Effects of Sucrose on Carbohydrate and Lipid Metabolism in NIDDM Patients

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Recently, there has been increasing interest toward the liberalization of sucrose in the diets of individuals with non-insulin-dependent diabetes mellitus (NIDDM). However, there is evidence from several well-controlled prospective studies demonstrating that the consumption of moderate amounts of sucrose may result in hyperglycemia, hyperinsulinemia, hypertriglyceridemia, hypercholesterolemia, and reduced high-density lipoprotein cholesterol concentrations. The fact that not all studies demonstrate these deleterious effects does not negate the positive data. The magnitude of the deleterious effects will probably vary with individual patients, baseline status, and amount of sucrose. Because these metabolic abnormalities are most disturbed in diabetes and are associated with increased risk of coronary artery disease, it would seem reasonable to continue to advise patients with NIDDM to limit sucrose consumption, at least until available data would allow us to predict in which individuals and at what level of sucrose consumption these adverse metabolic effects would not be present. *Diabetes Care* 12:62–66, 1989

There is general agreement that diet should serve as the cornerstone of any therapeutic program for the treatment of diabetes. Understanding the impact of variations in diet composition on the metabolic defects present in diabetes, however, is far from clear. This is particularly true in regard to what impact sucrose may have in controlling the abnormalities in carbohydrate and lipid metabolism present in diabetes. As interest in the dietary management of diabetes has intensified, attention has been directed toward the potential role that specific dietary manipulations might have in reducing the increased risk of coronary artery disease (CAD) associated with diabetes. In this regard, the issue of dietary sucrose must assume a prominent role in the discussion of the dietary treatment of diabetes. Recent statements from both the American Diabetes Association (1) and Food and Drug Administration (2) suggest there may be no adverse health effects associated with increased sucrose consumption in patients with diabetes. On the other hand, there is evidence from several well-controlled prospective studies suggesting that the consumption of moderate amounts of sucrose may result in a series of deleterious metabolic effects that are associated with an increased risk for the development of CAD (3–10). Specifically, studies have shown that the addition of moderate amounts of sucrose are associated with hyperglycemia, hyperinsulinemia, hypertriglyceridemia, hypercholesterolemia, and reduced high-density lipoprotein cholesterol (HDL-chol) concentrations. These metabolic abnormalities are most disturbed in diabetes (17,18 ,31,32) and are associated with the increased risk of CAD (30–34); therefore, it would seem reasonable to question the general recommendation liberalizing sucrose consumption in these individuals. In this article, we discuss the evidence from our group and others designed to assess the metabolic impact of moderate sucrose intake on carbohydrate and lipid metabolism in patients with non-insulin-dependent diabetes mellitus (NIDDM).

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CLINICAL STUDIES

Short-term studies. Much of the research conducted in patients with diabetes has focused solely on the acute effects of added sucrose on control of plasma glucose and insulin concentrations (11–13). For example, two recent studies showed that the replacement of sucrose for a portion of carbohydrate in a single meal for individuals with either insulin-dependent diabetes mellitus (IDDM) or NIDDM did not lead to an exaggerated increase in fasting or postprandial glucose or insulin concentrations (11,12). In another study, small doses of rapid-acting insulin was shown to attenuate the rise in plasma glucose levels after the ingestion of 100 g of ice cream in 10 patients with IDDM (13). These results in diabetic patients are all consistent with earlier observations of the acute effects of sucrose given as a single challenge to normal individuals and patients with abnormal glucose tolerance (14–16). These data suggest the addition of moderate amounts of sucrose to single meals would not result in an exaggerated plasma glucose or insulin response. On the other hand, these data should not be taken to support the notion that moderate amounts of sucrose may be safely added to the diets of individuals with diabetes. First, substitution of sucrose for other carbohydrates in the diet occurred for only a single meal. Second, assessment of the metabolic changes were limited to the acute effects of added sucrose on plasma glucose and insulin concentrations, even though previous studies have suggested that long-term sucrose feeding significantly alters both carbohydrate and lipid metabolism (3,5,6,8–10).

Long-term studies. For this discussion, long-term studies refer to studies lasting 1–6 wk. Although 6 wk is a relatively short period in terms of expected life span, to our knowledge there are no controlled metabolic studies in the literature lasting >6 wk. On the other hand, these studies provide insight into the metabolic disturbance that may be produced by increased dietary sucrose.

Although it would be ideal to limit our discussion to the effects of added sucrose given to patients with diabetes, at this time, few data exist that have assessed the long-term effects of added dietary sucrose in patients with diabetes under defined metabolic conditions. Therefore, our discussion of this issue begins with patients with diabetes and expands to include studies conducted on normal glycemic individuals (3–7) and patients with endogenous hypertriglyceridemia (8–10).

