Effect of Diet Restriction on 24-hr Urinary C-Peptide Excretion in Non-Insulin Dependent Non-Obese Diabetic Subjects

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OSHIMA, Y. Effect of Diet Restriction on 24-hr Urinary C-Peptide Excretion in Non-Insulin Dependent Non-Obese Diabetic Subjects. Tohoku J. exp. Med., 1985, 145 (3), 329-333 — Changes in insulin secretory responses by diet restriction were analyzed in non-insulin dependent non-obese diabetic subjects (NIDDM-NO) as well as in healthy volunteers by determining 24-hr urinary C-peptide immunoreactivity (24-hr UCPR). Insulin sensitivity for glucose utilization was measured by using cyclic somatostatin. Overnight fasting plasma glucose concentrations decreased in NIDDM-NO; however, 24-hr UCPR was reduced in both NIDDM-NO and healthy controls by diet restriction (25 kcal/kg) for 14 days. The level of 24-hr UCPR was higher but insulin sensitivity was lower in NIDDM-NO as compared with those in healthy controls. Therefore, diet restriction may be effective in controlling hyperglycemia and hypersecretion of insulin in NIDDM-NO, but it alone may not improve the reduced insulin sensitivity. —— 24-hr urinary C-peptide excretion; insulin sensitivity; diet restriction; non-insulin dependent non-obese diabetics

A few attempts have been made to elucidate the relationship between 24-hr urinary C-peptide immunoreactivity (24-hr UCPR) and metabolic control in diabetics (Horwitz et al. 1975; Pasquali et al. 1982). However, the previous studies did not observe the changes in 24-hr UCPR after dietary therapy in non-insulin dependent, non-obese diabetics (NIDDM-NO) in comparison with those in healthy subjects. The present study clarifies the differential effects of diet restriction on insulin secretory responses in NIDDM-NO and healthy controls.

SUBJECTS AND METHODS

The subjects in this study were 27 males and 13 females of recently diagnosed diabetics aged ranging from 34 to 79 years (mean = 54.4 years) who did not require insulin therapy, and 4 healthy volunteers (23-42 years old). The body weight of all the subjects ranged within ±18% of the standard weight. None had liver dysfunction or infectious disease. Their creatinine clearance rates were more than 65.0 ml/min.

All the patients were admitted to our hospital for dietary therapy. At first, 2100 kcal diet was given for 3 days, and then therapeutic diet (25 kcal/kg) was given for 14 days.

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Twenty-four-hr UCPR and overnight fasting plasma glucose levels (FPG) were determined before and after the dietary therapy. The insulin sensitivity test was made according to the method of Harano et al. (1977). The procedure was as follows (Fig. 1): glucose (6 mg/kg/min), monocomponent Act Rapid Insulin (Novo, 0.77 mU/kg/min) and cyclic somatostatin (Sigma Chemical, 125 µg in bolus followed by a constant infusion at a rate of 250 µg/hr) were simultaneously infused for over 120 minutes in a fluid volume, 100 ml/hr, through the antecubital vein by a constant infusion pump. Gelatin (0.35% Haemaccel, Hoechst) was added to avoid adsorption of insulin to the bottle wall. Blood was obtained 120 min after beginning the test.

Insulin sensitivity indices (ISI) were calculated as follows: V = KG; V: infusion rate of glucose (6 mg/kg/min); G: steady state plasma glucose level; ISI: $10^3 \times K = V/G \times 10^3$.

Plasma glucose levels were determined by the glucose oxidase method using a Beckman Glucose Analyser (Kadish et al. 1968), and for 24-hr UCPR, a radioimmunoassay Kit for human C-peptide (C-peptide Kit II, Dai-Ichi Radio Isotope Laboratory) was used.

Data were expressed as mean ± S.D. Statistical analysis was performed by Student’s paired and unpaired t test.

