A Comparison of Carbohydrate Metabolism After Sucrose, Sorbitol, and Fructose Meals in Normal and Diabetic Subjects

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Sucrose, sorbitol, and fructose (35 g) were fed to normal and diabetic subjects as a component of a 400-calorie breakfast. In both normal and diabetic subjects, the mean peak increment in plasma glucose was highest after the sucrose meals (44.0 mg/dl for normal subjects; 78.0 mg/dl for diabetic subjects); lowest after sorbitol meals (9.3 mg/dl for normal subjects; 32.3 mg/dl for diabetic subjects); and intermediate after the fructose meals (29.0 mg/dl for normal subjects; 48.0 mg/dl for diabetic subjects). In normal subjects, the mean peak increment of plasma immunoreactive insulin followed a similar pattern, but in diabetic subjects there was no significant difference between the three groups. We conclude that fructose or sorbitol, given as part of a meal, results in lower glucose levels in both normal and diabetic subjects, but that the latter is not related to a difference in insulin release. DIABETES CARE 3: 582–585, SEPTEMBER–OCTOBER 1980.

Interest in the use of sugars other than sucrose as a component of the diabetic diet stems from the earliest days of diabetes research. In 1874, Külz initially suggested that diabetic patients were able to metabolize oral fructose better than other sugars.[2] Fructose, but not glucose, was found to partially replete the hepatic glycogen stores of diabetic depancreatectomized dogs by Minkowski in 1893,[3] and Elliott Joslin published on the clinical usefulness of fructose in 1915.[4] Other nonsucrose sweetening agents used include sorbitol and xylitol, but they have not been investigated as extensively as fructose.[5]

Several groups have established a decreased plasma glucose and insulin rise after oral and i.v. administration of fructose and other sweetening agents compared with glucose in normal and diabetic subjects.[6] Bohannon and colleagues have also described the decreased reactive hypoglycemia after fructose.[7] Most studies used the pure sugar as a test substance. However, in analogy with the problems posed in interpreting the oral glucose tolerance test, it is clear that most patients do not consume large quantities of pure sugar. In a report prepared for the Food and Drug Administration in May 1978 by the Federation of American Societies for Experimental Biology, it was pointed out that adequate studies of the clinical effectiveness of fructose, xylitol, and sorbitol as part of mixed meals have not been conducted.

This report presents data on changes in glucose and insulin in normal and diabetic subjects after standardized meals containing fixed amounts of either sucrose, fructose, or sorbitol.

This study was presented, in part, at the 39th Annual Meeting of the American Diabetes Association, Los Angeles, California, June 1979.[1]

MATERIALS AND METHODS

Ten nondiabetic and six diabetic subjects participated in the study. The protocol was approved by the Human Safety Committee of the East Orange Veterans Administration Medical Center and written informed consent was obtained from each individual. No more than two tests were carried out in 1 wk, and the interval between any two tests was at least 3 days.

Studies in nondiabetic subjects. Ten nondiabetic males, aged 19–62 yr (mean age 43 yr) participated in the study. None of the subjects had a history of diabetes mellitus or chronic illness. Ten individuals were given a sucrose meal, six a sorbitol meal, and five received a fructose meal. Usually the sucrose meal was given first, although some patients received the meals in random order. All the nondiabetic volunteers underwent oral glucose tolerance testing (OGTT) with 100 g of dextrose after ingestion of at least 300 g of carbohydrates for 3 days. Fasting plasma glucose ranged between 71 and 93 mg/dl with a mean of 80 mg/dl. Each test meal, consisting of a scrambled egg, farina, low fat milk, and 120 ml of decaffeinated coffee, was given after an overnight fast. Of the 400 calories, 140 calories were comprised of 35 g sucrose, sorbitol, or fructose. A reason for choosing 35 g of various sugars is related to the fact that Adcock and Gray[9] showed

that 35 g ^{14}C-sorbitol is almost completely absorbed, and administration of more than this quantity would result in diarrhea in many patients. The first bite was considered zero time, and each subject finished the entire test meal in 5 min. Blood samples were drawn into heparinized tubes every 15 min up to 2 h, then at 150 and 180 min. Plasma glucose (PG) determinations were usually performed on the day of the test using the Beckman Glucose Analyzer. Pure solutions of either sorbitol or fructose were not detected by the analyzer. Determinations for plasma immunoreactive insulin (IRI) and growth hormone (GH) were performed by radioimmunoassay. All the determinations on one subject were carried out in the same assay to prevent interassay variability. All data were analyzed as the change from the mean of two baseline values. The paired Student's *t* test was used for statistical analysis in all tests except for comparison of sorbitol with fructose in normal subjects. In the latter, the *t* test for independent data was used.

