A Low–Glycemic Load Diet Facilitates Greater Weight Loss in Overweight Adults With High Insulin Secretion but Not in Overweight Adults With Low Insulin Secretion in the CALERIE Trial

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Lifestyle changes, in particular reducing energy intake, are the cornerstone of current approaches to weight loss and prevention of type 2 diabetes. However, there is currently no consensus that one dietary regimen is more effective than another for weight loss (1) or whether particular diets work better for identifiable groups of individuals. There is evidence, however, to suggest that both insulin resistance and insulin secretion play a role in body weight regulation (2–12). Therefore, dietary factors such as the dietary glycemic load (glycemic load = glycemic index [GI] × available carbohydrate amount) that influence these parameters may theoretically interact with subject-specific characteristics of glucose-insulin dynamics to influence the effect of different hypocaloric diets on weight loss or maintenance (13,14). Weight loss studies using the concept of the dietary glycemic index or glycemic load have shown conflicting results for heterogeneous groups of individuals (15–21).

In a 6-month controlled feeding trial in healthy overweight adults with normal glucose tolerance, we tested the hypothesis that individuals with higher insulin secretion lose more weight when randomized to a low–glycemic load diet compared with a high–glycemic load diet.

RESEARCH DESIGN AND METHODS

— This study was performed as part of the Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy (CALERIE) trial at the Human Nutrition Research Center on Aging at Tufts University with approval from the Tufts-New England Medical Center Human Investigation Review Committee. Written informed consent was obtained from all participants. Healthy women and men aged 24–42 years with a BMI of 25–29.9 kg/m^2 and fasting plasma glucose <100 mg/dl were recruited. After a 6-week baseline period when usual energy requirements for weight stability were assessed using the doubly labeled water method (22), participants were randomized for 24 weeks to either a high–glycemic load diet (60% carbohydrate, 20% protein, 20% fat, 15 g fiber/1,000 kcal, mean estimated daily glycemic index of 86, and glycemic load of 116 g/1,000 kcal) or a low–glycemic load diet (40% carbohydrate, 30% protein, 30% fat, 15 g giber/1,000 kcal, mean estimated daily glycemic index of 53, and glycemic load of 45 g/1,000 kcals) at 30% calorie restriction compared with baseline individual energy needs. The glycemic index and glycemic load of the diets were determined using the International Tables of Glycemic Index and Glycemic Load (23) and the Nutrition Data System for Research (version 4.05_33) developed by the Nutrition Coordinating Center, University of Minnesota, Food and Nutrient Database 33, released in 2002 (24). During the 6-month intervention period, all food was provided by the research center, and participants were requested to consume only this food and report additional foods if they were eaten. To maximize adherence to the study diet, regular behavioral group meetings and individual sessions with a dietitian were held. From participants' reports of leftover food and extra items, actual daily nutrient intake during the intervention period was calculated (24).

Height (±0.1 cm) was measured at baseline, and body weight (±100 g) was measured weekly. Insulin secretion was also estimated at baseline, as was the insulin value at 30 min (INS-30) after a 75-g oral glucose tolerance test (25). Insulin sensitivity in the fasting state was estimated at baseline by the homeostasis model assessment of insulin resistance (HOMA-IR) (26). Glucose was measured by the hexokinase method, and insulin was measured by radioimmunoassay. To examine change in weight at 6 months, we used general linear models adjusting for baseline weight, HOMA-IR and INS-30, and the interaction between diet × HOMA-IR and diet × INS-30 (PROC GLM procedure in SAS software, version 8.2; SAS Institute, Cary, NC).

