SUCROSE FEEDING IN MAN

Effects on Lipolysis and Antilipolytic Action of Insulin in the Adipose Tissue

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Abstract. In four patients with hyperlipoproteinemia and in one with a normal serum lipoprotein pattern 800 kcal of the daily caloric intake were replaced by sucrose for two weeks. Studies of the adipose tissue metabolism in vitro showed that the lipid synthesis from glucose, the basal as well as the noradrenaline-stimulated lipolysis, were considerably increased as compared to the controls. Furthermore, no antilipolytic effect of a physiological concentration of insulin was found. It was suggested that sucrose feeding induces changes in adipose tissue metabolism which may be of importance for the increased triglyceride levels noted in these patients.

The mechanisms behind the endogenous (carbohydrate-induced) hyperlipidemia are basically unknown. It is well known, however, that in patients with endogenous hyperlipidemia the degree of hyperlipoproteinemia can be modified by the diet. Furthermore, an increase in the plasma triglycerides is a normal response in almost every subject on a high carbohydrate diet.

In a recent study of patients with or without hyperlipoproteinemia (3) 800 kcal of the daily caloric intake were replaced by sucrose for 14 days. It was reported in that study that the sucrose feeding increased the triglyceride level, the plasma insulin level as well as the adipose tissue lipoprotein lipase activity in the normolipoproteinemic subjects. The latter effects would tend to inhibit lipid mobilization from the adipose tissue as well as to increase the elimination of the triglycerides. Since the increase in the hepatic glyceride–fatty acid synthesis was not of a sufficient order of magnitude to explain the increased triglyceride level it seems that the effect of sucrose feeding on adipose tissue metabolism should be studied. In the present communication some initial results of such studies are presented.

MATERIAL AND METHODS

The five patients subjected to sucrose feeding were admitted to the hospital for an operation of uncomplicated gall bladder disease. The liver function was normal according to our previous definition (3). None of the patients had any known disease apart from the gall bladder disease and in pertinent cases hyperlipoproteinemia. Clinical data of the patients are given in Table I. The plasma lipoprotein pattern was classified according to Fredrickson and Lees (7) using lipoprotein electrophoresis on agarose gel (13).

The patients subjected to sucrose feeding were hospitalized for 20 days. In the morning after the day of admission fasting capillary blood and heparinized venous blood samples were drawn for subsequent determinations of plasma insulin (10), triglycerides (4) and for lipoprotein electrophoresis (13). The patients were then given sucrose, 200 g/day from the third day through day 17. The ordinary hospital diet consists of an average of 2 500 kcal, distributed as 500 kcal protein, 900 kcal fat and 1 100 kcal carbohydrates, mainly as starch. With the aid of a dietician approximately 800 kcal (protein 160, fat 290 and carbohydrates 350 kcal) of the daily food intake were replaced by 200 g sucrose. Throughout the sucrose feeding period blood samples were drawn for the determination of triglycerides and plasma insulin. The patients were operated upon on day 19 after overnight fasting. Anesthesia was given as hexobarbital, nitrous oxide, oxygen and succinyl choline. Specimens of subcutaneous adipose tissue were obtained as soon as the abdominal cavity had been opened. The results obtained with these specimens are in the present study compared to the results previously obtained in this laboratory with specimens from patients who had not been subjected to carbohydrate feeding. Clinical data of part of the control material has
Table I. Clinical data of patients subjected to sucrose feeding for 14 days

<table>
<thead>
<tr>
<th>Subject no.</th>
<th>Before sucrose feeding</th>
<th>After sucrose feeding</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lipoprotein pattern^a</td>
<td>Triglycerides</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(mg/100 ml)</td>
</tr>
<tr>
<td>1</td>
<td>N</td>
<td>123</td>
</tr>
<tr>
<td>2</td>
<td>II A</td>
<td>131</td>
</tr>
<tr>
<td>3</td>
<td>II B</td>
<td>232</td>
</tr>
<tr>
<td>4</td>
<td>IV</td>
<td>198</td>
</tr>
<tr>
<td>5</td>
<td>II B</td>
<td>344</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td>206</td>
</tr>
</tbody>
</table>

^a Classified according to Fredrickson and Lees (7).

already been described in detail (11). These patients were operated upon for uncomplicated gall bladder disease or exploratory laparotomy after overnight fasting.

The incubation procedure in vitro has been described in detail previously (15). Briefly, small fragments, total weight 300–500 mg, were incubated in 2.0 ml Parker's medium 199 (Statens Bakteriologiska Laboratorium, Stockholm, Sweden) modified to a glucose concentration of 1.0 mM for 2 hours at pH 7.4 in the presence of 0.15 µC D-(1-^14C) glucose (New England Nuclear Corp., Frankfurt am Main, West Germany) and with or without the indicated concentrations of noradrenaline (Astra, Södertälje, Sweden) or insulin (recrystallized pork insulin, Vitrum, Stockholm, Sweden). The release of glycerol was taken as an index of the lipolysis and was determined enzymatically (12). The lipids were extracted with chloroform methanol (2:1, v/v) as described by Folch et al. (6) and the radioactivity in the chloroform phase was determined in a Packard Tri-Carb liquid scintillation spectrometer. Quenching was corrected for by means of internal standardization. Glyceride glycerol was determined according to Carlson (4). Mean cell size was determined on cells isolated with collagenase as described in detail elsewhere (16).

RESULTS

Since it now seems well established that adipocyte size is an important parameter for the rates of lipid synthesis and lipid mobilization in human adipocytes (1, 5, 8, 11), the data from the controls as well as those obtained after sucrose feeding were related to the mean cell size of the specimens. The control material consisted of individuals who had not been subjected to the carbohydrate-rich diet. Clinical data of part of this material has previously been published (11).

