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Indexes of Insulin Resistance using the Oral Glucose Tolerance Test (O-GTT) in Japanese Children and Adolescents

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Abstract

An oral glucose tolerance test (O-GTT) was conducted in 96 non-obese healthy children (7～11 years old) and adolescents (12～16 years old) to obtain the index of insulin resistance from the insulin (IRI) and C-peptide (CPR) values of fasting, 2-hour postload conditions and the Σ values, and the homeostasis model assessment ratio (HOMA-R) by assuming the value of the mean + 2SD to be the upper limit of the normal value for each clinical variable.

The results show that the adolescents, whose insulin resistance is thought to increase, showed higher IRI and CPR values of the 2-hour postload condition and Σ values compared to those of the children, but there were no differences between the 2 age groups in the values of the fasting condition, as well as in the HOMA-R values which were calculated from the fasting values.

These findings indicate that there is a limitation in using fasting values to judge insulin resistance. Instead, using the 2-hour postload values and/or the Σ values is more appropriate.
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Key words: insulin resistance, hyperinsulinemia, oral glucose tolerance test (O-GTT), homeostasis model assessment ratio (HOMA-R)

Introduction

In association with the increasing population of children and adolescents with obesity and/or type 2 diabetes mellitus[1–4], insulin resistance in these patients becomes problematic. However, there are very few reports on the standard value of insulin resistance[5]. Hyperinsulinemia is thought to result from a compensatory reaction induced by insulin resistance, except with insulin hypersecretion due to insulinoma or with insulin excretion disorder due to liver dysfunction.

This study obtains the indexes of insulin resistance in children and adolescents based on the results of the oral glucose tolerance test (O-GTT) in non-obese healthy children and adolescents.

Materials and Methods

An oral glucose tolerance test (O-GTT) was conducted in 96 non-obese healthy subjects classified into 2 age groups consisting of pre-pubertal children (7～11 years old), and adolescents (12～16 year old) (36 males and 36 females; 12 males and 12 females, respectively).

The weight and height of the subjects in the 2 age groups were within ± 20% of normal values, based

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Table 1 Values of BG, IRI, CPR and HOMA-R (mean ± SD) in non-obese healthy children and adolescents by O-GTT

Age		0min	30min	60min	120min	180min	Σ	HOMA-R
7～11 years	BG (mg/dl)	86.7 ± 5.8	131.9 ± 17.8	120.4 ± 17.0	103.5 ± 16.0	84.5 ± 13.2	528.8 ± 41.0	
	IRI (μU/ml)	11.0 ± 7.5	39.8 ± 19.2	32.7 ± 18.6	24.5 ± 14.2*	14.4 ± 11.2	122.0 ± 38.9**	2.4 ± 0.2
	CPR (ng/ml)	1.5 ± 0.2	5.0 ± 1.3	5.1 ± 0.9	4.5 ± 1.1*	2.6 ± 0.8	18.9 ± 4.5**	
12～16 years	BG (mg/dl)	86.9 ± 6.9	133.7 ± 11.7	127.8 ± 21.6	110.7 ± 18.1	94.7 ± 15.3	558.4 ± 46.8	
	IRI (μU/ml)	10.3 ± 6.4	49.1 ± 24.6	42.5 ± 23.3	42.3 ± 25.4*	25.9 ± 16.9	171.2 ± 66.1**	2.2 ± 0.2
	CPR (ng/ml)	2.0 ± 0.4	6.1 ± 1.6	6.9 ± 1.7	6.8 ± 1.7*	4.8 ± 1.6	26.9 ± 7.4**	

(*, **: P < 0.01 between two age groups)

on data collected in a 1,990 nationwide survey of school children. There was no significant difference in the mean percent overweight for the 2 age groups (1.8 ± 1.3% for children and 2.6 ± 1.1% for adolescents). And no subjects showed diabetic or impaired glucose tolerance patterns in O-GTT.

O-GTT was conducted by orally administering glucose at the 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. The homeostasis model assessment ratio (HOMA-R) was calculated according to the following equation: fasting IRI (μU/ml) × fasting BG (mg/dl)/405[6]. Student's t-test was used for the statistical analysis.

