Sugar-Sweetened Product Consumption Alters Glucose Homeostasis Compared with Dairy Product Consumption in Men and Women at Risk of Type 2 Diabetes Mellitus

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Abstract

Background: Dietary patterns characterized by high intakes of fruits and vegetables, whole grains, low-fat dairy products, and low glycemic load have been associated with lower type 2 diabetes mellitus (T2DM) risk. In contrast, dietary patterns that include high intakes of refined grains, processed meats, and high amounts of added sugars have been associated with increased T2DM risk.

Objective: This randomized, 2-period crossover trial compared the effects of dairy and sugar-sweetened product (SSP) consumption on insulin sensitivity and pancreatic β-cell function in men and women at risk of the development of T2DM who habitually consume sugar-sweetened beverages.

Methods: In a randomized, controlled crossover trial, participants consumed dairy products (474 mL/d 2% milk and 170 g/d low-fat yogurt) and SSPs (710 mL/d nondiet soda and 108 g/d nondairy pudding), each for 6 wk, with a 2-wk washout between treatments. A liquid meal tolerance test (LMTT) was administered at baseline and the end of each period.

Results: Participants were 50% female with a mean age and body mass index of 53.8 y and 32.2 kg/m², respectively. Changes from baseline were significantly different between dairy product and SSP conditions for median homeostasis model assessment 2–insulin sensitivity (HOMA2–%S) (1.3 vs. 21.3%, respectively, \( P = 0.009 \); baseline = 118%), mean LMTT disposition index (\(-0.03\) vs. \(-0.36\), respectively, \( P = 0.011 \); baseline = 2.59), mean HDL cholesterol (0.8 vs. \(-4.2\%\), respectively, \( P = 0.015 \); baseline = 44.3 mg/dL), and mean serum 25-hydroxyvitamin D \([25(OH)D]\) (11.7 vs. \(-3.3\%\), respectively, \( P = 0.022 \); baseline = 24.5 mg/L). Changes from baseline in LMTT Matsuda insulin sensitivity index (\(-0.10\) vs. \(-0.49\), respectively, baseline = 4.16) and mean HOMA2–β-cell function (\(-2.0\) vs. \(5.3\%\), respectively; baseline = 72.6%) did not differ significantly between treatments.

Conclusion: These results suggest that SSP consumption is associated with less favorable values for HOMA2–%S, LMTT disposition index, HDL cholesterol, and serum \([25(OH)D]\) in men and women at risk of T2DM vs. baseline values and values during dairy product consumption. This trial was registered at clinicaltrials.gov as NCT01936935.

Keywords: Insulin sensitivity, type 2 diabetes mellitus, dairy, sugars, lipoproteins

Introduction

The progression from normal glucose tolerance to the onset of type 2 diabetes mellitus (T2DM) is often protracted, with individuals early in the disease process exhibiting resistance to insulin-stimulated glucose uptake in skeletal muscle and adipose tissues, as well as impaired suppression of hepatic glucose output by a given circulating concentration of insulin (1). Normal glucose tolerance is maintained via compensatory hyperinsulinemia, thus preventing hyperglycemia (2). However, over time, the pancreatic β-cell response becomes impaired and eventually

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3 Supplemental Table 1 is available from the “Online Supporting Material” link in the online posting of the journal article and from the same link in the online table of contents at http://jn.nutrition.org.
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fails to produce sufficient insulin to maintain normoglycemia (1). By the time T2DM is diagnosed, the insulin secretory response is generally 70–80% below that which would be appropriate for the level of insulin sensitivity (3).

Diabetes prevention trials showed that interventions that increase insulin sensitivity substantially reduce the rate of conversion to diabetes in high-risk individuals (4). In the Diabetes Prevention Program, progression to diabetes was reduced by 58% in participants with elevated post-load plasma glucose who were randomly assigned to follow a lifestyle intervention with targets of at least 150 min/wk of physical activity and 7% weight loss, compared to a randomized control group that did not receive the lifestyle intervention (4). Both weight loss and increased physical activity enhance insulin sensitivity, which results in a reduced requirement for insulin secretion.

