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Factors responsible for elevation of 1-h postchallenge plasma glucose levels in Japanese men

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ABSTRACT

The 1-h postchallenge plasma glucose (1-h PG) level is considered to be a good index of the development of glucose intolerance and type 2 diabetes as well as of diabetic complications. In some cases, in Japanese, 1-h PG is elevated despite normal fasting glucose during oral glucose tolerance test (OGTT), but the factors responsible remain unclear. In the present study, subjects with normal glucose tolerance (NGT), isolated impaired fasting glucose (IFG), and isolated impaired glucose tolerance (IGT) were divided into subgroups at 1-h PG of 10.0 mM, and the four indices of insulin secretion and insulin sensitivity were compared. In all three categories, the insulinogenic index in subjects with elevated 1-h PG was remarkably lower than in those without elevated 1-h PG. In addition, the insulinogenic index was the strongest factor in elevated 1-h PG according to the multiple regression analysis. Interestingly, one third of the NGT subjects enrolled in this study had elevated 1-h PG. These subjects showed significantly elevated area under the curve of glucose (G-AUC) compared to NGT subjects without 1-h PG elevation. Thus, elevated 1-h PG in Japanese subjects indicates mildly impaired glucose tolerance due to decreased early-phase insulin secretion.

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1. Introduction

Type 2 diabetes is characterized by both decreased insulin secretion and reduced insulin sensitivity [1–3]. Some patients with glucose intolerance leading to type 2 diabetes show elevated postchallenge plasma glucose without elevated fasting glucose during oral glucose tolerance test (OGTT) [4–6]. Although elevated 1-h postchallenge plasma glucose involves a different regulatory mechanism than 2-h postchallenge plasma glucose (2-h PG), 1-h postchallenge plasma glucose (1-h PG) is also as reliable an index of glucose tolerance as 2-h PG generally [7,8]. However, the relevance of 1-h PG and 2-h PG for diabetes screening is controversial [9,10]. It has been reported that subjects with 1-h PG higher than 10.0 mmol/l show higher risk of developing diabetes than subjects with lower 1-h PG [11]. In addition, 1-h PG higher than 11.2 mmol/l was found to be an independent risk factor for mortality in cardiovascular disease [12–14]. It was recommended in a

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number of studies that subjects having normal fasting plasma glucose at OGTT together with high 1-h PG are followed as carefully as IGT subjects in cases of higher frequency of elevated HbA1c, hypertension, family history of diabetes, or peripheral vascular involvement [15]. In addition, 1-h PG is used in diagnosis of gestational diabetes mellitus (GDM) and risk of macrosomia and other perinatal complications [16,17].

In the present study, the insulin secretion and insulin sensitivity indices of Japanese subjects undergoing OGTT in three WHO categories, normal glucose tolerance (NGT), isolated impaired fasting glucose (IFG) and isolated impaired glucose tolerance (IGT), subdivided at 1-h PG of 10.0 mmol/l were evaluated and compared.

2. Subjects and methods

2.1. Subjects

We recruited subjects undergoing OGTT because of positive urine glucose test, >5.0% HbA1c level, >5.6 mmol/l fasting plasma glucose level, and family history of diabetes at initial examination for medical check-up at Kyoto University Hospital, Ikeda Hospital, Kansai Electric Power Hospital, Kansai Health Management Center, and Kyoto Preventive Medical Center from 1993 to 2005. Subjects in the three categories of glucose tolerance, NGT ($n = 179$: fasting plasma glucose (FPG) level < 6.1 mmol/l and 2-h PG level < 7.8 mmol/l), isolated IFG ($n = 44$: FPG level of 6.1–7.0 mmol/l and 2-h PG < 7.8 mmol/l), and isolated IGT ($n = 103$: FPG level < 6.1 mmol/l and 2-h PG level of 7.8–11.1 mmol/l) according to the diagnostic criteria of World Health Organization in 1998 [18] were enrolled in the study. All subjects were men with no signs of hypertension, hepatic or renal dysfunction, endocrine or malignant disease, engaging in heavy exercise, history of gastrectomy, or history of medication known to affect glucose metabolism. The study was designed in compliance with the ethics regulations of the Helsinki Declaration. After the subjects fasted overnight for 10–16 h, standard OGTT with 75 g glucose was administered according to the National Diabetes Data Group recommendations [16].

