Focus on Metabolic Tx in Schizophrenia Patients

BY SHERRY BOSCHERT

SAN FRANCISCO — Treating metabolic abnormalities in patients with schizophrenia may be a better way to deal with insulin resistance or dyslipidemia than switching antipsychotics, Dr. Sun H. Kim suggests.

Second-generation antipsychotics can cause weight gain, and some data suggest that these drugs may have direct effects on insulin resistance and the risk for diabetes, independent of body mass index. The psychiatric literature has focused on managing patients with schizophrenia who develop metabolic abnormalities by switching second-generation antipsychotics, because some drugs are associated with less weight gain than others.

The few studies on the topic, however, suggest that this strategy doesn't work and can psychiatrically harm patients who were stable on medication before switching, she said at the Sixth Annual World Congress on the Insulin Resistance Syndrome.

"Switching isn't likely to resolve their existing metabolic abnormalities," said Dr. Kim of Stanford (Calif.) University. "I think there should be more focus on directly treating the abnormalities."

A pilot study by Dr. Kim and her associates included 15 young outpatients with schizophrenia and a fasting glucose of 126 mg/dL or lower who tried to switch therapy after gaining more than 10 kg on a second-generation antipsychotic medication. They were obese (with a mean BMI of 34 mg/kg^2 and a mean waist circumference of 111 cm) and had very high triglyceride levels (252 mg/dL) and low HDL levels (40 mg/dL). Their average age was 34 years and the mean LDL cholesterol level was 110 mg/dL.

Oral glucose tolerance tests at baseline showed that 47% had diabetes (20%) or impaired glucose tolerance (27%). The mean fasting glucose was 97 mg/dL, and the mean 2-hour glucose was 150 mg/dL. "Based on our measurements, three-quarters of them were highly insulin resistant," Dr. Kim said. The patients had been taking quetiapine, olanzapine, risperidone, ziprasidone, or clozapine.

When they tried to switch to the antipsychotic aripiprazole, five patients (33%) could not tolerate the switch psychiatrically. After 4 months on aripiprazole, 3 of the other 10 patients had lost 6-13 kg, 1 patient had no change in weight, and 6 patients gained 1-11 kg. As a group, the mean weight did not change significantly. The weight changes "didn't have a tremendous impact on insulin resistance," she said, and no significant changes were seen in mean BMI, waist circumference, total triglycerides, HDL or LDL cholesterol levels, plasma glucose levels, or steady state plasma glucose (J. Clin. Psychopharmacol. 2007;27:365-8).

A larger, multicenter study by other investigators of 173 patients with schizophrenia or schizoaffective disorder who were being treated with olanzapine randomized them to continue on olanzapine (85 patients) or switch to aripiprazole (88 patients). The cohort had a mean BMI of 27 kg/m^2 or greater and a score of at least 4 on the Clinical Global Impressions–Severity scale of psychiatric disease.

Dropout rates were high in both groups—36% on aripiprazole and 26% on olanzapine. By the end of the 16-week study, mean weight had increased by 1.4 kg in the olanzapine group and decreased by 1.8 kg in the aripiprazole group—not an impressive change, Dr. Kim said. A slight benefit in triglyceride levels was seen in the aripiprazole group (a 14% decrease), compared with the olanzapine group (a 5% increase), but there were no significant changes in fasting glucose or insulin resistance. The Clinical Global Impressions–Improvement scores were statistically better with olanzapine than with aripiprazole, she added (J. Clin. Psychiatry 2008;69:1046-56).

"You have to weigh the risks and benefits of switching someone who is stable psychiatrically on one of these medications," and aggressively manage their metabolic abnormalities, she said. ■

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