Postprandial lipemia in pre- and postmenopausal women

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Abstract

Background and Objective: The increased risk for coronary artery disease observed in postmenopausal (PoW) women is partly explained by a more atherogenic lipoprotein profile. Moreover, natural menopause has been associated with an altered postprandial lipid profile. This study was designed to test the hypothesis that young premenopausal (PrW) and PoW may be independently associated with postprandial lipemia and indirectly associated with atherosclerosis.

Patients and Methods: A total of 46 healthy PrW and 44 healthy PoW participated in a 5-h intervention study. Blood samples were taken at the baseline and at 1, 2, 3, and 4 h after eating. Total cholesterol, LDL-cholesterol, HDL-cholesterol, fasting, and postprandial triglycerides (PPTG) were determined sequentially in blood samples.

Results: PPTG presented significant higher values in PoW compared to PrW (P < 0.05), but other lipids did not significantly differ between groups. PPTG concentrations in PoW were significantly higher than in PrW (P < 0.05). There was a significant time influence (P < 0.05) in TG in PrW and PoW, while time to peak and peak concentration were significantly higher in PoW than PrW. Other lipids were also decreased more in PrW than PoW, but not significantly so. Cholesterol concentrations showed a significant reduction after 2 h, to reach values similar to the baseline after 4 h in PrW but not in PoW. HDL-cholesterol concentration was decreased more in PoW compared to PrW but it was not significant.

Conclusions: Lipid postprandial response indicates a higher cardiovascular risk pattern in PoW compared to PrW.

Key words: Atherosclerosis, lipid profile, postprandial lipemia, postmenopause, premenopause

INTRODUCTION

Recent research shows close association of postprandial lipemia (PPL) with atherosclerosis. Triglycerides (TGs) are better predictors, although their predictive power has been underestimated in many epidemiological studies. Exaggerated PPL has invariably been observed in normolipidemic men and in one study of normolipidemic women with coronary artery disease (CAD). PPL is closely correlated with carotid intima-media thickness in normolipidemic and hyperlipidemic individuals independent of other risk factors. Higher daytime triglyceridemia with similar fasting triglyceride (FTG) levels was observed in subjects with premature CAD as compared to their first-degree relatives without CAD. Indeed some evidence suggests that postprandial plasma triglyceride (PPTG) levels predict future myocardial infarction better than FTG levels. Many studies have consistently shown that, in the hours following a meal, TG concentration is higher in patients with CAD than in subjects without, and this is an independent risk factor for CAD. Postprandial lipoprotein metabolism is affected by dietary habits, meal composition (amount and type of fat, carbohydrates, proteins, fiber, and alcohol), lifestyle practices, (physical activity and tobacco use), physiological factors (age, gender, and menopausal status), and pathological conditions (obesity, insulin resistance, diabetes mellitus (DM), etc). Abnormalities during the postprandial state contribute to the development of atherosclerosis and cardiovascular risk. The TG-rich lipoproteins are involved in many pathways leading to atherosclerosis. They are carriers of cholesterol esters to the vessel wall and they are toxic to the endothelial cells (ECs) and induce endothelial dysfunction. More and more research suggest that increased PPTG, not
very few data exist, and could not be taking vitamin, mineral, or phytoestrogen supplements. Medication known to affect bone and lipid metabolism or be receiving estrogen replacement therapy or any other medication known to affect bone and lipid metabolism or be taking vitamin, mineral, or phytoestrogen supplements. None of the women smoked.

Women for the postmenopausal group had to be amenorrheic for at least 1 year, non-hypertensive, non-diabetic, could not be obese (BMI < 30 kg/m²), could not be receiving estrogen replacement therapy or any other medication known to affect bone and lipid metabolism or be taking vitamin, mineral, or phytoestrogen supplements. None of the women smoked.