The three WHO categories of glucose tolerance were divided into subgroups at 1-h PG of 10.0 mmol/l in this study: NGT with higher 1-h plasma glucose (NGT-HG: NGT criteria and 1-h PG ≥10.0 mmol/l), NGT with lower 1-h plasma glucose (NGT-LG: NGT criteria and 1-h PG <10.0 mmol/l), isolated IFG with higher 1-h plasma glucose (IFG-HG: IFG criteria and 1-h PG ≥10.0 mmol/l), isolated IFG with lower 1-h plasma glucose (IFG-LG: IFG criteria and 1-h PG <10.0 mmol/l), isolated IGT with higher 1-h plasma glucose (IGT-HG: IGT criteria and 1-h PG ≥10.0 mmol/l), and isolated IGT with lower 1-h plasma glucose (IGT-LG: IGT criteria and 1-h PG <10.0 mmol/l).

2.2. Laboratory examination

Blood samples were collected at 0, 30, 60, and 120 min after OGTT, and plasma glucose and serum insulin levels were measured for all subjects. Plasma glucose and serum insulin levels at 90 min were measured for 75 NGT subjects. Blood samples for measurements of HbA1c, total cholesterol, HDL cholesterol, and triglycerides were drawn after an overnight fast.

The plasma glucose level was measured by glucose oxidase method using the Hitachi Automatic Clinical Analyzer 7170 (Hitachi, Tokyo, Japan). Serum insulin was measured by two-site radioimmunoassay (Insulin Riabead II, Dainabot, Tokyo, Japan) as reported previously [19]. Serum total cholesterol and triglycerides levels were measured as reported previously [20].

2.3. Measurement

Basal insulin secretion and sensitivity were evaluated by HOMA β-cell and HOMA-IR [21,22], respectively. Early-phase insulin secretion and systemic insulin sensitivity during OGTT were evaluated by insulinogenic index [23] and ISI composite [24,25]. The calculations were as follows:

$$\text{HOMA } \beta\text{-cell} = \frac{20 \times \text{fasting serum insulin level (FI) (mU/l)}}{\text{fasting plasma glucose level (FPG) (mmol/l)} - 3.5}$$

$$\text{HOMA-IR} = \frac{\text{FI (mU/l)} \times \text{FPG (mmol/l)}}{22.5}$$

$$\text{Insulinogenic index} = \frac{\text{30-min insulin} - \text{FI (pmol/l)}}{\text{30-min plasma glucose} - \text{FPG (mmol/l)}}$$

$$\text{ISI composite} = \frac{10{,}000}{[\text{FPG (mg/dl)}\ \text{FI (mU/ml)} \times \text{mean OGTT glucose (mg/dl)} \times \text{mean OGTT serum insulin (mU/ml)}]^{0.5}}$$

2.4. Statistical analysis

All analyses were performed using STATVIEW 5 system (Stat View, Berkeley, CA). Differences between two groups were assessed by unpaired *t*-test in terms of age, BMI, plasma glucose level, serum insulin level, HbA1c, triglyceride, total cholesterol, insulinogenic index, ISI composite, HOMA-IR, and HOMA β-cell. We used simple regression analysis and multiple regression analysis for comparison of the relationship between 1-h PG and the indices of insulin secretion and sensitivity. Probability (p) values less than 0.05 were considered statistically significant. Data are presented as mean ± S.E.

3. Results

Table 1 shows the clinical and metabolic characteristics of the six subgroups. NGT-HG had higher average age, BMI, FPG, 2-h PG and HbA1c than NGT-LG. IFG-HG had higher BMI than IFG-LG. IGT-HG had higher BMI, FPG, 2-h PG, 1-h insulin and HbA1c than IGT-LG. There were no significant differences in insulin (fasting and 2-h), triglycerides, total cholesterol and HDL-cholesterol levels between the two subgroups of NGT, isolated IFG, and isolated IGT.

The insulin secretion indices of insulinogenic index and HOMA β-cell indices in the three WHO categories are shown in

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