Relationship Between Pancreatic Insulin Content and Serum C-Peptide Response in Diabetic Subjects

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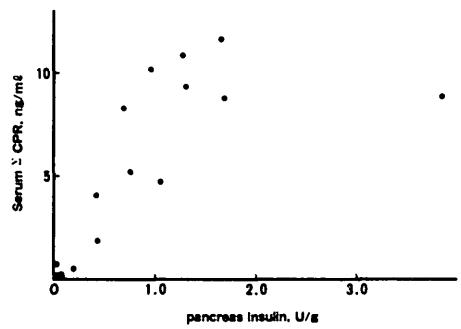

Figure 1—*The integrated C-peptide response (CPR) secretion and pancreatic insulin content are plotted for individual subjects.*

In diabetic subjects, the insulin content of the pancreas is decreased to a variable extent according to the severity or type of diabetes, as previously reported (1–3). The insulin or C-peptide response (CPR) also diminishes in diabetes, especially in insulin-dependent (type 1) diabetes mellitus (4–6). In diabetic subjects, the relationship between plasma immunoreactive insulin (IRI) or CPR response and insulin content in the diabetic pancreas has not been investigated. In this study, the extractable pancreatic IRI content and the plasma CPR response after a breakfast tolerance test were determined and their relationships were studied.

The materials consisted of 15 autopsied diabetic pancreases (11 men, 4 women; mean ± SE 57.6 ± 2.6 yr). Three pancreases were from type I diabetic patients and the rest were from non-insulin-dependent (type II) diabetic patients. Fourteen patients were treated with insulin and 1 patient was treated with diet alone. The patients were examined regularly, once or twice a month, at the outpatient clinic while in relatively good health, underwent the breakfast tolerance test within 3 yr of death, and died in our hospital. These data were collected from 1982 to 1989. The breakfast tolerance test was done as follows. After having the usual breakfast (~400 kcal: 35 g protein, 45 g carbohydrate, 11 g fat), after an overnight fast, blood was taken at 0, 60, and 120 min. The serum CPR level was determined each time and total integrated CPR value at each point was calculated (ΣCPR). Human pancreases obtained at autopsy within 6 h of death were used in this study. For determination of the extractable IRI content of the pancreas, the tail of the pancreas was minced and extracted with acidified alcohol; and the extract was assayed directly after dilution. Serum insulin and CPR levels were determined immunologically. Insulin antibodies were checked with I^{125}-labeled insulin. Subjects with insulin antibodies were excluded. Statistical analysis was done with Students' *t* test after semilogarithmic conversion.

The relationship between the serum ΣCPR and the extractable insulin content of the pancreas was studied. A sigmoidal curve described this relationship ($P < 0.02$; Fig. 1). Serum ΣCPR increased, along with pancreatic insulin content, to ~1.5 U/g insulin, and then it's increase became very mild. The mean ± SE pancreatic insulin content and ΣCPR of nondiabetic pancreases in our laboratory was 2.72 ± 0.34 U/g ($n = 21$) and 12.7 ± 2.0 ng/ml ($n = 7$), respectively.

In type I diabetes, a positive correlation between fasting serum CPR levels and β-cell insulin secretory capacity has been reported (7). The little data available in humans suggest that, in type II diabetes, the pancreatic mass is reduced ~60–70% of normal (8–9). Therefore, in most cases of type II diabetes, the relationship between extractable pancreatic insulin content and ΣCPR response seems to be near plateau.

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Refractory Changes of the Eyes in NIDDM During Treatment

Quantitative Analysis

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Most physicians observe the refractory changes of the eyes in diabetic patients during the course of treatment, although transitory, with or without subjective symptoms. However, the knowledge of quantitative contribution of changes in blood glucose levels to the severity of refractory changes, or the relationships of degree of refractory change with subjective complaint, such as blurred vision, has been poor. To address this issue, we examined the refractive condition of the eyes before treatment and after achieving euglycemia in 10 non-insulin-dependent diabetes mellitus (4 men, 6 women; age range 48–64 yr).

All patients were admitted to the hospital because of hyperglycemia (15.1 ± 4.0 mM; 271 ± 72.0 mg/dl) and three patients were treated with insulin, and seven with oral antidiabetic agents. Fasting plasma glucose (FPG) was monitored during admission. The changes in refraction of the eyes were examined by a single ophthalmologist before and 14 to 30 days after the treatment.

Refractive changes (ΔD) ranged from +0.25 to +2.75 diopter (0.68 ± 0.79) in 9 of 10 patients, with corresponding decrement of FPG (ΔFPG) from 3.6 (64.8) to 15.2 mM (273.6 mg/dl) (7.7 ± 4.0 mM; 138.6 ± 72.0 mg/dl). The changes in refraction (Y) in 20 eyes examined significantly correlated with ΔFPG (X) ($Y = 0.181X - 0.708$, $r = 0.86$, $P < 0.001$; Fig. 1, *left*). Furthermore, the rate of decrement of plasma glucose per day significantly correlated with ΔD ($r = 0.67$, $P < 0.01$; Fig. 1, *right*). Among 10 patients, 3 with ΔD >+0.5 but none with ΔD <+0.5 complained of blurred vision. In the former patients, ΔFPG was >5.6 mM (100 mg/dl), but no critical value on the rate of decrement of plasma glucose could be determined. Blurred vision in these 3 patients appeared 2 wk after the treatment and lasted for several months.

Although the accurate incidence of transitory refractory change in diabetic patients is unknown, it ranges from 5 to 50% in untreated or uncontrolled patients (1). However, our results showed higher incidence of 90%, which is in accordance with the recent observation (2). Moreover, our results indicated that the magnitude of FPG decrement during the treatment was closely associated with

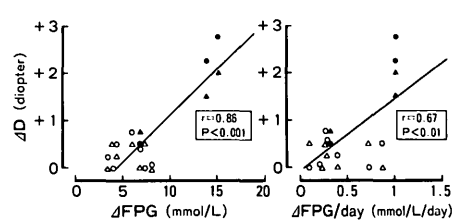

Figure 1—*Correlations between refractive changes and decrements of fasting plasma glucose level (left)* or the rate of decrement of fasting plasma glucose (*right*). ΔD, refractive change; ΔFPG, decrement of fasting plasma glucose during the treatment; ΔFPG/day, the rate of decrement of fasting plasma glucose per day during the treatment. ○, ●, right eye; △, ▲, left eye; ●, ▲, patient with blurred vision; ○, ▲, patient without blurred vision.

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