Metabolic effects of adding sucrose and aspartame to the diet of subjects with noninsulin-dependent diabetes mellitus1–3

Stephen Colagiuri, John J Miller, and Ronald A Edwards

ABSTRACT This study compared the effects of adding sucrose and aspartame to the usual diet of individuals with well-controlled noninsulin-dependent diabetes mellitus (NIDDM). A double-blind, cross-over design was used with each 6-wk study period. During the sucrose period, 45 g sucrose (9% of total daily energy) was added, 10 g with each main meal and 5 g with each between-meal beverage. An equivalent sweetening quantity of aspartame (162 mg) was ingested during the aspartame period. The addition of sucrose did not have a deleterious effect on glycemic control, lipids, glucose tolerance, or insulin action. No differences were observed between sucrose and aspartame. Sucrose added as an integral part of the diabetic diet does not adversely affect metabolic control in well-controlled NIDDM subjects. Aspartame is an acceptable sugar substitute for diabetic individuals but no specific advantage over sucrose was demonstrated. Am J Clin Nutr 1989;50:474–8.

KEY WORDS Sucrose, aspartame, noninsulin-dependent diabetes, glucose clamp

Introduction
The use of sweetening agents by diabetic individuals is common. A survey of our diabetic clinic population showed that 65% regularly use these products. Such individuals are instructed to avoid added sucrose and instead use one of the many alternative sweeteners. This advice is based on the assumption that refined carbohydrate, including sucrose, has a deleterious effect on postprandial glycemia. However, studies of the ingestion of sucrose alone (1) or as part of a mixed meal (2–6) (in both diabetic and nondiabetic individuals) have failed to confirm this belief. Medium-term studies that have examined the addition of sucrose to the diet of noninsulin-dependent diabetes mellitus (NIDDM) subjects for periods of 2–6 wk have produced conflicting results (7–10).

The aim of this study was to compare the metabolic effects of the daily addition of sucrose or an equivalent sweetening amount of aspartame to the usual diet of subjects with well-controlled NIDDM. The purpose was twofold: to further examine the issue of a possible deleterious effect of sucrose in the diabetic diet and to ascertain whether an alternative sweetener has any particular advantage. Aspartame was chosen as the comparative sweetener because it is now widely used by the diabetic population (11).

Subjects and methods
Subjects
Nine subjects (eight males, one female) who satisfied the criteria for NIDDM (12) were studied. The clinical details of the subjects are shown in Table 1. Glycosylated hemoglobin ranged from 5.7% to 9.1% with a mean of 7.2%, indicating good diabetes control. No patient was being treated with insulin; three were treated with diet alone and six were treated with diet and a sulphonylurea. All subjects were in good health apart from the diabetes and none was taking any medication (other than a sulphonylurea) known to interfere with glucose, insulin, or lipid metabolism.

Subjects were informed that the nature of the study was to compare two sweetening agents but the nature of the sweeteners was not disclosed prior to the study. The protocol was approved by the Committee on Experimental Procedures Involving Human Subjects of the University of New South Wales. Patients gave written informed consent prior to participation.

Study design
A double-blind, cross-over design was used. Potential subjects were assessed for ≥ 3 mo before the study and were selected because they were compliant with the prescribed diet.
TABLE 1
Characteristics of subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex</th>
<th>Age</th>
<th>BMI*</th>
<th>Duration of diabetes</th>
<th>Glycosylated Hb</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>y kg/m²</td>
<td>y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>M</td>
<td>70</td>
<td>26.5</td>
<td>6</td>
<td>9.1</td>
<td>Gliclazide (80 mg twice daily)</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>64</td>
<td>25.6</td>
<td>5</td>
<td>8.3</td>
<td>Diet</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>68</td>
<td>29.3</td>
<td>8</td>
<td>6.4</td>
<td>Gliphenclamide (2.5 mg in the morning)</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>63</td>
<td>24.6</td>
<td>6</td>
<td>8.2</td>
<td>Diet</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>56</td>
<td>28.9</td>
<td>3</td>
<td>7.1</td>
<td>Gliphenclamide (5 mg twice daily)</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>69</td>
<td>23.2</td>
<td>21</td>
<td>8.2</td>
<td>Gliphenclamide (5 mg in the morning)</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>71</td>
<td>24.9</td>
<td>12</td>
<td>8.2</td>
<td>Gliphenclamide (10 mg in the morning, 5 mg in the evening)</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>70</td>
<td>25.7</td>
<td>7</td>
<td>6.2</td>
<td>Gliphenclamide (5 mg twice daily)</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>62</td>
<td>28.6</td>
<td>9</td>
<td>5.7</td>
<td>Gliphenclamide (5 mg twice daily)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>26.4 ± 2.1</td>
<td>9 ± 5</td>
<td>7.2 ± 1.1</td>
<td></td>
</tr>
</tbody>
</table>