Studies in diabetic subjects. Six male individuals with non-insulin-dependent diabetes mellitus (NIDDM), aged 52–59 yr, participated in this study. Three patients exceeded ideal body weight (IBW) by 23%, 30%, and 35%; the other three were normal in weight. All patients met the criteria of the National Diabetes Data Group for the diagnosis of diabetes mellitus (fasting PG > 140 mg/dl on at least two occasions).[10] Fasting PG ranged between 90 and 197 mg/dl with a mean of 162 ± 15.4 (SEM ± mg/dl). Two patients had been taking oral hypoglycemic agents, which were discontinued at least 1 wk before the study was carried out. One patient had diabetic neuropathy but had no clinical evidence of enteropathy. The same format as in the control subjects was followed, with the exception that they did not have an OGTT. Since each diabetic patient received each of the three sweeteners with a test meal, the paired Student's *t* test was used uniformly.

RESULTS

Nondiabetic Subjects

Plasma glucose. The mean peak change in PG concentration (ΔPG) after sucrose, fructose, and sorbitol meals (Figure 1) was reached at 30 min, with mean values of 44 ± 5.4 (SEM) mg/dl, 29.0 ± 4.6 mg/dl, and 9.3 ± 2.3 mg/dl, respectively. When sucrose versus sorbitol meals were compared at individual times, statistically significant differences were noted at 15, 30, 45, and 60 min. When sucrose versus fructose meals were compared, ΔPG was significantly higher after sucrose at 15 and 30 min, and lower at 150 and 180 min.

An analysis of mean ΔPG by computing the areas under the curves by planimetry reveals a major and significant difference when sucrose is compared with sorbitol. There is no such difference in mean ΔPG for the entire sucrose versus fructose study, but when the total curve is separated into early (hyperglycemic) and late (reactive) phases, significant differences in opposite directions are noted.

Plasma IRI. The mean peak ΔIRI after a sucrose meal was seen at 30 min with a mean of 55.6 ± 10.0 μU/ml; at

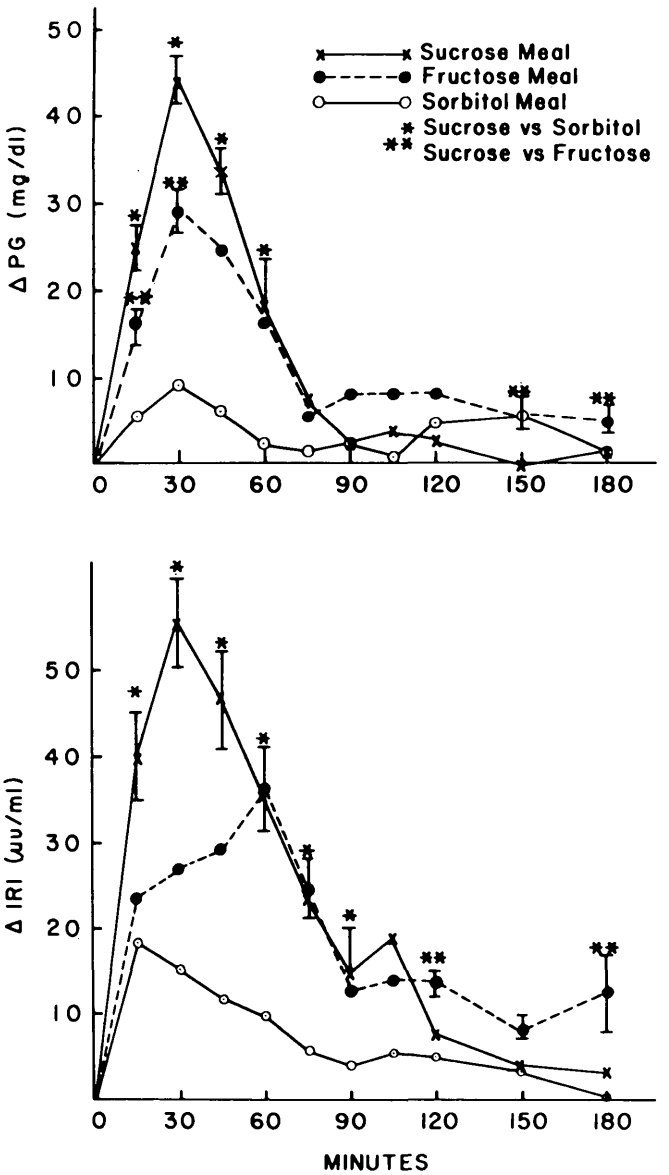

FIG. 1. ΔPG and ΔIRI after sucrose, fructose, and sorbitol meals in 10 normal subjects. Asterisks indicate $P < 0.05$.

