Postprandial changes in plasma and serum viscosity and plasma lipids and lipoproteins after an acute test meal\textsuperscript{1,2}

Christine C Tangney, Joanne M Hafner, Beth D McQuiston, Andrea J Domas, and Robert S Rosenson

ABSTRACT The influence of a fat-rich test meal on postprandial changes in plasma viscosity and serum viscosity was assessed in 12 normolipidemic adults. After a 12-14-h fast, volunteers (five men and seven women aged 23–50 y) were challenged with a test milk shake containing 50 g fat/m\textsuperscript{2} body surface area (BSA). Plasma viscosity, serum viscosity, and plasma lipids and lipoproteins were assessed at 0, 2, 3, 4, and 6 h. Viscosity values were determined by using a Mettler Contraves LS-40 rotational microviscometer. Postprandial changes in the study variables were assessed by area under the curve and included triacylglycerols (2.02 mmol/L), plasma viscosity (−0.10 mPa·s), and serum viscosity (−0.01 mPa·s). Peak plasma triacylglycerol concentrations were significantly greater than those observed at baseline \((P = 0.0022)\). There were no significant changes in any other variable when fasting and peak values were compared. Peak plasma viscosity increased in three and decreased in two subjects with no changes in the remaining seven subjects. Changes in peak plasma viscosity ranged from −7% to 7% with similar changes for serum viscosity, from −8% to 10%, and a slightly greater range for plasma fibrinogen, −16% to 10%. In this cohort of normotriacylglycerolemics, there were no significant postprandial changes in plasma viscosity or serum viscosity. \textit{Am J Clin Nutr} 1997;65:36–40.

KEY WORDS Plasma viscosity, serum viscosity, postprandial changes, normotriacylglycerolemia

INTRODUCTION

Changes in postprandial lipid concentrations have emerged as independent predictors of cardiovascular risk (1–5). Cross-sectional and case-control studies have shown that patients with coronary stenoses who are challenged with an acute fat load exhibit both a greater elevation in peak plasma triacylglycerol concentrations and a more prolonged lipemia than subjects without angiographically determined disease (1–3). In these studies, changes in postprandial triacylglycerol were predictive of coronary heart disease, whereas the fasting triacylglycerol concentration was not an important contributor.

Postprandial lipemia may modulate cardiovascular risk through delayed clearance or prolonged residence time of circulating factor VII (6, 7) or through hyperlipidemia-induced hyperviscosity (8, 9). Elevations in viscosity reduce capillary perfusion of poststenotic areas of coronary circulation (10, 11) and may predict cardiac events in patients with unstable angina (12) and in stroke survivors (13). Other than the immunoglobulins and fibrinogen, lipoprotein particles are important determinants of plasma viscosity (8, 9). Moreover, elevated plasma viscosity values have been found for patients with primary hyperlipoproteinemias, particularly triacylglycerol-enriched lipoproteins (14, 15).

Postprandial angina pectoris has been shown to be related to the severity of cardiovascular disease (16, 17). If changes in postprandial angina and postprandial triacylglycerol can predict cardiovascular risk in individuals with “normal” fasting lipid profiles, postprandial plasma viscosity measurements may improve characterization of this enhanced cardiovascular risk or provide a mechanistic explanation for the enhanced cardiovascular risk. Therefore, we evaluated postprandial changes in plasma lipids and lipoproteins and selected hemorheologic measures after ingestion of a standardized fat load by a cohort of normotriacylglycerolemics. Specifically, we determined whether a standardized fat-rich test load would elevate plasma viscosity and serum viscosity in such individuals. The latter was measured to evaluate the contribution of fibrinogen to plasma viscosity determinations.

SUBJECTS AND METHODS

Subjects

Twelve adult volunteers (five men and seven women aged 23–50 y) gave informed consent to participate in the study. Enrollment criteria included healthy nonsmokers with no active illness characterized by an acute-phase response or prior history of cardiac, hepatic, or endocrine diseases. Subjects were excluded if self-reported fasting total cholesterol concentrations were >6.22 mmol/L and triacylglycerols were >2.27 mmol/L or if these values exceeded the 90th percentile for their age (18). Participants were instructed to abstain from the consumption of any alcohol (including alcohol-containing products and medicines) for 72 h. One to 2 d before the designated test day, measurements of height, weight, waist circumference, and hip circumference were obtained from each.

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Received February 13, 1996. Accepted for publication August 27, 1996.
subject by the research nurse according to the *Anthropometric Standardization Reference Manual* (19). The “test” milk shake was prepared to reflect a standardized fat load for each subject by adjustment to body surface area (BSA) according to the Bootheby equation (20).

The study protocol was approved by the Rush-Presbyterian–St Luke’s Medical Center Human Investigation Committee.

