RESPONSE TO COMMENT ON PEPINO ET AL.

Sucralose Affects Glycemic and Hormonal Responses to an Oral Glucose Load. Diabetes Care 2013;36:2530–2535

M. Yanina Pepino and Samuel Klein

Diabetes Care 2014;37:e149 | DOI: 10.2337/dc14-0268

We appreciate the insightful comments by Grotz and Jokinen (1) regarding our study (2) that found that ingesting sucralose affects the metabolic response to subsequent glucose ingestion.

Grotz and Jokinen imply that the greater increase in peak plasma glucose concentration during the oral glucose tolerance test (OGTT) after sucralose than water ingestion was not clinically important because the concentrations were still within the normal range for an OGTT. However, sucralose ingestion also caused a 20% increase in total plasma insulin concentrations, which demonstrates insulin resistance, which is a known risk factor for diabetes, metabolic syndrome, and cardiovascular disease (3). The clinical relevance of this observation is not clear, as it is not known whether insulin resistance induced by sucralose increases the risk of developing metabolic diseases.

Grotz and Jokinen suggest that factors other than the consumption of sucralose, such as exercise, menstrual status, and varying food intake, could have been responsible for the differences in glucose and insulin responses to a glucose load that we observed after sucralose compared with water ingestion. This possibility is unlikely because *1*) subjects were instructed to avoid physical exercise for 3 days before all study visits, *2*) the number of subjects tested during different phases of the menstrual cycle was similar during the water and sucralose studies (27% were tested during menses, 27% during the follicular phase, and 46% during the luteal phase for both sucralose and water conditions), and *3*) we used a randomized crossover design, so each subject acted as his or her own control, which should reduce the potential influence of confounding factors, including variations in dietary intake.

Grotz and Jokinen also suggest that our test drink was five times sweeter than a typical diet soft drink, which could have influenced our outcome measures. However, it is not known whether sweetness, itself, has metabolic effects in people. In addition, we found the sweetness perception score of our test drink, assessed by using the general labeled magnitude scale (5 = weak, 16 = moderate, and 33 = strong), was 25.0 ± 4.0, which is below the "strong sweetness" intensity descriptor and below the perceived sweetness of either a diet (4) or a regular (5) cola.

Finally, our study was not designed to evaluate the safety of sucralose, and we completely agree with Grotz and Jokinen (1) that the results from our study should not be used to imply that sucralose is not safe. The objective of our study was to determine whether ingesting sucralose affects the metabolic response to glucose in insulin-sensitive, obese subjects who were not regular users of nonnutritive sweeteners. Our data demonstrate that sucralose is not inert, but affects the glycemic and insulin responses to an oral glucose load in this specific population. Further research is needed to better understand the potential effects of nonnutritive sweeteners on metabolic function and metabolic disease risk in people.

Funding. This work was supported by National Institutes of Health grant DK56341 (Nutrition Obesity Research Center).

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

References

1. Grotz VL, Jokinen JD. Comment on Pepino et al. Sucralose affects glycemic and hormonal responses to an oral glucose load. Diabetes Care 2013;36:2530–2535 (Letter). Diabetes Care 2014;37:e148. DOI: 10.2337/dc13-2972
2. Pepino MY, Tiemann CD, Patterson BW, Wice BM, Klein S. Sucralose affects glycemic and hormonal responses to an oral glucose load. Diabetes Care 2013;36:2530–2535
3. DeFronzo RA, Ferrannini E. Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. Diabetes Care 1991;14:173–194
4. Thai PK, Tan EC, Tan WL, Tey TH, Kaur H, Say YH. Sweetness intensity perception and pleasantness ratings of sucrose, aspartame solutions and cola among multi-ethnic Malaysian subjects. Food Qual Prefer 2011;22:281–289
5. Bartoshuk LM, Duffy VB, Fast K, Green BG, Prutkin J, Snyder DJ. Labeled scales (e.g., category, Likert, VAS) and invalid across-group comparisons: what we have learned from genetic variation in taste. Food Qual Prefer 2003;14:125–138

Center for Human Nutrition and Atkins Center of Excellence in Obesity Medicine, Washington University School of Medicine, St. Louis, MO

Corresponding author: M. Yanina Pepino, ypepino@dom.wustl.edu.