Insulin Resistance Status

Predicting Weight Response in Overweight Children

Doyle M. Cummings, PharmD, FCP, FCCP; Sarah Henes, MA, RD, LDN; Kathryn M. Kolasa, PhD, RD, LDN; John Olsson, MD; David Collier, MD, PhD

Objective: To assess the relationship between insulin resistance and body mass index (BMI) z score associated with dietary modification that focuses on limiting sweetened beverage consumption in overweight children.


Setting: Community-based primary care practices treating children.

Patients: Forty-five children (aged ≤18 years) at or above the 95th percentile of BMI for age and sex.

Intervention: Children and parents were instructed by a dietitian regarding caloric reduction and modification of sweetened beverage intake.

Main Outcome Measures: Insulin resistance at baseline was calculated from fasting insulin and glucose levels (ie, homeostatic model assessment [HOMA]) and change in BMI z score from baseline to 12-week follow-up.

Results: Change in BMI z score in response to a decrease in sweetened beverages correlated (Pearson product moment correlation coefficient = 0.42, P < .01) with baseline insulin resistance. Those with a decrease in or an unchanged BMI z score had significantly greater insulin resistance than those whose BMI z score increased (mean [SD] HOMA, 6.2 [4.2] vs 2.6 [2.0], P < .01). Linear regression confirmed that HOMA was a significant predictor of change in BMI z score when controlling for age, race, and sex.

Conclusions: Among overweight children in primary care practices, a significant relationship was found between insulin resistance and the change in BMI z score associated with a dietitian-mediated intervention that includes a focus on decreasing sweetened beverage consumption. Estimating insulin resistance may inform dietary recommendations for overweight children.

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Recent studies have identified a growing epidemic of childhood obesity in many of the world’s developed nations, including the United States, and lifestyle interventions are usually considered the initial treatment of choice. Dietary modifications have been an important component of these lifestyle interventions based on the premise that decreasing energy intake while maintaining or increasing energy expenditure will result in weight loss or limitation of weight gain beyond that associated with healthy growth and development. Limited caloric restriction has proved safe and modestly effective in producing weight loss in appropriately motivated children and families but may be less effective for weight maintenance.

More recent attention has focused on the composition of the diet and how alterations in nutrient content, rather than caloric restriction alone, may influence weight loss and other risk factors. Although evidence is increasing regarding the use of reduced-carbohydrate diets in overweight adults, less is known about their effectiveness in overweight children. In adults and children, reduced-carbohydrate diets appear to result in significant weight loss during short observation periods; consequently, despite relatively limited evidence, reduced-carbohydrate diets for children have rapidly increased in popularity.

Research on modifying specific carbohydrates ingested is also sparse. Several studies suggest that the ingestion of concentrated, sugar-sweetened drinks is independently associated with increasing body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) and that a dietary plan
that restricts such drinks significantly reduces caloric intake and weight.\textsuperscript{8} In a cluster-randomized trial in the United Kingdom, James et al\textsuperscript{10} reported on the effectiveness of a school-based educational program that focused on reducing consumption of carbonated drinks sweetened with sugar. Consumption decreased in the intervention schools and increased in the control schools in parallel with a slight reduction in the prevalence of overweight children in the intervention schools and an increase in the number of overweight children in the control schools. Despite this preliminary evidence regarding the overall response to restricting sugar-sweetened drinks, little is known about which children respond. We hypothesized, based on preliminary evidence in adults,\textsuperscript{9,11} that the magnitude of weight loss in children in response to a reduction in the ingestion of sweetened beverages may depend, in part, on the degree of insulin resistance, with higher insulin resistance leading to greater short-term weight loss.

**METHODS**

Data for this retrospective pilot study come from the prospective KIDPOWER Lifestyle Intervention Project, which included nutritional intervention in the usual-care atmosphere of a medical professional’s office. All data were abstracted from patient records.

**PATIENTS**

Children (aged 5-18 years) who were at or above the 95th percentile of BMI for age and sex and who expressed a willingness to participate in an educational program of lifestyle modification that included caloric restriction were referred from primary care practices in the community for further evaluation and treatment between July 1, 2004, and April 28, 2006. This study was approved by the East Carolina University Medical Center institutional review board for protection of human subjects.