In order to unify food intake the evening before the study, all participants followed written instructions with regard to a standardized dinner composition (known amount of vegetables and chicken curry with given quantity of rice). They were instructed to eat it before 21:00 h (in the previous evening) to avoid the effects of previous food intake and then refrained from all food and beverages (except water) until 08:30 h on the following morning. All participants had to be at the laboratory around 08:30 AM and remain at rest without ingesting any type of food, except the standard meal and water. The meal was ingested in up to 15 min and comprised sandwich loaf (two slices equivalent to 140 g) and butter (about 20 g). On the morning of the visit, blood pressure, weight, and height were measured and compliance with dinner instructions was verified with a questionnaire. After that, each participant underwent a structured examination, which included an interview. Height, weight, waist circumference (WC) and hip measurements, a fasting venipuncture, and sequential determination of serum lipids were done. Height and weight were measured to the nearest 0.5 cm and 0.1 kg, respectively. BMI was calculated as weight (kilogram) divided by height (in meter) squared. WC was determined to the nearest 0.1 cm using a measuring tape positioned at the midpoint between the lowest rib and the iliac crest and hips were measured at the largest gluteal circumference. These measurements were used to calculate the waist-to-hip ratio (WHR). Then, blood pressure was measured using a standard mercury sphygmomanometer. Postprandial blood samples were taken 1, 2, 3, and 4 h after the end of the study meal. To maintain hydration throughout the postprandial time, women drank 100 ml of demineralized water after 1, 2, and 3 h after eating. Samples were centrifuged; serum was collected and stored at 20 °C until analyzed. Lipid profiles comprising TC, HDL-C, LDL-C, and TG concentrations were measured at fasting and at 1, 2, 3, and 4 h post-load. Sample serum concentrations of TC, HDL-C, and TG were measured by enzymatic colorimetric methods using a Star Plus 21 semi-autoanalyser of Rapid Diagnostic Company. Calculation of LDL-C concentrations was based on the Friedewald equation. The diagnosis of DM was based on WHO criteria, i.e. a fasting plasma glucose level > 7.0 mmol/L or > 126 mg/dL, or a 2-h postprandial plasma glucose level > 11.1 mmol/L or > 200 mg/dL on more than one occasion, with symptoms of diabetes. All data were entered into an Excel spreadsheet, and were analyzed using standard statistical software such as SPSS. Chi-square test was used for categorical variables. All numerical data were presented as mean ± standard deviation. A P value of less than 0.05 was considered statistically significant.

Subjects of the premenopausal group were between the ages of 18 and 37, and those from the postmenopausal group were between 52 and 58 years of age. The anthropometric measurements and clinical characteristics of the groups of patients and the control subjects are summarized in Table 1. PrW (n = 46) and PoW (n = 44) were matched for BMI (mean ± SD = 26.1 ± 2.8 vs. 27.3...
± 2.4 kg/m², respectively), WC (mean ± SD = 92.1 ± 7.1 vs. 92.4 ± 8.7 cm, respectively), and WHR (mean ± SD = 0.92 ± 0.08 vs. 0.93 ± 0.01).

The result of the study on the relationship between the serum lipids in PrW and PoW are represented in Figures 1–4. The mean TC in mg/dL was 157, 168, 188, and 156 at fasting, 1, 2, 3, and 4 h in the PrW vs. 162, 175, 196, 180, and 173 in the PoW during the same duration. Cholesterol concentrations showed a significant reduction after 2 h, to reach values similar to the baseline after 4 h in PrW but not in PoW. The mean HDL-C in mg/dL was 47.34, 43.63, 42.1, 42.28 and 41.2 at fasting, first, second, third and fourth hours after the test meal in the PrW vs. 44.3, 42.8, 42.2, 43.11, and 39.14 in the PoW during the same time interval. This shows that HDL-C concentration was decreased more in PoW compared to PrW but it was not significant. The mean LDL-C in mg/dL was 121.39, 127.27, 106.3, 101, and 92.8 at fasting, 1, 2, 3, and 4 h in the PrW vs. 134.54, 139.3, 126, 128.3, and 114.1 in the PoW during the same amount of time.

### Table 1: Anthropometric measurements of the premenopausal and postmenopausal women

<table>
<thead>
<tr>
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<th>Premenopausal (n = 46) (mean ± SD)</th>
<th>Postmenopausal (n = 44) (mean ± SD)</th>
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<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>26.1 ± 2.8</td>
<td>27.3 ± 2.4</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>92.1 ± 7.1</td>
<td>92.4 ± 8.7</td>
</tr>
<tr>
<td>WHR</td>
<td>0.92 ± 0.08</td>
<td>0.93 ± 0.01</td>
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n: Number of women in the group; BMI: Body mass index; WHR: Waist-to-hip ratio; WC: Waist circumference

FTG was significantly related to PPTG in PrW and PoW. As FTG increased, PPTG also increased in the study group. The PPTG was increased significantly more in PoW (148 mg/dL, 178 mg/dL, 189 mg/dL, and 206 mg/dL in the first, second, third and fourth hours after the test meal) compared to PrW (94 mg/dL, 136 mg/dL, 168 mg/dL, and 153 mg/dL in the first, second, third and fourth hours after the test meal), P < 0.05. There was a significant time influence (P < 0.05) in TG in PrW and PoW, while time to peak and peak concentration were significantly higher in PoW than PrW. In this study postprandially, 43% of PoW had TG levels more than the highest TG level in PrW.

