INTERNAL MEDICINE

□ ORIGINAL ARTICLE □

Evaluation of Glucose Tolerance, Post-Prandial Hyperglycemia and Hyperinsulinemia Influencing the Incidence of Coronary Heart Disease

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Abstract

Background Recently, the frequency of patients who have glucose intolerance has been increasing in Japan. Glucose intolerance and insulin resistance/hyperinsulinemia are thought to influence the progression of atherosclerosis. The present study examined glucose tolerance, insulin resistance, post-prandial hyperglycemia/hyperinsulinemia and coronary risk factors by using 75 g oral glucose tolerance test (OGTT).

Patients and Methods Coronary risk factors were examined and OGTT with measurement of plasma glucose and serum insulin was done to evaluate the glucose metabolism and insulin resistance in 263 patients who underwent coronary angiography; 202 subjects were diagnosed as having coronary heart disease (CHD) and 61 subjects were normal. We compared the two groups.

Results The rate of having diabetes was significantly high in the CHD group. From the result of OGTT, 22.3% of CHD patients had diabetes mellitus and 36.6% had impaired glucose tolerance, thus the total glucose intolerance rate was 57.7% in the CHD group. No significant difference was noted in the homeostatic model assessment-R (HOMA-R), but glucose and insulin at 2 hours after OGTT were all significantly high in the CHD group.

Conclusion The rate of glucose intolerance and the levels of post-prandial glucose and insulin were high in the CHD group. We concluded that the post-prandial hyperglycemia and hyperinsulinemia influenced the incidence of CHD.

Key words: coronary heart disease, glucose tolerance, postprandial glucose, postprandial insulin

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In recent years, the number of type 2 diabetes mellitus (DM) patients has been increasing in Japan, and type 2 DM has become the main cause of death for coronary heart disease (CHD); moreover, hyperinsulinemia is the parameter of insulin resistance that is the cause of metabolic syndrome and has an effect on the progression of atherosclerosis (1, 2). Some reports have stated that impaired glucose tolerance and the serum insulin level affect the incidence and mortality of CHD (1-4). The purpose of this study was to evaluate whether or not the serum glucose and serum insulin levels influence the incidence of CHD in Japan by means of 75 g oral glucose tolerance test (OGTT).

In this study, OGTT was performed for 263 cases who were admitted to the hospital with suspicion of CHD, and the patients who underwent coronary angiography, and whose diabetic condition was not known. A comparative study of the results of OGTT, serum insulin level, homeostatic model assessment indices-R (HOMA-R) and other coronary risk factors was done for the CHD group and for the non-CHD (CONT) group.

Methods

Study population

The study subjects were 263 patients who underwent

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Table 1. Characteristics of the Study Population

	CONT group (n=61)	CHD group (n=202)	p-value
Age (years)	63.8 ± 12.0	63.9 ± 11.0	np
M/F (n)	30/31	135/57	**p=0.0010**
BMI (m/kg2)	23/9 ± 3.3	24.0 ± 3.3	np
LDL-C (mg/dl)	110 ± 32.3	121 ± 47.3	np
HDL-C (mg/dl)	55.2 ± 20.5	47.3 ± 15.6	**p=0.0015**
Triglycerides (mg/dl)	121 ± 73.7	122.1 ± 109.6	np
RLP-C (mg/dl)	5.02 ± 4.17	5.19 ± 11.35	np
Lp(a) (mg/dl))	21.6 ± 17.7	24.2 ± 20.6	np
Hypertension (%)	50.6	52.0	np
Diabetes Mellitus (%)	9.8	22.3	**p=0.0312**
Smoking (%)	24.6	51.6	**p=0.0002**

Values are exposed as mean ± SD M/F, male subjects/female subjects; BMI, body mass index; LDL-C, low density lipoprotein-cholesterol; HDL-C, high density lipoprotein-cholesterol; RLP-C, remnant like particle-cholesterol; Lp (a), lipoprotein (a).

