Single Administration of α-Glucosidase Inhibitors on Endothelial Function and Incretin Secretion in Diabetic Patients With Coronary Artery Disease
– Juntendo University Trial: Effects of Miglitol on Endothelial Vascular Reactivity in Type 2 Diabetic Patients With Coronary Heart Disease (J-MACH) –

Makoto Hiki, MD; Kazunori Shimada, MD; Takashi Kiyana, MD; Kosuke Fukao, MD; Kuniaki Hirose, MD; Hiromichi Ohsaka, MD; Yoshifumi Fukushima, MD; Atsumi Kume, MD; Rie Matsumori, MD; Katsuhiko Sumiyoshi, PhD; Tetsuro Miyazaki, MD; Hirotsushi Ohmura, MD; Takeshi Kurata, MD; Takashi Miida, MD; Hiroyuki Daida, MD

Background: Post-prandial hyperglycemia, hyperlipidemia, and endothelial dysfunction play an important role in the pathogenesis of atherosclerosis. Improvement in post-prandial hyperglycemia on α-glucosidase inhibitors (α-GIs) is associated with a risk reduction of cardiovascular diseases, but the post-prandial effects of α-Gls on endothelial function and incretin secretion in type 2 diabetic patients with coronary artery disease (CAD) remain unclear.

Methods and Results: The post-prandial effects of a single administration of miglitol and voglibose on endothelial function and changing levels of glucose, insulin, lipids, glucagon-like peptide (GLP)-1, and gastric inhibitory polypeptide (GIP) were compared after a standard meal loading in 11 diabetic patients with CAD, using a placebo-controlled cross-over design. The changing levels of glucose, insulin and triglycerides at 60 min were significantly lower in the miglitol group than in the voglibose and placebo groups (all P<0.01). GLP-1 levels were significantly higher at 120 min (P<0.05) and GIP levels were significantly lower at 30 min and 60 min (P<0.05) in the miglitol group compared to other treatments. The reactive hyperemia duration at 120 min was significantly maintained in the miglitol group compared to the other groups.

Conclusions: A single administration of miglitol significantly improved post-prandial glucose/lipid metabolism, incretin secretion, and endothelial dysfunction in diabetic patients with CAD, suggesting that miglitol may be a useful anti-atherogenic agent (UMIN000002264). (Circ J 2010; 74: 1471–1478)

Key Words: α-Glucosidase inhibitors; Coronary artery disease; Diabetes; Endothelial function; Incretin

Type 2 diabetes is a strong risk factor for coronary artery disease (CAD).1,2 In addition, diabetic patients with a previous history of CAD, especially myocardial infarction, have poor outcomes.3 Recently, much attention has focused on post-prandial hyperglycemia as a risk factor for atherosclerotic disease.4–8 The Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe/ASIA (DECODE/DECODA) Study demonstrated that blood sugar levels at 2 h after glucose loading have a superior predictive value for cardiovascular morbidity and overall mortality comparing to fasting blood sugar levels.9,10 In the Study to Prevent Non-Insulin Dependent Diabetes Mellitus (STOP-NIDDM), administration of the α-glucosidase inhibitor (α-GI) acarbose reduced the incidence of diabetes and the risk of developing cardiovascular events in patients with impaired glucose tolerance.11,12 Furthermore, in the Meta-Analysis of...
Risk Improvement under Acarbose 7 (MeRIA7), acarbose treatment significantly reduced hemoglobin A\textsubscript{1c} (HbA\textsubscript{1c}) and post-prandial blood sugar levels as well as the incidence of all cardiovascular diseases in diabetic patients.\textsuperscript{5} These results suggest the possibility that α-GI might exert suppressive effects on cardiovascular disease concomitantly with their ameliorating effects on post-prandial hyperglycemia.

