Type 2 Among Youths Triples Cardiovascular Risks

ARTICLES BY
MIRIAM E. TUCKER
Senior Writer

ROME — Youth with type 2 diabetes had an average of nearly three cardiovascular risk factors each, compared with just one in healthy controls in an analysis of 295 participants in a large, multicenter, U.S. case-control study.

The data come from 106 patients with type 2 diabetes and 189 healthy controls (matched for age, sex, and race/ethnicity) recruited by primary care providers at two sites (Colorado and South Carolina) of the six participating in the federally funded SEARCH for Diabetes in Youth, a study designed to investigate the prevalence and characteristics of diabetes in individuals aged younger than 20 years.

The current analysis, one of the first to focus on cardiovascular (CV) risk in this population, also showed that not all the risk factors could be accounted for by increased obesity and/or hyperglycemia.

The data appear to "support the statement that early prevention and treatment strategies [to reduce] the prevalence of cardiovascular risk factors in youth with type 2 diabetes mellitus are urgently needed," Dr. Dana Dabelea said at the annual meeting of the European Association for the Study of Diabetes.

The participants were aged 10-22 years, with a mean of 16 years for the diabetic group and 14 years for the controls—a statistically significant difference, despite attempts to age-match. Duration of diabetes in the type 2 group was 1.5 years. Females comprised 69% of the diabetic group and 60% of controls, not significantly different, said Dr. Dabelea, director of the epidemiology PhD program at the University of Colorado, Denver, and a principal investigator at the Colorado site.

The type 2 group was significantly more likely than were the controls to be African American (55% vs. 29%, respectively) and less likely to be non-Hispanic white (28% vs. 54%). Body mass index was significantly greater in the youth with diabetes (35 vs. 24 kg/m^2), as was waist circumference (108 vs. 80 cm in females; 110 vs. 77 cm in males). Mean hemoglobin A_{1c} in the diabetics was 7% (5% in the controls).

Consumption of saturated fat as a percent of total daily calories was slightly higher in the type 2 group, and the amount of daily physical activity was lower, but these were not statistically significant.

Highly statistically significant differences between the groups were seen in the proportions who had hypertension (27% in the type 2 group vs. 5% of controls), were on medication (5% of controls), had low HDL cholesterol (25% vs. 5%, respectively), and high triglycerides (27% vs. 6%).

Also highly significantly different were the proportions who were obese, defined as 95th percentile or greater BMI for age and sex (86% in the type 2 group vs. 26% of controls) and those with a large waist circumference, defined as 90th percentile or greater for age and sex (82% vs. 22%).

Elevated albumin/creatinine ratio of 30 mcg/mg or greater was present in 17% of the type 2 group, compared with 7% of controls, of borderline significance. Proportions of those with high LDL cholesterol and who were current smokers were not significantly different, she said.

Nearly half (45%) of the controls had none of these CV risk factors, compared with 3% of those with type 2 diabetes. In type 2 patients, 60% had three or more risk factors, compared with 13% of the nondiabetic controls. Those with type 2 diabetes had a mean of 2.9 CV risk factors each, compared with 1 for the controls.

In a series of multiple linear regression models, adjustment for differences in obesity accounted for the differences between the type 2 group and the controls in HDL cholesterol, systolic blood pressure, and adiponectin, while adjustment for hemoglobin A_{1c} between the groups accounted for the differences in apolipoprotein B and LDL particle size. Adjustment for obesity and HbA_{1c} accounted for the difference in triglycerides. But levels of the inflammatory markers fibrinogen and IL-6 remained significantly different between the two groups, even after adjustment for obesity and hemoglobin A_{1c}, Dr. Dabelea said. ■

Exenatide Plus Metformin Improves Metabolic, Hormonal Status in PCOS

ROME — Treating polycystic ovary syndrome with exenatide plus metformin was more effective than either medication alone in improving menstrual cycle frequency and hormonal and metabolic derangements, a study has found.

The findings were presented at the annual meeting of the European Association for the Study of Diabetes by Dr. Ted Okerson of Amylin Pharmaceuticals Inc. on behalf of the scheduled presenter Dr. Rajat Bhushan of the Metabolic Center of Louisiana Research Foundation, Baton Rouge, who was unable to attend the meeting. Dr. Karen Elkind-Hirsch of the same institution was the principal author of the study (J. Clin. Endocrinol. Metab. 2008;93:2670-8).

Metformin has been shown to reduce insulin resistance and androgen levels while increasing ovulation in women with polycystic ovary syndrome (PCOS). However, it does not alter insulin secretion. Exenatide (Byetta), used to treat type 2 diabetes, has been shown to restore first- and second-phase insulin secretion, which is attenuated in women with PCOS, as well as promote weight loss, thereby potentially further improving insulin sensitivity, Dr. Okerson said.

