

Original Article

Acute effects of acarbose on post-prandial glucose and triglycerides in type 2 diabetics following intake of different Malaysian foods

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Acarbose inhibits intestinal alpha-glucosidases resulting in diminished and delayed postprandial hyperglycaemia (PPH). Studies on effects of acarbose on postprandial lipaemia (PPL) have been inconclusive. Little is known about the effects of acarbose on PPH and PPL following intake of a polysaccharide diet. We studied 30 type 2 diabetic patients on dietary and/or oral hypoglycaemic agent(s). Thirty patients were recruited for food A (*nasi lemak*), 28 for food B (*mee goreng*) and 28 for food C (*roti telur*), which represent the typical diets of the three main races in Malaysia. Serial blood samples were taken at 15 min before and up to 240 min after each food intake, without acarbose. Subsequently, three doses of 50 mg acarbose were given orally and the same procedure was repeated the following day. There were significantly lower mean increments in plasma glucose levels after compared to before acarbose treatment 30, 45 and 60 min for food A and at 30, 45, 60, 120, 180 and 240 min for food C, but no significant difference was noted for food B. There was a significantly lower mean fasting glucose level after compared with before acarbose treatment following intake of food A and C but not food B. Short-term treatment with acarbose caused significant diminished and delayed PPH response with food A and C but not with food B. Acarbose was more effective in reducing PPH response in polysaccharide foods with a higher and earlier postprandial glucose peak than in those with a lower and lagged peak. There were no significant differences in the mean fasting or postprandial triglyceride levels before and after acarbose treatment, following intake of all three foods for up to 4 hours. Depending on the food absorption pattern, overnight low dose treatment with acarbose leads to diminished fasting and peak plasma glucose levels, and delayed PPH but insignificant reduction in postprandial lipaemia in poorly controlled type 2 diabetics following intake of racially different Malaysian food.

Key words: acarbose, alpha-glucosidase inhibitor, postprandial, glucose, triglyceride, type 2 diabetes.

Introduction

Acarbose is an antidiabetic agent that competitively and reversibly inhibits intestinal alpha-glucosidases, enzymes that are responsible for the metabolism of polysaccharides into absorbable monosaccharides. This results in a diminished and delayed rise in blood glucose following a meal, resulting in a reduction in postprandial hyperglycaemia (PPH)^{1–6} and glycated haemoglobin.^{1,3,7} After oral administration of acarbose, the postprandial rise in blood glucose is decreased in a dose-dependent manner, and glucose-induced insulin secretion is attenuated. Due to the diminished PPH and hyperinsulinaemia by acarbose, it would be expected that triglyceride (TG) uptake into adipose tissue, hepatic lipogenesis and TG concentration would be reduced.⁸ However, studies on the effect of acarbose on postprandial lipaemia have shown variable results.^{2,7,9–11}

Our group has previously shown that treatment with guar gum resulted in diminished PPH following intake of different Malaysian foods.¹² However, the effect of acarbose on the various polysaccharide Malaysian diets has not been evaluated. Intervention with agents that can affect risk factors such as postprandial hyperglycaemia and TG levels are expected

to reduce the risk of atherosclerosis. This study examines the acute effects of acarbose on fasting and postprandial plasma glucose and TG in poorly controlled type 2 diabetic patients following intake of different local Malaysian foods.

Materials and methods

Patients

A total of 30 type 2 diabetic patients (15 males and 15 females, mean age \pm SD = 51.3 \pm 10.8 years) attending the Universiti Kebangsaan Malaysia Hospital Diabetic Clinics and fulfilling the set criteria were recruited for this study. They comprised the three major ethnic groups of Malaysia (i.e. 16 Malay, six Chinese and eight Indian patients). This study was approved by the Ethics Committee of the hospital.