Vascular endothelial dysfunction contributes to the onset and the progression of atherosclerosis and serves as a predictive factor for cardiovascular events.\textsuperscript{14-16} A recent study showed that repetitive post-prandial fluctuation in glucose levels induced monocyte adhesion to the arterial endothelium and intimal thickening.\textsuperscript{5} In addition, reduction of post-prandial hyperglycemia improved the adhesion and atherosclerotic changes in rat models.\textsuperscript{2} Ceriello et al recently demonstrated that oscillating glucose levels have more deleterious effects than constant high glucose on endothelial function in diabetic patients.\textsuperscript{17}

Miglitol is a recently launched α-GI, which possesses particular pharmacokinetics. Miglitol is absorbed rapidly and almost completely from the small intestine after oral administration.\textsuperscript{18} Thus, it can strongly suppress the elevation of blood sugar levels shortly after a meal while causing relatively fewer side-effects in the digestive system such as abdominal bloating and diarrhea. The administration of miglitol has been demonstrated to suppress the progression of atherosclerosis associated with controlling fluctuations of blood sugar in apolipoprotein E knockout mice.\textsuperscript{19}

We therefore hypothesized that miglitol even in a single administration could improve post-prandial glucose and endothelial dysfunction in diabetic patients with CAD, who are at high risk for cardiovascular events. In the present study we examined post-prandial levels of blood sugar, insulin, lipids, oxidative and inflammatory markers, and incretin secretion such as glucagon-like peptide (GLP)-1 and total gastric inhibitory polypeptide (GIP), which have the potential to regulate glucose concentration and adiposity,\textsuperscript{20-22} as well as endothelial function after administration of single doses of 2 α-GIs such as miglitol and voglibose to diabetic patients with CAD.

**Methods**

**Subjects**

Eleven type 2 diabetic patients with CAD were enrolled in the present study. Inclusion criteria were age between 20 and 69 years, HbA\textsubscript{1c} levels ≤8.0%, patients with documented CAD defined as ≥50% diameter stenosis on coronary angiography, or history of myocardial infarction, prior percutaneous coronary revascularization, or prior coronary artery bypass surgery. Exclusion criteria were type 1 diabetes, treated with insulin therapy, symptomatic heart failure, acute coronary syndrome within 3 months prior to the examination, systemic disease including hepatic disease, renal disorders, collagen disease, and malignancy, and post-prandial hyperglycemia. No subjects changed either their internal medications or daily dietary habits during the examination period. Subjects received full verbal and written explanations of the nature and purpose of the study, and gave their written informed consent. The study was approved by the Ethics Committee of Juntendo University. This study has been registered in the UMIN Clinical Trials Registry System as trial ID UMIN000002264 and the abbreviated trial name as J-MACH.

**Study Design**

This study was a randomized, double-blind, placebo-controlled, cross-over design (Figure 1). The subjects visited Juntendo University Hospital after 12 h of fasting. Prior to the diet loading test, we administered 50 mg of miglitol, 0.3 mg of voglibose, or a placebo in a blind manner (Figure 1). A non-treating physician, using randomization envelopes, with no blocking, stratification, or other restrictions, randomized the order of administration of each drug. Concealment and double blinding was ensured by using easily soluble capsules. For the contents of the meal in the diet loading test, we used the test meal developed by the Committee on Standardization of Laboratory Testing Related to Diabetes of the Japan Diabetes Society (total energy: 1,925 KJ; carbohydrates, 49.1%; proteins, 15.7%; lipids, 35.2%).\textsuperscript{23} We selected 3 non-consecutive days in 1 week for 3 diet loading tests.

**Blood Sampling and Measurements**

Blood sampling was conducted at 4 points: 0 min (just before medication and diet loading), 30 min, 60 min, and 120 min after the diet loading. Plasma glucose, serum insulin, triglyceride (TG), low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), remnant-like protein cholesterol (RLP-C), malondialdehyde-modified low-density lipoprotein (MDA-LDL), inflammatory markers [soluble intercellular adhesion molecule (ICAM)-1 and E-selectin], and incretin (active GLP-1 and total GIP) were measured at each
Vascular Endothelial Functions

The response of forearm blood flow to reactive hyperemia (RH), an index of endothelium-dependent vasodilatation, was measured using a mercury-filled strain-gauge plethysmograph (EC-5R, DE Hokanson, WA, USA) at baseline, 60 min and 120 min after test meal loading, as described previously. In brief, examinations were performed in a quiet, dark, temperature-controlled (22–24°C) room. Subjects rested for at least 15 min before the examination. After basal forearm blood flow was measured, forearm blood flow was occluded by inflating a cuff around the left upper arm to a pressure of 200 mmHg for 5 min to induce RH. After acute release of the ischemic cuff occlusion, forearm blood flow was measured for 5 min. Forearm blood flow was expressed in ml·min⁻¹·100 ml⁻¹ of forearm tissue volume. The RH ratio was calculated as the maximal forearm blood flow during RH divided by the basal forearm blood flow to adjust for individual variation. The RH duration was defined as the time from release of the ischemic cuff occlusion to normalization of the forearm blood flow below the basal forearm blood flow.