![Fig. 1. Incorporation of (1-^14C) glucose into the total lipids of specimens of adipose tissue obtained in connection with sucrose feeding (•, regression line \(y = 0.16x - 3.46\)) and in the controls (▲, regression line \(y = 0.16x - 9.40\)). Mean cell size was determined on isolated cells.](image1)

![Fig. 2. Top. Basal lipolysis in specimens of human adipose tissue obtained in connection with sucrose feeding (•, regression line \(y = 1.14x - 84.11\)) and in the controls (▲, regression line \(y = 0.51x - 32.12\)). Bottom. Increment in glycerol release induced by 5 µM noradrenaline in specimens from sucrose-fed individuals (•, regression line \(y = 1.06x + 61.62\)) and in the controls (▲, regression line \(y = 3.61x - 251.84\)). Mean cell size was determined on isolated cells.](image2)
Table II. Effect of insulin on the noradrenaline-stimulated lipolysis in specimens of human adipose tissue obtained after sucrose feeding for 14 days

<table>
<thead>
<tr>
<th>Subject no.</th>
<th>Noradrenaline</th>
<th>Noradrenaline and insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>212.1 ± 9.2</td>
<td>219.0 ± 34.1</td>
</tr>
<tr>
<td>2</td>
<td>240.3 ± 11.6</td>
<td>244.1 ± 6.1</td>
</tr>
<tr>
<td>3</td>
<td>149.1 ± 10.0</td>
<td>185.1 ± 5.8</td>
</tr>
<tr>
<td>4</td>
<td>284.3 ± 8.2</td>
<td>285.1 ± 1.3</td>
</tr>
<tr>
<td>5</td>
<td>140.7 ± 2.3</td>
<td>134.8 ± 1.3</td>
</tr>
</tbody>
</table>

The incubations were performed for 2 hours in the presence of noradrenaline (5·10⁻⁴ M) and insulin (10² μU/ml), respectively. Results ± S.E.M. of duplicate determinations.

Lipid synthesis from glucose. In agreement with previous studies from carbohydrate-fed individuals (14) the rate of glucose conversion to lipids was for all cell sizes considerably enhanced as compared to the controls (Fig. 1). Addition of insulin (10² μU/ml) increased the incorporation of glucose by about 25% in the specimens with the smallest mean cell size.

Lipid mobilization. Sucrose feeding seems to increase the basal lipolysis considerably, and particularly in the larger adipose cells (Fig. 2, top). Furthermore, the glycerol increment induced by noradrenaline was considerably greater in the specimens obtained after sucrose feeding (Fig. 2, bottom). The apparent convergence of the regression lines is due to one subject (no. 5). Thus the rate of glyceride turnover in adipose tissue increased after sucrose feeding.

The antilipolytic effect of insulin at physiological concentrations (10² μU/ml) was also studied. As shown in Table II no effect of insulin at all was noted in the specimens from the sucrose-fed individuals. In the control material this concentration of insulin consistently inhibited the noradrenaline-stimulated lipolysis by at least 25–30% (11).

DISCUSSION

In a previous report (3) it was found that the sucrose feeding for 14 days used in the present study resulted in increased levels of plasma insulin and triglycerides. It was also reported that the lipoprotein lipase activity rose, which would lead to an increased uptake of triglycerides in the peripheral tissues. This finding, together with the fact that the increase in the fatty acid synthesis in the liver was rather limited, makes the adipose tissue a probable site for the provision of the substrate for the lipoprotein synthesis.

Most previous studies of human adipose tissue in connection with dietary manipulations have been concerned with the effect on lipid accumulation rather than lipid mobilization. Although no study with rat adipose tissue in connection with carbohydrate feeding is directly comparable to the present study it seems that the results obtained have varied between different laboratories. Braun and Fábray (2) reported that a high carbohydrate diet increased the lipolysis and the adenyl cyclase activity, while Gorman et al. (9) were unable to find this. Our findings of an increased lipolytic response would be consistent with an increased adenyl cyclase activity in connection with sucrose feeding. An unexpected finding was the complete loss of antilipolytic action of insulin at a concentration at which insulin has been consistently found to exert this action (11). The reason for this “insulin resistance” in connection with sucrose feeding is unknown. Since a stimulatory effect was found on the site of lipid accumulation, this dissociation of the actions of insulin does not seem to be due to any change in the insulin-receptor interaction.

To summarize, it seems that sucrose feeding leads to an increased rate of basal as well as noradrenaline-stimulated lipid mobilization, a loss of antilipolytic effect of insulin, while the effect of insulin on the side of lipid accumulation is maintained. From these results it would seem that sucrose feeding induced changes in adipose tissue metabolism which may be of importance for the increased triglyceride levels noted in these patients. However, since four of the five patients studied had hyperlipoproteinemia, it is not possible at present to draw valid conclusions whether the changes reported are specific for patients with a derangement in their lipoprotein pattern. The recent studies of Tashimo and Matsuda (17) on the metabolism of adipose tissue from rats with hyperlipidemia due to experimental nephrosis seem to be of relevance for this question. It was shown by these authors (17) that fat cells from nephrotic rats had increased rates of lipid mobilization and, in addition, insulin failed to exert an antilipolytic action. It may well be, then,

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that changes in adipose tissue metabolism are of importance for the development of the hypertriglyceridemia noted in different conditions. Further studies designed to elucidate these questions are at present in progress.

ACKNOWLEDGEMENTS

This investigation was supported by the Swedish Medical Research Council (project B73-03X-3506) and the Swedish Life Insurance Companies.

REFERENCES


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