**INTERVENTION**

After medical examination, each child and his or her parent entered a 12-week lifestyle intervention program (KIDPOWER) that included dietary modification. Each child and parent received a similar lifestyle education program from comparably trained staff members (S.H. and K.M.K.). The purposes of the program were to ensure that appropriate nutrient requirements were met for healthy growth and at the same time to limit further inappropriate weight gain, normalize metabolic abnormalities (eg, elevated insulin concentrations), and prevent complications associated with obesity. The initial dietary phase of the intervention involved a 12-hour fast before the visit. A follow-up message was also sent to the family, reminding them of the visit and the fast protocol. At the initial visit, the nurse verified that the patient had been fasting for at least 12 hours. The nurse then obtained a sample of venous blood from the antecubital fossa and delivered it to the hospital laboratory, where the serum was harvested and assayed for insulin concentrations (Immulite 2000 analyzer; Diagnostic Products Corporation, Los Angeles, California) according to an immunochemiluminometric method and for glucose (AU640 analyzer; Olympus Corporation, Center Valley, Pennsylvania) according to a hexokinase method. The homeostatic model assessment (HOMA) was used to estimate insulin resistance based on the work of Keskin et al,\textsuperscript{12} who found it to have acceptable sensitivity and specificity in diagnosing insulin resistance in children. The HOMA value was calculated as follows: (fasting plasma glucose concentration [measured in milligrams per deciliter] \times fasting plasma insulin concentration [measured in microunits per milliliter]) / 405. Data on daily consumption of sugar-sweetened and sugar-free beverages (collected in the following ordered categories: 0, <600, 600-959, 960-1439, 1440-2160, and >2160 mL), as well as fruit and vegetable intake, were collected by the dietitian (S.H. or K.M.K.) from the report of the parent(s) for children younger than 12 years and from the report of the child for children 12 years or older, using a modified 24-hour dietary recall that has been extensively used in the East Carolina University Pediatric Healthy Weight Research and Treatment Center.

**STATISTICAL ANALYSIS**

Data were analyzed using a commercially available software program (SPSS for Windows; SPSS Inc, Chicago, Illinois). Descriptive statistics were used to characterize the study population. Mean BMI at baseline was compared among categories of sweetened beverage consumption by analysis of variance. The change in BMI z score was correlated with HOMA values using a Pearson product moment correlation coefficient. Mean HOMA values were compared in children who had an increase in BMI z score with those who had a decrease in or an unchanged BMI z score using an independent-samples t test. Changes in mean BMI z score were also examined by race (white...
RESULTS

Ninety-one children enrolled in the study; 45 children (mean [SD] age, 10.9 [3.4] years; 29 females [64%]; 31 nonwhites [69%]) completed the 12-week study and had complete laboratory and dietary data available. At baseline, the mean (SD) BMI was 31.9 (6.9) (range, 19.8-51.5), the mean (SD) fasting insulin level was 18.7 (14.0) µIU/mL (range, 1.6-6814.0 [to convert to pico-international units per liter, multiply by 0.6945]), the mean fasting glucose level was 87.2 (15.7) mg/dL (range, 62-141 mg/dL [to convert to millimoles per liter, multiply by 0.05551]), and 13 of 45 patients (29%) had a HOMA value of 3.16 or greater, suggesting the presence of insulin resistance. As expected, the mean BMI in the insulin-resistant group was significantly higher than that in the non–insulin-resistant group (35 vs 30; \( P = .048 \)). Moreover, at baseline a significant trend was seen of increasing mean BMI values as a function of increasing levels of sweetened beverage consumption (Table 1).

Follow-up data showed that the dietitian intervention had a notable effect on sweetened beverage consumption. As indicated in Table 2, sweetened beverage consumption decreased significantly from baseline to the 12-week follow-up visit (\( P = .001 \)). This pattern of decreased consumption was not significantly different by age, race, sex, or insulin sensitivity (HOMA) status.

Change in BMI \( z \) score in response to a decrease in sweetened beverage consumption correlated (Pearson product moment correlation coefficient \( = 0.42; P < .01 \)) with baseline insulin resistance. Those with a decrease or no change in BMI \( z \) score had significantly greater insulin resistance than those whose BMI \( z \) score increased (mean [SD] HOMA value, 6.2 [4.2] vs 2.6 [2.0]; \( P < .01 \)). Among children with HOMA values of 3.16 or greater (insulin resistant), the mean BMI \( z \) scores remained unchanged (2.46 and 2.45, respectively), whereas children with HOMA values of less than 3.16 (insulin sensitive) had an increase in mean BMI \( z \) score (from 2.55 to 2.62, \( P < .01 \)) across the 12 weeks. Similarly, children with HOMA values of 3.16 or greater limited further weight gain during the 12-week dietary intervention (mean [SD] weight gain, 0.09 [1.66] kg), whereas children with HOMA values of less than 3.16 continued to gain weight (mean [SD] weight gain, 1.98 [3.33] kg; \( P = .06 \)). The linear regression model, in which the HOMA value was a significant predictor (\( \beta = .5, R^2 = 0.23, P < .01 \)) of the change in BMI \( z \) score even when controlling for age, race, and sex, further highlights the relative importance of insulin resistance.

The present study, completed in a community-based primary care environment, demonstrates several important findings. First, it adds to growing literature as reviewed by James and Vartanian and colleagues regarding the relationship between sweetened beverage consumption and a variety of outcomes, including body weight and BMI. Like others, we demonstrate a consistent and significant relationship between the magnitude of sweetened beverage consumption and BMI in children. We observed this relationship in all children across age, race, and sex categories. We believe this association occurs because sweetened beverage consumption constitutes a significant source of increased energy intake that is often uncompensated by an increase in energy expenditure.

