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

STEN MADSBAD  OLE K. FABER  CHRISTIAN BINDER
K. GEORGE M. M. ALBERTI  BARBARA LLOYD

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-depen-
dent diabetes mellitus was established according to the following criteria at onset:

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control.

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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 18.
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) 14. None of the subjects studied received medica-
tion 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 19. Plasma C-peptide (CPR) was measured using antibody
M1230, which has a detection limit of 0.06 pmol/ml 7.

Blood lactate, alanine, glycerol and β-hydroxybutyrate were determined as
described previously 12. Serum insulin binding IgG was also measured 4.

The β-hydroxybutyrate disappearance rate between 08 10 ~10 10 was calculated
from the slope of the regression line of log 10 plasma hydroxybutyrate from 08 10-10 10.
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 16
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).