Statistical Analysis

The results are represented as mean±SD. Statistical analysis was performed using SPSS (version 17.0, SPSS Japan, Tokyo, Japan). We used 2-way ANOVA to detect significant differences, which were later evaluated on post-hoc analysis (Tukey’s test). Because this study was a cross-over design, 2 independent variables between miglitol and placebo administration, between voglibose and placebo administration, and between miglitol and voglibose administration were needed for analyses. P<0.05 was considered to be significant.

Results

Baseline Characteristics

Table 1 lists the baseline patient characteristics. Of the 11 subjects, 10 were men with an average age of 65.3±7.3 years. The HbA₁c level was relatively controlled in the study subjects (6.3±0.5%). Table 2 lists the plasma glucose, serum insulin, TG, LDL-C, HDL-C, RLP-C, MDA-LDL, ICAM-1, and E-selectin before and after test meal loading. No significant differences were observed in each baseline level at point.

Plasma glucose, serum insulin, TG, and HDL-C were analyzed using standardized measurement methods. For the measurement of the following parameters, we utilized commercially available enzyme immunoassay kits: LDL-C was measured using a direct method (Sekisui Medical); RLP-C by RLP Cholesterol JIMRO II (Ohtsuka Pharmaceutical, Tokyo, Japan); MDA-LDL by a monoclonal antibody (Sekisui Medical); ICAM-1 by Quantifying Human sICAM-1/CD54 Immunoassay (R&D Systems, Minneapolis, MN, USA); E-selectin by Parameter Human E-Selectin (R&D Systems); GLP-1 by Glucagon-Like Peptide-1 (Active) ELISA Kit (Lincor Research, St Charles, MO, USA); and GIP by Human GIP (Total) ELISA Kit (Lincor Research).

In order to exclude the influence of posture and fluctuation of circulating plasma volume after diet loading, the lipids and MDA-LDA were adjusted with the serum albumin levels (ie, [Value]e=[Value]i×[Alb]/[Alb]i). [Value]e represents an adjusted value, with [Value]i, [Alb], and [Alb]i denoting a measured value, baseline serum albumin level, and serum albumin level during the measurement, respectively, as described previously.24

<table>
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<tr>
<th>Characteristics</th>
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<tr>
<td>Male (%)</td>
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<td>(91)</td>
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<tr>
<td>Age (years)</td>
<td>65.3±7.3</td>
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<tr>
<td>BMI (kg/m²)</td>
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<td>Waist circumference (cm)</td>
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<td>Fasting serum insulin (pmol/L)</td>
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<td>1.5-AG (µg/dl)</td>
<td>10.8±6.2</td>
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<tr>
<td>Triglyceride (mmol/L)</td>
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<tr>
<td>LDL-C (mmol/L)</td>
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<td>History of CABG, n (%)</td>
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<tr>
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<td>Nitrates/nitrates</td>
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<tr>
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Table 2. Baseline Characteristics

Miglitol, Incretin, and Endothelial Function

Changes of Blood Sugar and Insulin

The level of plasma glucose at 60 min after miglitol administration was significantly lower than that in the voglibose and the placebo groups (miglitol 100.7±18.9 mmol/L, placebo 121.8±19.7 mmol/L, miglitol vs voglibose P<0.01, miglitol vs placebo P<0.001; Table 2). The area under the curve (AUC) of plasma glucose between 0 and 120 min was significantly lower in the miglitol group than in the voglibose and the placebo groups (miglitol 8.6±7.3 mmol/L, Voglibose 14.8±9.5 mmol/L, miglitol vs placebo P<0.001; Figure 2A). Comparing the changes of the plasma glucose levels from each baseline, the level at 30 min after miglitol administration was significantly lower than that of the placebo group (P<0.01), and the level at 60 min after the administration of miglitol was significantly lower than that in the voglibose group (P<0.001) and the placebo group (P<0.001; Figure 2A). The levels of serum insulin at 60 min (miglitol 10.4±8.5 pmol/L, placebo 303.9±133.3 pmol/L, miglitol vs voglibose P<0.001, miglitol vs placebo P<0.001) and 120 min (miglitol 205.6±98.5 pmol/L, voglibose 322.4±151.8 pmol/L, placebo 339.5±118.0 pmol/L, miglitol vs voglibose P<0.01, miglitol vs placebo P<0.001) after miglitol administration.
were significantly lower than those of the voglibose and the placebo groups (Table 2). The AUC of serum insulin between 0 and 120 min was significantly lower in the miglitol group than in the voglibose and the placebo groups (miglitol 294.5±190.5 h·pmol/L, voglibose 488.3±204.8 h·pmol/L, placebo 503.2±190.5 h·pmol/L). The changes of the TG levels from each baseline, the level at 60 min after miglitol administration was significantly lower than that in the voglibose group (P<0.001) and the placebo group (P<0.001; Figure 2B).