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Both oral and written consent were obtained from each patient. Inclusion criteria included the following: duration of type 2 diabetes of at least 1 year; poorly controlled DM (HbA1c > 8%); body mass index (BMI) of 25–30 kg/m²; and a treatment regime consisting of diet and/or oral hypoglycaemic agent(s) only. Exclusion criteria included the following: type 2 diabetes of < 1 year duration; receipt of insulin treatment or antihyperlipidaemic agents; recent history of significant weight loss (> 5 kg over the previous 6 months); history of gastrointestinal disorders such as inflammatory bowel disease or malabsorption syndrome; or receipt of acid suppression therapy.

Food

The three types of food were *nasi lemak* (food A: carbohydrates, 58 g; fat, 13 g; protein, 10 g; 1628 kJ), *mee goreng* (food B: carbohydrates, 55 g; fat, 12 g; protein, 13 g; 1590 kJ) and *roti telur* (food C: carbohydrates, 45 g; fat, 13 g; protein, 14 g; 1486 kJ). Each food was assessed for the carbohydrate, fat, protein and calorie content by the hospital dietitian. Food A (*nasi lemak*) was rice-based while food B (*mee goreng*) and food C (*roti telur*) were noodle and dough-based foods, respectively. These represent the three different types of food of the three main ethnic groups, that is, Malay, Chinese and Indians, respectively. However, being a multiracial community, each food is consumed universally by all ethnic groups. Each type of food has a composite nature but all are mainly starch-based. The glycaemic index of the three foods is not known but the total glycaemic response is calculated by measuring the area under the curve of glucose concentration versus the time following food intake.

Methods

Thirty patients consented to participate in the study but two patients dropped out for the food B and C groups. Each patient was instructed to come for a total of three visits which were at least 2 weeks apart. The patients were instructed to be on their usual diet at least 1 week prior to the test and to fast overnight (10–12 h) prior to intake of one of the three specified foods for breakfast. On each visit, the patients were given one of the three different standardized Malaysian foods, prepared and quantified in a standard manner. The sequence at which the food was given was randomized between patients. In addition, the laboratory staff were also blinded on the sequence of the food given.

On day 1, serial venous blood samples were taken in the morning (8 am) at 15 min before and 0, 15, 30, 45, 60, 120, 180, and 240 min after food intake without acarbose. Subsequently, 50 mg acarbose was given to each patient together with lunch, dinner and breakfast the following morning (day 2). Similarly, blood samples were taken at 15 min before and 0, 15, 30, 45, 60, 120, 180, and 240 min after food intake with the third dose of acarbose given at breakfast. The corresponding pre-acarbose samples posed as controls for individual patients. The mean of the –15 and 0 min samples were taken as the baseline fasting value. The serial blood samples were analysed for glucose (enzymatic reference method with hexokinase) and TG (enzymatic calorimetric method) on an automated analyser (Cobas Integra; Roche Diagnostics Basel, Switzerland). The within run and day-to-day coefficient of variation (CV) for glucose method were 0.42% and

1.2% at glucose level of 5.6 mmol/L, and 0.43% and 0.97% at 19.7 mmol/L, respectively. The within run and day-to-day CV for the TG method were 0.97% and 1.0% at TG level of 1.5 mmol/L, 0.78% and 1.2% at 5.2 mmol/L, respectively. Delta glucose level was derived from the difference between postprandial and corresponding fasting glucose level.

Analysis of data

Significant difference of means for each variable between pre- and post-treatment groups were analysed by Student's paired *t*-test for those variables of Gaussian distribution and by Wilcoxon matched pairs signed-ranks test for those of non-Gaussian distribution. Pearson correlation coefficient was used to analyse correlation between two variables. Probability values of < 0.05 were taken as significant. The statistical analysis was performed on the Statistical Package for Social Sciences (SPSS) software (SPSS Inc., Chicago IL, USA) on an IBM-compatible computer.

