HYPERINSULINEMIA IN OBESITY: IMPORTANCE OF ADIPOSE TISSUE CELL SIZE

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Obese patients are considered to have a raised insulin level both in the fasting state and during stimulation [1, 2, 12]. Data have been published which indicate that the volume of fat cells is an important factor in regulating the fasting insulin level [3, 4].

The results of the authors' investigations, described below, show that not only the fasting insulin level, but also insulin liberation after stimulation by glucose are related to the size of the adipose tissue cells.

EXPERIMENTAL METHOD

The subjects were 17 persons not previously affected by diabetes or endocrine and other acute diseases. The body weight of these subjects did not change during the investigation. To differentiate the relationship between the index of ideal body weight and the volume of the fat cells, on the one hand, and the insulin level on the other hand, the subjects were divided into groups depending on the size of their fat cells. Under these conditions a volume of 0.45 nl was chosen as the limit beyond which hypertrophy of the fat cells was considered to be present.

Two groups of subjects were formed in this way — with the presence (group 1) and the absence (group 2) of hypertrophy of the fat cells: They differed statistically significantly in relation to size of fat cells but did not differ in relation to mean index of ideal body weight, age, or sex. The index of ideal body weight was calculated as the ratio of the real body weight to the ideal weight.

Before the beginning of the investigation particular attention was paid to the balanced calorie intake of all patients. They had to receive at least 200 g carbohydrates daily with their diet. The standard glucose tolerance test (SGTT; 50 g) was carried out on the hospitalized patients. The blood sugar level of all patients was normal and their triglyceride level did not exceed 250 mg/ml. The sugar level was determined by a modified Hagedorn—Jensen method in capillary blood taken from the lobe of the ear. The serum insulin concentration (immunoreactive insulin — IRI) was determined in venous blood [10, 14]. Adipose tissue was obtained from the subcutaneous layer of the abdominal wall. Cell volume was measured by the method in [8]. The results were subjected to statistical analysis by Student's t test.

EXPERIMENTAL RESULTS

The two groups chosen for study, with fat cells of different volume, differed statistically significantly in the trend of changes in the insulin level during SGTT and in their glucose tolerance. Correlation was found between the volume of the fat cells and the fasting blood insulin concentration. No correlation was found between the insulin level and the index of ideal body weight (Fig. 1). To show that the difference in the glucose level did not affect the difference in insulin liberation, data for a patient with the highest total

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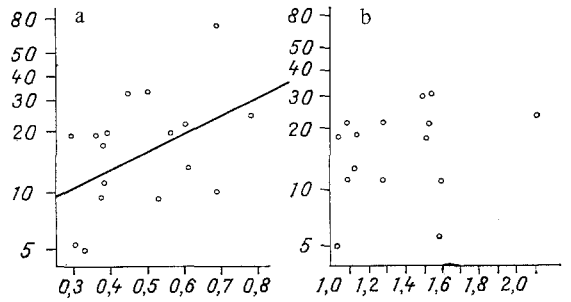

Fig. 1

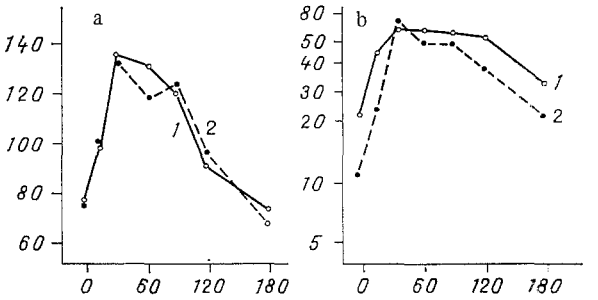

Fig. 2

Fig. 1. Correlation between fasting IRI level (logarithmic scale), volume of fat cells (a), and index of ideal body weight (b). Abscissa: a) volume of fat cells (in nl); b) index of ideal body weight; ordinate, IRI (in microunits/ml).

Fig. 2. Glucose (a) and insulin (b, logarithmic scale) levels during SGTT. Abscissa, time (in min); ordinate: a) glucose concentration (in mg/100 ml), b) IRI (in microunits/ml). 1 and 2) Mean volume of fat cells 0.626 ± 0.101 and 0.367 ± 0.054 nl respectively.

glucose concentration in group 1 and the patient with the lowest total glucose concentration in group 2 were excluded from further analysis. In the remaining patients of the two groups the SGTT revealed an equal mean glucose concentration (Fig. 2). Meanwhile the insulin concentration and mean volume of fat cells continued to differ (Fig. 2). Obesity developed on the basis of hypertrophy and (or) hyperplasia of the adipose tissue, depending in all probability on age at the beginning of the disease [7, 13]. Differentiation between hyperplasia and hypertrophy of fat cells is interesting in view of changes in metabolism associated with an increase in volume of the fat cells [5, 7, 9].

The results of these investigations showed that the fasting insulin level correlates statistically significantly with the volume of the fat cells. This fact has been noted previously by only two groups of workers [3, 4, 13]. In addition, the present investigations showed that the insulin concentration during the SGTT also depends on the volume of the fat cells. Under conditions of comparable glucose tolerance, more prolonged liberation of insulin was observed in subjects with increased volume of their fat cells than in patients with smaller fat cells (Fig. 2).

The greater the volume of the fat cells, the later the insulin concentration reaches a maximum after administration of glucose. Before hyperinsulinemia can be diagnosed in patients with obesity, the fasting insulin level, the maximum level in response to stimulation, and the duration of insulin liberation must all be analyzed. Since hyperinsulinemia in obese patients is reversible after reduction of the body weight, in our opinion it is a secondary process, due to resistance of the hypertrophied fat cells to insulin. Some workers consider that hyperinsulinemia corresponds to the process which induces enlargement of the fat cells and thereby increases resistance to insulin [6, 11, 12]. An increased calorie intake or unbalanced diet may evidently modify hyperinsulinemia. Support for the endogenous origin of hyperinsulinemia is given by the results of the writers' study of patients with hyperlipoproteinemia. Even extreme variations in the composition of the diet of these patients had no effect on their raised serum insulin concentration.

The present investigation thus confirms the importance of fat cell size in regulation of the basal and stimulated insulin secretion levels in patients with obesity.

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