RESULTS

— A total of 32 (25 women and 7 men) of 34 enrolled participants completed the 6-month intervention period and necessary measurements. At baseline, their mean age was 34.6 years,

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Abbreviations: HOMA-IR, homeostasis model assessment of insulin resistance; INS-30, insulin value at 30 min.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

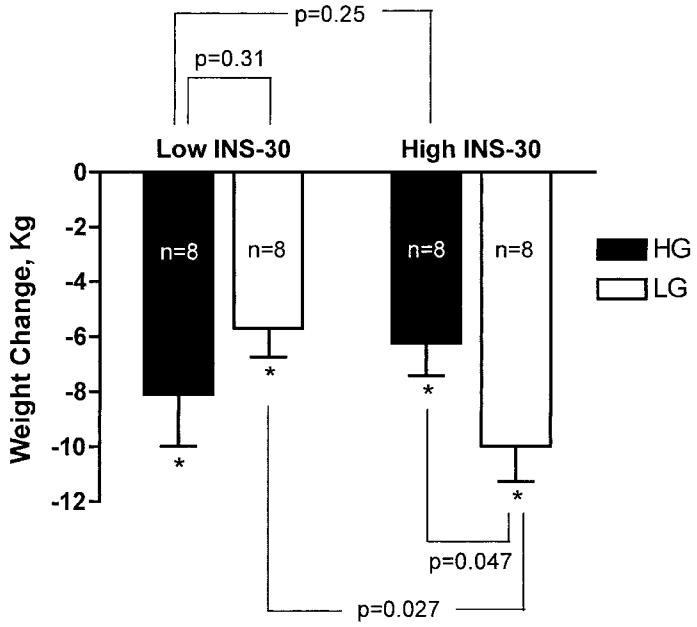

Figure 1—*Mean (±SEM) weight change during a 6-month feeding study of a high– (HG) vs. low– (LG) glycemic load diet in overweight adults stratified by baseline insulin secretion based on serum insulin at 30 min after a 75-g oral glucose tolerance test (low INS-30 < 473 pmol/l [66 mU/l] < high INS-30). P values are adjusted for baseline weight. *P < 0.005 for within-group change in weight from baseline.*

BMI was 27.5 kg/m^2, and fasting insulin was 82.5 pmol/l. The mean target energy intake was 1,966 kcal/day, and the mean reported daily energy intake during the intervention did not differ between the two groups (2,017 kcal in the high–glycemic load diet vs. 1,972 kcal in the low–glycemic load diet, $P = 0.70$).

We examined whether baseline INS-30 predicted change in weight over the 6-month intervention period. We found a diet × INS-30 interaction ($P = 0.02$) in the multivariate prediction model, and the weight data were stratified into two groups separated by the median INS-30 value (Fig. 1). Participants with high baseline INS-30 lost more weight if randomized to the low–glycemic load diet compared with the high–glycemic load diet ($P < 0.05$). The reverse was observed in the low–INS-30 group, namely, low–INS-30 participants in the high–glycemic load diet lost more weight than those in the low–glycemic load diet, but the difference was not statistically significant ($P = 0.25$). We also examined whether baseline HOMA-R predicted weight change, and we found no diet × HOMA-R interaction.

CONCLUSIONS — The main finding from this pilot study was that healthy overweight women and men with relatively greater insulin secretion in response to a standard oral glucose tolerance test lost more weight when assigned to a low–glycemic load hypocaloric diet than to a high–glycemic load diet, but there was no differential effect of the two diets on weight loss in individuals who had relatively lower insulin secretion.

Data from human studies on whether insulin secretion predicts future weight gain (4,6,27–29) or affects the ability of overweight individuals to lose weight in response to a hypocaloric diet (7,30) are controversial. However, the influence of postchallenge hyperinsulinemia on weight loss may be particularly important for specific dietary compositions, in particular diets that differ in glycemic load or glycemic index, as suggested by animal studies (31–33). High–glycemic load diets increase postprandial hyperinsulinemia, which favors fatty acid uptake, inhibition of lipolysis, and energy storage leading to weight gain (34). High–glycemic load diets also lead to other postprandial metabolic changes, including a lower glucose nadir and increase in counterregulatory hormones that may explain increased hunger and increased energy intake in the postabsorptive period, presumably leading to weight gain over time (32). All of these mechanisms may be exacerbated in individuals with high insulin secretory capacity at baseline, which makes them more susceptible to weight gain upon exposure to a high–glycemic load diet (35). These individuals can be hypothesized to do best on low–glycemic load diets, a hypothesis supported by our present findings.

Our results require confirmation in further studies with larger numbers of subjects, but nevertheless offer the first evidence that simple indexes of insulin secretion may help enhance weight loss success in overweight individuals through the use of targeted dietary recommendations specific for insulin secretion status.

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