Comparison of monounsaturated fatty acids and carbohydrates for reducing raised levels of plasma cholesterol in man

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ABSTRACT
To compare monounsaturated fatty acids and carbohydrates for actions on lipid and lipoprotein levels from solid-food diets, 10 men were studied on three diets. One diet was high in saturated fatty acids and very high in cholesterol (High Sat+Chol), a second was high in monounsaturates but low in cholesterol (High Mono), and a third was low in fat, high in carbohydrates, and low in cholesterol (Low Fat). All diets were consumed for 6 wk. Compared with the High Sat+Chol diet, the High Mono and Low Fat diets significantly and similarly reduced plasma cholesterol and LDL cholesterol. In contrast, the Low Fat diet significantly lowered HDL cholesterol whereas the High Mono diet did not. Therefore, a solid-food diet rich in monounsaturated fatty acids is equivalent to a low-fat, high-carbohydrate diet for cholesterol lowering but does not reduce the HDL-cholesterol level.


KEY WORDS
Monounsaturated fatty acids, carbohydrates, saturated fatty acids, dietary cholesterol, plasma cholesterol

Introduction

Two dietary factors that raise the plasma cholesterol concentrations are saturated fatty acids and cholesterol. A rise in plasma cholesterol during the feeding of diets high in saturated fatty acids occurs in almost all individuals (1-5). The response to dietary cholesterol is more variable although carefully controlled studies revealed that most people demonstrate some increase in cholesterol levels on high-cholesterol diets (3, 6, 7). It further was reported that saturated fatty acids and cholesterol are additive in their action to raise the cholesterol level (8). The relatively high intakes of saturated fatty acids and cholesterol by Americans are considered by many investigators to be a significant factor in the high prevalence of coronary heart disease (CHD) in the United States (9).

In other regions of the world where dietary habits are different from those of most Americans, rates of CHD are lower. For example, in China, Japan, and other countries of the orient, intakes of total fat are relatively low and so are rates of CHD (10). Further, in Greece, Crete, southern Italy, and other Mediterranean countries, the traditional diet is rich in olive oil and total fat intakes can be relatively high but, even so, rates of CHD are relatively low (10). Olive oil contains large amounts of oleic acid, a monounsaturated fatty acid. A recent study from our laboratory (11) demonstrated that a diet low in total fat and another high in monounsaturated fatty acids caused comparable lowering of plasma cholesterol as compared with a diet high in saturated fatty acids. However, the applicability of this finding to the general population has been questioned because the study was carried out for a relatively short period with liquid-formula diets and carbohydrates consisted entirely of simple sugars. For this reason our purpose was to carry out a similar investigation that was longer in duration and that made use of mixed, solid-food diets.

Subjects and Methods

Subjects

Ten men were investigated in the domiciliary-care unit of the Sam Rayburn Memorial Veterans Administration Medical Center, Bonham, the Veterans Administration Medical Center, Dallas; and the Center for Human Nutrition, University of Texas Southwestern Medical Center, Dallas, TX.

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Center, Bonham, TX. This facility provides medical and psychiatric care, rehabilitation assessments, and other therapeutic measures to ambulatory eligible veterans. Many of the patients in the domiciliary-care unit reside for long-term care. The patients were selected by the following criteria: 1) they were mentally competent and willing to volunteer for a dietary study, 2) they did not have recent history of alcohol or drug abuse; 3) they were generally healthy and did not have liver or kidney dysfunction, diabetes mellitus or other endocrine diseases, hypertension, or congestive heart failure; 4) they were not taking cardiac medications; and 5) they were not markedly overweight.

The patients ranged in age from 61 to 70 y (mean ± SD, 64 ± 2 y). Their body mass indices ranged from 20.8 to 30.5 (mean, 25.9 ± 3.4). At the time of admission to the study, average lipids and lipoproteins for the group were total cholesterol, 227 ± 12 (SEM) mg/dL (5.87 ± 0.3 mmol/L); triglycerides, 127 ± 21 mg/dL (1.43 ± 0.24 mmol/L), low-density-lipoprotein (LDL) cholesterol 143 ± 5 mg/dL (3.70 ± 0.13 mmol/L) and high-density-lipoprotein (HDL) cholesterol 51 ± 3 mg/dL (1.3 ± 0.08 mmol/L). Several patients carried a diagnosis of atherosclerotic disease, either coronary heart disease or peripheral vascular disease. Six of the 10 patients smoked cigarettes throughout the study. All patients gave informed consent for the study.