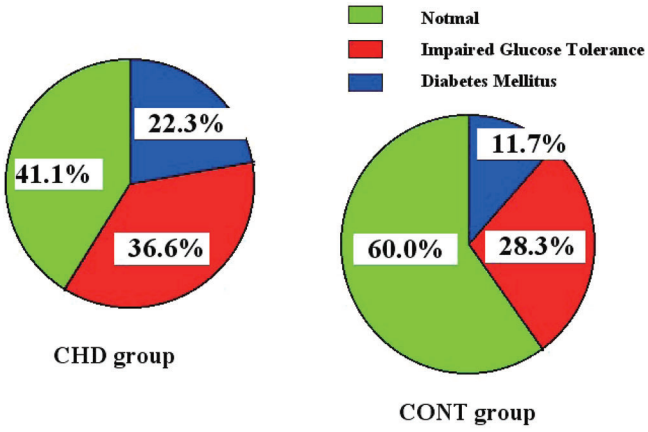

Figure 1. Result of glucose metabolism confirmed by OGTT in two groups. The rate of diabetes mellitus was significantly high in CHD group (p=0.0489). The total of impaired glucose tolerance and diabetes was 59.9%.

coronary angiography under suspicion of CHD but with an unknown diabetic condition between April 2000 and March 2005. The patients were divided into two groups according to following criteria: (1) 202 patients who had over 75% stenosis in AHA category in their coronary artery by coronary angiography were classified the CHD group and (2) 61 patients with normal coronary arteries were the CONT group. The CONT group patients were denied to have valvular disease and myocardial disease by ECG and echocardiography. The CHD group contained 86 patients of acute coronary syndrome and 116 effort angina.

Methods

In patients of acute coronary syndrome, height and weight were measured and blood samples were obtained after a 12-hour fast when the clinical status was stable, about two weeks after admission. In other patients, height and weight were measured at admission and blood samples were obtained after a 12-hour fast, second day of admission. Homeostatic model assessment indices-R (HOMA-R) were used as markers of insulin resistance and calculated as follows: HOMA-R = [fasting insulin (μU/ml) × fasting serum glucose (mg/dl)]/405 (5). HOMA-R of over 1.73 was considered insulin resistant (6) and over 64 μU/ml for 2h serum insulin by OGTT was considered to have hyperinsulinemia (7).

Statistical results were expressed as means ± standard deviation. Age, LDL-cholesterol, HDL-cholesterol, triglyceride were analyzed by student's t-test, and others were by Mann-Whitney test. Categorical data were analyzed by chi-square statistics.

Results

Clinical characteristic data are shown in Table 1. The percentage of males, frequency of diabetes mellitus (DM) and smoking are significantly high in the CHD group. Lipid data showed that HDL-cholesterol was markedly low value in the CHD group; however, no difference was noted in other lipid data. Fig. 1 shows the result of glucose metabolism confirmed by OGTT. The total of impaired glucose tolerance and diabetes was 58.9% in the CHD group and 40% in the CONT group (p=0.0489). In the data of glucose tolerance and insulin resistance taken from OGTT, no significant difference was noted in HOMA-R and possession rate of insulin resistance confirmed by HOMA-R. However, CHD group showed a high tendency ratio to have hyperinsulinemia by 2 hours after OGTT (Table 2).

The results of blood sugar (BS) and serum insulin level by OGTT are shown in Figs. 2, 3. The 2h BS and the serum

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Table 2. **Insulin Resistance Data of the Two Groups**

	CONT group (n=61)	CHD group (n=202)	p-value
HOMA-R	1.46 ± 0.97	1.58 ± 1.12	np
Insulin Resistance by HOMA-R (%)	25.0	30.2	np
Insulin Resistance by serum insulin 2h after OGTT(%)	31.1	45.0	p=0.0509

CHD group showed high tendency ratio to have hyperinsulinemia by 2 hours after OGTT.

