Dietary Trans Fatty Acids and Serum Lipoproteins

ABSTRACT

Trans fatty acids are produced during industrial hydrogenation of vegetable and marine oils. Hydrogenation is used to change the characteristics of oils so that they can be incorporated into food items, such as margarines, shortenings, salad oils, and high-fat baked goods. Hydrogenated oils, however, are not the only source of trans fatty acids in the human diet. Fat from ruminants also contains small amounts of trans fatty acids due to “natural” biohydrogenation by bacteria in the rumen. Most trans fatty acids have 18 carbon atoms and one double bond (trans–C18:1). Information on the average intake of trans fatty acids as well as on the variation in intake between individuals is scarce because of missing and unreliable figures for trans–C18:1 in most food composition tables.

The health aspects of trans–C18:1 have been evaluated, and the general conclusion was that intakes of trans–C18:1 had no adverse effects on health. Five years ago, however, interest in trans–C18:1 revived because it was reported that trans–C18:1 raised low-density lipoproteins and Lp(a), and lowered high-density lipoproteins as compared with oleic acid (cis–C18:1). The results from all of the recent studies combined suggest that effects of trans–C18:1 on low-density lipoproteins and high-density lipoproteins—which may be mediated by cholesterol ester transfer protein—are dose-dependent with no threshold effect. This suggests that the intake of trans–C18:1, like that of the cholesterol-raising saturated fatty acids, should be as low as possible to minimize coronary heart disease risk.

Introduction

Trans fatty acids have been called unnatural substances because they are produced during the industrial hydrogenation of vegetable oils.
and—in a few countries—of marine oils. Hydrogenation, or hardening, is applied to change the characteristics of the liquid oils so they can be incorporated into food items, such as margarines, shortenings, salad oils, and high-fat baked goods.

The most abundant trans fatty acid in the diet has 18 carbon atoms and one double bond (trans–C18:1). This molecule is formed after hydrogenation of linoleic acid, which has two double bonds in the cis configuration. “Cis” means that the two carbon chains, adjacent to the double bond, point in the same direction. In this way, a bend is introduced in the molecule, which impairs crystallization and keeps the oil liquid. In the trans configuration, however, the two carbon chains point in opposite directions and stretch the molecule. The melting point of the oil increases and the liquid oil becomes more solid. Commercially hydrogenated oils, however, are not the only source of trans fatty acids in the human diet. Fat from ruminants also contain small amounts of trans fatty acids because of biohydrogenation by bacteria in the rumen.

The health aspects of trans fatty acids have been evaluated in many studies and the general conclusion was that intakes of trans fatty acids had no major impact on health (1). Recently, however, interest for trans–C18:1 revived because it was reported that these fatty acids may have an unfavorable effect on serum lipid and lipoprotein levels (2).

Intake of Trans Fatty Acids

Information on the intake of trans fatty acids is scarce because of missing or unreliable figures in most food composition tables and databases. Data for trans fatty intake, however, have been estimated using figures for average per capita consumption of foods and mean values of trans fatty acids in various food groups or by analysis of duplicate portions.

Table 1 shows the intake of trans–C18:1 acids in four different countries (3–6), as determined by duplicate portion analysis. Duplicate portions were sampled by free-living subjects. For Finland, however, the average food consumption data were estimated mainly from food balance sheets and a representative daily diet was composed in spring and autumn. When results were expressed as percent of total fatty acids or as proportion of daily energy, the intake of trans–C18:1 was similar in Sweden, the Netherlands, and the United States. The consumption of
trans fatty acids by the vegans and lacto-vegetarian subjects studied by Akesson et al. (3), however, was substantially lower.

The calculated intake of trans fatty acids from availability data or as calculated from dietary surveys (7–11) in the United States is shown in Table 2. It is evident that the estimated intake depends on the method used. Using food availability data shows higher values than data from dietary surveys. This can be partially explained by the fact that not all available food is actually consumed. It is also evident, that the actual consumption is difficult to estimate. For example, Hunter (8) and Enig

Table 1. Mean Daily Intake of Trans Fatty Acids in Four Different Countries as Determined by Duplicate Portion Analysis