60 min after a fructose meal with a mean of 36.2 ± 10.6 μU/ml (Figure 1); and at 15 min after a sorbitol meal with a mean of 18.6 ± 6.0 μU/ml. When ΔIRI after sucrose and sorbitol meals were compared, there was statistical significance at 15, 30, 45, 60, 75, and 90 min. When ΔIRI after sucrose and fructose meals were compared, ΔIRI was significantly higher after a fructose meal at 120, 150, and 180 min.

When areas under the curves of mean ΔIRI after sucrose versus fructose or sorbitol meals are compared, results similar to mean ΔPG were obtained.

Diabetic Subjects

Plasma glucose. The mean peak ΔPG after sucrose meals was 78.0 ± 12.0 mg/dl, after fructose meals 48.0 ± 11.0 mg/dl,

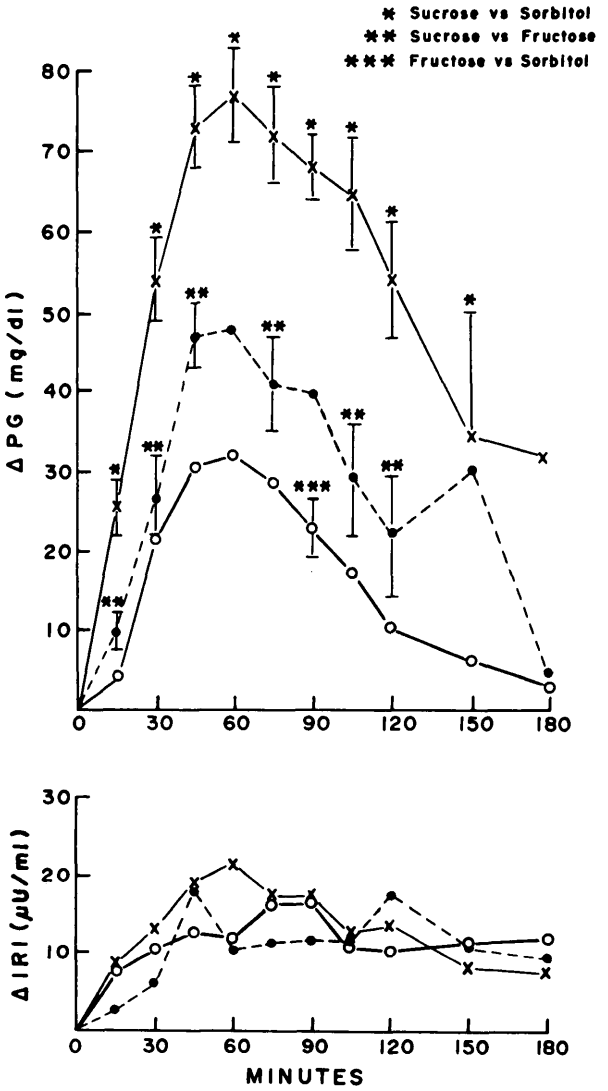

FIG. 2. ΔPG and ΔIRI after sucrose (x), fructose (●), and sorbitol (○) meals in six diabetic subjects. Asterisks indicate $P < 0.05$.

and after sorbitol meals 32.3 ± 7.3 mg/dl (Figure 2). There was a statistically significant difference between paired ΔPG after sucrose versus sorbitol meals at every individual point in time between 15 and 150 min. When ΔPG after sucrose was compared with ΔPG after fructose, significant differences were noted at 15, 30, 45, 75, 105, and 120 min. Lastly, comparison of fructose versus sorbitol yielded statistical significance only at 90 min. An analysis of mean ΔPG by examining areas under the curves (Figure 3) revealed significant differences when sucrose, fructose, and sorbitol meals were compared with each other.

Plasma IRI. The mean peak ΔIRI after sucrose meals was 21.9 ± 6.8 μU/ml at 60 min, after fructose meals 18.0 ± 3.2 at 45 min, and after sorbitol meals 16.2 ± 3.6 at 90 min. Comparison of ΔIRI after the three types of meals revealed no statistical significance whether one looks at individual points in time (Figure 2) or areas under the curve (Figure 3).

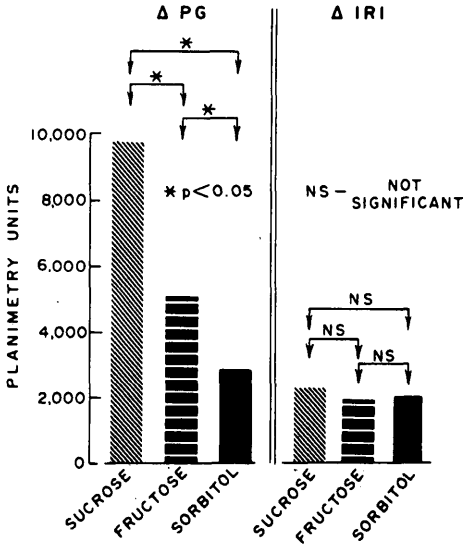

FIG. 3. Areas under the curves of total ΔPG and ΔIRI after sucrose, fructose, and sorbitol meals in six diabetic subjects.