*Body mass index.

and the general requirements of diabetes management and their diabetes was well controlled.

The subjects' usual diet plan was analyzed (13) during the pre-study period and details are contained in Table 2 and are typical of the diet consumed by Australians with diabetes (14). Carbohydrate, fat, and protein represented 43%, 39%, and 18% of total energy, respectively. Complex and simple carbohydrates were 67% and 33% of total carbohydrate intake, respectively. No added sucrose was used and sucrose in the diet was calculated as between 1% and 2% of total energy. The mean fiber content of the diet was 29 g.

Subjects were randomly allocated to one of two groups. 1) Sucrose (45 g) was added to the usual diet. The three main meals were supplemented with 10 g sucrose, and 5 g sucrose was added to the midmorning, midafternoon, and supper tea or coffee. 2) Aspartame (162 mg) was added to the usual diet. This quantity of aspartame was chosen to provide a sweetness level equivalent to the amount of sucrose used in the first group (18 mg aspartame is equivalent to 5 g sucrose). Each of the three main meals was supplemented with 36 mg aspartame, and 18 mg aspartame was added to the between-meal beverages.

Subjects remained in each group for 6 wk and then transferred to the comparative treatment group for a further 6 wk. The subject's ability to comply with the study requirements was assessed regularly throughout both dietary periods.

TABLE 2
Composition of diet*

<table>
<thead>
<tr>
<th></th>
<th>Energy kcal/d</th>
<th>Energy kJ/d</th>
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<tbody>
<tr>
<td></td>
<td>1966 ± 200</td>
<td>8100 ± 850</td>
</tr>
</tbody>
</table>

Carbohydrate (% of total energy) | 43 ± 2
Complex (% of total carbohydrate) | 67 ± 14
Simple (% of total carbohydrate) | 33 ± 15
Protein (% of total energy) | 18 ± 3
Fat (% of total energy) | 39 ± 5
Fiber (g) | 29 ± 9

* x ± SD.

Packaging of sweeteners

The sucrose and aspartame were packed in plain sachets labeled A or B according to a code. Each sachet contained 5 g sucrose or 18 mg of aspartame (Equal®, Searle Laboratories, Crows Nest, New South Wales, Australia) bulked to 0.5 g with lactose.

Assessments

Body weight, glycosylated hemoglobin (Hb), and fasting concentrations of plasma glucose and serum lipids (total and high-density lipoprotein [HDL] cholesterol and triglycerides) were measured at entry and at the end of each dietary period. Subjects continued the usual monitoring of their diabetes. All subjects performed urinalysis at least twice daily and four subjects also monitored their capillary blood glucose levels with a reflectance meter. Pre- and postprandial tests were performed and results were recorded and used to estimate glucosuria and to calculate an average blood glucose concentration for each subject.

Carbohydrate tolerance and in vivo insulin action were measured at entry and again at the end of each dietary period. Carbohydrate tolerance was assessed by the glycemic rise after ingestion of a standard test breakfast (1050 kJ [250 kcal]; 52 g carbohydrate) after an overnight fast. Blood was collected for measurement of plasma concentrations of glucose and insulin 30 min before, immediately before, and at 30-minute intervals for 2 h after ingestion of the breakfast. The glycemic and insulin responses were calculated as the incremental area under the respective glucose and insulin curves.

