

Effect of insulin on serum lipids in juvenile diabetes

By

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In diabetic children, the effect on serum lipids of insulin by itself and combined with glucose or with Aminosol + glucose has been studied. The level of serum free fatty acids decreased significantly in every case. The cephalin level decreased under the effect of insulin and insulin + Aminosol, whereas it rose after insulin and glucose infusion. The triglyceride level remained unchanged when insulin was applied by itself, and decreased significantly under the effect of insulin + Aminosol, while it showed a rising tendency after insulin + glucose infusion.

In the absence of insulin production, disturbances of glucose metabolism are usually accompanied by changes in the metabolism of lipids. Hyperglycaemia and hyperinsulinism elicit a rise in the triglyceride level [3, 7]. On the other hand, an increase of the protein level has a significant influence on the activity of enzymes playing a role in lipolysis and lipogenesis [16].

In the present study, the serum lipid level has been studied as follows:

- (i) subcutaneous administration of the usual morning dose of insulin on an empty stomach;
- (ii) simultaneous application of insulin and infusion of Aminosol;
- (iii) insulin treatment followed by infusion of 5% glucose solution.

MATERIALS AND METHODS

The material consisted of 19 diabetic children ranging in age from 5 to 20 years. In every case the disease had manifested itself prior to the 14th year of life. The patients had no acetonuria or polyuria. The first test was performed on an empty stomach 12 hours after the evening insulin dose. Fast acting insulin was employed. The intravenously administered Aminosol solution contained a 3,3% mixture of amino acids and 5% glucose. The 5% glucose was administered in 50% Ringer's solution; the dose was 1000 ml for 1.73 sq. m. body surface applied in drip infusion for three hours.

Blood sugar values were determined by the ortho-toluidine method. Blood pH was measured according to Astrup, total lipids by the method of Donhoffer et al. [6]; triglyceride by that of Laurell [11]; phospholipids according to Bartlett [1] and their fractions by the combined method of Gjone [9] and Walaas [17]; and the

free fatty acid level by Dole's procedure [5]. The percentual amounts of the fatty acids in the above fractions were determined by gas chromatography after extraction by the method of Folch et al. [8]. Lipids extracted in this way were separated by thin layer chromatography in a petrol ether: ether: acetic acid (85 : 15 : 3) system. The fractionated lipids were transformed to methylester and estimated by means of a Hewlett-Packard 402 gas chromatograph at 170°C, using a 180 cm long Gas Chrom Q column filled with 8% DEGS. Statistical evaluation was performed by Student's *t* test.

RESULTS

The blood sugar levels are shown in Fig. 1. The lowest value was recorded after insulin had been applied by itself and the highest after insulin + Aminosal infusion. In the cases with a history of diabetes of more

than 6 years a relative resistance to insulin had developed and in the Aminosal experiment the blood sugar level remained in the hyperglycaemic range and the blood pH rose from 7.30 ± 0.020 to 7.37 ± 0.015 .

Serum FFA values are seen in Fig. 2; they displayed a significant fall in every experiment. No remarkable difference was noted in the total lipid and total phospholipid values. Insulin alone caused a significant decrease in the percentual amount of cephalin in the phospholipid fraction, while insulin combined with glucose induced a significant increase in the cephalin content. In all the cases in which Aminosal loading elicited a blood sugar decrease below 180 mg per 100 ml a significant ($p < 5\%$) fall in cephalin content ensued (Fig. 3). The essential fatty acids