We have recently published two studies in which the effects of increased dietary sucrose on glucose, insulin, and lipid metabolism in patients with NIDDM were evaluated (17,18). In one study, the only variable was the amount of total calories present as sucrose (17). After 15 days of diets containing 16% of the total calories as added sucrose, there was a significant increase in day-long plasma glucose and triglyceride (TG) concentrations. In addition, there were significant elevations in fasting total plasma and very-low-density lipoprotein (VLDL) TG and cholesterol concentrations compared with a sucrose-free diet. Twenty-four-hour urinary glucose excretion was also significantly greater when sucrose was present in the diet, despite no change in the total carbohydrate content of the diet.

Because the recent recommendations of the American Diabetes Association include both an increase in dietary carbohydrate and the use of moderate amounts of sucrose (19), we felt it was imperative to document the effects of parallel changes in both carbohydrate and sucrose in patients with diabetes. To accomplish this, diets containing 40% of the total daily calories as carbohydrate and 3% as sucrose were contrasted with diets containing 60% of total calories as carbohydrate and 10% sucrose in patients with NIDDM (18). The combination of these two dietary manipulations appeared to exacerbate the metabolic changes seen with increased dietary sucrose alone. Plasma glucose, insulin, and TG concentrations were significantly elevated throughout the day as a result of the high-carbohydrate moderate-sucrose diets. Further evidence that the 60% carbohydrate diet resulted in a deterioration of day-long glycemic control is supported by the observation that mean 24-h urinary glucose excretion was more than doubled during this dietary period (25 vs. 56 g/24 h). Although fasting plasma glucose and insulin concentrations were unchanged, total plasma and VLDL TG and VLDL-chol concentrations were significantly increased, and HDL-chol significantly decreased as a result of the high-carbohydrate moderate-sucrose diet. The results of these controlled metabolic studies in patients with NIDDM are clear. The addition of moderate amounts of sucrose to the diets of individuals with diabetes, in amounts comparable to those typically consumed by the general population (20), resulted in significant increases in day-long hyperglycemia, hyperinsulinemia, fasting and postprandial hypertriglyceridemia, fasting hypercholesterolemia, and decreased fasting HDL-chol concentrations.

In contrast with these studies, there are five reports that suggest that increased dietary sucrose consumption over a period of 8 days to 6 wk did not result in adverse metabolic effects (21–25). In one of these studies the authors reported no significant metabolic effects of replacing 45 g of complex carbohydrate with an equal amount of sucrose (21). However, dietary sucrose intake was not controlled in this study. Patients were merely given dietary advice and asked to alter their consumption of sucrose. Without control of dietary intake it is difficult to accept these results as proof that increased dietary sucrose has no adverse metabolic effect.

In a second outpatient study, Chantelau et al. (22) reported no significant differences in the degree of blood glucose control or plasma lipid concentrations after diets containing either sucrose or sodium cyclamate in 10 patients with IDDM receiving continuous subcutaneous insulin-infusion therapy. However, the level of dietary sucrose reportedly consumed in their study was only 24

g/day. The amount of sucrose contained in their diets (4% of total daily calories) is roughly equivalent to the amount of sucrose contained naturally in fruits and vegetables in diets of individuals on sucrose-restricted diets. Therefore, this level of dietary sucrose hardly constitutes an adequate test of the effects of an increase in the consumption of sucrose.

In two other studies, the nature of the experimental design made actual comparisons between the sucrose-added and sucrose-restricted diets difficult (23,24). Specifically, in one of these studies the two dietary periods used were ~11 mo apart, and the degree of metabolic control in these individuals before the experimental diets differed between the two periods (24). For example, mean ± SE fasting plasma glucose concentration was 187 ± 25 mg/dl before the low-sucrose diet and 237 ± 26 mg/dl before the high-sucrose diet. As a result, the investigators could not make direct comparisons between the two dietary periods and reported changes in glucose, insulin, and TG metabolism from two separate baseline periods. Unfortunately, the effects of this difference in baseline values on the glycemic response is difficult to evaluate. More important, fasting hypertriglyceridemia was noted in both of these studies after the high-sucrose diet (23,24). Thus, there appears to be only a single well-controlled metabolic study on patients with diabetes conducted over an 8-day period in which the authors reported no significant differences in metabolic control as a result of increased dietary sucrose (25).

In this study, fasting, 1- and 2-h postprandial, and overall mean plasma glucose concentrations were higher after the sucrose diet in both IDDM and NIDDM subjects. In addition, fasting and postprandial peak TG concentrations were increased in the sucrose-containing diets in both groups. The fact that the differences reported did not reach levels of significance may be a result of the specific statistical analysis used or the length of time over which the studies were conducted. This study lasted only 8 days, and the magnitude of these metabolic changes may have increased with duration of diet. Given these observations, and the uncertainty surrounding the metabolic effects of added sucrose at this time, the appropriateness of encouraging sucrose intake in patients with diabetes is questionable.