<table>
<thead>
<tr>
<th>First author</th>
<th>Year of sampling</th>
<th>Country</th>
<th>grams</th>
<th>% of fatty acids</th>
<th>% of energy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Åkesson</td>
<td>1968/1975</td>
<td>Sweden</td>
<td>3.7</td>
<td>5.0</td>
<td>2.0</td>
</tr>
<tr>
<td></td>
<td>1978</td>
<td>Sweden*</td>
<td>0.9</td>
<td>1.8</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>1980</td>
<td>Sweden*</td>
<td>3.0</td>
<td>3.9</td>
<td>1.3</td>
</tr>
<tr>
<td>van den Reek</td>
<td>1982</td>
<td>USA</td>
<td>2.6 (3.1)</td>
<td>5.3 (6.5)</td>
<td>1.8 (2.2)</td>
</tr>
<tr>
<td>Van Dokkum</td>
<td>1984/1985</td>
<td>Netherlands</td>
<td>—</td>
<td>5.0</td>
<td>1.8</td>
</tr>
<tr>
<td>Heinonen</td>
<td>1987</td>
<td>Finland</td>
<td>1.4 (1.7)</td>
<td>1.5 (1.9)</td>
<td>0.5 (0.6)</td>
</tr>
</tbody>
</table>

*Values in parentheses refer to total trans fatty acids.
*Subjects were vegans.
*Subjects were lacto-vegetarians.
*The duplicate diet referred to the average Finnish diet. Food consumption data were derived mainly from the food balance sheets.

Table 2. Mean Daily Intake of Trans Fatty Acids in the United States, as Calculated from Availability Data or Dietary Surveys

<table>
<thead>
<tr>
<th>First author</th>
<th>Method</th>
<th>Year</th>
<th>Trans fatty acids (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hunter</td>
<td>Availability</td>
<td>1970</td>
<td>7.7</td>
</tr>
<tr>
<td></td>
<td>Availability</td>
<td>1980</td>
<td>7.6</td>
</tr>
<tr>
<td></td>
<td>Availability</td>
<td>1984</td>
<td>7.6</td>
</tr>
<tr>
<td>Hunter</td>
<td>Availability</td>
<td>1989</td>
<td>8.1</td>
</tr>
<tr>
<td>Enig</td>
<td>Availability</td>
<td>1983</td>
<td>12.3</td>
</tr>
<tr>
<td>London</td>
<td>Dietary survey</td>
<td>1986–1987</td>
<td>3.4</td>
</tr>
<tr>
<td>Troisi</td>
<td>Dietary survey</td>
<td>1987–1990</td>
<td>3.4</td>
</tr>
</tbody>
</table>
et al. (9) used comparable methods to measure the intake, but the difference between estimates is about 30%–40%.

It is also possible to estimate the intake of trans–C18:1 by fatty acid analyses of blood lipid fractions (12). The proportion of trans–C18:1 in the diet correlates with trans–C18:1 in serum triglycerides and platelet phospholipids. In this way, information of the habitual dietary intake over the last days (serum triglycerides) to several weeks (platelet phospholipids) can be obtained. The ratio of trans–C18:1 in dietary fat to trans–C18:1 in serum triglycerides was 1.15, which suggests that the proportion of trans–C18:1 in serum triglycerides is close to its proportion in the dietary fat. To obtain information over longer periods of time, measurements in adipose tissue can be made. From the study of London et al. (10), it appears that the ratio of trans–C18:1 in adipose tissue to dietary trans–C18:1 is also close to unity.

**Trans Fatty Acids and Serum Total Cholesterol:**

**"Older" Studies**

Results of the older studies (13–19) on the effects of trans fatty acids on serum total cholesterol conflict. Anderson and colleagues (13) concluded that replacement of 1% of energy from carbohydrates in the diet by trans fatty acids increased serum cholesterol levels by about 1.2 mg/dL (0.031 mmol/L). Later studies, however, did not confirm this finding (Table 3). Most authors reported no hypercholesterolemic effect of trans fatty acids (14, 15, 18), while Vergroesen et al. (17) found that trans–C18:1 was only hypercholesterolemic in the presence of dietary choles-

