles of these medications play a role, through the disruption of normal metabolic processes.

We hope this report adds to the growing body of evidence regarding these adverse effects and alerts clinicians to the possibility of abnormal glucose and lipid regulation with atypical antipsychotic use in the pediatric population.

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