Diets

At entrance into the study, the patients were being fed from the domiciliary kitchen. The food served in this kitchen typically is high in total fat, saturated fatty acids, and cholesterol. Meat usually is offered twice daily and eggs always are offered for breakfast. At entry none of the patients was receiving a special diet. For this investigation three different solid-food diets were fed from the same kitchen but the diets were prepared and served under the close supervision of one of the authors (DN). Each dietary period lasted 6 wk. The diets were prepared from mixed foods. The composition of each diet was estimated from a standard handbook (12). For each diet 2-wk menus were prepared and they were rotated three times in each period. The participants ate at a special table and their adherence to the diet was monitored either by a dietitian or a food-service attendant. The patients were urged not to eat extra food and they had no access to alcohol.

One diet was designated High Sat+Chol; it was rich in saturated fatty acids and cholesterol. It contained 40% of calories as fat, 45% as carbohydrate, and 15% as protein. Fatty acid calories were distributed as follows: 19% saturated fatty acids, 15% monounsaturated fatty acids, and 6% polyunsaturated fatty acids. The saturated fatty acids in this diet were calculated to have the following composition: 2.2% of calories had a chain length of 4–10 carbon atoms; 13.0% of calories had a chain length of 12–16 (lauric, myristic, and palmitic acids), and 3.8% of calories had a chain length of 18 (stearic acid). Cholesterol intake in this diet averaged 900 mg/d. The second diet was called High Monoo; it contained 40% fat, (7% saturated, 27% monounsaturated, and 6% polyunsaturated fatty acids), 45% carbohydrate, and 15% protein. Cholesterol intake averaged 200 mg/d. The third diet was designated Low Fat; it contained 20% fat (7% saturated, 7% monounsaturated, and 6% polyunsaturated fatty acids), 65% carbohydrate, and 15% protein. Cholesterol intake was averaged to be 200 mg/d. In the High Monoo and Low Fat diets most saturated fatty acids had a C chain length of 14 and 16 (myristic and palmitic acids). All diets were composed of mixed foods (cereals, breads, vegetables, fruits, meat, whole eggs, egg whites, milk, fats, and oil). The High Sat+Chol diet was rich in products containing butter fat and it included two eggs per day. The High Mono diet was enriched in high-oleic safflower oil and unhydrogenated peanut butter. Butter and safflower oil were added to salads, vegetables, bread, and toast. The order of the dietary periods was randomized. The patients were weighed twice weekly and caloric intake was adjusted to maintain a constant weight throughout the study. Patients maintained their normal activity level and no special exercise regimen was employed.

Lipid and lipoprotein

After allowing 1 mo for equilibration on each new diet, the patients were sampled three times per week for the last 2 wk of the 6-wk period. Blood samples were drawn after a 14-h fast and plasma was obtained by centrifugation at 1232 × g for 30 min. Each plasma sample was analyzed by Lipid Research Clinics procedures (13) for levels of total cholesterol, triglycerides, and lipoprotein cholesterol; plasma total cholesterol and triglycerides were measured enzymatically (14, 15). The HDL-cholesterol level was determined enzymatically after precipitation of lipoproteins containing apolipoprotein B with heparin-manganese (13). Through the appropriate use of blanks and standards in the enzymatic reaction, this method was shown to give the same values for HDL cholesterol whether cholesterol in HDL was estimated enzymatically or by gas-liquid chromatography (16). To obtain the concentration of LDL cholesterol, the very-low-density-lipoprotein (VLDL) cholesterol of density < 1.006 g/mL was removed by ultracentrifugation (13) after cholesterol was determined in the infranatent, the level of LDL cholesterol was calculated as infranatant cholesterol minus the HDL cholesterol.

Statistical analysis

For comparison of means among the three dietary periods, a repeated-measures analysis of variance was carried out (16, 17). Mean values for the six measurements of each period were used for the analysis. When the analysis indicated that the results for the three periods were different, paired t tests were used to compare individuals diet periods with Bonferroni adjustments to control the overall a level (17, 18).

Results

The data for individual patients are given in Figure 1 and for the group are given in Table 1. On average the plasma total cholesterol was 13% lower on both High Mono and Low Fat diets than on the High Sat+Chol diet (p < 0.001). There were no significant differences for plasma triglycerides among any of the groups. LDL-cholesterol levels were 19% lower on both High Mono and Low Fat diets. In contrast HDL-cholesterol levels were significantly lower on the Low Fat diet than on both High Mono and High Sat+Chol diets (p < 0.02) but there was no difference between the latter two diets. As shown in Figure 1, the trends noted for group means were fairly uniform for individual patients.

