Postprandial hypertriglyceridaemia in type 2 diabetic subjects

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Postprandial hyperlipidemia is a major risk factor for cardiovascular diseases in type 2 diabetes. The dyslipidemia of diabetes in the postprandial phase is a major determinant of the atherogenicity of LDL. This study was done to study the postprandial triglyceride levels in patients with type 2 diabetes mellitus; to assess the relationship between fasting and postprandial triglyceride levels and postprandial triglyceride levels and fasting blood sugar values in type 2 diabetes; and to analyze the relationship between postprandial hypertriglyceridaemia and conventional coronary risk factors.

One hundred type 2 diabetic subjects (M:F - 67:33, mean age 56.6 ± 11.9 years, mean body mass index 24.83 kg/m²) were studied and compared with controls. Fasting and 2-hour postprandial responses with respect to plasma glucose and triglycerides (TG) were measured after a breakfast meal, usually consumed by the patient with usual dose of insulin or oral hypoglycemic drugs. Postprandial hypertriglyceridaemia was taken as a postprandial TG value greater than 15% of the corresponding fasting TG value. There was significant postprandial hypertriglyceridaemia in diabetics in comparison to controls. FBG was significantly related to fasting and postprandial triglycerides. As FBG increased, both fasting and postprandial TG increased. Fasting TG was significantly related to postprandial TG. As fasting TG increased, postprandial TG increased. There was no correlation between postprandial TG and age, sex, smoking, hypertension, total and LDL cholesterol.

KEY WORDS: Coronary risk factors, postprandial hypertriglyceridaemia, type 2 diabetes

Diabetes mellitus (DM) is an important risk factor for the development of premature atherosclerosis. The increased rate of coronary artery disease (CAD) in patients with DM is attributable in part to specific disorders of lipoprotein metabolism. These include disordered metabolism of VLDL and chylomicrons that may be atherogenic. The dyslipidemia of diabetes in the postprandial phase is a major determinant of the atherogenicity of LDL, which may account for the up to fivefold increase in atherosclerosis in the diabetic patient.

Elevated postprandial triglycerides, peak postprandial triglyceridaemia have been associated in clinical trials with both early coronary artery and carotid artery atherosclerosis for persons with hyperlipidemia, independent of established risk factors.[4,5] Various clinical trials both in India (Chennai) and the West (Spain, USA, Sweden) have shown that postprandial hypertriglyceridaemia is common in type 2 DM. Normalization of the postprandial phase in diabetes will yield important cardiovascular benefits.

Hence this study is being carried out to find out the characteristics of postprandial triglyceride levels in patients with type 2 diabetes mellitus in comparison with healthy population and also to analyze the significance of postprandial triglyceridaemia as a risk factor for CAD in diabetes.

Methodology

The study was conducted over a period of 6 months - during March to August 2005. The study was designed as a case control study. One hundred consecutive patients meeting the inclusion criteria on treatment at the Department of Internal Medicine, Medical College Hospital, Thiruvananthapuram, were included. Normal healthy controls, age and sex matched, were selected.

Inclusion criteria
Diagnosed type 2 diabetes mellitus patients on treatment, in the age group 45-65 years.

Control: Healthy controls in the age group 45-65 years.
Exclusion criteria
Overt thyroid dysfunction
Familial hyperlipidemia
Nephrotic range proteinuria
On drugs like antihyperlipidemic agents, beta blockers, thiazides, oral contraceptive pills, steroids

Data collection
A detailed pro forma was filled up for each patient, which included age, sex, IP number, past history of coronary artery disease and cerebrovascular accident, family history of CAD, history of smoking and history of hypertension; and laboratory parameters including fasting and postprandial blood glucose, renal function tests, liver function tests, serum total cholesterol, serum triglycerides (fasting and postprandial), LDL cholesterol, HDL cholesterol and VLDL were noted. A detailed physical examination was done, including examination of the cardiovascular system. Blood pressure was recorded with a standard manometer using WHO guidelines.