**Changes of Lipids and MDA-LDL**

The level of TG at 60 min after miglitol administration was significantly lower than in the placebo group (1.25±0.53 mmol/L vs 1.74±0.83 mmol/L, P<0.01; Table 2). The AUC of TG between 0 and 120 min was significantly lower in the miglitol group than in the placebo group (2.65±1.14 h·mmol/L vs 3.41±1.59 h·mmol/L, P<0.05; Table 2). Comparing the changes of the TG levels from each baseline, the level at 60 min after miglitol administration was significantly lower than that in the voglibose group (P<0.001) and the placebo group (P<0.001; Figure 2C). The level of RLP-C at 60 min after miglitol administration was significantly lower than that in the placebo treatment (0.097±0.034 mmol/L vs 0.137±0.068 mmol/L, P<0.01, **Table 2**). Comparing the changes of the RLP-C levels from each baseline, the level at 60 min was significantly lower in the miglitol group than in the placebo group (2.06±0.53 mmol/L vs 3.06±0.16 mmol/L, P<0.01; **Table 2**). Comparing the changes of HDL-C, LDL-C, and MDA-LDL between each drug administration group, the AUCs were significantly different between each drug administration group (Table 2).
Changes of ICAM-1 and E-Selectin

No significant changes were observed in ICAM-1 or E-selectin levels after the administration of the α-GIs or placebo (Table 2).

Changes of Vascular Endothelial Function

After test meal loading, the RH duration and RH duration ratio (divided by RH duration at 0 min) at 60 min were significantly decreased in the voglibose group (both P<0.01) and placebo group (both P<0.001; Figure 3A). The RH duration and RH duration ratio at 120 min were also significantly decreased in the voglibose and placebo groups (all P<0.001; Figure 3A). No significant reductions, however, of RH duration or RH duration ratio were observed in the miglitol group (Figure 3A).

The reduction of RH duration at 120 min was significantly preserved in the miglitol group (104.2 ±14.1 s vs 75.6 ±14.9 s, P<0.001) and the voglibose group (93.1 ±16.3 s vs 75.6 ±14.9 s, P<0.05) compared with the placebo group (Figure 3A). The reduction of RH duration ratio at 120 min was significantly preserved in the miglitol compared to the placebo group (93±19% vs 72±16%, P<0.05; Figure 3B). The reduction of RH duration ratio at 120 min was significantly higher in the miglitol group than in the voglibose group (93±19% vs 72±16%, P<0.05; Figure 3B). The same trends in the RH ratio were observed in these subjects (data not shown).

Changes of Incretin

Figure 4 shows the changes of GLP-1 and GIP levels after the test meal loading in each drug group. The level of GLP-1 was significantly higher at 60 min after the administration of miglitol than in the placebo group (6.5±3.8 pmol/L vs 3.7±1.2 pmol/L, P<0.05), and significantly higher at 120 min after the administration of miglitol than in the voglibose group (6.8±4.7 pmol/L vs 3.9±2.1 pmol/L, P<0.05) and the placebo group (6.8±4.7 pmol/L vs 3.6±1.2 pmol/L, P<0.05; Figure 4A). The level of GIP was significantly lower at 30 min after the administration of miglitol than in the voglibose group (37.9±19.1 pmol/L vs 73.7±20.9 pmol/L, P<0.05) and the placebo group (37.9±19.1 pmol/L vs 78.8±25.0 pmol/L, P<0.05), significantly lower at 60 min after the administration of miglitol than in the voglibose group (30.2±11.7 pmol/L vs 62.0±19.9 pmol/L, P<0.05) and the placebo group (30.2±11.7 pmol/L vs 68.6±32.0 pmol/L, P<0.01), and significantly lower at 120 min after the administration of miglitol than in the placebo group (33.1±17.6 pmol/L vs 48.8±22.2 pmol/L, P<0.01; Figure 4B).