Although weight loss and physical activity have received the most attention for diabetes prevention, a number of other factors may have important influences on T2DM risk. For example, dietary patterns characterized by high intakes of fruits and vegetables, whole grains, low-fat dairy products, and a low glyemic load were associated with lower T2DM risk and a more favorable T2DM risk factor profile (5, 6). In contrast, dietary patterns that include high intakes of refined grains, processed meats, and foods containing high amounts of added sugars were associated with increased T2DM risk (7). Individuals who habitually consume sugar-sweetened beverages may be particularly at risk of the development of T2DM. A recent meta-analysis of prospective cohort studies showed that those in the highest quintile of sugar-sweetened beverage intake (most often 1–2 servings/d, ~355–710 mL/d) had a 26% greater risk of developing T2DM than those in the lowest quintile (none or <1 serving/mo, ~355 mL/mo) (RR: 1.26; 95% CI: 1.12, 1.41). More recently, data from the Health Professionals Follow-Up Study, a prospective cohort of 40,389 healthy men, showed that those in the top quintile of sugar-sweetened beverage intake (4.5–7.5 servings/wk, or ~1.6–2.7 L/wk) had a 25% increased risk of the development of T2DM (HR: 1.24; 95% CI: 1.09, 1.40; P-trend < 0.01) compared with nonconsumers, after adjustment for multiple potential confounders (8).

In contrast to intake of sugar-sweetened beverages, a higher intake of dairy products was associated with lower T2DM risk (5, 9). For example, in the Health Professionals Follow-Up Study cohort, higher dairy intake was associated with a 23% lower RR (0.77; 95% CI: 0.62, 0.95) for T2DM in the highest (≥2.9 servings/d) vs. lowest (<0.9 servings/d) quintiles in a fully adjusted model (10). A serving of fluid milk is 237 mL, whereas serving sizes for yogurt and most cheeses are 170 g and 30 g, respectively. The inverse association was strongest for low-fat dairy products (RR: 0.73; 95% CI: 0.59, 0.89; P-trend < 0.001). Each serving/d increase in low-fat dairy intake was associated with a 12% lower risk of T2DM (RR: 0.88; 95% CI: 0.81, 0.94).

Despite growing evidence of the inverse relation between dairy product consumption and T2DM risk, little is known about the influences of increased dairy product intake on insulin sensitivity and pancreatic β-cell function. Because many people consume fewer than the recommended number of daily servings of dairy products (11), and more servings than recommended of sugar-sweetened products (SSPs) (12), an evaluation of the metabolic effects of substituting a dairy beverage (milk) and food (yogurt) for a sugar-sweetened beverage (soda) and food (nondairy pudding) is of interest. We hypothesized that consumption of dairy products, compared with SSPs, would favorably affect insulin sensitivity and pancreatic β-cell function in habitual consumers of high-sugar beverages.

Methods

Study design. This randomized, controlled crossover trial was conducted in accordance with Good Clinical Practice Guidelines, the Declaration of Helsinki (13), and the United States 21 Code of Federal Regulations. An appropriately constituted institutional review board (Quorum Review IRB, Seattle, Washington) approved the study protocol and informed consent documents before the study commencement. Subjects provided signed informed consent and authorization for disclosure of protected health information before the initiation of any protocol-specific procedures. In addition, subjects were informed of their right to withdraw from the study at any time.

Treatments. This study included 2 6-wk treatment periods and a 2-wk washout between treatments. Subjects were randomly assigned to a treatment sequence that included consumption of SSPs (710 mL/d of nondiet soda and 108 g/d of nondairy pudding) or dairy products (474 mL/d of 2% milk and 170 g/d low-fat yogurt with no added sugar). A randomization list was created with the use of SAS (SAS Institute) with the seed number recorded. Based on this list, a series of envelopes was created, with each envelope showing the subject’s treatment sequence (dairy products then SSPs or SSPs then dairy products) and opened by the study coordinator at the time of random assignment. The nutrient composition of each study product is presented in Supplemental Table 1. All subjects were instructed to consume ≤1 serving/d of nonstudy-related dairy products during each treatment period. Subjects were counseled on incorporating the study products into their habitual diets while maintaining caloric balance. Compliance with study product consumption was evaluated by the study staff based on the returned food items from the provided products and recorded as the percentage of scheduled servings of study products consumed.