Results

The mean \pm SD of HbA1c of the patients recruited was 9.7 ± 1.9 (range 8.0–13.4%), duration of type 2 diabetes was 9.8 ± 7.7 (range 2.0–30.0 years) and BMI was 26.6 ± 1.6 (25.0–30.0 kg/m²).

Glucose absorption pattern

The plasma glucose levels peaked at 60 min for food A and C, while those for food B peaked later at 120 min. At 60 min, the difference between the peak and fasting glucose (delta peak glucose) levels for food B was lower than that for A (2.30 ± 0.58 vs 4.02 ± 0.41 mmol/L, $P < 0.05$) or C (2.30 ± 0.58 vs 3.74 ± 0.34 mmol/L, $P < 0.05$), but there was no significant difference in the delta peak glucose levels between food A and C (4.02 ± 0.41 vs 3.74 ± 0.34 mmol/L, $P > 0.05$) (Fig. 1)

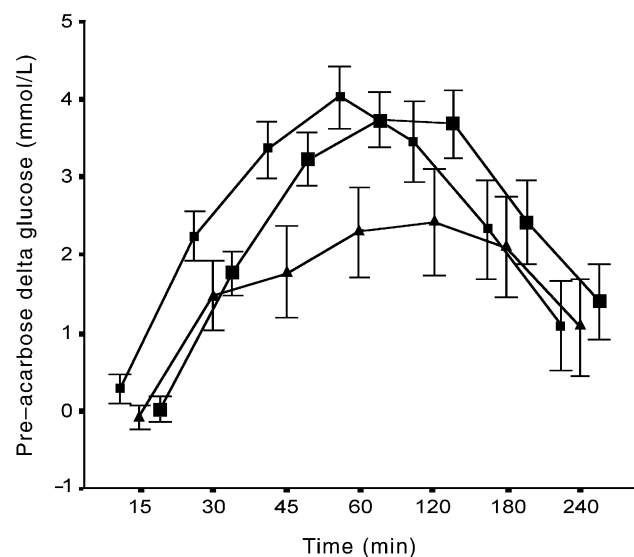


Figure 1. Absorption pattern of glucose following intake of different polysaccharide foods (mean \pm SEM). (■) Food A; (▲) food B; (●) food C.

Triglyceride absorption pattern

There was no significant difference in the pre-acarbose mean delta TG levels (difference between postprandial and corresponding basal TG levels) between food A, B and C ($P > 0.05$) at all timed intervals. There was no significant difference in the highest TG level achieved ($P > 0.05$) and the time taken to attain this level (at about 4 h) between foods A, B and C (Fig. 2).

Effects of acarbose on fasting and postprandial glucose level and triglyceride level

The mean fasting glucose levels were significantly lower after only three doses of acarbose compared to before acarbose treatment. This was observed with foods A and C but not with food B (Table 1).

For food A (*nasi lemak*), there were significantly lower mean increments in plasma glucose levels following treatment with three doses of acarbose compared with pre-acarbose treatment at 30, 45 and 60 min after food intake (Table 1, Fig. 3). For food C (*roti telur*), there were significantly lower mean increments in plasma glucose levels following treatment with acarbose compared with pre-acarbose treatment at 30, 45, 60, 120, 180 and 240 min after food intake (Table 1, Fig. 4). For food B (*mee goreng*), there was no significant difference between the mean increment in plasma glucose levels without and with acarbose treatment across all timed postprandial samples [Table 1, Fig. 5].