**Intervention**

All subjects were instructed to report on the test day between 0800 and 0900 after a minimum 12-h overnight fast. On the test day, subjects were asked to maintain a constant, nonstrenuous activity level throughout that day. A hematocrit sample from every subject was evaluated at the beginning of each session to avoid phlebotomies from anemic individuals. Anemia was defined as a hematocrit < 0.40 for males and < 0.36 for females.

On the test day, the antecubital vein was catheterized with an intravenous cannula by a trained perfusion nurse using a tourniquet. The catheter was flushed with saline and the first 5 mL blood discarded to avoid any dilutional effects. Baseline blood samples were collected into evacuated tubes. Then the subject consumed the test milk shake within 10 min. The preparation represents a 50-g/m² fat load. The dietary composition is described in Table 1. Insensible water losses were replaced by 330 mL premeasured drinking water that was consumed by all subjects during the study. No other food or beverage was permitted for the next 6 h. Subsequent blood samples were obtained at 2, 3, 4, and 6 h.

**Analytical measurements**

Viscosity measurements were made at 37 °C on plasma and serum aliquots by using a Contraves LS-40 coaxial cylinder microviscometer and DIN 412 measuring cup (Mettler-Toledo AG, Greifensee, Switzerland). Viscosity determinations were obtained at 25 shear rates between 100 and 0.2 s⁻¹, and the results were averaged. The batch CV for plasma viscosity was 2.8% and was 2.3% for serum viscosity. Plasma concentrations of total cholesterol (CV = 1.3%), high-density-lipoprotein cholesterol (CV = 3.2%), low-density-lipoprotein cholesterol (CV = 7.8%), and triacylglycerols (CV = 3.5%) were assayed with standard chemical techniques by Rush Medical Laboratories at Rush-Presbyterian-St Luke’s Medical Center. Plasma fibrinogen measurements (21) represented an average of three individually acquired measurements that were selected to minimize previously recognized methodologic variability, batch CV = 5.8% (22).

**Data analyses**

Changes in postprandial lipids and viscosity were quantified in two ways:

1. The maximum changes from fasting values (either positive or negative) for each variable were identified in each subject. The magnitude of change was calculated as one-half of the sum of the two highest (or lowest) postprandial values minus the fasting values (23). This “peak” value was compared with that at baseline by using Wilcoxon’s matched-pairs signed-rank test to assess whether the acute test meal was responsible for significant changes from baseline measures (24, 25).
2. To estimate the magnitude of the postprandial changes in lipids, fibrinogen, plasma viscosity, and serum viscosity, the area for the 6-h period above the 0-h baseline value was integrated (23, 26). This expression will be referred to as the area under the curve.

Because of the small sample size and the nature of the variables studied, most statistical analyses used nonparametric procedures. Mann-Whitney U tests, Wilcoxon signed-rank tests, and Spearman rank correlations were performed by using SPSS-PC software, version 5.01 (27).

**RESULTS**

**Physical characteristics of the subjects**

The energy load of the test meal varied from 4150 to 6431 kJ (992 to 1537 kcal) and the total fat content varied from 75.5 to 117 g, based on the BSA of each subject. As illustrated in Table 2, one female and one male subject had a body mass index (BMI; kg/m²) indicative of obesity (BMI > 30). However, all subjects had desirable waist-hip ratios (WHR): < 1.0 for males and < 0.85 for females (28).

Fasting concentrations of triacylglycerols, fibrinogen, total cholesterol, and high-density-lipoprotein cholesterol, and plasma viscosity and serum viscosity are provided in Table 3. Plasma viscosity and serum viscosity values were consistent with “normal” values in our laboratory (± SD): 1.39 ± 0.08 mPa · s for plasma viscosity and 1.27 ± 0.06 mPa · s for serum

**TABLE 1**

Composition of oral fat load standardized to body surface area

<table>
<thead>
<tr>
<th>Ingredients (g)</th>
<th>264</th>
<th>116</th>
<th>35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haagen Dazs ice cream</td>
<td>Haagen Dazs ice cream</td>
<td>Haagen Dazs ice cream</td>
<td>Haagen Dazs ice cream</td>
</tr>
<tr>
<td>Cream of coconut</td>
<td>Cream of coconut</td>
<td>Cream of coconut</td>
<td>Cream of coconut</td>
</tr>
<tr>
<td>Pasteurized egg</td>
<td>Pasteurized egg</td>
<td>Pasteurized egg</td>
<td>Pasteurized egg</td>
</tr>
</tbody>
</table>