DISCUSSION

The presence of obesity and/or diabetes mellitus does not seem to decrease the desire for sweets in the diet. In the United States, 80% of diabetic patients use dietetic foods.[11] The need for dietetic foods in diabetes has been questioned on the basis of cost versus nutritional benefits,[12] but there is little doubt that such products will continue to be used in great volume. Since the disapproval of cyclamates, there has been a growing interest in the nonsucrose nutritive sweeteners, fructose and sorbitol.

Studies using the pure carbohydrate showed lower levels of PG after ingestion of both fructose and sorbitol compared with sucrose or glucose in normal and diabetic subjects.[6] Bohannon and colleagues confirmed these findings in normal subjects using fructose and also showed a lesser insulin increase.[7] Despite these studies, little scientific work has been performed looking at the effects of fructose and sorbitol as components of meals. Arvidsson-Lenner[13] has been cited in many reviews as showing no significant differences among sucrose, fructose, and sorbitol meals with respect to blood glucose levels or glycosuria. However, this study was performed in diabetic and healthy subjects over the age of 60 yr, without prior carbohydrate feeding and without standardized meals between subjects. In addition, she used relatively small quantities of sweeteners (14–21 g) and did not perform insulin determinations. The metabolic effects of 75 g of fructose compared with an equal amount of dietary starch was studied in two insulin-dependent diabetic patients.[14] Fructose feeding did not alter blood glucose levels or urinary excretion of glucose; insulin values were not measured. In an acute study, fructose was given to 26 hospitalized diabetic children by isocalorically substituting 1.0 g/kg fructose for other carbohydrates at breakfast.[15] Blood glucose values from 30 to 120 min after ingestion were significantly lower on fructose days. A longer 4-wk trial of fructose, compared with isoca-

loric sugar-free diets, did not result in impaired control of diabetes, and it was concluded that fructose could be used as a sweetening agent in such patients. Steinke et al. gave sorbitol (up to 40 g in three divided doses) during meals for 8–48 days to diabetic children at camp.[16] When compared with control periods without sweetening agents, sorbitol resulted in no significant variation in either glycosuria or daily insulin dose. Shuman et al. also evaluated sorbitol and found no alteration of diurnal blood glucose values when sorbitol was added to the usual diets.[17]

While the current studies do not answer the question of long-term effects of nonglucose nutritive sweeteners as a substitute for glucose and sucrose in diets of patients with diabetes mellitus, they do provide information that is more useful than that obtained by administration of the pure sugars fructose and sorbitol. In normal subjects, both fructose and sorbitol meals resulted in lower PG and IRI levels than corresponding amounts of sucrose also given as parts of a meal, with sorbitol resulting in lower PG levels during the first hour. The patients did not describe any difference in sweetness between the three meals, but half of the patients eating the sorbitol meals complained of either mild abdominal cramps or diarrhea. These side effects, while mild, led to better acceptance of fructose as a sweetening agent.

The changes in PG in diabetic patients followed the same relative patterns as in nondiabetic subjects, but both the absolute levels and differences from baseline were greater. The achievement of peak levels of PG was delayed after the ingestion of all three sugars. In the nondiabetic subjects, the peak levels of PG were seen at 30 min in 18 of 22 studies. In the diabetic subjects, the peak PG was seen at 60 min in 9 of the 18 studies, at 75 min in 2 studies, and at 45 min in the remaining 7 tests. The delayed peak is in agreement with other studies.[18] The mean baseline plasma IRI concentration was higher in diabetic subjects compared with control subjects (19.3 ± 1.8 μU/ml versus 12.9 ± 2.4 μU/ml). This is compatible with the higher fasting PG in this group with NIDDM.[19] Insulin secretion in the diabetic subjects was markedly impaired in response to sucrose and fructose meals, but there were no significant differences in either peak insulin values or integrated insulin secretion when the three sugars were compared. Therefore, the difference in PG after the various meals cannot be attributed to differences in insulin secretion.

It is clear from our studies that both fructose and sorbitol in meal form result in lower PG levels when compared with sucrose in normal and diabetic subjects. Many investigators currently believe that prolonged elevations of PG play a role in the development of the vascular complications of diabetes.[20] Although our experiments do not address the problem of long-term effects of fructose and sorbitol on plasma glucose and insulin values, it is possible that such agents may be advantageous in the diabetic diet when sweeteners are desired.

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