The Association of Carotid Intima-Media Thickness and Postprandial Dyslipidemia in Patients with Type 2 Diabetes

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This research aimed at investigating the correlation between postprandial dyslipidemia and carotid intima-media thickness in people with diabetes.

Materials and Methods: In 28 diabetic patients and 22 age and sex-matched healthy adults, the carotid intima-media thickness was measured using Doppler ultrasound. Blood glucose, total cholesterol, triglycerides, LDL and HLD cholesterol level were measured after overnight fasting and again 4 hours after a standard high-fat meal.

Results: The carotid intima-media thickness of diabetic patients was greater than normal subjects (0.96±0.29 mm vs. 0.75±0.17 mm, respectively p=0.008). Diabetic patients showed postprandial hypertriglyceridemia (P=0.03). In patients with fasting hyperglycemia and postprandial hypertriglyceridemia, carotid intima-media thickness was greater than in patients with normal levels (p=0.04 and p=0.03 respectively).

Conclusion: Postprandial hypertriglyceridemia and fasting hyperglycemia may be an independent risk factor for early atherosclerosis and macrovascular disease in individuals with type 2 diabetes.

Key Words: Carotid intima-media thickness (IMT), Type 2 Diabetes

Introduction
Cardiovascular disease (CVD) is the leading cause of death among diabetic patients. Two-thirds of patients with diabetes mellitus (DM) will eventually die of CVD. The risk of macrovascular complications (peripheral arterial disease, congestive heart failure, coronary artery disease, myocardial infarction and sudden death) increases up to fivefold in patients with diabetes.1 Mortality and morbidity of CVD significantly decrease in the non-diabetic population through restricted control of traditional risk factors, namely hypertension, smoking, and hyperlipidemia; however, this is not true for diabetic patients. The rising prevalence of type 2 diabetes increases the global burden of cardiovascular disease. Since the so-called traditional risk factors cannot fully explain the excessive cardiovascular disease risk of type 2 diabetic patients, other risk factors need to be identified.2 Several studies indicate that postprandial metabolic derangements, most notably hyperglycemia and hypertriglyceridemia, are important cardiovascular risk factors since they in-

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duce oxidative stress and endothelial dysfunction, although the mechanism is unclear. Measurement of carotid intimae-media thickness, (IMT) by ultrasonography is a noninvasive and quantitative method of evaluating early atherosclerotic changes in the vasculature. It has been shown that an increase in carotid IMT is associated with an increased risk of ischemic heart disease (IHD) or cerebrovascular disease. In fact, increase in thickness of the intimae and media of the carotid artery is directly associated with an increased risk of myocardial infarction and stroke in older adults without a history of cardiovascular disease. In this study, we investigate the association between postprandial metabolic derangements (hyperglycemia and dyslipidemia) and carotid intimae-media thickness.

Materials and Method
A total of 28 people (10 males and 18 females) with type 2 diabetes and 22 healthy individuals as a control group (10 males and 12 females) were recruited in 2005 at the outpatient clinic of the Iran Institute of Endocrinology and Metabolism, affiliated to Iran University of Medical Sciences in Tehran. The diagnosis of diabetes mellitus was made as per criteria laid down by WHO and patients aged over 30 years with fasting or postprandial hyperglycemia or both were included in the study. The subjects were excluded if they had a history of ketonuria or ketoacidosis, insulin requirement or any evidence of acute metabolic complications, acute infections, cerebrovascular accidents or ischaemic heart disease.

Blood glucose, total cholesterol, triglycerides and HDL cholesterol were measured after overnight fasting, and again after a standard high fat meal, the total energy content of which was 725 kcal, 38% of which was obtained from fat, 22% from protein, and 40% from carbohydrates; it consisted of two boiled-eggs, 15 gr butter, six slices of white bread, and 240 ml of milk. Blood glucose was measured by enzymatic calorimetric photometry with glucose oxidize enzyme test. Blood triglycerides, cholesterol and HDL cholesterol were measured by GPO-PAP diagnostic kit. LDL cholesterol was calculated using the Freidwald formula.

Carotid intimae-media thickness was measured with high resolution B-mode ultrasonography by AUS harmonic operator’s manual device (code 830 0219 000 Rev.C). For each subject, four measurements from the right and left common carotid arteries and the internal carotid arteries were done. The mean value of these measurements was calculated; the procedure was done by the same person.

For assessing the differences between groups, analysis of variance was used and Tukey-Duncan multiple comparison test was applied when appropriate. The difference of IMT in high and low levels of variables was determined by t-test (independent-samples t test and paired-samples t test). P value of <0.05 was considered statistically significant.

Results
The clinical and biochemical characteristics of the diabetic and control groups are presented in Table 1. The mean age of the diabetic subjects was 52.9 (SD=3.4) years while that of the control group was 50.8 years (SD=6.3). Females were more predominant in both groups. The mean duration of diabetes was 11.3 (SD=6.5) years.