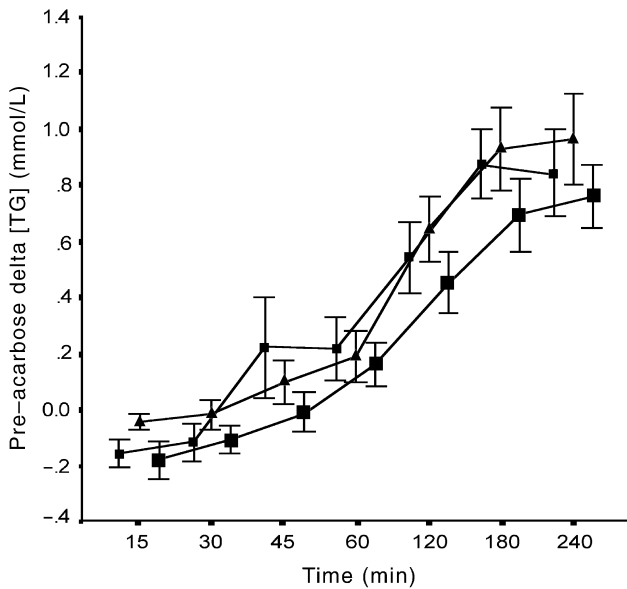


Figure 2. Absorption pattern of triglycerides following intake of different polysaccharide foods (mean \pm SEM). (■) Food A; (▲) food B; (●) food C.

Without acarbose treatment, the mean postprandial increment in plasma glucose peaked at 60 min for foods A and C but at 120 min for food B. With foods A and C, treatment with acarbose resulted in delayed (to 75 and 120 min, respectively) and diminished peak increments in glucose level ($P < 0.01$ and $P < 0.0001$, respectively). With food B, treatment with acarbose did not result in significant delay or reduction in postprandial plasma glucose response ($P > 0.05$).

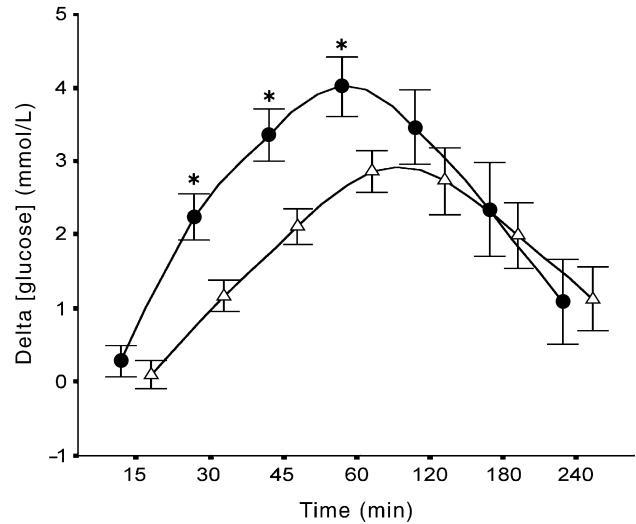


Figure 3. Pre- and post-acarbose delta glucose levels following intake of food A (mean \pm SEM). *Significant P value. (●) Pre-acarbose; (△) post-acarbose.

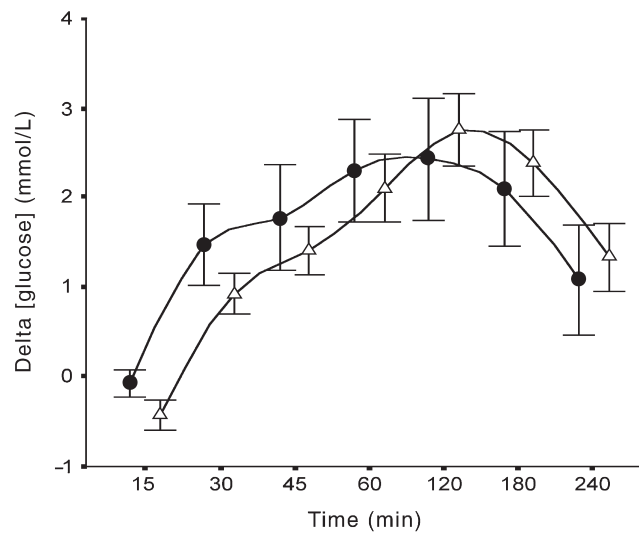


Figure 4. Pre- and post-acarbose mean delta glucose levels following intake of food B (mean \pm SEM). (●) Pre-acarbose; (△) post-acarbose.

