Caffeine Worsens Insulin Resistance in Prediabetics

BY JEFF EVANS
Senior Writer

WASHINGTON — Caffeine intake appears to exaggerate postmeal insulin resistance in prediabetic adults who regularly drink several cups of coffee each day, according to preliminary results of a randomized, double-blind, crossover study of 50 individuals.

The results "suggest that caffeine consumption promotes the development of type 2 diabetes in those people who are at greatest risk for this disease," James D. Lane, Ph.D., said at the annual meeting of the Society of Behavioral Medicine.

This is the first time that caffeine's effects on insulin resistance have been measured in habitual coffee drinkers with prediabetes, said Dr. Lane of the department of psychiatry and behavioral medicine at Duke University, Durham, N.C. More than 12 other studies have shown that caffeine administration acutely raises insulin resistance both in healthy, nondiabetic volunteers and in patients with type 2 diabetes.

Other studies have shown that coffee drinking is associated with a significantly reduced risk of type 2 diabetes, but these conclusions have been "based on correlational observations, not controlled, experimental studies," he noted.

In the current study, all participants had prediabetes (average impaired fasting blood glucose level of 111 mg/dL) and drank at least 2 cups of coffee per day, which was confirmed by a 7-day food diary. Each person fasted overnight and did not consume any caffeine, which preserved any tolerance that they had developed from their continued exposure to caffeine.

On the first day of testing, the participants received either 250 mg caffeine or placebo pills and had their fasting blood glucose levels measured. On the second day, they received the opposite of what they had taken on day 1. After 60 minutes, they had their blood glucose levels measured again, and they received a booster dose of 125 mg caffeine or placebo. They also drank a BoostPlus liquid meal replacement shake (75 g carbohydrates, plus fat and protein), which is similar to an oral glucose tolerance test except that it is more like a real meal, Dr. Lane said. Blood samples were drawn during each of the next 3 hours.

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The total 375-mg dose of caffeine was equivalent to about 3 cups of brewed coffee, similar to what subjects consumed on average each day (409 mg).

For the first 41 participants with full results available, caffeine increased the 3-hour area under the curve (AUC) for plasma glucose by 15% more than placebo, though the result was not statistically significant. But the 3-hour AUC for plasma insulin was 18% greater with caffeine than with placebo—a significant difference. AUC is the standard method for measuring responses to oral glucose tolerance tests, said Dr. Lane. "This pattern of results shows that caffeine did increase insulin resistance in these prediabetic subjects."

A normal response to the extra insulin produced with caffeine would have been to reduce the peak glucose level to a point lower than what was seen with placebo. But "the glucose response was, if anything, a little larger in the caffeine condition," he said. "Given the conditions of our study, we think that this insulin resistance effect occurs every day as these prediabetic individuals and others like them consume caffeinated beverages in the real world."

If the results can be replicated in a larger, long-term prospective study, it would suggest that people who have prediabetes should curtail caffeine consumption to reduce their risk, Dr. Lane said. ■

Oral Alternatives Show Promise For Treating Gestational Diabetes

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Two oral medications deserve further investigation as alternative therapies for gestational diabetes, results of separate small studies suggest.

Acarbose or metformin might be helpful if additional research supports these preliminary findings, investigators said in separate poster presentations at the annual meeting of the Society for Maternal-Fetal Medicine.

Neither drug is approved for the treatment of gestational diabetes. Both are Food and Drug Administration pregnancy category B. Injected insulin or oral glyburide are approved to treat gestational diabetes.

An oral option other than glyburide might allow patients to be managed on one or potentially two oral agents before resorting to injections of insulin, Dr. Jacquelyn Cortez said in an interview at one of the posters. She and her associates conducted a prospective, double-blind trial that randomized 59 women diagnosed with gestational diabetes in their second or third trimester, prior to 34 weeks' gestation, to 50 mg acarbose t.i.d. or identical placebo pills taken with meals. All had failed diet therapy.

At regular follow-ups, if more than half of the patient's fasting glucose values were above 95 mg/dL, or more than half of her postprandial glucose values were above 135 mg/dL, the dosage was increased to 100 mg t.i.d. If this did not control blood glucose levels, she was considered to have failed single-agent therapy and started on a second agent.

Fewer patients in the acarbose group failed monotherapy and required a second agent, compared with the placebo group, but the difference did not quite reach statistical significance. Women in the acarbose group gained significantly less weight (19 pounds) than did those on placebo (27 pounds), said Dr. Cortez of the department of reproductive medicine at the University of California, San Diego.