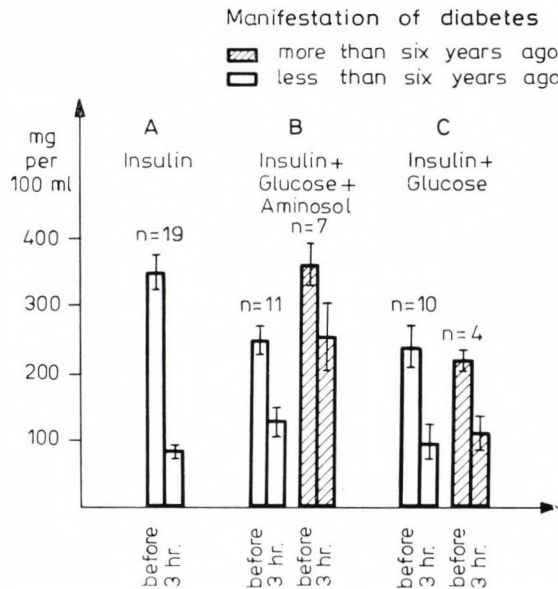


FIG. 1. Blood sugar level

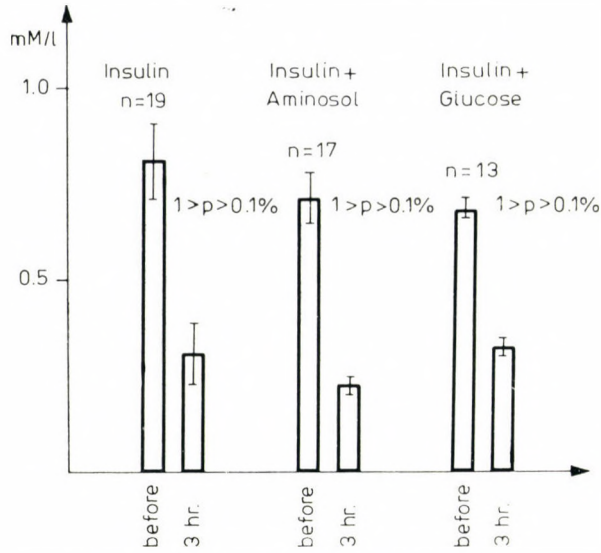


FIG. 2. Serum free fatty acid level

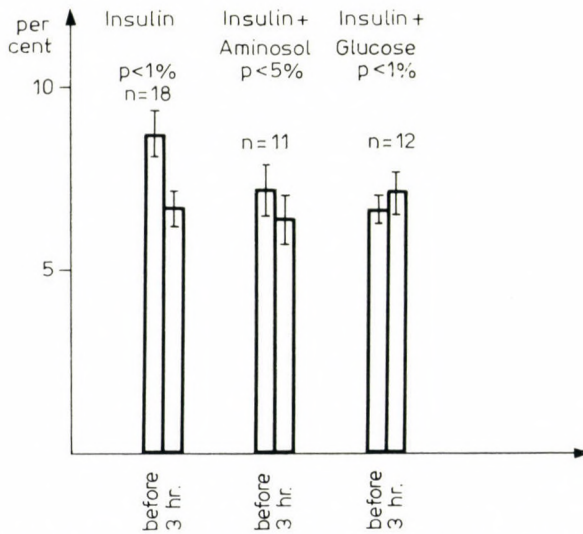
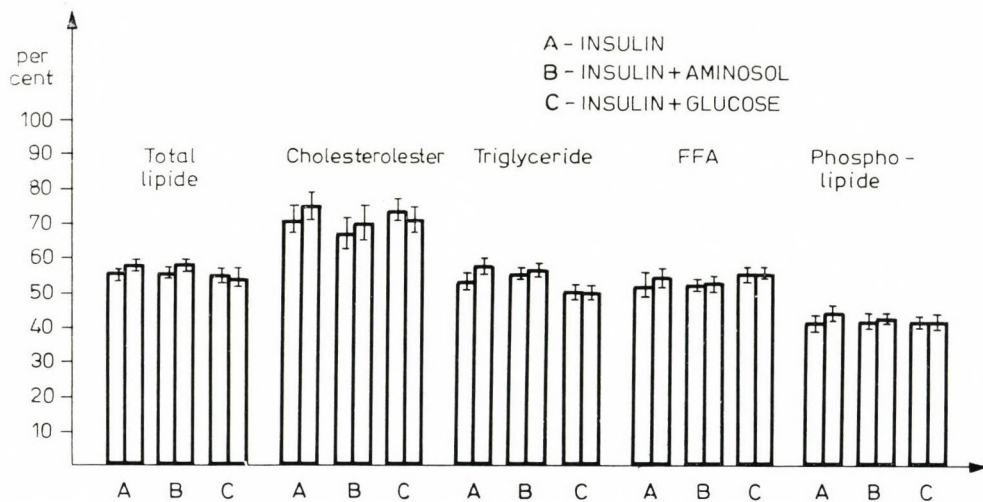