**Nutrients**

<table>
<thead>
<tr>
<th>Energy (kJ)</th>
<th>4481</th>
<th>69</th>
<th>16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrate (g)</td>
<td>Carbohydrate (g)</td>
<td>Carbohydrate (g)</td>
<td>Carbohydrate (g)</td>
</tr>
<tr>
<td>Protein (g)</td>
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<td>Protein (g)</td>
</tr>
<tr>
<td>Fat (total) (g)</td>
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<td>Fat (total) (g)</td>
</tr>
<tr>
<td>Saturated fat (g)</td>
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</tr>
<tr>
<td>Monounsaturated fat (g)</td>
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<tr>
<td>Polyunsaturated fat (g)</td>
<td>Polyunsaturated fat (g)</td>
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<td>Polyunsaturated fat (g)</td>
</tr>
<tr>
<td>Cholesterol (g)</td>
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<td>Cholesterol (g)</td>
</tr>
<tr>
<td>Carbohydrate (% of energy)</td>
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<td>Carbohydrate (% of energy)</td>
</tr>
<tr>
<td>Protein (% of energy)</td>
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<td>Protein (% of energy)</td>
</tr>
<tr>
<td>Fat (% of energy)</td>
<td>Fat (% of energy)</td>
<td>Fat (% of energy)</td>
<td>Fat (% of energy)</td>
</tr>
</tbody>
</table>

1. A typical “test” milk shake as presented to subject 1129 with a body surface area of 1.63 m².
2. Haagen-Dazs Co, Inc, Teaneck, NJ.
TABLE 3
Postprandial changes as compared with fasting values

<table>
<thead>
<tr>
<th>Variable</th>
<th>Fasting</th>
<th>Peak change*</th>
<th>AUC†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triacylglycerols (mmol/L)*</td>
<td>0.62 (0.29 to 0.87)</td>
<td>0.47 (0.13 to 1.81)</td>
<td>2.02 (0.31 to 6.58)</td>
</tr>
<tr>
<td>Plasma viscosity (mPars)</td>
<td>1.33 (1.24 to 1.43)</td>
<td>−0.01 (−0.96 to 0.08)</td>
<td>−0.10 (−0.42 to 0.23)</td>
</tr>
<tr>
<td>Serum viscosity (mPars)</td>
<td>1.25 (1.18 to 1.32)</td>
<td>0.01 (−0.11 to 0.12)</td>
<td>−0.01 (−0.44 to 0.45)</td>
</tr>
<tr>
<td>Fibrinogen (g/L)</td>
<td>2.42 (2.15 to 3.50)</td>
<td>−0.75 (−0.38 to 0.42)</td>
<td>0.10 (−1.55 to 0.90)</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>4.69 (3.21 to 5.87)</td>
<td>0.01 (−0.23 to 0.23)</td>
<td>−0.21 (−1.27 to 0.80)</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>1.40 (1.06 to 1.63)</td>
<td>−0.05 (−0.21 to 0.13)</td>
<td>−0.25 (−0.97 to 0.46)</td>
</tr>
</tbody>
</table>

* Medians; minimum and maximum values, or range, in parentheses.
† Maximal postprandial peak reflects the maximum change, whether positive or negative.
‡ Area under the curve per hour, as calculated by the trapezoidal rule, normalized to the 0-h concentration (23).
§ Fasting values were significantly different from that of peak, P = 0.0022.

viscosity (15). Similarly, fibrinogen concentrations were consistent with values obtained for normal healthy subjects in our laboratory (2.58 ± 0.58 g/L) (22).

Postprandial changes in lipids and rheologic measures

An identifiable peak in triacylglycerol concentrations was identified in all subjects after they ingested the “test” milk shake. The peak postprandial triacylglycerol concentration reflected a significant increase from baseline values (P = 0.0022). The magnitude of the peak response was highly variable among subjects, ranging from a minimum of 17% to a maximum of 229% above baseline concentrations (Table 3). The time of the peak triacylglycerol response varied from subject to subject; one subject exhibited the peak response at 2 h, two at 3 h, six at 4 h, and three at 6 h.

There were no significant differences for any other variables examined by peak response. The absence of change in hematocrit and total serum protein concentrations may support the contention that no volume depletion probably occurred or that these variables were too insensitive to detect meaningful changes in volume. Examination of “batch” CVs for the primary variables of interest dictates that the only meaningful postprandial changes are those that exceed methodologic variation. With the selection of a 2.8% minimal change in plasma viscosity, only two subjects had reductions in plasma viscosity postprandially, and three subjects had elevations in plasma viscosity. No other changes were observed in the remaining subjects. Postprandial fibrinogen values had to exceed a 6% change to be considered biologically meaningful. Five subjects had increases ranging from 6.3% to 18.4% whereas four volunteers had decreases from −9.3% to −16%.

When postprandial changes were quantified by area under the curve, a similar pattern was observed (Table 3). All subjects manifested a positive area under the curve for plasma triacylglycerols. The area under the curve for plasma viscosity and fibrinogen was positive in the same individuals who exhibited elevations in peak response. Similarly, those subjects with a negative peak response in plasma viscosity or fibrinogen also showed negative changes in area under the curve for that variable. The same eight individuals with a negative peak change in high-density-lipoprotein cholesterol response also exhibited an overall negative area under the curve. On the other hand, six subjects had a negative area under the curve for serum viscosity, but only five subjects had a negative peak response. Seven subjects displayed a negative area under the curve for total cholesterol, but only five subjects had negative peak responses and one subject manifested no change.