Subjects. Eligibility for the trial was based on self-reported use of high-sugar beverages (≥2 serving/d; serving sizes were 355 mL nondiet soda and 240 mL fruit juice cocktails) and being at high risk of the development of diabetes based on 1 or more of the following, without the presence of T2DM: an impaired fasting glucose concentration of 100–125 mg/dL; a glycated hemoglobin concentration of 5.7–6.4% (14), or a ≥20% risk of developing T2DM in the next 7.5 y based on the San Antonio Heart Study prediction equation (15). Eligible subjects were men and women 18–74 y of age, inclusive, with BMI ≤45.0 kg/m², who had a waist circumference of ≥83.8 cm (33.0 inches) for women and ≥91.4 cm (36.0 inches) for men at the screening visit. Premenopausal female subjects were scheduled for their end-of-treatment visits during the follicular phases of their menstrual cycles, defined as days 1–14, where day 1 is the first day of menses. In addition, eligible subjects were those who were willing to maintain a stable body weight, maintain their habitual diet (including coffee, tea, and alcoholic beverages) and exercise routines with the exception of the study products, and limit nonstudy-related dairy product intake to ≤1 serving/d (1 serving is ~237 mL of milk, 170 g of yogurt, and 30 g of most cheese) during each treatment period.

Subjects were excluded from the study for the following reasons: uncontrolled hypertension (systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥100 mm Hg); abnormal laboratory test results of clinical importance (at the discretion of the investigator), including TGs ≥400 mg/dL, fasting creatinine ≥1.5 mg/dL, and fasting blood glucose ≥126 mg/dL; a history or presence of clinically important cardiac (including coronary artery disease), renal, hepatic, endocrine (including type 1 diabetes mellitus or T2DM), pulmonary, biliary, gastrointestinal, pancreatic, or neurologic disorders; a recent history or presence of cancer, except nonmelanoma skin cancer; weight loss or gain of >4.5 kg in the month before screening or extreme dietary habits (e.g., very-low–carbohydrate diet); and a history within the last 12 mo or strong potential for alcohol abuse (>14 servings/wk) or substance abuse. Women who were pregnant, lactating, or planning to be pregnant or during the study period or of childbearing potential and unwilling to commit to the use of a medically approved form of contraception were not enrolled. Individuals who reported habitual consumption of ≤4 serving/d of dairy foods and beverages were excluded from the study. Further, individuals were excluded if use of medications or supplements known...
to alter carbohydrate or lipid metabolism, or weight-loss drugs or programs, were reported within 4 wk before the screening visit. Participants who used antibiotics within 4 wk before the screening visit were excluded from the study; if an infection occurred during the study, clinic visits were rescheduled to allow at least 5 d to elapse after resolution of the infection or completion of the antibiotic therapy (whichever was later).

Assessments. Plasma chemistry and whole blood hematology profiles were measured at screening. Fasting (9–15 h, water only) plasma lipid profiles, plasma glucose and serum insulin responses to a liquid meal tolerance test (LMTT), and serum 25-hydroxyvitamin D [25(OH)D] were measured at baseline and the end of each 6-wk treatment period. Biochemical measurements were completed by Elmhurst Reference Laboratory. Serum total 25(OH)D concentrations were assessed with the use of the DiaSorin Liaison Total-D chemiluminescence immunoassay. Plasma glucose was determined with the use of the glucose oxidase method and serum insulin was determined with the use of a chemiluminescent immunoassay. The plasma lipid profile assessment included total cholesterol (TC), HDL cholesterol, and TG, and was analyzed with the use of the Beckman Coulter LX20 PRO as previously described by the Standardization Program of the CDC and the National Heart, Lung, and Blood Institute (16). The Friedewald equation (17) was used to estimate LDL cholesterol concentrations in milligrams per deciliter as follows: LDL cholesterol = TC − HDL cholesterol − TGs/5. Non-HDL cholesterol was calculated as non-HDL cholesterol = TC − HDL cholesterol.