Postprandial blood glucose levels were significantly lower on acarbose therapy (122 mg/dL), compared with placebo (130 mg/dL). There were no differences between groups in perinatal outcomes.

The failure rate with acarbose in this study and failure rates with glyburide in other studies are high, but women on acarbose in the present study did not develop the hypoglycemia sometimes seen with glyburide, Dr. Cortez noted. Acarbose is a glycosidase inhibitor that prevents intestinal breakdown of starches to glucose in the upper small bowel.

Metformin, an insulin sensitizer, was the subject of a separate review of data from two randomized trials in which 67 women with gestational diabetes took the drug. Of these, 59 met glycemic goals of fasting glucose values lower than 105 mg/dL and 2-hour postprandial glucose values lower than 120 mg/dL, reported Dr. Lisa E. Moore of the University of New Mexico, Albuquerque, and associates. The eight who did not meet glycemic goals started insulin therapy.

Macrosomia occurred in four infants (6%), and all were delivered vaginally. The primary cesarean delivery rate (excluding elective repeat C-sections) was 15% (10 patients). There were no cases of fetal anomalies or maternal or fetal hypoglycemia. Eight neonates had hyperbilirubinemia, and two had 5-minute Apgar scores lower than 5.

The efficacy rate with metformin seemed similar to success rates with glyburide in other studies, Dr. Moore said. Failure of metformin was not predicted by maternal BMI or the value of the 1-hour glucose challenge test. Metformin is not approved in the United States for this indication, but there are data from other countries on its use in gestational diabetes. Dr. Cortez and Dr. Moore have no financial relationships with the drugs' manufacturers. ■

ALT Elevation May Point to Metabolic Syndrome in Children

BY PATRICE WENDLING
Chicago Bureau

NEW ORLEANS — Serum alanine aminotransferase, a noninvasive marker commonly used to assess nonalcoholic fatty liver and related liver dysfunction, appears to be useful in identifying children with metabolic syndrome and its components.

"Elevations of alanine aminotransferase within normal range relate strongly to metabolic syndrome and its components and may help improve the risk assessment of this condition in the pediatric population," Dr. Dharmendrakumar Patel said at the Southern regional meeting of the American Federation for Medical Research.

Dr. Patel and colleagues from the Tulane (University) Center for Cardiovascular Health in New Orleans reported data from 1,524 children aged 4-11 years (62% white, 51% male) and 1,060 adolescents aged 12-18 years (58% white, 51% male) examined as part of the Bogalusa Heart Study.

Serum alanine aminotransferase (ALT) and cardiovascular risk factors were measured at baseline. The acceptable cutoff points for the metabolic variables aren't established for children, so adverse levels were defined as values above the age-, race-, and gender-specific 75th percentiles of body mass index (BMI), systolic blood pressure, ratio of total cholesterol to HDL cholesterol, and homeostatis model assessment: insulin resistance (HOMA-IR). A clustering of adverse levels of all four variables denoted metabolic syndrome. Age-, race-, and gender-specific quartiles of ALT were used for analysis.

Overall, 25% of children and 29% of adolescents in the top quartile of ALT had adverse levels of three or four metabolic syndrome risk factors. This clustering was significantly higher than expected, Dr. Patel said.

When the researchers used an area under the receiver operating curve, the diagnostic accuracy of ALT to classify pediatric patients with metabolic syndrome was 67% in children and 82% in adolescents.

ALT levels were significantly higher in white children, compared with black children and in male adolescents, compared with female adolescents, said Dr. Patel, a research analyst and field epidemiologist at the center.

In children, the average ALT level was 17 U/L in both white boys and girls, compared with 16 U/L in black boys and 15.3 U/L in black girls.

In adolescents, the average ALT level was 19 U/L in both white and black boys, compared with 16 U/L in white girls and 14.6 U/L in black girls.

Children and adolescents with ALT levels in the top quartiles, compared with the bottom quartiles, had an increased prevalence of adverse levels of body mass index, systolic blood pressure, ratio of total cholesterol to HDL cholesterol, and HOMA-IR index, as well as metabolic syndrome.

Upon multivariate analyses, body mass index was the most important independent predictor of ALT levels in both groups. The odds ratio for an abnormal or elevated ALT level was 2.2 for children and 1.8 for adolescents with BMIs above the 75th percentile for age, gender, and race. Other significant independent predictors were white race in children; and total cholesterol to HDL cholesterol ratio, HOMA-IR, and male gender in adolescents. ■