In vivo insulin action was measured using the euglycemic glucose clamp technique (15). An intravenous cannula was inserted into each forearm. One cannula, kept patent with a slow infusion of normal saline, was used for blood collection. Blood glucose concentration was measured immediately after collection at 5–10-min intervals and blood collected for serum insulin measurement, at 10-min intervals. Two hours after commencing the tritiated glucose infusion an insulin infusion was commenced at a rate of 40 mU·m⁻²·min⁻¹. When the blood glucose concentration was reduced to ~6 mmol/L the clamp study proper was commenced and continued for 120 min. The blood glucose was maintained at a constant level by a variable-
TABLE 3
Indices of metabolic control at entry to the study and after the sucrose
and aspartame periods*

<table>
<thead>
<tr>
<th></th>
<th>Initial</th>
<th>Sucrose</th>
<th>Aspartame</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>75.7 ± 2.6</td>
<td>75.9 ± 3.0</td>
<td>75.3 ± 2.8</td>
</tr>
<tr>
<td>Fasting plasma glucose (mmol/L)</td>
<td>5.7 ± 1.1</td>
<td>6.2 ± 1.6</td>
<td>6.0 ± 1.2</td>
</tr>
<tr>
<td>Glycosylated Hb (%)</td>
<td>7.2 ± 0.4</td>
<td>7.5 ± 0.5</td>
<td>7.3 ± 0.3</td>
</tr>
<tr>
<td>Cholesterol (mmol/L)</td>
<td>5.2 ± 0.2</td>
<td>5.3 ± 0.2</td>
<td>5.4 ± 0.2</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>0.91 ± 0.10</td>
<td>0.96 ± 0.09</td>
<td>0.93 ± 0.11</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.9 ± 0.3</td>
<td>2.1 ± 0.3</td>
<td>2.1 ± 0.5</td>
</tr>
</tbody>
</table>

* x ± SEM.

rate glucose infusion by use of the Pacberg program (16). Glucose utilization rate was determined during the clamp studies using [3-3H]glucose. An intravenous bolus (3.7 x 10^6 Bq) was injected 2 h before the start of the insulin infusion, followed by a constant infusion of 3.7 x 10^6 Bq/h until the end of the clamp study. Blood was collected at 10-min intervals for measurement of radioactivity. Samples were precipitated with Ba(OH)2 and ZnSO4 and centrifuged at 1500 x g and the protein-free supernatant was evaporated in a scintillation vial. Glucose specific activity was calculated from blood glucose concentration and radioactivity. In the steady-state conditions that prevailed the rate of appearance of glucose (Ra) was equal to the rate of disappearance of glucose (Rd). Rd was calculated for the period from 90 to 120 min of the clamp by use of the Steele equations (17). Rd as the rate of glucose utilization was used to assess insulin action during the clamp study.

Biochemical analyses

A hexokinase method (18) was used for measuring the plasma glucose concentration. Serum insulin concentration was determined by a standard double-antibody radioimmunoassay; human antiinsulin antibody RD10 and insulin standard RD13 (Wellcome Laboratories, Dartmouth, UK) and porcine 125I tracer (CIS, Paris) were used. The detection limit of this assay is 14–28 pmol/L and the coefficient of variation between and within assay is 5%. Glycosylated Hb was measured by ion-exchange chromatography with disposable minicolumns supplied by Bio-Rad Laboratories (Richmond, CA); range for non-diabetic persons, 5.2–8.4%. Total cholesterol and HDL cholesterol (after isolation from plasma by polyethylene glycol [PEG] precipitation) were measured by a standard enzymatic technique (CHOD-PAP, Boehringer Mannheim, Ryde, New South Wales, Australia) and total triglycerides were measured (19) after enzymatic hydrolysis.

Statistics

Differences between the results at entry and after the two dietary periods were analyzed by two-way analysis of variance (ANOVA) (20).

Results

Antidiabetic treatment remained unchanged during the study. No significant changes in mean body weight of the group occurred. Eight of the nine subjects gained a mean of 1.2 kg during the sucrose period. One subject lost 4 kg during the aspartame period and maintained this weight loss during the sucrose-supplemented diet. Glycemic control (as assessed by the mean glycosylated Hb concentration, by the mean fasting plasma glucose concentration on the morning of the test breakfast, and assessment of in vivo insulin action) remained unchanged during the study (Table 3). No subject showed any change in glucosuria during either dietary period. Mean (±SEM) capillary blood glucose values in the four subjects who performed self blood glucose monitoring were 6.5 ± 0.7 mmol/L before entry, 6.6 ± 0.7 mmol/L during the sucrose period, and 6.7 ± 0.7 mmol/L during the aspartame period.