Study participants completed an LMTT at baseline and at the end of each treatment period by consuming a liquid meal load (2 237-mL servings of Ensure Creamy Milk Chocolate or Homemade Vanilla Shake, Abbott Nutrition Division, Abbott Laboratories) within 10 min. Blood samples were obtained for measurement of plasma glucose and serum insulin at 0, 30, 60, 90, and 120 min; 0 min was the start of the liquid meal load. Adverse events and waist circumference at the iliac crest were assessed at baseline, beginning, and end of each treatment period, and vital signs were measured (seated, resting blood pressure and heart rate taken at 0, 3, 6, 9, and 12 min with the final 4 measurements averaged and the first discarded). Subjects completed 3-d diet records recording all food and beverage intake 3 d before baseline and at the end of each treatment period to capture habitual food intake. The diet records from each subject’s baseline visit were intended to capture habitual intake and were returned to the subject with instructions to replicate the foods and beverages consumed, with the exception of the study products, on the day before the end of each treatment visit. Diet records were analyzed with the use of Food Processor SQL Nutrition Analysis and Fitness Software (version 10.4.0, ESHA Research).

Statistical analysis and calculations. Sample size calculations were performed to test for a difference between the dairy and SSP conditions for the change from baseline to the end of each treatment. An evaluable sample size of 32 subjects was expected to provide 80% power (2-sided for the change from baseline to the end of each treatment) with the use of Food Processor SQL Nutrition Analysis and Fitness Software. An evaluable sample, which included all subjects who provided at least 1 post-random-assignment outcome data point during both diet phases, was obtained for measurement of plasma glucose and serum insulin at 0, 30, 60, 90, and 120 min; 0 min was the start of the liquid meal load. Adverse events and waist circumference at the iliac crest were assessed at baseline, beginning, and end of each treatment period, and vital signs were measured (seated, resting blood pressure and heart rate taken at 0, 3, 6, 9, and 12 min with the final 4 measurements averaged and the first discarded). Subjects completed 3-d diet records recording all food and beverage intake 3 d before baseline and at the end of each treatment period to capture habitual food intake. The diet records from each subject’s baseline visit were intended to capture habitual intake and were returned to the subject with instructions to replicate the foods and beverages consumed, with the exception of the study products, on the day before the end of each treatment visit. Diet records were analyzed with the use of Food Processor SQL Nutrition Analysis and Fitness Software (version 10.4.0, ESHA Research).

Statistical analyses were performed with the use of SAS version 9.2. Analyses for safety measures were completed for data collected from all subjects who were randomly assigned and consumed at least 1 dose of study product. Analyses of outcomes were completed on an efficacy evaluable sample, which included all subjects who provided at least 1 post-random-assignment outcome data point during both diet phases. The primary outcome variable was the difference between treatments in the change from baseline in the MISH.

Secondary outcome variables included differences between treatments for changes or percent changes from baseline to the end of each treatment period, and included the following: waist circumference, systolic and diastolic blood pressures, lipoprotein lipids, serum 25 (OH)D, fasting and 2-h insulin and glucose responses to the LMTT, homeostasis model assessment 2-insulin sensitivity (HOMA2-%S) and homeostasis model assessment 2–β-cell function (HOMA2-%B) from LMTT data, total AUC for glucose and insulin during the LMTT, the insulin secretion index (ISI) and disposition index during the LMTT, and the insulin-to-glucose ratio (Δ insulin:Δ glucose) over the first 30 min after the liquid meal load (23). Total AUC for glucose and insulin concentrations during the LMTT were calculated with the use of the trapezoidal rule (24) and ISI was calculated as total AUC for serum insulin from 0 to 120 min divided by the total AUC for plasma glucose from 0 to 120 min (21, 25). HOMA2-%S and HOMA2-%B were calculated with the use of fasting values for glucose and insulin as previously described (26). The LMTT disposition index, an indicator of pancreatic β-cell function and a measure of the appropriateness of insulin response relative to insulin sensitivity, was calculated as the product of the MISH and ISI (21, 27).