Criteria for dyslipidemia were those recommended by the National Cholesterol Education Programme ATP III guidelines. All individuals with a history of smoking (either present or within the past year) were classified as smokers. This included bidi smokers and tobacco chewers. Hypertension was diagnosed and classified according to the JNC VII criteria. A fasting plasma glucose 126 mg/dl or previous history of diabetes mellitus was required for the diagnosis of diabetes. In this study, a value of 15% above fasting triglyceride value was taken as cutoff for postprandial hypertriglyceridaemia.

Blood was collected from patients after an overnight (12-hour) fast and 2-hour postprandial (after a breakfast meal) for lipid profile measurements.

Results

Majority of the patients with diabetes were male (67% vs. 33% female). The mean age of patients with diabetes was 56.6 ± 11.9 years, and that of the controls was 53.5 ± 12.7 years. The maximum number of people in both the cases (42%) and controls (40%) were in the 50-59 years age group. As many as 27% of the patients in the study group had past history of coronary artery disease or cerebrovascular accident compared to 10% of controls (P < 0.001). Family history of coronary artery disease was present in nine patients, while none of the controls had it. The prevalence of systemic hypertension was seen to be significantly higher in the cases (28% of the cases vs. 14% of controls) (P < 0.001). As many as 60% of the cases were smokers compared to 12% of the controls. The difference was statistically significant (P < 0.01). The lipid profiles showed significantly higher levels of total cholesterol (P < 0.05) and postprandial triglyceride (P < 0.01) in diabetics compared to the controls [Table 1]. The HDL, LDL cholesterol and fasting triglyceride levels were not significantly different in the two groups. Our results differ with the study by Ceriello et al., in which 42% of cases had FBG >200 (P < 0.001). As many as 45% of controls had IGT (FBS 110-126) (P < 0.001). FBG was found to be significantly related to F-Tg (r - 0.209) [P < 0.05] and PP-Tg. (r - 0.201) [P < 0.05]. As FBG increased, both F-Tg and PP-Tg increased. There was no significant relation between FBS and F-Tg and PP-Tg in controls. F-Tg was significantly related to PP-Tg (r - 0.909) [P < 0.01] in diabetics. As F-Tg increased, PP-Tg increased in the study group. There was significant postprandial hypertriglyceridaemia (P < 0.001) in diabetics when compared to controls [Table 2]. There was no correlation between postprandial triglyceride level and age, sex, smoking, hypertension, total and LDL cholesterol.

Discussion

The mean age of patients with diabetes in this study was 56.6 years. Majority of patients with diabetes were in the 50-59 years age group, indicating that there was an increased incidence of diabetes with increasing age. Majority of cases were males, and male-to-female ratio was 7:3. The prevalence of systemic hypertension was seen to be significantly higher in the cases. There was a significantly higher incidence of CAD and CVA in the cases. The lipid profiles showed significantly higher levels of total cholesterol and postprandial triglyceride in the cases compared to the controls. The HDL, LDL cholesterol and fasting triglyceride levels were not significantly different in the two groups. As many as 42% of the cases had fasting blood glucose >200, showing that diabetes was poorly controlled in a significant number of cases. FBG was significantly related to fasting and postprandial triglycerides. As FBG increased, both fasting and postprandial triglycerides increased. Fasting triglyceride was significantly related to postprandial triglycerides. As fasting triglyceride increased, postprandial triglycerides increased.

There was significant postprandial hypertriglyceridaemia in cases when compared to controls. There was no correlation between postprandial triglyceride level and age, sex, smoking, hypertension, total and LDL cholesterol.
Further studies should also clarify which carbohydrate diets have fewer propensities to cause PPHL.\[5,6\] Diet-gene interactions of PPHL should be investigated, although practical implications are limited. Several drugs could improve postprandial lipoprotein metabolism, including ω-3 fatty acids,\[7,8\] HMG Co-A reductase inhibitors\[9,10\] and thiazolidinediones. However, usefulness of these drugs in those with PPHL alone remains to be investigated.