The means of fasting triglyceride levels in the diabetic and control groups were 146.1 and 112.1 mg/dL respectively and those of postprandial triglyceride were 194.1 and 161.7 mg/dL in these groups respectively. There was no statistically significant difference between these groups (Table 1, Fig.1.).
Intima – media thickness and dyslipidemia

Table 1. Demographic and biochemical characteristic of the study sample

<table>
<thead>
<tr>
<th>Variables</th>
<th>Diabetic group (n=28)</th>
<th>Non-diabetic group (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female/ Male (number)</td>
<td>10/18</td>
<td>10/12</td>
</tr>
<tr>
<td>Age (years)*</td>
<td>52.9±9.3</td>
<td>50.8±13.2</td>
</tr>
<tr>
<td>Duration of diabetes (years)</td>
<td>11.3±6.5</td>
<td>-</td>
</tr>
<tr>
<td>Fasting Blood Glucose (mg/dL)</td>
<td>167.2±45.2</td>
<td>80.8±14.2</td>
</tr>
<tr>
<td>Fasting Triglyceride (mg/dL)</td>
<td>146.1±63.5</td>
<td>112.1±48.3</td>
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<tr>
<td>Fasting Cholesterol (mg/dL)</td>
<td>180.2±33.4</td>
<td>172.3±38.9</td>
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<tr>
<td>Fasting HDL (mg/dL)</td>
<td>47.2±10.6</td>
<td>91.4±6.2</td>
</tr>
<tr>
<td>Fasting LDL (mg/dL)</td>
<td>100.8±22.5</td>
<td>107.5±33.8</td>
</tr>
<tr>
<td>Postprandial Glucose (mg/dL)</td>
<td>194.5±69.1</td>
<td>87.8±14.4</td>
</tr>
<tr>
<td>Postprandial Triglyceride (mg/dL)</td>
<td>194±106.4</td>
<td>161.7±46.4</td>
</tr>
<tr>
<td>Postprandial Cholesterol (mg/dL)</td>
<td>189.8±46.9</td>
<td>171.3±37.2</td>
</tr>
<tr>
<td>Postprandial HDL (mg/dL)</td>
<td>47±18.6</td>
<td>37±7.5</td>
</tr>
<tr>
<td>Postprandial LDL (mg/dL)</td>
<td>103±32.2</td>
<td>107.5±41.1</td>
</tr>
</tbody>
</table>

*Mean±SD

The carotid IMT was higher among the diabetic group compared with the control group and this difference was statistically significant (0.96±0.2 VS 0.75±0.1, P=0.008) (Fig.2).

We used the regression model to adjust the gender (sex) and also duration of diabetes but these factors were not associated with intima thickness.

Discussion

The findings of our study showed that postprandial triglycerides and fasting blood glucose are two important factors that may affect carotid intima-media thickness. Although several studies have shown fasting triglyceride levels to be associated with CHD in both diabetic and non-diabetic subjects,5-9 relatively little attention has been given to...
postprandial triglycerides in this regard, especially in diabetic subjects. Teno et al. showed that postprandial triglyceride levels showed the strongest statistical association with carotid IMT in a cohort of type 2 diabetic subjects despite normal fasting triglyceride levels. The finding of this study showed that there is no significant difference of IMT between males and females and this is accordance with other reports.

It is evident that postprandial dyslipidemia can induce oxidative stress and endothelial dysfunction since endothelial dysfunction is accompanied by a significant nitric oxide increase. In fact, the postprandial state as produced by ingestion of a fat-enriched meal, is associated with endothelial activation, as indicated by the increased circulating levels of the proinflammatory cytokines such as IL-1, IL-6 and adhesion molecules ICAM-1 and VCAM-1. The most common presentation of diabetes is elevated fasting blood sugar. Hyperglycemia via glycation and increase in activity of the protein kinase C pathway appears to cause oxidative stress. Postprandial dyslipidemia also interacts with the process of thrombosis and an elevated postprandial triglyceride-rich lipoprotein concentration has the ability to activate coagulation factor 7 and the plasminogen activator inhibitor.

Similar to postprandial hyperglycemia, postprandial increases in triglycerides are proinflammatory, prothrombotic, and adversely affect several endothelial functions, by inducing oxidative stress. Therefore it is feasible that prolonged postprandial hypertriglyceridemia leads to an atherogenic environment.

Our study supports the association of fasting hyperglycemia and postprandial increases in triglyceride level with carotid intima-media thickness in patients with type 2 diabetes. Therefore control of fasting hyperglycemia plus hypertriglyceridemia, especially in the postprandial state, may be beneficial in reducing the rate of macro-vascular complication, namely coronary heart disease and stroke, in patients with type 2 diabetes.

References