Repeated measures ANCOVA was used to assess differences in responses between test conditions. The initial models included terms for treatment, sequence, sex, treatment by sex, period, and baseline, with subject as a random effect. Models were reduced in a stepwise manner until only significant (P ≤ 0.05) terms or treatment and baseline value remained. If the normality assumption was rejected at the 1% level with the Shapiro–Wilks test on the model residuals (28), an analysis with the use of rank-transformed data was performed. All tests of statistical significance were 2-tailed and completed at α = 0.05. Results for continuous variables are reported as means ± SEMs or medians with interquartile range limits. Paired t tests or Wilcoxon rank sums tests with Bonferroni corrections for 2 comparisons (0.05/2 = 0.025) to declare statistical significance were used to test within-treatment changes from baseline.

Results

In total, 116 participants were screened and 43 subjects met all of the inclusion and none of the exclusion criteria, resulting in random assignment of subjects in 2 sequences: dairy products and then SSPs (n = 21) and SSPs and then dairy products (n = 22). A total of 33 subjects completed the trial and 34 subjects were included in the efficacy evaluable sample, which included only data for subjects who provided at least partial outcome data on both treatments (participant flow diagram; Figure 1). Of the subjects in the efficacy evaluable sample, 50% were women, 65% were nonHispanic white, 24% were nonHispanic black, and 9% were Hispanic/Latino. Mean age, BMI, and waist circumference were 53.8 ± 2.1 y, 32.2 ± 0.8 kg/m², and 106 ± 1.7 cm, respectively. Of the 10 subjects who did not complete the study, 3 were lost to follow-up, 6 withdrew consent, and 1 did not complete the second treatment because of an adverse event unrelated to study product consumption.

Median (interquartile range limit) overall compliance with study product consumption was 100% (98.8%, 102%) and 100% (99.4%, 103%) for the dairy product and SSP treatments, respectively (P = 0.49). Results from 3-d diet record analyses at baseline and during dairy product and SSP treatments are presented in Table 1. No differences were observed between the dairy product and SSP conditions for energy, cholesterol, or sodium intakes. Reported intakes of carbohydrates, sugars, and dietary fiber were significantly (P < 0.05) lower during the dairy product condition. Reported intakes of protein, total fat, SFAs, unsaturated FAs, and calcium were significantly (P < 0.05) higher during the dairy product condition.

Mean or median values for indicators of glucose homeostasis at baseline and end of treatments and changes from baseline to the end of each treatment period are shown in Table 2. Fasting insulin increased from baseline during the SSP condition, and was slightly reduced during the dairy product condition (1.2 vs.

Dairy vs. sugar-sweetened products
TABLE 1 Energy, macronutrient, and mineral intakes of men and women at risk of type 2 diabetes mellitus at baseline and during dairy product and SSP conditions

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Dairy products</th>
<th>SSPs</th>
<th>p2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy, kcal/d</td>
<td>2230 ± 95.7</td>
<td>2090 ± 83.7</td>
<td>2160 ± 91.7</td>
<td>0.18</td>
</tr>
<tr>
<td>Carbohydrate, % energy</td>
<td>52.3 ± 1.4</td>
<td>47.2 ± 1.2***</td>
<td>57.2 ± 1.5*** &lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Sugar, g/d</td>
<td>123 ± 8.4</td>
<td>93.4 ± 5.6**</td>
<td>148 ± 6.4*** &lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Fiber, g/d</td>
<td>17.5 ± 1.4</td>
<td>15.2 ± 0.9*</td>
<td>16.9 ± 0.8 0.005</td>
<td></td>
</tr>
<tr>
<td>Protein, % energy</td>
<td>15.3 ± 0.4</td>
<td>19.3 ± 0.6***</td>
<td>15.2 ± 0.4 &lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Fat, % energy</td>
<td>32.5 ± 1.1</td>
<td>33.0 ± 1.0</td>
<td>29.0 ± 1.2** &lt;0.001</td>
<td></td>
</tr>
<tr>
<td>SFA</td>
<td>10.8 ± 0.5</td>
<td>11.6 ± 0.5</td>
<td>9.1 ± 0.5** &lt;0.001</td>
<td></td>
</tr>
<tr>
<td>UFA</td>
<td>21.7 ± 0.7</td>
<td>21.4 ± 0.6</td>
<td>19.9 ± 0.8* 0.022</td>
<td></td>
</tr>
<tr>
<td>Cholesterol, mg/d</td>
<td>245 (179, 364)</td>
<td>258 (186, 306)</td>
<td>263 (179, 321) 0.82</td>
<td></td>
</tr>
<tr>
<td>Calcium, mg/d</td>
<td>719 ± 49.7</td>
<td>1250 ± 30.1***</td>
<td>721 ± 36.9 &lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Sodium, mg/d</td>
<td>3260 ± 203</td>
<td>3070 ± 188</td>
<td>3170 ± 207 0.25</td>
<td></td>
</tr>
</tbody>
</table>