Table 1. Mean \pm SEM of fasting glucose levels of the pre- and post-acarbose treated groups with different types of food

Types of food	Before acarbose fasting glucose level (mmol/L)	After acarbose fasting glucose level (mmol/L)	P value (paired t -test)
Food A (<i>nasi lemak</i>) ($n = 30$)	11.10 \pm 0.62	10.36 \pm 0.63	<0.05*
Food B (<i>mee goreng</i>) ($n = 28$)	11.15 \pm 0.81	10.56 \pm 0.68	NS
Food C (<i>roti telur</i>) ($n = 28$)	10.96 \pm 0.75	10.21 \pm 0.77	<0.01*

*Significant P values; NS, not significant.

Thus, acarbose caused diminished and delayed postprandial hyperglycaemic response following intake of foods A and C but not food B. The peak mean increment in plasma glucose level without acarbose was significantly higher in foods A and C compared with food B ($P < 0.05$) but no significant difference was noted between foods A and C ($P > 0.05$). Acarbose treatment resulted in a reduction of peak mean increment in plasma glucose levels in foods A and C but not in food B, as clearly indicated by the lack of significant difference in the post-acarbose glucose peaks between all three foods ($P > 0.05$) (Table 2).

There were no significant differences in the mean fasting or corresponding serial increment in plasma TG levels between 'before' and 'after treatment' with acarbose, across all three different types of food. Without acarbose treatment, there were significant positive correlations between fasting and 4 h postprandial TG levels with foods A ($r = 0.784$; $P < 0.0001$), B ($r = 0.784$, $P < 0.0001$) and C ($r = 0.741$; $P < 0.0001$). Similarly, with acarbose treatment, there were significant positive correlations between fasting and 4 h postprandial TG levels with foods A ($r = 0.789$; $P < 0.0001$), B ($r = 0.802$; $P < 0.0001$) and C ($r = 0.874$; $P < 0.0001$). However, fasting TG level did not significantly correlate with increment in TG level at 4 h. There was a significantly higher mean TG level at 4 h in those with fasting TG level > 2.3

mmol/L than in those with a fasting TG level < 2.3 mmol/L, with or without acarbose treatment ($P < 0.05$). In contrast, there was no significant difference in the 4 h increment in plasma TG level between those with fasting TG level > 2.3 mmol/L and < 2.3 mmol/L ($P > 0.05$). Therefore, fasting TG level is predictive of postprandial TG level but not of increment in plasma TG level at 4 h.

Discussion

This study showed that different local Malaysian foods have different patterns of absorption, differing in their peak increment in plasma glucose levels and the time taken to achieve these peak levels. With foods A and C, acarbose treatment resulted in lower fasting plasma glucose levels, and a diminished and delayed peak increment in plasma glucose response. These effects were not observed with food B. This study clearly indicated that with only three doses of 50 mg acarbose, effective lowering of fasting plasma glucose was achieved with two (*nasi lemak* and *roti telur*) out of the three types of composite food studied. In addition, this showed that low-dose acarbose treatment for a short duration (overnight) led to attenuation of postprandial hyperglycaemic response with local Malaysian foods that were either rice- (food A) or dough-based (food C), but not noodle-based (food B). These foods are popular among the three major ethnic groups in Malaysia.

