COMMENT ON PEPINO ET AL.

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

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We are interested in the recent publication by Pepino et al. (1), given that the body of evidence supports the safe use of sucralose.

Pepino et al. was a small, nonblinded, randomized, cross-over study in a select group of mostly female (15/17), predominantly African American (13/17), relatively young (mean age 35 years), morbidly obese (BMI 42.3 $\pm$ 1.6 kg/m^2), insulin-sensitive subjects. The study evaluated the response to a 75-g oral glucose tolerance test (OGTT) conducted 10 min after consumption of 60 mL of either distilled water or an aqueous 2 mmol/L sucralose solution. OGTTs were conducted about 1 week apart in the morning after a self-reported overnight fast.

While a statistically significant difference in peak plasma glucose change was reported, the actual peak plasma glucose concentration following the postsucralose OGTT was within the normal range for a 75-g OGTT (2). These results indicate no clinically significant impact on glycemic control. Consistent with this, there was no accompanying statistically significant treatment group difference in mean glucose area under the curve.

Small changes in insulin sensitivity, such as those reported in this study, can be the result of many factors. For example, varying food intake and menstrual status can produce insulin sensitivity changes and have been particularly difficult to control in outpatient studies. There was no record or control of exercise or food intake in the days preceding the self-reported overnight fast, or information on menstrual status in this study of mostly women of menstruating age. The test drink in this study was also about five times sweeter than a typical diet soft drink, and there was no control to assess the impact of sweetness alone. Other factors, such as gastric emptying rates, can also significantly impact OGTT outcomes. Such confounding variables could impact the results of repetitive OGTTs in this small ($N = 17$) study, and thus explain the nominal differences observed in the insulin and glucose measures reported.

In some animal and in vitro studies, sucralose has been shown to interact with gut sweet-taste receptors, with different effects, including a GLP-1 response. However, multiple clinical studies in humans do not support a clinically meaningful effect on GLP-1 or a biological effect on carbohydrate metabolism (3–5). These studies report that sucralose does not alter glucose homeostasis or adversely affect insulin response, either acutely or chronically, in normal and diabetic people. The results of these studies also strongly suggest that no adverse effect on glucose homeostasis would result from the interaction of sucralose or, indeed, any nonnutritive sweetener with sweet-taste receptors in the body.

Regulatory health authorities around the world have concluded that sucralose is safe for use. In the U.S. Food and Drug Administration ruling that sucralose is safe for its intended use (6), including for both normoglycemic and diabetic individuals, it stated that studies show that sucralose has no influence on insulin secretion or postprandial or fasting blood glucose levels in animals or humans.

Therefore, the available evidence indicates that sucralose is safe, with no clinically significant effect on either acute or long-term blood glucose control.

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