1 Values are means ± SEMs or medians (interquartile range limits). Complete data were available only for nutritional components on food labels; therefore, results for nutrients not consistently listed, including vitamin D, were unavailable. However, differences in vitamin D consumption between the 2 conditions would be expected to be mainly attributed to the differences in the vitamin D content of the assigned study products consumed daily; dairy condition: 280 IU/d vitamin D; SSP condition: 60 IU/d vitamin D. Different from baseline: *P < 0.05, **P < 0.01, ***P < 0.005 after Bonferroni correction for 2 comparisons. SSP, sugar-sweetened product; UFA, unsaturated fatty acid.

2 Calculated from repeated measures ANCOVA models for the comparisons between dairy product and SSP conditions, with baseline value included in each model as a covariate (n = 34).

FIGURE 1 Participant flow diagram. Men and women at risk of type 2 diabetes mellitus were randomly assigned to 1 of 2 treatment sequences, consuming dairy products then SSPs, or SSPs then dairy products. A total of 33 subjects completed the trial and 34 subjects were included in the efficacy evaluable sample, which included only data for subjects who provided at least partial outcome data on both treatments. SSP, sugar-sweetened product.

-0.1, respectively; P = 0.036). There were no statistically significant differences in responses in fasting glucose, 2-h glucose or insulin, or AUC for glucose or insulin over 120 min during the LMTT. No significant difference in response between conditions was present for the MISI, but HOMA2-%S declined significantly during the SSP condition compared with the dairy product condition (-21.3 vs. 1.3, respectively; P = 0.009). The LMTT disposition index was significantly decreased from baseline during the SSP condition vs. the dairy product condition (-0.4 vs. 0.0, respectively; P = 0.011), but other indicators of pancreatic β-cell function did not differ between treatment conditions.

Mean fasting lipoprotein lipid concentrations and serum 25(OH)D at baseline and end of treatments and the percent changes from baseline to the end of each treatment are shown in Table 3. Mean HDL cholesterol responses were slightly increased by 0.8% after consumption of dairy products, compared with a 4.2% reduction after SSP consumption (P = 0.015). Also, mean serum 25(OH)D increased by 11.7% during the dairy product condition, compared with a 3.3% decrease during SSP consumption (P = 0.022). No differences were observed for other lipoprotein lipid variables. Changes in body weight did not differ between the 2 treatment conditions (0.1 and 0.4 kg in the dairy product and SSP conditions, respectively, P = 0.22). In addition, changes in heart rate, blood pressure, and waist circumference did not differ between conditions (data not shown).

Although limited data are available from which to infer that a 2-wk washout is sufficient for a complete return to the pretreatment state, each treatment period was 6 wk in length, which should have allowed ample time for a new steady state to manifest. There was no statistical evidence to suggest carryover effects (treatment by sequence interaction) for any of the variables assessed.

