Neuropsychiatric Illness Linked to Type 2 Diabetes

The relationship between the two is not completely clear and is likely to have many factors.

BY DAMIAN McNAMARA
Miami Bureau

ORLANDO, FLA. — Nearly 20% of children and adolescents have a neuropsychiatric diagnosis at the time they are diagnosed with type 2 diabetes, according to a retrospective study presented at the annual scientific sessions of the American Diabetes Association.

"Adolescents with neuropsychiatric disease and other risk factors may have a higher risk for glucose intolerance or type 2 diabetes, and may benefit from screening," Lorraine E. Levitt Katz, M.D., said. "The risk of type 2 diabetes may be greatest for obese children on atypical antipsychotics."

The relationship between neuropsychiatric illness and type 2 diabetes is not completely clear and is likely multifactorial. Weight gain, caused by neuropsychiatric illness or antipsychotic medication, may play a role; obesity is a risk factor for type 2 diabetes in children and adolescents. Neuropsychiatric illness may promote a sedentary lifestyle, another factor associated with weight gain. Some medications may cause hyperglycemia through insulin resistance or effects on beta cells. Other risk factors for pediatric type 2 diabetes include family history, ethnicity, and female gender, said Dr. Levitt Katz, a pediatric endocrinologist at the Children's Hospital of Philadelphia.

"At [Children's Hospital of Philadelphia], we've seen an increase in new type 2 diabetes cases. The number has increased steadily each year, up to 55 in 2002," said Dr. Levitt Katz, also of the University of Pennsylvania.

She and her colleagues reviewed the charts of 237 children and adolescents newly diagnosed with type 2 diabetes, to determine the prevalence of neuropsychiatric illness. They identified 46 such patients (19%). Diagnoses included depression, behavioral disorders (including attention-deficit hyperactivity disorder), mental retardation, autism, and developmental delay.

"A large number of pediatric patients with type 2 diabetes have neuropsychiatric disease," Dr. Levitt Katz said. Pediatric endocrinologists diagnosed most of the diabetes in the study population, but primary care physicians diagnosed some patients. The study findings may not even reflect the true prevalence. "We would argue our data are an underestimation of neuropsychiatric illness among children with diabetes."

Depression was the leading diagnosis (13 patients). A meeting attendee asked if preexisting depression interferes with a patient's motivation regarding diabetes. "It's an enormous challenge that will require creative thinking to address," Dr. Levitt Katz said. Although the study focused on neuropsychiatric illness at the time of diagnosis, she added that there is also depression after diagnosis and a large number of undiagnosed disorders.

Investigators next looked at patient demographics for any factors that might be more strongly associated with neuropsychiatric illness. For example, they compared body mass index (BMI) Z scores between diabetics with a neuropsychiatric condition and those without. "We did not find statistically significant differences in BMI, unlike we expected," she said.

Neither gender nor age at diabetes diagnosis was associated with a higher prevalence of neuropsychiatric illness. There was a trend toward a difference by ethnicity. The patient population included children who were African American (67%), Caucasian (24%), Asian Pacific (6%), and other (3%). "We found the African American population in the affected group was overrepresented at 79%, but it was not significantly different," said Dr. Levitt Katz.

The large number of comorbid conditions was a limitation of the study. In addition, the frequency of neuropsychiatric disease was not studied in a comparable pediatric population without diabetes.

The researchers looked for an association between the use of antipsychotic medication and diabetes. They found that 37.5% of children taking antipsychotics were on one agent and 27.5% were on two agents, but there was no correlation. Dr. Levitt Katz said, "We were somewhat surprised by these results; we initially thought type 2 diabetes was associated with psychiatric medications."

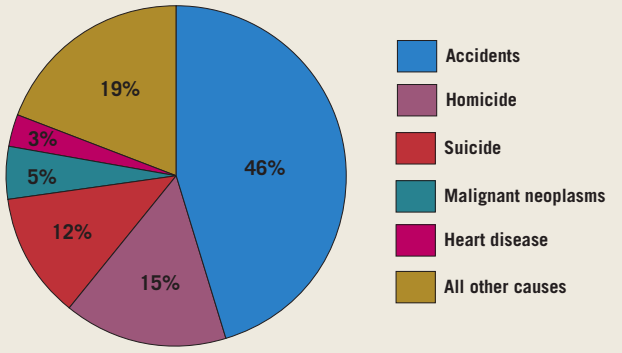
Twenty patients were taking mood stabilizers and eight were taking selective serotonin reuptake inhibitors. There were 17 patients on atypical antipsychotics, most commonly risperidone and olanzapine.