The results of longer-term studies in nondiabetic individuals also raises questions about the safety of increasing sucrose in the diets of individuals with diabetes. This is particularly true of individuals who may not have diabetes but are not completely normal metabolically. For example, Reiser et al. (6,7) have demonstrated in normoglycemic hyperinsulinemic individuals that the isocaloric addition of sucrose for 6 wk increased fasting plasma glucose, insulin, and total and VLDL TG concentrations. Moreover, these increases were proportional to the amount of sucrose added. Similarly, Liu et al. (8) have demonstrated the magnitude of the increase in fasting total and VLDL TG concentrations in patients with endogenous hypertriglyceridemia varied as a function of the sucrose content of the diet. Kuo and Bassett (26) reported significantly increased total plasma TG, cholesterol, and phospholipid concentrations in patients with endogenous hypertriglyceridemia when switched from starch- to sucrose-containing diets. Comparative studies made of fatty acid composition for the plasma lipid suggested that the sucrose-induced hyperlipidemia resulted primarily from active endogenous lipogenesis. Further evidence that increased sucrose results in increased TG synthesis is provided by Nikkila (9), who demonstrated increased fasting TG concentrations in a group of individuals with primary endogenous hypertriglyceridemia when a sucrose-containing diet was compared with either starch- or fructose-containing diets. The increase in TG levels in these individuals appeared to result from an increase in the production rate of TG rather than a change in total-TG turnover rates.

Finally, using a somewhat different approach, Roberts (10) pointed out that plasma TG levels fell when nondiabetic individuals were switched from a normal to a sucrose-free diet but only in subjects in whom TG levels were >120 mg/dl with the normal diet. In contrast, the sucrose content of the diet did not seem to affect plasma TG levels in individuals with basal TG levels <120 mg/dl. Similarly, plasma cholesterol concentrations decreased in individuals with a fasting cholesterol concentration >225 mg/dl, whereas plasma cholesterol levels were slightly increased in individuals with fasting cholesterol levels <225 mg/dl. Thus, individuals with higher levels of plasma TG or cholesterol seemed to benefit from the dietary restriction of sucrose.

In individuals with normal carbohydrate and lipid metabolism, the results of moderate variations in the sucrose content of the diet on carbohydrate and lipid metabolism appear to be mixed. Several investigators have reported increased plasma glucose, insulin, and total VLDL TG concentrations with the addition of sucrose to the diet for periods up to 6 wk (3–5). Again, these increases were proportional to the amount of sucrose added (3,4). On the other hand, not all investigators have observed these metabolic changes in normal individuals (5,27). Note, however, that Dunnigan et al. (5) who concluded that "glucose tolerance, plasma insulin, and serum lipids are not significantly altered by the substitution of sucrose for starch at levels of sucrose intake comparable to those in the Western diet," documented that fasting plasma glucose concentration increased significantly ($P < .001$) in response to the added sucrose. Although the mean response only increased 4 mg/dl, subjects were all normal glucose tolerant. It is possible that the magnitude of this change would not be as modest in patients with diabetes.

Larger intakes of sucrose (1000 kcal/day or 35% of total calories) have been shown to result in decreased insulin binding to human monocytes and decreased insulin sensitivity (28). Unfortunately, these diets were also hypercaloric, and it is not clear how much of the changes noted are a result of the hypercaloric nature of the diets and how much is related to the increased sucrose content of the diets. However, it is interesting that insulin

sensitivity and average daily sucrose intake were significantly negatively correlated ($r = -.52$; $P < .01$) before dietary intervention, and this correlation was enhanced after hyperalimentation with sucrose ($r = -.95$; $P < .05$). Subsequent studies by the same group identified fructose as the moiety responsible for the impaired insulin binding and insulin sensitivity induced by sucrose (29).

CONCLUSION

In conclusion, there is evidence that increasing dietary sucrose consumption can significantly increase postprandial glucose, insulin, TG, and fasting total and VLDL TG and cholesterol concentrations and can significantly decrease HDL-chol concentrations. The fact that similar changes have been demonstrated to occur in normal subjects (3–7) and patients with endogenous hypertriglyceridemia (8–10,26) and NIDDM (17,18) suggests that these findings should be viewed as the expected sequelae of such diets. Furthermore, these deleterious effects on carbohydrate and lipid metabolism can occur at levels of dietary sucrose comparable to those consumed by the average American adult (17% of total calories; 20). It is believed that elevated plasma and VLDL TG concentrations may predispose otherwise healthy individuals to CAD, and there is evidence that high plasma TG concentrations are involved in the pathogenesis of CAD in diabetes (30–32). Similarly, published evidence indicates that elevations in plasma glucose and insulin levels constitute definite risk factors favoring the development of CAD (33,34). Finally, changes in the LDL-chol–to–HDL-chol ratio observed when dietary sucrose is increased are strongly associated with increased incidence and prevalence of CAD.

Although it could be argued that many of the changes may be modest in magnitude, the changes may be of great clinical significance. This may be particularly true given the multiplicity of the deleterious metabolic effects that have been described to occur when dietary sucrose consumption is increased. The fact that all studies do not show these deleterious effects does not negate the positive data. It is likely that the magnitude of the deleterious effects will vary with individual patients, baseline status, and amount of sucrose. Because current data do not permit the prediction of which patients may be adversely affected, perhaps the best advice is to limit sucrose consumption, be aware of the potential deleterious effects, monitor patients closely, and modify sucrose consumption appropriately in accordance with any change in the patient's metabolic status.

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