Table 1. Changes in body weight and fasting plasma glucose level in diabetic subjects and healthy controls

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<th>before</th>
<th>14 days</th>
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<tr>
<td><strong>Body weight (kg)</strong></td>
<td></td>
<td></td>
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<tr>
<td>Diabetic subjects (n = 40)</td>
<td>54.9 ± 7.6</td>
<td>NS</td>
</tr>
<tr>
<td>Healthy controls (n = 4)</td>
<td>51.1 ± 4.7</td>
<td>NS</td>
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<tr>
<td><strong>Fasting plasma glucose level (mg/100 ml)</strong></td>
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<tr>
<td>Diabetic subjects (n = 40)</td>
<td>168.6 ± 43.7</td>
<td>$p &lt; 0.001$</td>
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<tr>
<td>Healthy controls (n = 4)</td>
<td>87.5 ± 4.5</td>
<td>76.5 ± 2.1</td>
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RESULTS

Changes in body weight and FPG (Table 1)

Both NIDDM-NO and healthy controls showed no significant decrease in body weight. However, FPG significantly \( p < 0.001 \) decreased in NIDDM-NO.

Comparison of the changes in 24-hr UCPR of the NIDDM-NO with those of healthy controls (Table 2)

Both NIDDM-NO and healthy controls showed a significant \( p < 0.001, p < 0.05 \), respectively decrease in 24-hr UCPR excretion by diet restriction. There was no significant difference in the values of 24-hr UCPR between both groups before the dietary therapy. NIDDM-NO, however, showed a higher level of 24-hr UCPR than healthy controls after the dietary therapy \( p < 0.05 \).

ISI (Fig. 2)

ISI of NIDDM-NO, \( (36.5 \pm 20.7) \times 10^3 \), were significantly lower than those of healthy controls, \( (85.8 \pm 32.4) \times 10^3 \).
DISCUSSION

Levin (1980) described that the objective of the diet for lean diabetic patients is to keep body weight stable and to prevent, as much as possible, wide swings from extremely high to extremely low levels of plasma glucose. All the cases of NIDDM-NO in this study showed a decrease in FPG, and the fluctuation of diurnal plasma glucose levels diminished. In terms of these results, this diet regulation appeared to be effective, but plasma glucose levels could not be controlled well with dietary therapy alone in some cases. Seventeen of 40 diabetics were therefore treated additionally with sulfonylurea.

Kaneko et al. (1975) found that C-peptide excretion in urine was increased by stimulation of insulin secretion. It was subsequently demonstrated that the urinary excretion rate of C-peptide may serve as a practical indicator for estimating the secretion rate of insulin in normal and diabetic subjects (Horwitz et al. 1977; Meistas et al. 1981, 1982). Furthermore, 24-hr UCPR excretion could be an indicator of the metabolic information for diabetes therapy (Pasquali et al. 1982). In the present study, the values of 24-hr UCPR were followed up as a marker to evaluate the effect of diet restriction on the insulin secretory rate. Significant decreases in 24-hr UCPR were seen in both NIDDM-NO and healthy subjects. A significant reduction of the plasma glucose level was observed in NIDDM-NO, but not in healthy subjects. Therefore, it was thought that healthy subjects so responded to diet restriction as to maintain the plasma glucose level within the physiologic range by means of diminishing insulin secretion. Hyperglycemia of NIDDM-NO tended to subside with diet restriction to some extent. However, its control was insufficient during the observation period even after diet restriction. The high levels of 24-hr UCPR in NIDDM-NO were thought to be induced by uncontrolled plasma glucose levels.

Harano et al. (1977) reported that reduced insulin sensitivity could not be improved with dietary therapy in his evaluating system using cyclic somatostatin to suppress the endogenous secretions of insulin, glucagon and growth hormone in adult-onset, non-obese, untreated diabetics. In the present study, ISI in NIDDM-NO, obtained according to the method of Harano et al. (1977), were significantly lower than those in healthy subjects. These results appear to be important for the high level of 24-hr UCPR in NIDDM-NO.

A previous study (Ichihara et al. 1975) revealed that restricted diet could improve the β-cell function of the pancreatic islet in adult-onset non-obese diabetics. The observation period in the present study seemed to be too short to elucidate this point.

It was concluded that diet restriction in NIDDM-NO was effective to control their hyperglycemia and hypersecretion of insulin, but might not be able to improve the reduced insulin sensitivity which must participate in this type of abnormalities.
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References