A total of 24 adverse events during the dairy product condition and 21 during the SSP condition were reported by subjects (P = 0.84). None of the adverse events were characterized as severe or serious, and 4 were classified as possibly, probably, or definitely related to consumption of the study products, all during the SSP treatment, including diarrhea (n = 1), dyspepsia (n = 1), flatulence (n = 1), and increased stool frequency (n = 1).
Discussion

In this randomized, controlled crossover trial, consumption of 3 servings/d of dairy products (474 mL low-fat milk and 170 g yogurt) for 6 wk resulted in more favorable values for some indicators of carbohydrate homeostasis (HOMA2–%S, LMTT disposition index, and fasting insulin), as well as higher circulating concentrations of plasma HDL cholesterol and serum 25(OH)D, compared with consumption of 3 servings/d of SSPs (710 mL nondiet soda and 108 g nondairy pudding) in habitual consumers of sugar-sweetened beverages. The Dietary Guidelines for Americans recommend 3 servings/d of dairy products; however, results from the NHANES indicate that median consumption of dairy products in the United States is lower—only 2 servings/d in men and 1.5 servings/d in women (11). It is not clear at present whether the reduced T2DM risk associated with higher dairy product intake is associated with lower risk of T2DM development, whereas greater consumption of sugar-sweetened beverages is associated with increased T2DM incidence (5, 7, 10, 29–33). It is not clear at present whether the reduced T2DM risk associated with higher dairy product intake is due to favorable effects of dairy products, displacement of other foods and beverages from the diet that may increase risk, such as sugar-sweetened beverages, or other factors (8, 9). Although the results from the present study cannot resolve these questions, they do not clearly support beneficial effects of the dairy products consumed, because no marked changes in indicators of carbohydrate homeostasis from the habitual diet at baseline were observed during the dairy product condition. HOMA2–%S and the LMTT disposition index worsened compared with the dairy product condition (and with baseline) during the SSP condition, which would be expected to increase T2DM risk if maintained over an extended period. Accordingly, although these findings support the view that dairy products represent healthier alternatives to SSPs with regard to the T2DM risk factor profile, further research will be needed to assess whether consumption of dairy products or components thereof produce favorable effects on indicators of glucose homeostasis.

Dairy fat may be 1 component of dairy foods with the potential to provide benefits related to glucose metabolism. Recent data from observational studies indicate that concentrations of plasma or phospholipid FAs that serve as biomarkers of milk fat intake (15:0; 17:0; and trans-16:1,n–7) are associated with higher hepatic and/or systemic insulin sensitivity and other indicators of enhanced glucose homeostasis (34, 35). Therefore, the use of low-fat dairy products may have reduced the ability to demonstrate an effect. Additional randomized controlled trials designed to evaluate the impact of dairy fats on metabolic outcomes are warranted.

Several nutritional components differed between treatment conditions. Therefore, it is not possible to attribute differences in outcome variable responses to any single difference. The 10% difference in dietary carbohydrate (47.2 vs. 57.2%) in the dairy product and SSP conditions, respectively) was largely because of a difference in dietary carbohydrate (47.2 vs. 57.2% in the dairy product condition (and with baseline) during the SSP condition, which would be expected to increase T2DM risk if maintained over an extended period. Accordingly, although these findings support the view that dairy products represent healthier alternatives to SSPs with regard to the T2DM risk factor profile, further research will be needed to assess whether consumption of dairy products or components thereof produce favorable effects on indicators of glucose homeostasis.
2 treatment conditions, approximately half (~5% of total energy) of which was fructose (from sucrose and high-fructose corn syrup). Results from previous studies suggested that higher intakes of fructose may produce insulin resistance (36, 37). For example, Stanhope et al. (36) provided 25% of energy as fructose or glucose for 10-wk treatment periods. No change from baseline in insulin sensitivity index was observed during the glucose condition, but a 17.3% reduction \( (P < 0.001) \) was noted during the fructose period. Thus, the decline observed in HOMA2–%S in the SSP condition in the present study may be, at least in part, attributable to higher fructose consumption.