Acarbose was more effective in reducing postprandial hyperglycaemic response in polysaccharide foods with higher and earlier postprandial glucose peaks (foods A and C) than in that with a lower and delayed peak (food B). Acarbose reduced postprandial response within 18 h of 150 mg of acarbose treatment with the peak increment in plasma glucose levels delayed for 15–60 min. This study clearly showed that within 18 h of three small doses of acarbose, a significant reduction in fasting and peak increment in plasma glucose levels could be seen in certain types of Malaysian food without altering TG absorption in all of the patients studied for up to 4 h of the postprandial period. The results of the Diabetes Intervention Study indicate that PPH and TG levels are independent risk factors for myocardial infarction and total mortality in newly detected type 2 diabetes.¹³ The results of this study highlight the potential use of acarbose treatment in attenuating postprandial hyperglycaemic response following intake of foods with higher and earlier glucose peaks. These results are very encouraging in terms of the potential role of acarbose in reducing risk of myocardial infarction, atherosclerosis and total mortality in type 2 diabetes by virtue of its ability to attenuate PPH.¹³

The typical Asian diet is generally composed of high carbohydrate content compared with European food. This study clearly showed that the absorption pattern of glucose in the three typical ethnic-based foods did not depend on the carbohydrate content but on the complexity of the food. With the given carbohydrate content of food B being between food A and C, it would be predicted that the glycaemic response would be that between A and C. However, it was observed that food B exhibited a lower and delayed postprandial hyperglycaemic response. The TG absorption of food B, though, did not differ from that of A or C. This suggests the possibility of complex fibers in food B affecting its glucose but not fat absorption pattern up to 4 h after food.

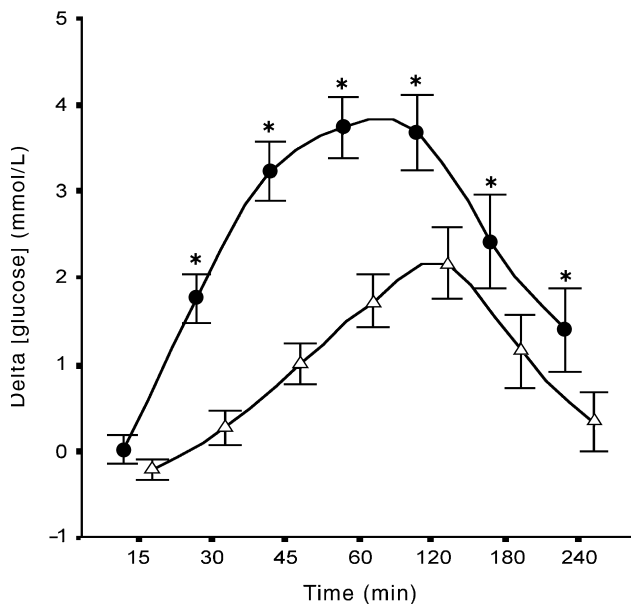


Figure 5. Pre- and post-acarbose delta glucose levels following intake of food C. *Significant P value. (●) Pre-acarbose; (△) post-acarbose.

Table 2. Total glycaemic response (area under the curve) before and after acarbose treatment following intake of different types of food

	Total glycaemic response* (min mmol/L)		Difference in area under the curve [†] (min mmol/L)
	Before AT	After AT	
A	619.6	474.0	145.6
B	438.9	465.9	-27.0
C	620.6	296.4	324.2

*Area under the curve; [†]before compared with after acarbose treatment; AT, acarbose treatment.

Fasting TG levels can be used to differentiate between patients with normal TG metabolism and those with high postprandial levels. In addition, TG levels 4 h after a standard oral lipid load were better than the fasting TG level for discriminating between normal and abnormal TG metabolism.¹⁴ This study also clearly showed that fasting TG levels were predictive of postprandial TG but not of increment in TG levels at 4 h after food with and without acarbose treatment. This is in agreement with previous studies which showed that poorly controlled type 2 diabetic patients with fasting hypertriglyceridaemia exhibited higher postprandial chylomicron remnant levels than did normotriglyceridaemic type 2 diabetics and normal controls.^{15,16}

Depending on the food absorption pattern, overnight low-dose treatment with acarbose leads to diminished fasting and peak plasma glucose levels as well as delayed PPH, but an insignificant reduction in postprandial lipidaemia, up to 4 h after food in poorly controlled type 2 diabetics following intake of rice- and dough-based Malaysian food.

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