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Original Article

Postprandial triglyceride responses and endothelial function in prediabetic first-degree relatives of patients with diabetes

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KEYWORDS:
Postprandial triglycerides;
Endothelial dysfunction;
Prediabetes;
Family history;
Dyslipidemia

BACKGROUND: Only a few studies have reported on postprandial lipid responses and endothelial function in prediabetic subjects. None of the study has compared role of familial predisposition in determining postprandial endothelial dysfunction and postprandial hypertriglyceridemia in subjects with prediabetes.

OBJECTIVE: The objective was to study the postprandial triglyceride (PPTG) responses and endothelial function in prediabetic first-degree relatives of patients with diabetes.

METHODS: Thirty-nine subjects were recruited on the basis of oral glucose tolerance test into 3 groups: group 1, prediabetic subjects who had a first-degree relative with diabetes; group 2, prediabetic subjects without family history of diabetes; and group 3, normal glucose tolerance subjects without family history of diabetes. Oral fat challenge test was performed in all study subjects and PPTG responses were measured up to 8 hours. Postprandial endothelial function after 4 hours of fat challenge was estimated by flow-mediated dilation.

RESULTS: Postprandial endothelial dysfunction was greatest in group 1 and significantly higher in group 1 compared with group 2 ($P < .001$) and group 2 compared with group 3 ($P < .001$). PPTG responses (TG-AUC, TG-peak, TG-6 hour, and TG-8 hour) were significantly higher in group 1 compared with groups 2 and 3. However, they were similar between groups 2 and 3. Endothelial function showed significant negative correlation with TG-6 hour and TG-8 hour.

CONCLUSION: Prediabetic subjects respond to fat challenge with a greater degree of TG response and endothelial dysfunction compared with normal glucose tolerance subjects especially if they have a first-degree relative with diabetes. This may contribute to enhanced cardiovascular risk reported in prediabetic individuals.

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Introduction

Atherosclerosis is believed to be a postprandial phenomenon.[1] The postprandial state is associated with acute and transient elevation of blood glucose and lipids, which are believed to increase the risk of vascular complications particularly in subjects with diabetes[2,3] and prediabetes.[4,5] Determining postprandial responses is complex and challenging. However, studies evaluating lipids and atherosclerosis should include postprandial parameters.

It has been reported that postprandial lipemia particularly hypertriglyceridemia can cause endothelial dysfunction,[6] which is recognized as an early process of atherosclerosis even in healthy subjects.[7] It has been reported that the risk of coronary heart disease is related more closely to postprandial serum triglyceride (TG) level or to delayed chylomicron remnant clearance than to fasting serum TG level.[7] Postprandial hypertriglyceridemia after a high-fat meal can cause endothelial dysfunction even in healthy subjects.[8] The mechanism of postprandial hypertriglyceridemia–induced endothelial dysfunction is still not clear, although it has been suggested that oxidative stress or direct injury to the vascular wall by TG-rich lipoprotein particles may cause endothelial dysfunction.[6] This endothelial dysfunction is an early process of atherosclerosis and consequently a very sensitive parameter of the early stage of atherosclerosis and thereby useful in the early diagnosis of patients with high risk of coronary artery disease.[8,9]

There are only a few studies in literature about postprandial lipid responses and their effects on endothelial function affecting cardiovascular morbidity in subjects with impaired glucose tolerance.[4,10–12] To the best of our knowledge, there is no study which has compared role of familial predisposition in determining postprandial endothelial dysfunction and postprandial hypertriglyceridemia in subjects with prediabetes. The present study was therefore designed to ascertain whether subjects with prediabetes have abnormal postprandial endothelial function and postprandial TG (PPTG) responses after fat challenge and whether there is any effect of family history of diabetes on these parameters.

Materials and methods

The study was approved by Institutional Ethical Committee for Human Research, University College of Medical Sciences, Delhi. An informed consent was obtained from each of the study participant, and guidelines of ethical committee were followed during the study.

Healthy male subjects between age group of 20 and 60 years were included in the study. Subjects with evidence of liver or kidney disease, endocrine disease affecting lipids (hypothyroidism, Cushing's syndrome), hypertriglyceridemia (fasting serum TGs ≥250 mg/dL), recent systemic illness, inherited disorder of lipid metabolism, hypertension, congestive heart failure, smoking, and those receiving drugs affecting lipid metabolism were excluded. Details of history and physical examination including anthropometric evaluation were recorded in a predesigned performa. Screening investigations included hemoglobin concentration, liver and kidney function tests, serum uric acid, and fasting serum lipid profile.

Thirty-nine subjects were recruited and divided on the basis of oral glucose tolerance test (OGTT) into 3 groups of 13 each: group 1, prediabetic subjects (impaired glucose tolerance ± impaired fasting glucose) who had a first-degree relative with diabetes; group 2, prediabetic subjects without family history of diabetes; and group 3, normal glucose tolerance (NGT) subjects without family history of diabetes. Prediabetes was diagnosed only if this was confirmed after a repeat OGTT. All the 3 study groups were matched for age, sex, body mass index, waist circumference, waist-to-hip ratio, and blood pressure. Fasting serum insulin on the day of OGTT was also measured. Subjects with fasting plasma glucose between 100 and <126 mg/dL were labeled as impaired fasting glucose and subjects with 2-hour post-OGTT plasma glucose (2 h PG) ≥140 to <200 mg/dL were labeled as impaired glucose tolerance subjects.

After 14 hours of overnight fasting, standardized oral fat challenge test[13] was performed in all the study subjects after hospitalization as follows. Blood was collected for fasting lipid parameters (0 hour). The subjects were then given a fatty meal in the form of whipped cream with sugar and fruits according to body surface area (729 kcal/m^2). The fatty meal included 65.2 g fat (saturated fat 64%, monounsaturated fatty acids 31%, and polyunsaturated fatty acids 5%), 240 mg cholesterol, 24.75 g carbohydrate, and 5.3 g protein per 729 kcal/m^2. Blood samples for lipid parameters were again drawn at 2, 4, 6, and 8 hours of the oral fat challenge and serum samples stored at −20°C for future analysis. All the biochemical estimations were done by commercially available kits. Serum insulin was estimated by immunoradiometric assay method. The very low-density lipoprotein cholesterol (VLDL-C) and low-density lipoprotein cholesterol (LDL-C) were calculated as follows: VLDL-C = TG/5 and LDL-C = [Total CHL − (HDL-C + VLDL-C)] and homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as HOMA-IR = [fasting insulin (mIU/L) × fasting glucose (mmol/mL)]/22.5.

Noninvasive flow-mediated dilation (FMD) was performed in all study subjects at 4th hour post oral fat challenge (high-resolution B-mode ultrasonography, P-700 Philips, transducer frequency 7.5 MHz). The scanning was conducted at the gain setting at time gain compensation appropriate for superficial structures.

The endothelial function was evaluated radiologically, by measuring FMD of the right brachial artery. Subjects were made to rest for 10 minutes in supine position before scanning. Right brachial artery longitudinal scans were taken 3.5 cm proximal to the antecubital fossa.

Baseline brachial artery diameter (D-0) was measured. Reactive hyperemia was created by placing a cuff on the forearm and inflating it to 250 mm Hg for 5 minutes, thereby occluded blood flow to the forearm, and endothelium-