HOMA2–%S declined by a median of 21.3% from a baseline median value of 118% (i.e., a reduction of ~18% of the baseline value) during the SSP condition. The MISI showed a smaller decline of ~12% of the baseline value (0.5 units) during the SSP condition, whereas the difference from the dairy product condition was 0.4 units. The study was designed to have the power to detect a difference of 0.54 units between conditions for the MISI response, so the failure to detect a difference in the MISI could be a type II statistical error (insufficient power), or could represent a difference in the processes measured by the 2 indices of insulin sensitivity. HOMA2–%S is a fasting index that primarily reflects hepatic insulin sensitivity with a secondary contribution from skeletal muscle, whereas the MISI likely reflects skeletal muscle insulin sensitivity to a greater degree than HOMA2–%S (38). The results are therefore consistent with an adverse effect of SSP consumption on hepatic insulin sensitivity.

The LMTT disposition index showed a statistically significant decline of 0.4 units (~15%) during the SSP condition, but was unchanged from baseline during dairy product consumption. In contrast, HOMA2–%B showed a nonsignificant \( (P = 0.105) \) trend toward an increase during the SSP condition compared with the dairy product condition (a difference of 7.8%, or ~11% of the baseline value of 72.6%). The LMTT disposition index is derived from a combination of the premeal insulin concentration and both the first and second phase peripheral insulin responses to a carbohydrate load. Because these 2 indices of β-cell function reflect different aspects of the pancreatic insulin response (after hepatic insulin extraction), it is not surprising that the results do not fully align. The decline in LMTT disposition index during SSP consumption suggests that the pancreatic β-cell response (relative to insulin sensitivity) deteriorated. Additional research will be needed to define the mechanisms responsible for the changes observed in indices of carbohydrate homeostasis in the present trial.

HDL cholesterol declined by 4.2% during the SSP period, but was essentially unchanged during dairy product consumption (change of 0.8%). Intakes of carbohydrates and sugars were increased in the SSP condition and protein consumption was lower relative to the dairy product condition. A likely explanation for the change in HDL cholesterol relates to the displacement of carbohydrate (especially fructose) in the SSP condition with protein and fat in the dairy product condition. Increased dietary carbohydrate intake was associated with lower HDL cholesterol (39), whereas higher dietary protein was associated with reductions in circulating TGs and increases in HDL cholesterol in some studies (40, 41). There was a nonsignificant reduction in TG concentration in the dairy product condition, which may have been accompanied by a larger reduction in postprandial TGs (36). Postprandial TG is a strong determinant of the HDL cholesterol concentration (42).

Serum 25(OH)D concentrations were significantly higher during the dairy product condition. A positive correlation was observed between 25(OH)D and HDL cholesterol in cross-sectional studies (43), but dietary supplementation with vitamin D has not been found to increase circulating concentrations of HDL cholesterol (44).

After 6 wk of dairy product consumption, blood pressure was not significantly altered. This result is consistent with that from a previous trial conducted by our group (39). However, results from previous studies, such as the Dietary Approaches to Stop Hypertension trial and others, indicate that dietary patterns that include low-fat dairy products may lower blood pressure in some subjects, and may reduce the risk of developing hypertension (45, 46).

To the authors’ knowledge, results from only a few studies that directly investigated the effects of dairy product consumption on carbohydrate metabolism have been published (47, 48). The effects of dairy product interventions on insulin sensitivity were recently reviewed by Turner and colleagues (48), who found mixed results, with 4 studies showing improved homeostasis model assessment insulin sensitivity, 1 showing worsened values, and 5 showing no effect. Additional studies will be needed to more clearly define the influence of dairy products and components thereof on carbohydrate metabolism.

Limitations of the present work include the fact that subjects were free-living; thus, there was potential for confounding by other dietary and lifestyle factors. Because the study foods were so different, it was not possible to blind the study subjects or staff to treatment assignment. The sample included those with normal and impaired fasting glucose; however, the sample size was not large enough to complete meaningful subgroup analyses. Because treatment periods were relatively short (6 wk), longer-term effects are uncertain. Finally, subjects were habitual consumers of sugar-sweetened beverages; thus, generalizability to other groups is unknown.

In summary, results from the present trial suggest that SSP consumption is associated with less favorable values for HOMA2–%S, LMTT disposition index, HDL cholesterol, and...
References


