Ingestion of Diet Soda Before a Glucose Load Augments Glucagon-Like Peptide-1 Secretion

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OBJECTIVE — The goal of this study was to determine the effect of artificial sweeteners on glucose, insulin, and glucagon-like peptide (GLP)-1 in humans.

RESEARCH DESIGN AND METHODS — For this study, 22 healthy volunteers (mean age 18.5 ± 4.2 years) underwent two 75-g oral glucose tolerance tests with frequent measurements of glucose, insulin, and GLP-1 for 180 min. Subjects drank 240 ml of diet soda or carbonated water, in randomized order, 10 min prior to the glucose load.

RESULTS — Glucose excursions were similar after ingestion of carbonated water and diet soda. Serum insulin levels tended to be higher after diet soda, without statistical significance. GLP-1 peak and area under the curve (AUC) were significantly higher with diet soda (AUC 24.0 ± 15.2 pmol/l per 180 min) versus carbonated water (AUC 16.2 ± 9.0 pmol/l per 180 min; P = 0.003).

CONCLUSIONS — Artificial sweeteners synergize with glucose to enhance GLP-1 release in humans. This increase in GLP-1 secretion may be mediated via stimulation of sweet-taste receptors on L-cells by artificial sweetener.
pharmacologic doses of GLP-1 used in incretin effect (10–12). However, the delayed gastric emptying rather than an insulin secretion, an effect due primarily to prandial blood glucose and decreased intestinal GLP-1. In contrast, exogenous GLP-1 in either plasma glucose or insulin after diet soda exposure and does not occur with pure oral glucose or artificial sweeteners (8), and cephalic-phase GLP-1 response has not been observed in humans (9). Instead, we postulate that the enhancement of GLP-1 release observed here after diet soda ingestion was due to stimulation of gut taste receptors by artificial sweeteners in a commercially available soda, suggesting that the effect may be relevant in everyday life.

Because artificial sweeteners were given by mouth in the form of diet soda, one might hypothesize that increases in insulin and GLP-1 were due to cephalic-phase insulin release. This is unlikely, because cephalic-phase insulin release typically occurs 2–10 min after taste exposure and does not occur with pure oral glucose or artificial sweeteners (8), and cephalic-phase GLP-1 response has not been observed in humans (9). Instead, we postulate that the enhancement of GLP-1 secretion observed here after diet soda ingestion was due to stimulation of gut taste receptors by artificial sweetener, synergizing with glucose-mediated stimulation of GLP-1 release.

The metabolic consequences of increased GLP-1 release after ingestion of both artificial sweeteners and glucose remain uncertain. In the present study, no significant differences were observed in either plasma glucose or insulin after diet soda versus carbonated water ingestion, despite the significant differences in GLP-1. In contrast, exogenous GLP-1 in healthy volunteers results in lower postprandial blood glucose and decreased insulin secretion, an effect due primarily to delayed gastric emptying rather than an incretin effect (10–12). However, the pharmacologic doses of GLP-1 used in these studies resulted in plasma levels 3- to 10-fold higher than those seen here after diet soda. In addition, artificial sweeteners likely play a role in glucose metabolism beyond changes in GLP-1. There is evidence in animals that activation of intestinal sweet-taste receptors by artificial sweeteners enhances intestinal glucose absorption via upregulation of GLUT2 (1). Thus, the kinetics of glucose and insulin observed in the present study may have been affected both by changes in GLP-1 and by altered intestinal glucose absorption.

In summary, artificial sweeteners in combination with glucose increase GLP-1 secretion, but the clinical significance of this observation remains to be determined. Additional studies are needed to isolate the effects of individual sweeteners in diet sodas and should include individuals with metabolic abnormalities such as type 2 diabetes, a condition typically associated with loss of the incretin effect. In light of the large number of individuals using artificial sweeteners on a daily basis, it appears essential to carefully investigate the associated effects on metabolism and weight.

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