Results

The results of O-GTT are shown in **Table 1**. In the pre-pubertal age group (7～11 years old), the BG, IRI and CPR values in the fasting condition were 86.7 ± 5.8 mg/dl, 11.0 ± 7.5 μU/ml and 1.5 ± 0.2 ng/mg, respectively, while the 2-hour postpload values were 103.5 ± 16.0 mg/dl, 24.5 ± 14.2 μU/ml and 4.5 ± 1.1 ng/mg, and their Σ values were 528.8 ± 41.0 mg/dl, 122.0 ± 38.9 μU/ml and 18.9 ± 4.5 ng/mg, respectively. The HOMA-R value of this group was 2.4 ± 0.2. On the other hand, in the adolescent age group (12～16 years old), the fasting BG, IRI and CPR values were 86.9 ± 6.9 mg/dl, 10.3 ± 6.4 μU/ml and 2.0 ± 0.4 ng/mg, respectively, while the 2-hour postpload values were 110.7 ± 18.1 mg/dl, 42.3 ± 25.4 μU/ml and 6.8 ± 1.7 ng/mg, and their Σ values were 558.4 ± 46.8 mg/dl, 171.2 ± 66.1 μU/ml and 26.9 ± 7.4 ng/mg, respectively. The HOMA-R value of this group was 2.2 ± 0.2.

Although the adolescent age group showed higher values in both the 2-hour postpload IRI, CPR and Σ values with a statistical significance (P < 0.01 for each value) than those of the pre-pubertal age group, there were no differences in the fasting values between the 2 age groups. In addition, no differences were observed in the HOMA-R values. There were no gender differences in these values for each age group.

The individual values of the mean + 2SD are shown in **Table 2**. Assuming that the values shown in **Table 2** to be the upper limit of the normal range of each clinical variable, the judgment criteria of insulin resistance were estimated to be IRI > 25 μU/ml, CPR > 3.0 ng/mg and HOMA-R > 3.0 in the fasting condition for both age groups, while the following different judgment criteria were considered for the 2 age groups when the 2-hour postload values and Σ values are used: with the 2-hour postload values, IRI > 50 μU/ml and CPR > 7 ng/mg for the prepubertal age group, and IRI > 100 μU/ml and CPR > 10 ng/mg for the adolescent age

Table 2 The mean + 2SD values of BG, IRI, CPR and HOMA-R in non-obese healthy children and adolescents by O-GTT

Age		fasting	120min	Σ	HOMA-R
7～11 years	IRI (μU/ml)	26	52.9	200	2.8
	CPR (ng/ml)	1.9	6.7	27.9	
12～16 years	IRI (μU/ml)	23	93.1	303	2.6
	CPR (ng/ml)	2.8	10.2	41.7	

Table 3 Indexes of insulin resistance in non-obses healthy children and adolescents by O-GTT

Age		fasting	120min	Σ	HOMA-R
7～11 years	IRI (μU/ml)	＞25	＞50	＞200	＞3
	CPR (ng/ml)	＞3	＞7	＞30	
12～16 years	IRI (μU/ml)	＞25	＞100	＞300	＞3
	CPR (ng/ml)	＞3	＞10	＞40	

group; with the Σ values, IRI＞200 μU/ml and CPR ＞30 ng/mg for the pre-pubertal age group, and IRI ＞300 μU/ml and CPR＞40 ng/mg for the adolescent age group (**Table 3**).

Discussion

Insulin resistance in obese and/or type 2 diabetic children and adolescents is a physiological condition in which insulin sensitivity of a target organ of insulin action declines, requiring more insulin to maintain the same extent of insulin action as healthy children and adolescents. This is similar to the phenomena observed in adults. Hyperinsulinemia is thought to result from a compensatory reaction induced by insulin resistance, except with insulin hypersecretion due to insulinoma or with insulin excretion disorder due to liver dysfunction. Therefore, with obesity or type 2 diabetes mellitus, where the function of insulin secretion is maintained at the normal level, hyperinsulinemia reflects the presence of insulin resistance[7].

To confirm insulin resistance, methodologies such as the glucose clamp method[8] and minimal model[9] are available. However, these methods are inconvenient. Therefore, in this study, we conducted the widely used O-GTT in children and adolescents to obtain the index of insulin resistance more simply. In the age adolescent group, where insulin resistance is thought to be augmented[10], significantly higher 2-hour postload IRI and CPR values, as well as higher Σ values, were observed compared to those observed in the pre-pubertal age group, but we observed no differences in the fasting values or in the HOMA-R values that were calculated from the fasting values.

These findings suggest that there is a limitation in using of the values of the fasting condition as an index of insulin resistance, and it is preferable to instead use the 2-hour postload values and/or the Σ values. Although the adiponectin value[11] and the leptin value[12] have recently drawn attention as indices of insulin resistance in years, more convenient indices of insulin resistance were obtained through this study by conducting O-GTT, which is the most widely used in routine medical practice as a basic diabetic examination.

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