DIURNAL PROFILES OF INTERMEDIARY METABOLITES IN INSULIN-DEPENDENT DIABETES AND THEIR RELATIONSHIP TO DIFFERENT DEGREES OF RESIDUAL B-CELL FUNCTION

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The prevalence of residual B-cell function is almost 100% in patients with a duration of diabetes up to two years. With longer duration the prevalence declines and reaches a level of about 15% after 15 years of disease. This residual B-cell function may play an important role in the stabilization of glucose metabolism. Even a minimal insulin secretion has been found to prevent the development of severe ketoacidosis when insulin administration is stopped. Patients with residual B-cell function also needed less exogenous insulin to obtain a similar degree of metabolic control as found in patients without B-cell function.

Insulin-dependent patients, however, show abnormal diurnal profiles of many products of intermediary metabolism other than just glucose. Therefore, the present study was designed to assess the effect of different degrees of preserved B-cell function on diurnal profiles of intermediary metabolites during daily life conditions.

PATIENTS AND METHODS

Eighteen subjects with insulin-dependent diabetes (IDD) were studied after 6 to 18 months of insulin treatment (clinical data in tab. 1). The diagnosis of insulin-dependent diabetes mellitus was established according to the following criteria at onset:

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random blood glucose higher than 12 mmol/l, significant ketonuria (more or equal to ‑+‑, Ketostix®), body weight below 110% of the ideal for sex and height. All were treated with insulin once daily. For comparison five healthy men were investigated. They were between 22 and 42 years old and their body weight was within normal range (100% ± 10%). None of the subjects studied received medication other than insulin.

The patients were examined in a situation as near to their normal daily life as possible. They were ambulant but took no significant exercise between samples. After an overnight fast, free flowing venous blood samples were taken 30, 10 and 0 min before and 30, 60, 90, and 120 min after breakfast, lunch and dinner. The normal subjects followed the same protocol including the diabetic diet.

Blood glucose concentration was measured using a glucose oxidase method, plasma insulin concentration (IRI) was measured after ethanol precipitation of the antigen-antibody complex. Plasma C-peptide (CPR) was measured using antibody M1230, which has a detection limit of 0.06 pmol/ml. Blood lactate, alanine, glycerol and β-hydroxybutyrate were determined as described previously. Serum insulin binding IgG was also measured.

The β-hydroxybutyrate disappearance rate between 0800-1000 was calculated from the slope of the regression line of loge plasma hydroxybutyrate from 0800-1000. The endogenous insulin response in the same period was calculated as the incremental area under the C-peptide curve using the mean of the three fasting samples as baseline.

Statistical evaluation was made by means of the Mann-Whitney rank sum test comparing mean concentration; coefficients of correlation were calculated using Spearman’s rank correlation test. The level of type I error (2α) was set at 0.05.

As we earlier have shown that a stimulated C-peptide value equal to or above 0.30 pmol/ml characterizes patients who have a better degree of glycemic control than patients with lower or without CPR, the patients with CPR above 0.30 pmol/ml were analyzed separately.

RESULTS

Comparison of diabetics with endogenous insulin secretion above and below 0.30 pmol/ml - Seventeen of the 18 patients had plasma CPR concentrations above 0.06 pmol/ml, and 7 of the patients had one or more CPR values equal to or above 0.30 pmol/ml (tab. 1). The mean ± SEM of the metabolites and hormones measured in the two groups of diabetics is shown in fig. 1. No difference regarding age and duration of disease was found between the groups (tab. 1), but the 7 patients with the highest CPR were treated with significantly less (p<0.01) insulin (mean 0.25 ± SEM 0.04 IU/kg/24 h vs 0.40 ± 0.04 IU/kg/24 h) (tab. 1). No difference (p>0.05) was found between the two groups regarding amount of insulin binding IgG (tab. 1).

Mean C-peptide concentrations were at all sample times different between the two groups. The mean blood glucose was significantly lower in the 7 patients with highest CPR, but the increase in blood glucose seen after meals was not different between the two groups. For all 18 patients a direct correlation was found between mean blood glucose and mean β-hydroxybutyrate concentrations (r = 0.54, p<0.05), but no difference in mean β-hydroxybutyrate concentrations was found between the two groups (fig. 1).