Insulin Resistance in Japanese Adolescents with Type 2 Diabetes Mellitus

Yukashi Ohki, Megumi Kishi, Hiromi Orimo and Takuya Ohkawa

Department of Pediatrics, Nippon Medical School

Abstract

An oral glucose tolerance test (O-GTT) was conducted in 22 patients with type 2 diabetes mellitus whose ages at onset were less than 18 years old. They were classified into 2 groups, obese and non-obese at onset, and insulin secretory function was compared with that of a non-obese healthy group. The results show that, in the group of obese subjects with type 2 diabetes mellitus, both values of fasting IRI and ΣIRI were significantly higher than those in the healthy group. In the non-obese adolescent group with type 2 diabetes mellitus, both values of fasting IRI and ΣIRI were also significantly higher than those in the healthy group, although the difference was not as prominent as in the obese subjects with type 2 diabetes mellitus.

It was revealed that insulin resistance is present not only in obese adolescents with type 2 diabetes mellitus, but also in non-obese adolescents with type 2 diabetes mellitus. (J Nippon Med Sch 2004; 71: 88-91)

Key words: type 2 diabetes, insulin resistance, hyperinsulinemia, adolescents, oral glucose tolerance test (O-GTT)

Introduction

Compensatory hypersecretion of pancreatic β cells against insulin resistance in obese patients is a physiologically important compensatory mechanism to maintain the function of glucose tolerance, and the failure of this compensatory mechanism is thought to cause relative insulin secretory disorders leading to the onset of type 2 diabetes mellitus\(^2\). In contrast to adult cases, there are very few reports on insulin resistance covering the disease period between onset and early-stage type 2 diabetes mellitus in adolescents\(^3\). With this background, we performed an oral glucose tolerance test (O-GTT) in patient groups of non-obese and obese adolescents with type 2 diabetes mellitus and compared their insulin secretory function with that of non-obese healthy group\(^1\).

Materials and Methods

A total of 22 study subjects (including 12 males and 10 females) were recruited from among patients with type 2 diabetes mellitus whose ages at onset were less than 18 years old, and who visited our department for medical examination in the period from January to December 2002. Their ages, ages at onset and morbidity periods were 12~25 (17.8±3.4 years), 8~17 (13.4±2.6 years) and 3 months~12
years (4.6 ± 2.9 years), respectively. Of these patients, 17 were obese and 5 were non-obese at the onset of the disease. The family history of type 2 diabetes mellitus (relative within the second degree) was noted in about 2/3 of the patients. Half of the patients were receiving drug therapy, and the mean value of HbA1c in the last six months was 7.7 ± 2.7%.

They were classified into 2 groups, obese and non-obese at onset, and insulin secretory function was compared with that of 24 non-obese healthy subjects aged 12~16 years. The percent overweight at onset in the obese, non-obese type 2 diabetes and healthy group were 57.0 ± 23.4%, 32 ± 35% and 26 ± 1.1%, respectively.

Diabetes mellitus was diagnosed according to WHO criteria. O-GTT was conducted by administering glucose at a fixed dose of 1.75 g/kg per standard body weight, and blood samples were collected 0, 30, 60, 90, 120, 150, and 180 minutes after administration. The Σ values were calculated by the sum of the values at 0, 30, 60, 120 and 180 minutes after administration for the following 3 clinical variables. Blood glucose (BG) was determined using the glucose oxidase method, while the insulin (IRI) and the C-peptide (CPR) values were determined using the RIA solid phase technique.

Obesity was diagnosed when the weights of the subjects were more than 20% over normal values, based on the data collected in a 1990 nationwide survey of school children.

For the between-subgroup-comparison of the 3 groups of healthy adolescents, non-obese and obese adolescents with type 2 diabetes mellitus, Dunkan’s multiple range test (significance criteria of P < 0.005) was used.

Results

The IRI values of the fasting condition for each group are shown in Fig. 1. The fasting IRI values were 37.3 ± 28.8 μU/ml for the obese diabetic group and 15.0 ± 5.3 μU/ml for the non-obese diabetic group, showing significantly higher values with a statistical significance (P < 0.05) even in the non-obese diabetic group compared to the value of 10.3 ± 6.4 μU/ml in the healthy group. The ΣIRI values (Fig. 2) were 446.8 ± 380.3 μU/ml in the obese diabetic group and 227.8 ± 239.4 μU/ml in the non-obese diabetic group, also showing higher values with a statistical significance (P < 0.05) even in the non-obese diabetic group compared to the value of 171.2 ± 66.1 μU/ml in the healthy group.

Discussion

The onset of diabetes mellitus not only of type 1 but also of type 2 in children and adolescents has been successively reported in recent years. However, type 2 diabetes mellitus in obese adolescents, the disease stage of which is thought to be an early phase differing from that in adult patients, has been little investigated considering whether insulin is hypersecreted due to insulin resistance or secretory dysfunction. There are no reports on type 2 diabetes mellitus in non-obese adolescents in this mechanism-based context.

Hyperinsulinemia is thought to be a compensatory reaction caused by insulin resistance, except for insulin hypersecretion due to insulinoma or insulin secretion disorder due to liver dysfunction.
Therefore, with obesity or type 2 diabetes mellitus where the function of insulin secretion is maintained at a normal level, hyperinsulinemia reflects the presence of insulin resistance. With this background, we conducted an oral glucose tolerance test (O-GTT) in adolescents with type 2 diabetes mellitus and compared their insulin secretory function with that of an age-matched healthy group to examine the presence or absence of insulin resistance in non-obese and obese adolescents with type 2 diabetes mellitus. The results show that the type 2 diabetic obese group showed significantly higher values of both fasting IRI and ΣIRI compared to those of the healthy group, and higher fasting IRI and ΣIRI values were also observed even in the type 2 non-obese diabetic group, although the difference was not as prominent as found in the obese diabetic group. The results confirm the presence of insulin resistance not only in obese adolescents with type 2 diabetes mellitus but also in non-obese adolescents with type 2 diabetes mellitus. In our section, therapeutic protocols to treat children with type 2 diabetes have been designed separately for obese and non-obese patients until now. These study results suggest that insulin resistance is primarily involved in type 2 diabetes mellitus in adolescents as
a common pathogenic basis, irrespective of obesity or non-obesity, and we developed a unified therapeutic protocol to treat both patient types (Fig. 3).

Efforts will continue to establish a better therapeutic methodology by accumulating details of treatment cases according to the newly designed therapeutic protocol for children and adolescents with type 2 diabetes mellitus.

References


(Received, September 1, 2003)
(Accepted, September 26, 2003)