Discussion

This study was designed to compare a low-fat, high-carbohydrate (Low Fat) diet with a diet high in monoun-
DIETARY MONounsaturates vs Carbohydrates

but which diet employed at the lowest level of fat intake of saturated fatty acids and cholesterol but total fat intakes were twice as high.

According to several reports (6, 20, 21), intakes of dietary cholesterol > 500 mg/d produce a diminishing increment in the cholesterol concentration beyond the 500 mg level. For example, consider the equation of Keys et al (6) for dietary cholesterol:

\[ y = 1.5(X_2^{0.5} - X_1^{0.5}) \]  

(1)

where \( y \) is the change in serum cholesterol in mg/dL, and \( X_2 \) and \( X_1 \) are the cholesterol content of the two diets expressed as mg/1000 kcal. Raising dietary cholesterol from 200 to 500 mg/d for an individual consuming 2500 kcal/d should increase plasma total cholesterol by \( \sim 8 \) mg/dL (0.21 mmol/L). A further increment in dietary cholesterol to 900 mg/d should produce an additional rise in total cholesterol of 7 mg/dL (0.18 mmol/L). Thus, the increment in dietary cholesterol from 200 to 900 mg/d, as used in our study, should have raised the cholesterol level by \( \sim 15 \) mg/dL (0.39 mmol/L). A significant portion of the reduction in plasma total cholesterol on High Mono and Low Fat diets therefore could have been the result of a decreased intake of cholesterol.

On the High Sat+Chol diet, intakes of saturated fatty acids averaged 19% of total calories. According to the data of Keys et al (22) and Hegsted et al (3), all saturated fatty acids do not raise the cholesterol level to the same extent. Both these reports (3, 22) indicated that the C18 stearic acid does not raise the total cholesterol level compared with oleic acid. A preliminary study (23) from our laboratory in humans confirmed this finding, and several studies in animals are in accord with this response (24-26). Further, several reports (27-29) suggest that medium-chain saturated fatty acids (chain length 4-10) do not raise the plasma cholesterol levels. Therefore, if we subtract fatty acids of chain lengths 4, 6, 8, 10, and 18 from the total saturates, the High Sat+Chol diet contained only 13% of cholesterol-raising saturated fatty acids (chain lengths 12, 14, and 16). Keys et al (22) indicated that these latter saturated fatty acids raise the plasma cholesterol by 2.7 mg/dL (0.07 mmol/L) for every 1% of calories. Thus for the High Sat+Chol diet compared with the High Mono diet for cholesterol-raising saturates, the High Mono diet should have caused a mean reduction in plasma cholesterol of 16.2 mg/dL (0.42 mmol/L). This decrease combined with the 15 mg/dL (0.39 mmol/L) decrease predicted for the lower cholesterol intake should have reduced the plasma total cholesterol level by 31 mg/dL (0.80 mmol/L). This predicted reduction closely approximated the observed mean reduction of 32 mg/dL (0.83 mmol/L).

Both Keys et al (2) and Hegsted et al (3) reported that carbohydrates have approximately the same effect as monounsaturated fatty acids on plasma total cholesterol levels. A similar relationship was noted previously in a study from our laboratory (11). The current results are in complete accord. On average the plasma total cholesterol fell to the same extent on both High Mono and Low Fat diets. Likewise, the LDL-cholesterol concentration de-

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**Figure 1.** Plasma levels of total, LDL, and HDL cholesterol and triglycerides in 10 patients on High Sat+Chol, High Mono, and Low Fat diets. Each point represents the mean of six determinations done during the last 2 wk of 6-wk periods. (To convert values for cholesterol and triglycerides to mmol/L, multiply by 0.02586 and 0.01129, respectively.)

saturated fatty acids (High Mono) in which calories were consumed mainly as solid foods. These two diets in turn were compared to a diet high in both saturated fatty acids and cholesterol (High Sat+Chol). The latter diet was employed to obtain maximally high levels of cholesterol in total plasma and in LDL and HDL subfractions. On the High Sat+Chol diet, intakes of both saturated fatty acids (19% of calories) and cholesterol (\( \sim 900 \) mg/d) exceeded current American intakes, and this cholesterol-raising diet should have provided a plasma cholesterol ceiling by which the two cholesterol-lowering diets could be compared. In other words, the experimental design not only facilitated comparison of two cholesterol-lowering diets but also allowed us to determine the maximal degree of cholesterol reduction that can be obtained by therapeutic diets that are low in both saturated fatty acids and cholesterol. The Low Fat diet was equivalent to the American Heart Association Phase III diet for treatment of hypercholesterolemia (19); the High Mono diet had the same
TABLE 1