Correlations Between Endothelial Function and Each Parameter

We investigated the correlations between endothelial function and each parameter. Modest but significant negative correlations were observed between the RH duration ratio at 120 min and the changes of plasma glucose level at 60 min (r=−0.49, P<0.01), and between the RH duration ratio at 120 min and the changes of plasma glucose level at 120 min (r=−0.38, P<0.05) after test meal loading. Interestingly, strong
Figure 3. Effects of miglitol, voglibose or placebo on post-prandial levels of (A) RH duration and (B) RH duration ratio (divided by RH duration at 0 min) in 11 type 2 diabetic patients with coronary artery disease. Data are presented as mean ± SD. Two-way ANOVA and Tukey multiple comparisons were used for continuous variables. †P<0.05, miglitol vs voglibose; ***P<0.001, *P<0.05, miglitol vs control; ‡P<0.05, voglibose vs placebo, 2-way ANOVA and Dunnett type multiple comparisons were used for continuous variables. #P<0.01, ###P<0.001 vs 0 min. RH, reactive hyperemia.

Figure 4. Effects of miglitol, voglibose or placebo treatment on post-prandial levels of (A) active GLP-1 and (B) total GIP in seven type 2 diabetic patients with coronary artery disease. Data are presented as mean ± SD. Two-way ANOVA and Tukey multiple comparisons were used for continuous variables. †P<0.05, miglitol vs voglibose; **P<0.01, *P<0.05, miglitol vs placebo. GIP, gastric inhibitory polypeptide; GLP, glucagon-like peptide.
and significant negative correlations were demonstrated between the RH duration ratio at 120 min and the level of GIP at 60 min after test meal loading ($r = -0.68, P<0.01$), and between the RH duration ratio at 120 min and the AUC of GIP ($r = -0.74, P<0.01$).

**Discussion**

We have clearly demonstrated that a single administration of miglitol to type 2 diabetic patients with CAD has beneficial effects on their post-prandial state of hyperglycemia, insulinenia, hyperlipidemia, vascular endothelial dysfunction, and incretin secretion, using a randomized, double-blind, placebo-controlled, cross-over design. The present study is, to the best of our knowledge, the first report to investigate the effects of $\alpha$-GIs on vascular endothelial function and incretin secretion after standard meal loading in type 2 diabetic patients with CAD.

Vascular endothelial dysfunction profoundly affects the initiation and progression of arteriosclerosis.\(^\text{16}\) Several non-invasive methods have been developed to measure endothelial function. Flow-mediated vasodilatation of the brachial artery can be used to assess the endothelial function of the forearm conduit artery. RH measured using strain-gauge plethysmography can evaluate the endothelial function of resistance artery and changes in the flow response resulting from endothelial-derived vasoactive substances,\(^\text{17}\) as in the present study. A previous study reported that RH duration in the forearm can also be used to assess vascular endothelial function.\(^\text{18}\) In addition, RH duration significantly reflected cardiovascular risk factors and its decrease correlated with the number of risk factors.\(^\text{19}\) Therefore, RH duration measured on strain-gauge plethysmography could be potentially useful in assessing vascular endothelial function. In the present study, a single administration of miglitol preserved vascular endothelial function after test meal loading. A recent study also demonstrated that a single administration of acarbose abolished the post-prandial decrease of indices of endothelial function in type 2 diabetic patients.\(^\text{20}\) The present results are concordant with the previous study, but we emphasize the differences of patient characteristics. In the present study we enrolled type 2 diabetic patients with already documented CAD, who are at much higher risk for cardiovascular events than those without CAD.\(^\text{21}\) The impact of preservation of endothelial function in the post-prandial state must imply clinical benefits even in these high-risk patients. Although we assessed the possibility of involvement of inflammation and oxidative stress on endothelial function in the post-prandial state, no significant changes were observed in relation to these putative factors. The precise mechanisms are still unidentified, but negative correlations between endothelial function and the indices of changing of post-prandial glucose levels were demonstrated. A previous study also reported the association between post-prandial endothelial function and post-prandial glucose levels.\(^\text{22}\) In addition, swings in glucose levels affect monocyte adhesion to the endothelium in animal models,\(^\text{19}\) and oscillating glucose levels cause much deleterious impairment on endothelial function rather than constant high glucose.\(^\text{23}\) Therefore, post-prandial endothelial function could, in part, be improved by amelioration of post-prandial glucose levels by administration of miglitol.