### DISCUSSION

This study clearly shows the differences in PPTG response between PoW and PrW with similar age, BMI, daily intake, even after careful matching. PoW displays higher PPL than PrW, and the TG concentration in PoW does not return to baseline levels within 4 h. Even when adjusting for TG baseline values, these differences were still observed. We studied nonsmoking women of similar age and BMI, because smoking, obesity, and age influence both lipid metabolism and the occurrence of menopause. In theory, the selection of age-matched groups might be a problem, because the fact that menopause was reached at a different chronological age could be an indication of under menopausal changes in fasting plasma lipids in our study were highly comparable to those found by others.
in longitudinal\cite{37,38} or cross-sectional\cite{39,40} studies. Several clinical studies have shown that the magnitude and duration of PPL are positively related to the pathogenesis and progression of coronary heart disease (CHD). Postprandial lipid metabolism refers to the series of metabolic events that occur following the ingestion of a meal containing fat. Dietary fat is principally composed of TG; PPL therefore being characterized by an increase in plasma TG concentration.\cite{44} PPL is influenced by various parameters such as gastric emptying time, intestinal absorption, and lipoprotein lipase activity. Some studies have shown that the gastric emptying of liquids and solids decreases with age,\cite{42} but intestinal motility is not altered with age.\cite{43} Pancreatic secretion slightly decreases with age.\cite{44} However, Arora et al\cite{45,46} studying healthy individuals have reported that fecal excretion, and, consequently, fat absorption changes slightly with age, suggesting that the decrease in pancreatic secretion is not enough to hinder the normal digestive process. One could imagine that because older individuals have a longer gastric emptying time, the absorption of fat would be slowed, justifying a late elevation in triglyceridemia. With age, gastric emptying rate and lipoprotein lipase activity are known to decrease, and a reduction of pancreatic lipase secretion and a delay in the clearance of TG-rich lipoproteins have also been observed.\cite{41} Bibliographical data on postprandial metabolism in PrW and PoW women are scarce and the studies that have been undertaken involve very small numbers of subjects. It is also difficult to compare data due to of the variety of food employed in the different studies. The lower PPL displayed by the PrW in this study was also found in other studies, with levels of TG for PrW and PoW similar to our data.\cite{47} Nabeno et al.\cite{41} reported similar results, but differ in the baseline characteristics of the women studied and in the food consumed, which was given as a fat-rich cream. Hyperinsulinemia usually induces an overproduction of TG-rich lipoproteins in the liver by increasing the availability of free fatty acids, which are the most important precursors of de novo TG synthesis. However, it has been seen that the postprandial response is complex, and both lipoprotein concentrations and composition are affected.\cite{48} In the study by Pirro et al., it has been seen that PoW women with mixed hyperlipemia show a greater PPTG increase and a more pronounced reduction in the HDL-C level and LDL-C size than hypercholesterolemic and normolipemic subjects. The presence of the features of insulin resistance syndrome could contribute to the deterioration of postprandial lipemic response in those subjects.\cite{49} Data collected over 25 years ago from the Framingham Heart Study demonstrated that TG levels could influence the CAD risk only in patients with a low HDL-C concentration.\cite{50} After numerous reports, the association of high TG concentration with low HDL-C levels is now well established among patients with CAD.\cite{51} Other factors besides TG that have a further influence on HDL-C levels are BMI, adipose tissue distribution, serum glucose and insulin levels, smoking, and alcohol intake.\cite{52,53} A positive correlation between BMI and PPL has been reported in some studies where an elevated BMI seemed to aggravate the postprandial response.\cite{54} Prolonged exposure of the endothelium to TG-rich atherogenic remnant particles might be the reason why postprandial increases in TG account for greater CAD risk.\cite{55} Furthermore, the clearance of chylomicrons and their remnants is impaired in coronary atherosclerosis.\cite{56} Also, for those individuals at risk for CHD, chylomicrons can be poorly hydrolyzed and their clearance via hepatic receptor-mediated pathways delayed.\cite{57,58} Therefore, we can say that natural menopause is associated with aggravated PPL in women matched for age and BMI. Higher PPL potentially explains the relation of TGs and CHD mortality risk in PoW.\cite{59}

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