Second, the study illustrates the impact of intensive counseling by a trained dietitian on sweetened beverage consumption in overweight children. Although variable, consumption decreased in most children across age, race, and sex categories and regardless of insulin sensitivity status, demonstrating the potential for intensive dietary intervention to significantly alter patterns of energy intake. As busy primary care physicians contemplate the growing complexities of dietary intervention in overweight children, especially the importance of modifying specific macronutrients to maximize benefit, the crucial role of the dietary professional in education and counseling becomes increasingly clear. Furthermore, focusing on sweetened beverage consumption is a concrete target for dietary modification even in busy practices. In the present study, parents were also included as a target of the dietary intervention to significantly alter patterns of energy intake. In older children, however, parental influence may play a lesser role.

The third and main finding of the present study was a significant effect of insulin sensitivity status on the re-
response to a dietary intervention that focused on decreasing sweetened beverage consumption. Children who had a decrease in or an unchanged BMI z score were more insulin resistant, whereas those children who had an increase in BMI z score were more insulin sensitive. The association of insulin sensitivity status (HOMA) and BMI z score response to dietary intervention remained significant even when controlling for age, race, and sex in the linear regression model. These findings are similar to those described by Cornier et al. and colleagues in adults. The exact mechanism for these findings remains unclear. Cornier et al., in a subset analysis, described the increased expression of FOXC2, a transcription factor in adipose tissue that regulates uncoupling protein 1 and, therefore, may influence energy expenditure in insulin-resistant adult patients with greater weight loss after a carbohydrate-restricted diet. However, these findings are preliminary and their relevance in overweight children is uncertain. Studies in animals by Pawlak et al. appear to confirm the impact of high-glycemic index diets on adiposity. According to the work of these investigators, high-glycemic load diets, as might be expected from substantial ingestion of sweetened beverages, increase postprandial hyperinsulinemia, thus favoring fatty acid uptake, inhibition of lipolysis, and energy storage, resulting in weight gain. Such a diet may also be associated with a lower glucose nadir, leading to increased counterregulatory hormone production and further compensatory energy intake. According to Pittas et al., these mechanisms would be expected to be exaggerated in individuals with increased insulin secretory capacity (ie, increased insulin resistance) at baseline and may form the basis for a more pronounced response to a carbohydrate-reduced diet, such as that associated with decreasing sugar-sweetened beverage consumption.

The pathophysiologic importance of insulin resistance, previously described in adults, carries significant cardiovascular risk. The association of insulin resistance with the cluster of cardiovascular risk factors from childhood to adulthood has also been described. The present study adds to this literature by suggesting that baseline insulin resistance status influences response to specific dietary interventions in overweight children that include reduction in sweetened beverage consumption. Accordingly, the present study builds on the work of Keskin et al. to suggest that estimating insulin resistance using HOMA in overweight children may be of benefit in planning a dietary intervention.

Limitations of the present study are its short duration, small number of children, and lack of a control group. However, mean age, race, and sex were not significantly different between those who were insulin resistant and those who were insulin sensitive. Because we did not carefully monitor physical activity patterns in these children, we cannot rule out the possibility that differences existed in energy expenditure between groups. Furthermore, because the lifestyle intervention included a variety of dietary recommendations, we cannot rule out the possibility that the changes in BMI z score were related to other dietary changes and not solely to changes in sweetened beverage consumption. Because a comprehensive 24-hour dietary recall was not obtained, we are unable to document the overall decrease in carbohydrate intake. However, all children received the same lifestyle intervention by trained staff members and reduced sweetened beverage consumption to a similar degree, and yet weight maintenance or decrease was apparent only in those with increased insulin resistance. Despite these limitations, the present data suggest that the role of insulin resistance in weight loss should be further evaluated through a randomized trial of dietary intervention focused on decreasing sweetened beverage consumption by overweight children.

In conclusion, among overweight children in primary care practices, a significant relationship was seen between insulin resistance as estimated by HOMA and the change in BMI z score associated with a dietitian-mediated intervention that includes a focus on decreasing sweetened beverage consumption. Overweight children with increased insulin resistance may limit weight gain and stabilize BMI z score after this dietary modification, whereas overweight children who are not insulin resistant may continue to gain weight. If confirmed, these results suggest that reducing sweetened beverage consumption should be a particular initial focus within a broader dietary intervention in overweight children who have heightened insulin resistance. Additional research should be undertaken on the potential influence of baseline insulin resistance status on the response to sweetened beverage reduction in obese children.

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Correspondence: Doyle M. Cummings, PharmD, FCP, FCCP, Department of Family Medicine and Pediatrics, Brody School of Medicine at East Carolina University, 600 Moye Blvd, Greenville, NC 27834 (cumingsd@ecu.edu).

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REFERENCES

2. Hedley AA, Ogden CL, Johnson CL, Carroll MD, Curtin LR, Flegal KM. Preva-

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