We showed dramatic changes in incretin secretion due to miglitol treatment. Miglitol administration significantly maintained the levels of GLP-1 at 120 min and significantly decreased the levels of GIP at 30 min and 60 min after test meal loading. These findings are consistent with previous studies reported by Lee et al,\(^\text{24}\) Arakawa et al,\(^\text{25}\) and Narita et al.\(^\text{26}\) As we described in the previous section, however, we demonstrated these effects and endothelial function simultaneously, in type 2 diabetic patients with CAD. These findings suggest that miglitol strongly stimulates endogenous GLP-1 secretion and inhibits GIP secretion. Miglitol, but not voglibose or acarbose, is absorbed in the upper small intestine.\(^\text{18,27}\) Accordingly, miglitol is absorbed by a relatively higher amount of carbohydrate in the lower intestine, where GLP-1 secreting L-cells exist, in comparison to other unabsorbed $\alpha$-GIs. This may explain the strong GLP-1 secretion action of miglitol.

A recent study reported that iv administration of GLP-1 improves endothelial dysfunction in diabetic patients with CAD,\(^\text{28}\) suggesting that incretin should be associated with endothelial function. In the present study, strong and significant negative correlations were found between RH ratio and GIP, but not GLP-1 levels. It was reported that GIP directly acts on adiposity and insulin resistance.\(^\text{29}\) Further investigations are needed to clarify the association between incretin and endothelial function in the next step.

A single administration of miglitol, but not voglibose, ameliorated the elevation of glucose levels shortly after test meal loading. This may, in part, be associated with the unique pharmacokinetics, which involves rapid and almost complete absorption in the small intestine, as described here.\(^\text{18,21}\) Therefore, miglitol may have a powerful inhibitory effect against $\alpha$-glucosidase without increasing adverse effects. The results of STOP-NIDDM, which demonstrated that $\alpha$-GIs reduced cardiovascular events even in patients with impaired glucose tolerance, suggest the importance of interference to post-prandial glucose swings.\(^\text{11,12}\) It was reported that the post-prandial glucose fluctuations, rather than stable hyperglycemia, promoted monocyte adhesion to endothelial cells.\(^\text{5}\) We have reported that high levels of glucose at 120 min after oral glucose tolerance test were associated with CAD, even in patients with normal glucose tolerance.\(^\text{8}\) Miglitol also inhibited the increase of TG and RLP-C shortly after test meal loading. Post-prandial hyperlipidemia as well as hyperglycemia plays an important role in endothelial dysfunction.\(^\text{16,33}\) Although the mechanism of lipid metabolism has not been clarified, a previous study suggested that it might result from delays in gastric emptying.\(^\text{22}\) Taken together with these findings, miglitol may be one of the useful drugs associated with the reduction of cardiovascular risks in subjects with problems of drug compliance.

**Study Limitations**

There are several potential limitations in the present study. First, this study involved a small sample size. We conducted a randomized, double-blind, placebo-controlled, cross-over study. Therefore, we believe that the positive results of miglitol found in the present study must be reliable. Other $\alpha$-GIs, including voglibose, might have beneficial effects as well as miglitol in the post-prandial condition even for a single administration of each drug. Indeed, the reduction of RH ratio at 120 min was significantly preserved in the voglibose group compared with the placebo group. Second, the present study assessed the effects of single administration of $\alpha$-GIs on post-prandial state. The investigation of impact of long-term effects, including post-prandial parameters and clinical outcomes, is needed as the next step. Third, as described here, the mechanisms by which miglitol ameliorated endothelial dysfunction after test meal loading in type 2 diabetic patients with CAD, have still not been elucidated. Additional effects
on glucose reduction or some other novel mechanism such as incretin metabolism could affect endothelial function. Further studies are needed to assess these points. Fourth, we used mainly RH duration in analysis of endothelial function. There are several parameters that can be used to assess endothelial function on strain-gauge plethysmography, but the same trends were observed with regard to RH ratio (data not shown).

**Conclusion**

A single administration of miglitol provides beneficial effects against post-prandial hyperglycemia, insulinemia, hyperlipidemia, vascular endothelial dysfunction, and incretin secretion in diabetic patients with CAD. Miglitol may be one of the useful drugs associated with the reduction of cardiovascular risks via amelioration of endothelial dysfunction in the post-prandial state even in diabetic patients who already have CAD. Further prospective studies are required to confirm these findings.

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The article continues with a list of references.