Plasma lipids and lipoproteins in the three diet periods*

<table>
<thead>
<tr>
<th>Diet</th>
<th>Total cholesterol (mg/dL)</th>
<th>Total triglycerides (mmol/L)</th>
<th>LDL cholesterol (mg/dL)</th>
<th>HDL cholesterol (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Sat+Chol</td>
<td>240 ± 11</td>
<td>113 ± 11</td>
<td>172 ± 9</td>
<td>52 ± 4</td>
</tr>
<tr>
<td></td>
<td>(6.20 ± 0.28)</td>
<td>(1.27 ± 0.12)</td>
<td>(4.45 ± 0.23)</td>
<td>(1.34 ± 0.10)</td>
</tr>
<tr>
<td>High Mono</td>
<td>208 ± 10†</td>
<td>104 ± 9</td>
<td>140 ± 8‡</td>
<td>50 ± 4</td>
</tr>
<tr>
<td></td>
<td>(5.37 ± 0.26)</td>
<td>(1.17 ± 0.10)</td>
<td>(3.62 ± 0.21)</td>
<td>(1.29 ± 0.10)</td>
</tr>
<tr>
<td>Low Fat</td>
<td>208 ± 7†</td>
<td>113 ± 8</td>
<td>139 ± 5‡</td>
<td>46 ± 4§</td>
</tr>
<tr>
<td></td>
<td>(5.37 ± 0.18)</td>
<td>(1.27 ± 0.09)</td>
<td>(3.59 ± 0.13)</td>
<td>(1.19 ± 0.10)</td>
</tr>
</tbody>
</table>

*Mean ± SEM; n = 10.
†High Mono and Low Fat significantly different from High Sat+Chol at p < 0.0010.
‡High Mono and Low Fat significantly different from High Sat+Chol at p < 0.0002.
§Low Fat significantly different from High Sat+Chol and High Mono at p < 0.0182.

clined identically on the two diets. These results suggest that there is nothing gained by way of LDL-cholesterol reduction merely by lowering intakes of total fat. A diet high in monounsaturated fatty acids but low in saturates appears just as effective for lowering of plasma LDL-cholesterol as a diet low in total fat. The converse of course also is true.

In a previous report from this laboratory (11) in which liquid-formula diets were used, a low-fat diet caused a reduction in levels of HDL cholesterol compared with a diet high in saturated fatty acids whereas a diet high in monounsaturates did not. The same result was obtained in this study. The HDL-cholesterol concentration on the current Low Fat diet was significantly lower than the High Sat+Chol diet by an average of 6 mg/dL (0.16 mmol/L). In contrast, the High Mono diet did not cause a significant reduction in HDL cholesterol. Thus the HDL-lowering effect of a low-fat diet apparently occurs with solid-food diets as well as with liquid-formula diets. Recently, a similar response was reported by Mensink and Katan (30), who found that a low-fat, high-carbohydrate diet caused a reduction of HDL-cholesterol levels whereas a diet high in monounsaturates did not. Their investigation also employed solid-food diets.

A high-carbohydrate diet was reported to cause an increase in plasma triglycerides (11, 31, 32). This response was not observed in the present investigation. On the Low Fat diet the plasma triglyceride level was essentially the same as on High Sat+Chol and High Mono diets. Whether this lack of rise in triglyceride levels on the Low Fat diet was due to the patients' inherently low triglycerides, the use of solid-food diets, or the nature of the carbohydrates is not clear.

In summary, this study confirms that a diet low in total fat has essentially the same effect on plasma total cholesterol and LDL cholesterol as a diet high in monounsaturated fatty acids. Both produce a significant reduction in total cholesterol compared with a diet high in saturated fatty acids and reductions correspond to those predicted by Keys et al (2, 6, 22). However, the investigation further supports recent reports (11, 30) that low-fat diets significantly reduce HDL-cholesterol levels whereas diets high in monounsaturates do not. Thus, data obtained on solid-food diets indicate diets high in monounsaturated fatty acids induce changes in lipoprotein-cholesterol levels that are at least as beneficial from the viewpoint of coronary risk as a diet low in fat and high in carbohydrates. This finding may allow for a greater flexibility in choice of dietary constituents for achieving reduced levels of cholesterol for the American population.

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References