The future
Guidelines for a cut off value of postprandial hypertriglyceridaemia have to be published. Some questions remain unanswered. These are:
1. Should postprandial triglyceride be measured routinely in diabetes?
2. What are the treatment options for postprandial hypertriglyceridaemia?

Hence studies of postprandial triglyceride have to be continued into the future.

Table 1: Lipids in diabetics and controls

<table>
<thead>
<tr>
<th></th>
<th>Group</th>
<th>Mean</th>
<th>Ceriello et al.[1]</th>
<th>C.R Soman et al.[2]</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL (mg/dl)</td>
<td>Controls</td>
<td>41.16 ± 7.9</td>
<td>42.50 ± 15.42</td>
<td>54.1 ± 13.2</td>
</tr>
<tr>
<td></td>
<td>Cases</td>
<td>41.20 ± 11.9</td>
<td>42.11 ± 15.42</td>
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<tr>
<td>LDL (mg/dl)</td>
<td>Controls</td>
<td>127.88 ± 32.9</td>
<td>122.66 ± 37.9</td>
<td>145.9 ± 41.0</td>
</tr>
<tr>
<td></td>
<td>Cases</td>
<td>141.36 ± 50.6</td>
<td>130.04 ± 48.5</td>
<td></td>
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<tr>
<td>Total Cholesterol (mg/dl)</td>
<td>Controls</td>
<td>197.16 ± 37.1</td>
<td>190.46 ± 37.6</td>
<td>223.7 ± 45.3</td>
</tr>
<tr>
<td></td>
<td>Cases</td>
<td>214.12 ± 53.0</td>
<td>194.67 ± 34.9</td>
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<tr>
<td>FTG (mg/dl)</td>
<td>Controls</td>
<td>170.90 ± 15.5</td>
<td>176.2 ± 16.31</td>
<td>167 ± 18.2</td>
</tr>
<tr>
<td></td>
<td>Cases</td>
<td>170.43 ± 14.9</td>
<td>163.04 ± 15.5</td>
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<tr>
<td>PPTG (mg/dl)</td>
<td>Controls</td>
<td>180.53 ± 15.2</td>
<td>191.13 ± 14.2</td>
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</tr>
<tr>
<td></td>
<td>Cases</td>
<td>204.44 ± 15.9</td>
<td>209.34 ± 16.7</td>
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</table>

Table 2: Mean percent difference between fasting and postprandial triglycerides

<table>
<thead>
<tr>
<th>Mean % difference between FTG and PPTG</th>
<th>Present study</th>
<th>Thesis Ceriello et al.[1]</th>
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<tbody>
<tr>
<td>Cases</td>
<td>23.2</td>
<td>21.46</td>
</tr>
<tr>
<td>Controls</td>
<td>12.7</td>
<td>13.21</td>
</tr>
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</table>

Issues to be addressed about postprandial hypertriglyceridaemia (PPHL)

Despite the growing literature on PPHL, several issues remain unanswered. First, the precise cut off point for PPHL is not yet known. Several studies use 15% or greater of F-Tg as cutoff for postprandial hypertriglyceridaemia.\[11\]

Second, how important is PPHL in the causation of CAD in Asian Indians? Heterogeneous etiological factors for CAD preclude simple answers to this question. PPHL should be viewed as an important cardiovascular risk factor in the realm of abdominal obesity and metabolic syndrome in Asian Indians.\[2-4\] Whether it contributes independently to the risk of CAD in Asian Indians remains to be investigated.

Third, should PPHL be investigated routinely? No guidelines are available on this issue. One could presume that PPHL is present in patients with fasting hypertriglyceridaemia. It would be rational to investigate for PPHL in those with normal fasting lipid levels but having abdominal obesity.

Fourth, what are the treatment options for PPHL in Asian Indians? Diet and physical exercise should be advised to reduce abdominal obesity and insulin resistance. An important issue would be ‘how low should be a low-carbohydrate diet to effectively prevent PPHL?’

References


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