FIG. 3. Cephalin fraction of serum phospholipide, per cent

(linoleic acid, linolic acid, arachidonic acid) showed a rising tendency both on fasting and on Aminosol infusion; these changes did not prove significant. Following glucose infusion the percentual amounts of essen-

tial fatty acids remained unchanged (Fig. 4).

The triglyceride level was not affected by insulin itself (116 ± 22 and 112 ± 32 mg per 100 ml) while the combined effect elicited by glucose



FIRST COLUMNS : before test. Second columns : 3 hr

Fig. 4. Serum triglyceride level, per cent

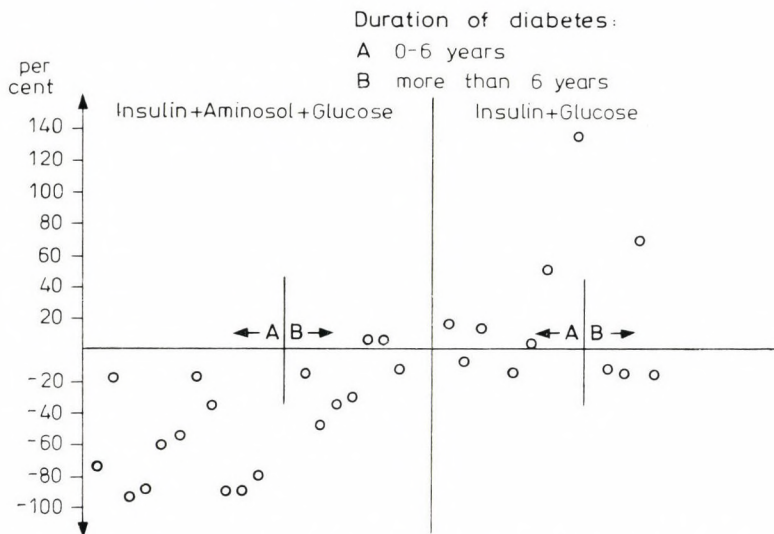


FIG. 5. Duration of diabetes: A 0-6 years B more than 6 years

and Aminosol or glucose is demonstrated in Fig. 5.

It is seen that in each case of diabetes with a history of less than 6 years, Aminosol infusion evoked a significant ($p < 1\%$) decrease in the triglyceride level. However, in two

patients with a history of more than 6 years, a minimum rise in the triglyceride value was noted without a fall in blood sugar. At the same time, the amino acid level in serum and urine was left unchanged and so was the haematocrit.

DISCUSSION

In our patients the cephalin fraction showed a significant fall after the application of insulin and of insulin + Aminosol, while an increase ensued under the effect of glucose. Cephalin was found to promote blood coagulation [4, 13, 15] by enhancing thrombin formation and thus has presumably a role in the development of microangiopathy. In this respect, the change elicited by insulin alone and in combination with Aminosol was favourable and the change caused by glucose infusion was disadvantageous. Arachidonic and linoleic acids are essential components of intracellular phosphatides [14] and an inverse connexion was found between the incidence of vascular obstructions and the serum linoleic acid concentration. In this respect, the rise in the essential fatty acids has to be considered advantageous.

Under the present experimental conditions, the changes observed in the serum triglyceride level must have been correlated with the fat uptake of adipose tissue and with the triglyceride production by the liver [2] where lipogenesis from glucose also takes place [12].

It is assumed that in comparatively recent diabetes, insulin production is increased by amino acids. This may explain that in diabetes of more than six years standing a relative resistance to insulin develops under the effect of Aminosol. Therefore, the changes in the serum lipide level

elicited by insulin + Aminosol are metabolically advantageous but those induced by insulin + glucose act unfavourably.

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