Fasting concentrations for serum total cholesterol, HDL cholesterol, and triglycerides were not significantly different at the end of the sucrose- or aspartame-supplemented periods compared with pretreatment levels (Table 3). The two patients (#2 and #3) who had significantly elevated fasting triglyceride concentrations when they entered the study (3.5 and 3.5 mmol/L, respectively) recorded values of 2.8 and 3.6 mmol/L, respectively, at the end of the period of ingestion of sucrose.

The glycemic and insulin responses to the test breakfast are shown in Figure 1. There were no statistically significant differences between fasting and postmeal glucose and insulin concentrations after either dietary period compared with the pretreatment values. Mean glycemic responses were 305 ± 36 mmol·min⁻¹·L⁻¹ at entry, 315 ± 24 mmol·min⁻¹·L⁻¹ after sucrose, and 330 ± 30 mmol·min⁻¹·L⁻¹ after aspartame. The corresponding insulin responses were 17 648 ± 4229. 19 188 ± 3367,
TABLE 4
Assessment of insulin action*

<table>
<thead>
<tr>
<th></th>
<th>Initial</th>
<th>Sucrose</th>
<th>Aspartame</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rd (mg·kg⁻¹·min⁻¹)</td>
<td>4.7 ± 0.4</td>
<td>4.5 ± 0.4</td>
<td>4.4 ± 0.4</td>
</tr>
<tr>
<td>Plasma glucose (mmol/L)</td>
<td>5.2 ± 0.4</td>
<td>5.7 ± 0.5</td>
<td>5.5 ± 0.4</td>
</tr>
<tr>
<td>Serum insulin (pmol/L)</td>
<td>574 ± 36</td>
<td>610 ± 43</td>
<td>589 ± 43</td>
</tr>
</tbody>
</table>

* x ± SEM.
† Rd, rate of glucose utilization.

and 19 788 ± 4286 pmol·min⁻¹·L⁻¹, respectively. None of these differences were statistically significant.

The results of the assessment of in vivo insulin action are shown in Table 4. Clamped plasma glucose concentrations and plateau serum insulin levels were similar on the test days. The coefficient of variation of the clamp ranged from 3% to 7% and did not differ between test periods. Glucose utilization rates were not significantly different after ingestion of either sucrose or aspartame.

Discussion

Our study did not show a detrimental effect on glycemic control, lipid levels, carbohydrate tolerance, or in vivo insulin action as the result of the daily addition of 45 g sucrose ingestion over a 6-wk period. No differences were observed when compared with a period of ingestion of an equal sweetening quantity of aspartame. The quantity of added sucrose amounted to 9% of total daily energy, which raised the average sucrose ingestion to between 10% and 11% of total daily energy during the sucrose-supplemented dietary period. The way the sucrose was consumed was restricted in that subjects were instructed to add it to tea or coffee, sprinkle it on breakfast cereals, or use it to sweeten fruit eaten as dessert.

Previous studies that examined the addition of sucrose to the diet of diabetic subjects gave conflicting results (7–10). The study by Peterson et al (8) examined the effect of substituting an average of 45 g complex carbohydrate with 45 g sucrose per day (~10% of total daily energy) in the diets of groups of NIDDM and IDDM subjects. Subjects were given a sucrose-exchange list and were instructed to substitute 15 g portions of complex carbohydrate at each main meal with sucrose or low-fat sucrose-containing foods. Sucrose consumption was not controlled but was determined from analysis of 3-d food records and interviews with the dietitian. No alteration of diabetes control, diurnal glucose profiles, and lipid levels was noted. The background diet in this study was high in fiber, containing a daily average of 53.5 g fiber, and was also low in fat. This fiber content is considerably greater than that consumed in the usual diet and may have influenced the results. Another negative result was reported by Bantle et al (9) in subjects with IDDM and NIDDM who ingested over an 8-d period a diet in which 23% of total energy was sucrose compared with a conventional diet containing <5% sucrose. Mean and pre- and postprandial plasma glucose levels, 24-h urinary glucose, and fasting and postprandial triglyceride levels were not adversely affected.

