Metformin Improves Weight Loss, Satiety in Kids

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

SAN FRANCISCO — Metformin is associated with modest weight loss and some improvements in signs of metabolic syndrome in obese children with severe hyperinsulinemia, a government-sponsored randomized controlled trial has concluded.

But because this is the first such study in children, the drug can't yet be recommended for routine use in this population, Dr. Jack Yanovski said at the annual meeting of the Endocrine Society.

Dr. Yanovski, chief of the National Institutes of Child Health and Human Development's Unit on Growth and Obesity, presented the results of the first placebo-controlled trial of metformin in children aged 6-12 years. The 100 children who participated (mean age 10 years) were all obese (mean body mass index [BMI] 34.6 kg/m^2) and severely hyperinsulinemic, with fasting insulin of at least 15 mcU/mL.

The cohort consisted mostly of female children (60%). Children randomized to metformin (53) were started at 1,000 mg/day; this was ramped up to a final dosage of 1,000 mg twice a day for the duration of the 6-month trial. All children but one were able to tolerate the dose. All children also took a daily multivitamin supplement.

By the study's end, mean BMI had decreased in the active group and increased in the placebo group (–1 kg/m^2 vs +0.23 kg/m^2—a significant difference). Children taking metformin also had a significantly decreased BMI *z* score, compared with those taking placebo (–0.11 vs –0.04). Mean body fat mass also decreased significantly in the active group (–1.7 kg) and increased significantly in the placebo group (2 kg).

Some signs of metabolic syndrome improved in children taking metformin, although the changes were not significant. Serum glucose, homeostatic assessment model algorithm (HOMA) insulin resistance index, and total cholesterol all improved in the treated children.

Children in the metformin group experienced a significant decrease in serum vitamin B_{12} concentrations, although all remained within normal range, and no child required additional supplementation.

The most commonly reported adverse events were liquid stool (60% metformin vs. 2.5% placebo), nausea (24% vs. 8%), and fatigue (14% vs. 5%). All were significantly more common in the metformin group; however, by the study's end, the incidence of liquid stool had decreased by 20% and the incidence of nausea had decreased by 8%.

Metformin also appears to exert its weight-loss effects in obese children by reducing their desire to eat and thus decreasing their food intake, according to a substudy of the same government-sponsored trial, Rachael Sorg said in a poster session at the Endocrine Society meeting.

Some of the children (45 metformin-treated and 39 placebo-treated) participated in both a pre- and posttreatment meal study to evaluate the drug's effect on food intake. One study was conducted before the drug trial commenced, and one at the end of the 6-month treatment period.

Each meal study included two buffet lunches, each containing 28 items (9,835 calories total). The first lunch was consumed after children fasted through the night. The second was consumed after they drank a 790-calorie nutrient shake for breakfast.

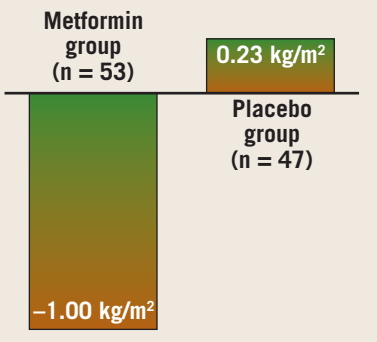
Subjects completed a scale of hunger, fullness, and desire to eat before after each test meal, and also kept a food diary of everything they consumed for 7 days before and after the test.

Compared with baseline measurements obtained in the pre-metformin meal study, children taking metformin consumed significantly fewer calories in the meal after the breakfast shake. They also reported significantly decreased feelings of hunger and increased feelings of fullness after the shake. They reported lower hunger after the postshake meal, lower desire to eat the postshake meal, and lower caloric intake at the postfast meal as well, although none of these differences were significant.

"These data suggest that one of the mechanisms whereby metformin treatment reduces body weight in overweight, hyperinsulinemic children is by decreasing food intake and perceived hunger," said Ms. Sorg, a research assistant at the National Institutes of Child Health and Human Development.

Dr. Yanovski and Ms. Sorg said they had no financial disclosures to make with regard to metformin. ■

6-Month Change in Body Mass Index of Obese Children



Note: Based on a study of children with a mean age of 10 years that were obese and severely hyperinsulinemic.
Source: Dr. Yanovski

ELSEVIER GLOBAL MEDICAL NEWS

Study Shows Favorable Gastric Banding Outcomes in Teen Cohort

BY ALICIA AULT
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SAN FRANCISCO — Teens who underwent laparoscopic gastric banding surgery had improvements in hemoglobin A_{1c}, triglyceride, and C-reactive protein measures, according to 6-month follow-up results for 14 patients.