There were no significant correlations between fasting plasma viscosity values and fasting concentrations of any of the lipids other than a strong inverse relation with total triacylglycerols (ρ = −0.729, P < 0.01). Fasting serum viscosity values were also inversely associated with both measures of postprandial change in serum viscosity, for area under the curve (ρ = −0.762, P < 0.001) and for peak value (ρ = −0.587, P < 0.045).

DISCUSSION

This is the only report to describe rheologic changes in normotriacylglycerolemic subjects after consumption of an oral test fat load that was standardized to BSA. In this cohort of 12 normotriacylglycerolemic volunteers, there were no significant changes in either plasma viscosity or serum viscosity after ingestion of the test milk shake. Several other groups have also found that an oral fat-containing challenge did not result in significant changes in plasma viscosity. More than 30 y ago, Charm et al (29) reported no change in plasma viscosity measured 3 h after the consumption of 250 mL 30% cream by seven subjects. In yet another study of eight men who ingested 110 g butter on toast (3577 kJ, or 855 kcal), there was no change in plasma viscosity 3.5 h later (24). In contrast, Schütz et al (25) challenged 10 normolipidemic adults with 200 mL corn oil (6799 kJ, or 1625 kcal) and reported significant elevations in plasma viscosity and triacylglycerols at 2 h. These investigators reported that the fasting triacylglycerol concentration was the key predictor of postprandial plasma viscosity changes. Moreover, Schütz et al showed that very-low-density-lipoprotein particles had a marked influence on fasting plasma viscosity (a difference of 0.04 mPa · s) after comparing native samples from normotriacylglycerolemic subjects with the same samples centrifuged to remove triacylglycerol-rich lipoproteins. This difference was greater in plasma than in serum samples. In the present cohort of subjects, we observed a significant inverse association between fasting plasma viscosity and fasting triacylglycerol concentrations. In another report, six subjects who consumed a meal higher in fat content (85 g fat, 75% of energy as fat, and 3774 kJ, or 902 kcal) than our milk shake yet similar in energy load to that of ours, exhibited an average increase in plasma viscosity (0.05 mPa · s) 3 h postprandially that paralleled a 120% increase in plasma tria-
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cyglycerols (30). However, not all subjects had an increase in plasma viscosity (30). Unlike our report and others (24, 25, 29), Leschke et al (30) were the only investigators to report a marked change in an increase of ~60% in fibrinogen postprandially.

There are several methodologic differences between the postprandial viscosity studies. A capillary tube viscometer was used for plasma viscosity determinations in all the studies except ours. Each report measured viscosity at a variety of time points. Unlike the aforementioned reports (24, 25, 29, 30), we defined postprandial changes in terms of peak response and area under the curve for the selected variables of interest. In all studies except that by Schütz et al (25), the intervention was a "mixed" fat load that also contained some carbohydrate and protein. Finally, our study provides more detailed information on subject volunteers, including ages, sex, and anthropomorphic profiles.

The postprandial triacylglycerol response after a standardized fat load was described by both peak response and area under the curve (1–3, 23, 26). Considerable between-subject variability in postprandial triacylglycerol response was noted (23, 31). Our study and two others (25, 30) reported considerable between-subject variation in the postprandial response of plasma viscosity, serum viscosity, and fibrinogen. Whereas fasting plasma measures reflect the equilibrated state of lipid transport, the postprandial "state" probably reflects variable synthesis, secretion, and metabolism of chylomicrons and very-low-density lipoproteins.

Other sources of variation included measurement variation in outcome variables. There was no subject who displayed the magnitude of change in plasma fibrinogen concentrations reported by Leschke et al (30) despite the fact that the same assay and similar time points were evaluated. We measured three replicates of fibrinogen to account for this known methodologic variation (22). For viscosity measurements, replicate measures were not feasible because of the large sample volume required (4 mL plasma or serum per determination).

Although postprandially mediated triacylglycerol changes are independent predictors of coronary artery disease risk, the magnitude of these changes in this cohort of normolipidemic, healthy, active adults was insufficient to elevate plasma viscosity or serum viscosity. Whether these expressions of rheologic variables are predictive of cardiovascular risk in other high-risk patient groups merits further study (32, 33). Further studies necessitate evaluation of cohorts of subjects that may include subjects with established coronary heart disease, a family history of premature coronary artery disease and the presence of other major established coronary artery disease risk factors such as hyperlipidemia and non-insulin-dependent diabetes mellitus.

REFERENCES

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