Dietary cis and trans Monounsaturated and Saturated FA and Plasma Lipids and Lipoproteins in Men

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ARTICLES

ABSTRACT: Trans monounsaturated fatty acids (TFA) are hypercholesterolemic compared to oleic acid to a degree approaching or equivalent to saturated FA. However, it is unknown to what extent these effects may be due to cholesterol lowering by oleic acid rather than elevation by saturated FA and TFA. In order to better understand the impact of replacing TFA in foods, it is first necessary to know the relative lipid-modifying effects of the major FA that change as TFA are lowered or removed. For 5 wk, 50 normocholesterolemic men were fed controlled diets providing approximately 15% of energy from protein, 39% from fat, and 46% from carbohydrate in a randomized, 6 × 6, crossover design. Eight percent of energy was replaced across diets with the following: carbohydrate (CHO) (1:1 simple to complex); oleic acid (OL); TFA; stearic acid (STE); TFASTE (4% of energy from each); carbon 12:0–16:0 saturated FA (LMP). LDL cholesterol concentrations (mmol/L) were as follows (different superscripts indicate significance at P ≤ 0.01): OL 2.95; CHO 3.05; STE 3.10; LMP 3.21; TFA + STE 3.32; and TFA 3.36. HDL cholesterol concentrations (mmol/L) were as follows: STE 1.16; TFA 1.16; TFASTE 1.17; CHO 1.19; OL 1.24; and LMP 1.30. Triacylglycerides were highest after STE (1.13) and lowest after OL (0.88) (P < 0.001). Thus, compared to the carbohydrate control diet, TFA raised LDL cholesterol at least equivalent to LMP but had no effect on HDL cholesterol; STE had no effect on LDL cholesterol but lowered HDL cholesterol; and oleic acid raised HDL cholesterol but had no effect on LDL cholesterol.

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In a study performed in our laboratory, dietary trans monounsaturated FA (TFA) were found to be intermediate between cis monounsaturated FA and long-chain saturated FA in their hypercholesterolemic effect on plasma total cholesterol (TC) and low density lipoprotein cholesterol (LDL-C) concentrations in adult male and female volunteers (1). Recommendations to lower or replace TFA in the diet have been the subject of considerable discussion in both lay and scientific forums (2–5). In general, reviewers of TFA and cardiovascular disease (CVD) risk have concluded that, whereas consumption of TFA may raise plasma cholesterol concentrations, their benefit lies in their ability to substitute for saturated FA whose intake is of greater concern. To fully understand the impact of replacing TFA in foods, it is first necessary to know the lipid-modifying effects of the major FA that replace TFA. This is difficult to determine because there is no energy-yielding, “neutral” dietary control to which FA effects on various components of the plasma lipid profile can be compared. To compare effects of TFA on LDL-C and high density lipoprotein cholesterol (HDL-C), the relative plasma lipid and lipoprotein-modifying effects of replacing equicaloric amounts of several major energy-yielding nutrients were assessed. In the current investigation, effects of equicaloric replacement of carbohydrate by stearic acid (STE), TFA, oleic acid (OL), and C12:0–C16:0 saturated FA were determined in men fed diets with carefully controlled FA profiles.

METHODS AND MATERIALS

Study design. A controlled feeding trial was conducted at the Beltsville Human Nutrition Research Center (BHNRC) with 50 men. The feeding period was divided into two phases with an 8-wk break between phases. Two blood samples were collected during the 4-d period immediately preceding initiation of the controlled diet for both phases, and values for plasma lipids and lipoproteins were compared to determine if the subjects returned to initial baseline levels during the break (Table 1). Participants consumed all six diets for 5 wk/diet. Diet assignments were determined according to a 6 × 6 Latin square crossover design. This design was chosen to ensure complete balance of the number of diets administered in each study period as well as the number of occurrences of each diet sequence (6). The random sequence of diet assignments was

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balanced with respect to body mass index (BMI) and baseline plasma LDL-C concentration. During the fifth week of each period, replicate blood samples were collected on two different days, from one-half of the subjects on Tuesday and Thursday, and from the other one-half on Wednesday and Friday. Subjects were switched from one diet to the next without a washout between periods except as described between phases 1 and 2.

**Blinding of study results.** Dietary treatments including menus and menu food items were color-coded during the study. Although study participants could recognize differences in appearance, taste, and other characteristics between the different fats and foods prepared with the fats, they were unaware of the overall nutrient and FA profiles of the diets. For determination of plasma lipids, all samples were coded to blind analysts to treatments. Analytical data, blinded to those who performed the controlled feeding and sample collection phases of the investigation, were sent directly from the analytical laboratory to the statistician. After all data for plasma lipids and lipoproteins were in place and the database was locked, a preliminary statistical analysis was performed with treatments coded; the treatments were then decoded by the statistician (M. Iwane), and final analyses of the data were performed.