The Lap-Band, made by Inamed Inc., a division of Allergan Inc., was approved by the Food and Drug Administration in 2001 for adults. It has been used off label for adolescents, but many institutions are discouraging those unapproved procedures and are urging providers instead to enroll patients at one of the three study sites, said Dr. Ilene Fennoy, who presented results from the Columbia University, New York, site at the annual meeting of the Endocrine Society.

At Columbia University, 38 adolescents aged 14-17 years have received the Lap-Band, and 14 of those have had 6 months of follow-up, said Dr. Fennoy, a pediatrician at Columbia and medical director of the comprehensive adolescent bariatric surgery program at the Morgan Stanley Children's Hospital of New York–Presbyterian. Study participants, all of whom were Tanner stage IV or V, underwent psychological evaluation and had to have demonstrated failure to lose weight after participation in a documented weight-loss program for at least 6 months, Dr. Fennoy said.

Values for the children were assigned based on references; what might be considered normal for an adult is not so for a pediatric patient, according to Dr. Fennoy. Overall, the 14 patients have lost an average of 20 pounds each. The body mass index *z* score declined from 2.88 to 2.69, and waist circumference declined from 145.5 cm to 132.2 cm. Hemoglobin A_{1c} values declined from 5.59% to 5.48%, while triglycerides went from 128.9 mg/dL to 95 mg/dL. C-reactive protein levels dropped from 9.4 mg/L to 5.7 mg/L.

There were no significant differences in blood pressure.

Dr. Fennoy said that the adolescents tolerated the surgery "very well," and returned to school within a week, but that "the hardest part for them usually is eating smaller portions." Postoperative complications included some increased bleeding in one patient and the need to reposition a band in another. The study cohort will be followed for 5 years, Dr. Fennoy said.

Overall, "for the extremely obese adolescent, [the Lap-Band] offers the opportunity to lose significant weight, which really is not present from pharmacologic and lifestyle interventions," she noted. Her data will be part of Allergan's application to the FDA for approval of the Lap-Band in adolescents, but the company is not funding the study, Dr. Fennoy said. She had no disclosures to report. ■

Mediterranean, Low-Carb Diets Found as Effective as AHA Diet

BY MARY ANN MOON
Contributing Writer

Both the Mediterranean diet and the low-carbohydrate (Atkins) diet proved to be as safe and effective for inducing weight loss in moderately obese subjects as was the American Heart Association's low-fat, restricted-calorie diet, according to a report.

In a 2-year randomized controlled trial in which adherence rates ranged from 78% to 90%, the low-carb and Mediterranean diets produced beneficial metabolic effects in addition to weight loss, suggesting that their dietary strategies might be considered for use in clinical practice and that "diets might be individualized according to personal preferences and metabolic needs," said Dr. Iris Shai of Ben-Gurion University of the Negev, Beer-Sheva, Israel, and her associates.

In particular, the low-carbohydrate diet that allows unrestricted caloric intake as long as carbohydrate content is kept to a minimum "may be optimal for [patients] who will not follow a restricted-calorie dietary regimen," they noted.

The researchers compared the three diets in a workplace study involving 322 participants with a mean body mass index (BMI) of 31 kg/m^2 and a mean age of 52 years, most of whom (86%) were men. Dietitians met with the participants frequently, for a total of 18 sessions, each for 90 minutes. They also conducted brief motivational telephone calls with those who were having trouble adhering to their diet. The participants' spouses were educated to be supportive of dietary goals at home.

The participants were weighed monthly in the workplace, and adherence to diets was monitored with food frequency questionnaires. At 2 years, the adherence rates were 78% with the low-carbohydrate diet, 85% with the Mediterranean diet, and 90% with the AHA low-fat, low-calorie diet.

"We believe that similar strategies to maintain adherence could be applied elsewhere" outside of the workplace environment, Dr. Shai and her associates wrote.

Daily energy intake decreased significantly and to a similar extent in all three groups. The mean weight loss was 3.3 kg with the AHA diet, 4.6 kg with the Mediterranean diet, and 5.5 kg with the low-carbohydrate diet, the investigators said (New Engl. J. Med. 2008;359:229-41).

All three groups also had significant and similar decreases in BMI, waist circumference, blood pressure, and insulin levels.

The low-carbohydrate diet produced the greatest improvement in lipid profiles, with a 20% relative decrease in the total cholesterol to HDL cholesterol ratio, compared with a 12% decrease for the AHA diet. ■