By contrast the Stanford group (7, 10) reported deleterious effects of sucrose addition on both glucose and lipid profiles. The initial publication (7) compared eucaloric diets that differed in sucrose content (16% vs 1% of total daily energy) in 11 NIDDM subjects. Each of the dietary periods was 15 d and the sucrose-added diet resulted in significantly elevated daylong glucose and triglyceride levels as well as elevated fasting total cholesterol, triglycerides, and lipid fractions. The comparative sucrose-free diet used in this study derived 57% of carbohydrate energy from sugars other than sucrose. High-fructose diets are known to lower postprandial glucose responses (9). This might explain the results of Coulston et al (7) if their comparative diet contained a significant percentage of the sugar as fructose. A second study (10) in nine NIDDM subjects compared a high-carbohydrate (60%), low-fat (20%), sucrose-containing (10%) diet with a conventional carbohydrate (40%), fat (40%), and sucrose (3%) diet. Adverse effects of the high-carbohydrate, sucrose-containing diet were demonstrated on glucose, insulin, and lipid profiles, again emphasizing the relevance of the background diet on the metabolic effects of adding sucrose.

Factors that may account for some of the differences in the results of these published studies include patient factors such as the degree of diabetes control and the severity of diabetes, the amount of added sucrose, the background diet, and the nature of the sugars used in the comparative diets. In our study the subjects’ diabetes was well controlled, with mean glycosylated Hb in the normal range, and none had severe hyperglycemia during the study period. The amount of sucrose added was similar to that reported to be consumed in a survey of relatives of diabetic individuals (14). Our subjects had a mean duration of diabetes of 9 y and their diets reflected past dietary instruction lower in carbohydrate content and higher in fat content than current recommendations.

A further issue addressed in our study was whether the use of an alternative sweetener, aspartame, conferred any benefits compared with sucrose. Aspartame, a synthetic dipeptide, was chosen as the sweetener because it has been the subject of an extensive marketing campaign and is being used commonly by the diabetic population. We were unable to identify any variable studied that was improved by the use of aspartame compared with sucrose. The small amount of lactose used as a bulking agent for the aspartame, a total of 4.3 g/d, was unlikely to have masked any beneficial effects. Furthermore, such bulking agents remain a component of commercially available sweeteners and their usage is to be judged on that basis. The negative finding of this study does not exclude a possible beneficial effect of using aspartame in a different manner. If aspartame were used as a substitute for existing carbohydrate in the diet, thereby reducing total energy intake, a beneficial effect on blood glucose
and other indices of metabolic control might be achieved.

We caution against the overinterpretation of the results of our study. Our subjects’ diabetes was well controlled and the subjects had proven compliance and attended a diabetes clinic regularly for review. Three further points require emphasis. First, the form in which the sucrose is added would seem to be important. In this study sucrose was used solely as an additive and our results should not be extended to include, for example, confectionery and baked goods that may also have a high fat content. Second, detailed monitoring of postprandial blood glucose levels was not performed in all subjects and a deleterious cumulative effect of sucrose on these measurements cannot be excluded. Finally, our study does not address in detail the potential effects of sucrose addition on the various lipid fractions. We measured those lipids (total cholesterol, HDL cholesterol, and triglycerides) that we routinely measure to assess the clinical progress of our NIDDM patients. No adverse effects on these were demonstrated during the study period. The more detailed assessment of lipids in the studies by the Stanford group (7, 10) indicated that more subtle but potentially serious changes in lipid fractions may be attributable to sucrose and further work is required to resolve this issue.

Many aspects of the diabetic food plan are currently being reappraised and a number of traditional beliefs are being challenged. Although there is no specific nutritional need for sweetening agents, they are commonly used by individuals with diabetes and may have important therapeutic implications and improve an individual’s ability to adhere to the requirements of the diabetic food plan. There is evidence that the fat restriction now recommended becomes increasingly difficult to achieve once sucrose is removed from the diet (21). Despite the availability of alternative sweetening agents the omission of all added sucrose remains a hardship to some diabetic individuals. Our study suggests that the controlled use of sucrose can be considered in certain individuals. Aspartame is an acceptable sucrose substitute for diabetic individuals but has no specific advantage over sucrose when used solely as a sweetening agent except perhaps in weight-reducing diets.

Aspartame (Equal®) was supplied by Searle Laboratories, Division of Searle Australia Propriety Limited, Crows Nest, New South Wales, Australia.

References