**Subjects.** Volunteers were recruited by advertisement in the area of the Beltsville Agricultural Research Center (Beltsville, MD). Men of all races between the ages of 25 and 60 yr were recruited regardless of smoking habits. From the 207 respondents, 58 met the eligibility criteria, described next, and were selected to enter the study. Four of those selected dropped out before initiation of the first feeding period. Of the 54 subjects who started the diets, 50 completed all six diets, and only data from these 50 participants are included in the present report (Table 1). Samples from dropouts were not analyzed. Three dropped prior to the end of the first feeding period, and one was dropped for noncompliance during the third feeding period.

Minimum eligibility criteria were based on general health, eating habits, age, BMI, and fasting plasma LDL-C, HDL-C, and triacylglyceride (TG) concentrations. Volunteers were required to be within 85–120% of gender-specific ideal BMI specified by life insurance reference tables (7). Volunteers who reported taking lipid-lowering drugs, blood pressure medications, or dietary supplements or who had eating habits inconsistent with the study protocol (e.g., those on vegetarian or low-fat diets) were excluded. Volunteers were evaluated by a physician and determined to be in good health with no signs or symptoms of hypertension, hyperlipidemia, diabetes, peripheral vascular disease, gout, liver or kidney disease, or endocrine disorders. Subjects selected for the study were required to have fasting plasma HDL-C concentrations greater than 0.65 mmol/L (25 mg/dL) and TG concentrations less than 3.39 mmol/L (300 mg/dL). From the volunteers who met all other selection criteria, those selected to participate had plasma LDL-C concentrations between the 25th and 75th percentiles of those screened.

Exercise was not a selection criterion nor was it controlled during the study, but volunteers who reported participation in major physical activities such as routine jogging for long distances, weight lifting, or other strenuous exercise programs were not selected for the study. Otherwise, subjects were encouraged to maintain their normal exercise patterns (type, duration, and frequency) throughout the study and were required to record major departures from their normal pattern of exercise on a daily questionnaire.

Volunteers were fully informed of study requirements. They were required to read and sign a consent form detailing the study objectives, risks, and benefits before final selection as subjects for the study. Participants received monetary compensation commensurate with the effort required of them by the study. All procedures and payments were approved by the Johns Hopkins University Committee on Human Research.

**Controlled feeding procedures.** On Monday through Friday subjects consumed breakfast and dinner at the BHNRC’s Human Study Facility under the supervision of a dietitian. At breakfast, each subject was provided with a carry-out lunch to be consumed that day. Snack items were included in the daily menu, and subjects were provided the option of consuming the snacks at dinner or later in the evening. Meals for the weekend were packaged for home consumption and provided to the subjects with written instructions after dinner on Friday. Coffee and tea were allowed in unlimited amounts.

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**TABLE 1**

**Baseline Characteristics of Men Who Completed All Diets (n = 50)**

<table>
<thead>
<tr>
<th></th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Difference (Phase 1 – Phase 2)</th>
<th>P-valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body weight (kg)</strong></td>
<td>83.1 ± 1.7</td>
<td>82.7 ± 1.7</td>
<td>0.46 ± 0.32</td>
<td>0.153</td>
</tr>
<tr>
<td><strong>Triglycerides (mmol/L)</strong></td>
<td>1.149 ± 0.081</td>
<td>1.157 ± 0.081</td>
<td>−0.008 ± 0.056</td>
<td>0.884</td>
</tr>
<tr>
<td><strong>Total cholesterol (mmol/L)</strong></td>
<td>4.768 ± 0.092</td>
<td>4.781 ± 0.083</td>
<td>−0.013 ± 0.069</td>
<td>0.850</td>
</tr>
<tr>
<td><strong>LDL cholesterol (mmol/L)</strong></td>
<td>3.082 ± 0.072</td>
<td>3.037 ± 0.072</td>
<td>0.045 ± 0.056</td>
<td>0.428</td>
</tr>
<tr>
<td><strong>HDL cholesterol (mmol/L)</strong></td>
<td>1.160 ± 0.038</td>
<td>1.124 ± 0.043</td>
<td>−0.054 ± 0.016</td>
<td>0.002</td>
</tr>
</tbody>
</table>

aMean age was 42 yr and mean body mass index was 26.2 kg/m².

bProbability of significant difference between phases calculated from a paired t-test.