An open-label, prospective 24-week pilot study of 60 obese oligoovulatory women with PCOS was funded by a grant from Amylin Pharmaceuticals and Eli Lilly & Co. In the study, 40 white and 20 African American women with PCOS were randomized to receive either 1,000 mg metformin twice daily, exenatide 10 mcg twice daily, or a combination of the two, for 24 weeks. The women were aged 18-40 years, with a body mass index above 27 kg/m^2 and six or fewer menses per year. Forty-two patients (14 in each group) completed the study, with equal racial distribution across groups.

Menstrual cycle frequency, the primary study end point, was significantly increased in all treatment groups at 24 weeks and to a significantly greater degree with the combination, compared with metformin. The proportion of normal cycles in the group increased from a mean of 22% at baseline to 57% with exenatide, from 21% to 49% with metformin, and from 29% to 83% with both drugs. Ovulatory rates also improved with all three regimens, but significantly more so with the combination. Ovulation occurred in 86% of the combination patients, compared with 50% in the exenatide group, and 29% on metformin.

Body weight changes were significant in both groups receiving exenatide, but not in those receiving metformin alone. At 24 weeks, mean weight loss was 6 kg in the combination group and 3.2 kg with exenatide vs. 1.6 kg with metformin. Similar reductions were seen in body mass index, Dr. Okerson reported.

Total testosterone was significantly decreased from baseline in all treatment groups, by 10.2 ng/dL with exenatide alone, 3.6 ng/dL with metformin alone, and 18.4 ng/dL with the combination. The free androgen index was significantly more reduced with the combination, compared with metformin alone but not compared with exenatide alone. Levels of sex hormone–binding globulin were increased, but not significantly, with all treatments, whereas levels of dehydroepiandrosterone sulfate and thyroid-stimulating hormone were not significantly altered in any group.

Insulin sensitivity improved significantly with all treatments, and was significantly higher in the combination group than in the metformin group. After therapy, the calculated mean insulin secretion sensitivity index was 516 with combination therapy, 395 with exenatide, and 232 with metformin. Total cholesterol and triglycerides decreased significantly with combination therapy vs. metformin, which did not consistently improve those levels. HDL and LDL cholesterol levels did not change significantly with treatment. Adiponectin levels increased significantly with all treatments, while other inflammatory markers did not change.

The most common adverse events were mild or moderate gastrointestinal problems, including nausea in 15% with exenatide, 20% with metformin, and 45% with the combination. Vomiting occurred in 5% of each monotherapy group and in 10% of those on the combination. Diarrhea was more common with metformin (30%) than with the combination (10%), and did not occur with exenatide. No patient left the study because of GI side effects; four left the study because they became pregnant. ■

Oral Test Tracks Level Of Glucose in PCOS

ROME — Oral glucose tolerance testing identified abnormal glucose metabolism in 10% more patients with polycystic ovary syndrome than did fasting glucose tests alone, a study has found.

Other clinical and paraclinical factors associated with type 2 diabetes were not highly predictive of impaired 2-hour glucose levels, suggesting that all patients with PCOS should be screened with an oral glucose tolerance test (OGTT), Dr. Simona Fica and her associates reported in a poster at the annual meeting of the European Association for the Study of Diabetes.

The 258 patients in the study had a mean age of 25 years and mean body mass index of 29 kg/m^2. All had presented with chronic oligoanovulation and hyperandrogenism, with or without polycystic ovary on ultrasound. All were screened with a fasting glucose test and a 2-hour OGTT.

Abnormal blood glucose levels were found in a total of 18.9% of the patients, with impaired fasting glucose in 5.4%, impaired glucose tolerance in 8.5%, and diabetes mellitus in 5%. Of the 247 patients with a fasting glucose level less than 126 mg/dL, OGTT revealed 10.1% with either impaired glucose tolerance (8.9%) or diabetes (1.2%) at 2 hours.

Abnormal 2-hour glucose values were significantly associated with an age of 30 years or older, a BMI of 27 or greater, a waist-hip ratio of 0.8 or greater, a fasting blood glucose value of 100 mg/dL or greater, a homeostasis model assessment index at or above 3, a total cholesterol level greater than 200 mg/dL, and triglyceride levels of 150 mg/dL or above.

However, the positive predictive value of these factors for abnormal 2-hour glucose values was low: 42.9% for fasting glycemia; 23.7% for triglycerides; and 13.4% for both BMI and waist-hip ratio, said Dr. Fica of the endocrinology department at Carol Davila University of Medicine and Pharmacy and Elias Hospital, both in Bucharest, Romania.

Neither the presence of acanthosis nigricans nor having first-degree relatives with type 2 diabetes was associated with 2-hour OGTT abnormalities in this population, despite the known association between the two factors and type 2 diabetes.

"Due to the low value of clinical and paraclinical data to predict 3-hour abnormal glucose levels, we suggest all patients be screened with OGTT," they concluded. ■