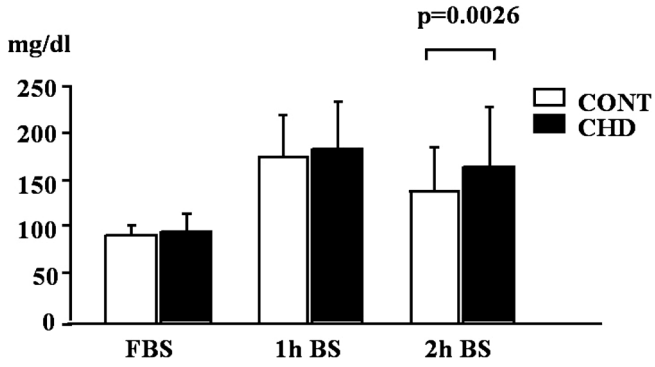

Figure 2. **Blood suger levels from OGTT in two groups. 2 hours blood suger level was significantly high in CHD group.**

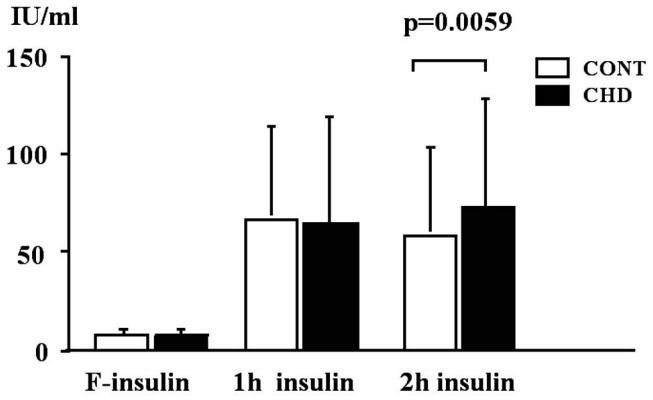

Figure 3. **Serum insulin levels from the OGTT in two groups. 2 hours serum insulin level was significantly high in CHD group.**

insulin level were significantly high in the CHD group.

Discussion

It is considered that glucose intolerance makes progresses to CHD (1, 2). Also, in a report, glucose intolerance was confirmed in 65% of acute myocardial infarction patients for which the existence of diabetes mellitus had not been clear (8). The findings of this study also noted a high ratio of glucose intolerance of 59.9% of the CHD group. The same tendency can be considered in Japan. In the results of OGTT, no difference of FBS and 1-hour BS level were noted in the 2 groups, however, the 2-hour blood sugar level was significantly high in the CHD group. Even though blood sugar level showed that 1-hour sample was higher than 2-hour sample, the difference between two groups was confirmed only in the 2-hour sample. This means that the elevation of BS was prolonged after consumption of meal and the post-prandial hyperglycemia badly affected the coronary artery. The insulin value also showed that the 2-hour sample was higher than the 1-hour sample in the CHD group. This is the compensatory change to prolonged post-prandial hyperglycemia, but the existence of insulin resistance is indicated as well. Generally, HOMA-R which calculated from FBS and fasting insulin, is used as a parameter of insulin resistance. As for HOMA-R, there was no difference between the two groups. Regarding risk factors of CHD, post-prandial hyperglycemia and hyperinsulinemia may indicate an early abnormality rather than HOMA-R.

The mechanism of the bad effect of post-prandial hyperglycemia to atherosclerosis progression was due to fluctuation of BS after the consumption of meal. And it is reported that the fluctuation of BS exerts its effects by producing free radicals (9).

It is reported that the fasting rather than the 2 hours hyperinsulinemia is a significant risk factor for recurrence of cardiovascular event (CVE) for past CHD patients (10). However, this study showed that the 2 hours insulin was at a remarkably higher level than the fasting insulin for the occurrence of CHD. A persistently high level of serum insulin may badly affect atherosclerosis.

It is said that the influence of insulin starts from post-prandial hyperinsulinemia and elevates to fasting insulin, and continues to CVE.

There are some reports that post-prandial hyperglycemia itself plays an important role in the onset of CHD (11, 12);

it seems that control of post-prandial hyperglycemia is important. HbA_{1c} does not show the fluctuation of BS, therefore post-prandial hyperglycemia needs to receive more attention. It will be necessary to more carefully note impaired glucose tolerance cases, especially post-prandial hyperglycemia.

In order to control post-prandial hyperglycemia, alpha-glucosidase inhibitor [to suppress sugar absorption] (13), pioglitazone hydrochloride [to improve insulin resistance] (14), Meglitinides [non-sulphonylurea insulin secretagogus] or rapid acting insulin analogues have already been used. More detailed studies are needed to clarify whether or not the control of post-prandial hyperglycemia and hyperinsulinemia prevent CHD.

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