The atypical agents were prescribed for a wide range of diagnoses, including behavioral problems, bipolar disorder, schizophrenia, depression, and seizure disorder secondary to head trauma. Dr. Levitt Katz said, "This suggests there may be a lot of off-label use of these antipsychotics in children."

One year ago, there was a consensus conference on antipsychotics, obesity, and diabetes. The recommendations that emerged from the meeting include performing a risk-benefit assessment before starting medications, tracking BMI and waist circumference, doing a baseline screening for diabetes, and monitoring patients regularly. ■

DATA WATCH

Accidents Cause Almost Half of All Deaths in 15- to 24-Year-Olds



Note: Percentages represent the fraction of 33,009 deaths in 2002.
Source: Centers for Disease Control and Prevention

RICHARD FRANKI, RESEARCH/DESIGN

Pioglitazone Improved Lipids Better Than Rosiglitazone

BY MITCHEL L. ZOLER
Philadelphia Bureau

NEW ORLEANS — Treatment with pioglitazone led to better improvements in serum lipid measures compared with rosiglitazone in a study of 735 patients with type 2 diabetes and dyslipidemia.

"Whether these differences in lipid measures translate into differences for the future risk of cardiovascular disease has not yet been determined," but a comparison study of the two drugs using clinical end points is underway, Ronald B. Goldberg, M.D., said at the annual scientific sessions of the American Heart Association.

The study enrolled patients with type 2 diabetes who had fasting serum triglyceride levels of 150-599 mg/dL and fasting serum LDL-cholesterol levels lower than 131 mg/dL. The study was done at centers in the United States, Mexico, Puerto Rico, and Colombia, and was sponsored by Takeda Pharmaceuticals Co. and Eli Lilly and Co., which comarket pioglitazone (Actos) in the United States. Dr. Goldberg receives research support from and is on the speakers' bureau for Lilly and Takeda.

After a 4-week washout period, patients were randomized to treatment with either 30 mg pioglitazone or 4 mg rosiglitazone (Avandia) daily for 12 weeks. At the end of this first treatment phase, patients receiving pioglitazone had their daily dosage boosted to 45 mg, and patients on rosiglitazone upped their daily dosage to 8 mg. The higher dosages were continued for another 12 weeks. The full 28-week study was completed by 299 patients in the pioglitazone group and 286 patients who took rosiglitazone.

By the end of the study, several serum lipid values had substantially improved in the patients taking pioglitazone, compared with the measures taken at baseline at the end of the washout period (see box). These improvements were significantly better than the changes seen in the rosiglitazone group, said Dr. Goldberg, professor and chief of the division of diabetes and metabolism at the University of Miami.

The study's primary end point was the change in serum triglyceride levels. In the pioglitazone group, the average triglyceride level was 259 mg/dL at baseline, which then fell by an average of 52 mg/dL with treatment. Among patients treated with rosiglitazone, the average triglyceride level was 240 mg/dL at baseline, which then rose by 13 mg/dL with treatment.

The number and severity of treatment-related adverse events were similar in the two treatment groups, said Dr. Goldberg, but his report at the meeting did not include any details from the safety analysis.

It's not known why these two drugs—which are both thiazolidinediones and had similar effects on glycemic control in the study—would differ in their effects on serum lipids. This is the first head-to-head comparison of the two drugs, Dr. Goldberg told this newspaper. ■

Changes in Serum Lipids After 24 Weeks

	Pioglitazone Patients	Rosiglitazone Patients
Triglycerides (mg/dL)	–52	13
HDL cholesterol (mg/dL)	5	2
LDL cholesterol (mg/dL)	12	21
LDL particle concentration (nmol/L)	–50	110
LDL particle size (nm)	0.46	0.33

Source: Dr. Goldberg