<table>
<thead>
<tr>
<th>Year</th>
<th>First author</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1961</td>
<td>Anderson</td>
<td>Hypercholesterolemic</td>
</tr>
<tr>
<td>1962</td>
<td>McOsker</td>
<td>No effect</td>
</tr>
<tr>
<td>1964</td>
<td>Erickson</td>
<td>No effect</td>
</tr>
<tr>
<td>1965</td>
<td>De Jongh</td>
<td>Very small effect</td>
</tr>
<tr>
<td>1972</td>
<td>Vergroesen</td>
<td>Moderate effect</td>
</tr>
<tr>
<td>1975</td>
<td>Maltson</td>
<td>No effect</td>
</tr>
<tr>
<td>1982</td>
<td>Laine</td>
<td>Slight negative effect</td>
</tr>
</tbody>
</table>
terol. However, when all of the studies are combined, it appears that dietary trans fatty acids increase the serum total cholesterol level. Table 4 shows the results of four regression equations relating dietary trans fatty acid intake to changes in serum total cholesterol levels. For equation one, only trans fatty acids were part of the regression equation. The estimated change in the serum total cholesterol level when 1% of dietary carbohydrates is replaced isocalorically by trans fatty acids is 1.10 mg/dL (0.028 mmol/L). The estimate changed slightly depending on the other fatty acids in the model. Thus, when saturated and cis-mono-unsaturated fatty acids became part of the regression equation (equation 3), the estimated effect of trans fatty acid relative to that of carbohydrates was 1.26 mg/dL (0.032 mmol/L). However, the coefficient for trans fatty acids was statistically significant for each equation and close to 1.10 mg/dL (0.028 mmol/L), very similar to the estimate of Anderson et al. (13).

**Trans Fatty Acids and Serum Lipoproteins: Recent Studies**

A few years ago, we examined the effects of trans fatty acids on the distribution of cholesterol over the various lipoproteins (2). In that

<table>
<thead>
<tr>
<th>Equation</th>
<th>Saturates</th>
<th>Trans</th>
<th>Cis-Monoenes</th>
<th>Cis-Polyenes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equation 1</td>
<td>mg/dL</td>
<td>1.10</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>mmol/L</td>
<td>0.028</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$P &lt; 0.01$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Equation 2</td>
<td>mg/dL</td>
<td>1.12</td>
<td>1.11</td>
<td></td>
</tr>
<tr>
<td></td>
<td>mmol/L</td>
<td>0.029</td>
<td>0.029</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$P = 0.05$</td>
<td>$P &lt; 0.01$</td>
<td></td>
</tr>
<tr>
<td>Equation 3</td>
<td>mg/dL</td>
<td>1.17</td>
<td>1.26</td>
<td>0.29</td>
</tr>
<tr>
<td></td>
<td>mmol/L</td>
<td>0.030</td>
<td>0.032</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$P = 0.04$</td>
<td>$P &lt; 0.01$</td>
<td>$P = 0.51$</td>
</tr>
<tr>
<td>Equation 4</td>
<td>mg/dL</td>
<td>0.87</td>
<td>0.96</td>
<td>-0.31</td>
</tr>
<tr>
<td></td>
<td>mmol/L</td>
<td>0.022</td>
<td>0.025</td>
<td>-0.008</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$P = 0.19$</td>
<td>$P = 0.01$</td>
<td>$P = 0.49$</td>
</tr>
</tbody>
</table>
study, 59 volunteers received three different diets. The composition of
the diets was similar, except for 10% of energy that was provided by
either oleic acid, trans isomers of oleic acid, or by lauric plus myristic
plus palmitic acid, the cholesterol-raising saturated fatty acids. We
found that serum low-density lipoprotein (LDL) cholesterol levels were
the lowest on the diet high in oleic acid and increased with 14 mg/dL
(0.37 mmol/L) on the trans fatty acid–rich diet and with 18 mg/dL (0.47
mmol/L) on the saturated fat diet. These results clearly show that trans
fatty acids have an unfavorable effect on serum LDL cholesterol. HDL
cholesterol levels were 7 mg/dL (0.17 mmol/L) lower on the diet high
in trans–C18:1 as compared with the other two diets. This study, how-
ever, was criticized because the amount of trans fatty acids was rela-
tively high. It could be argued that effects are only observed at higher
intakes and that the effect is not proportional to the amount consumed.
Therefore a comparable study was carried out at lower intakes of trans–
C18:1 (7.9% of total energy intake), and results were similar (20). More
recently, Judd et al. (21) examined the effects of trans–C18:1 on serum
lipids and lipoproteins at even lower intakes. All subjects consumed a
diet with a high level of oleic acid and no trans–C18:1, a moderate (2.5% 
of total energy) and a high level of trans–C18:1 (5.9% of total energy),
and a high level of saturated fatty acids. Compared with oleic acid, 
trans–C18:1 raised serum LDL cholesterol levels, although less than sat-
urated fatty acids. Also, a significant decrease in the HDL cholesterol
level was observed on the diet that provided 5.9% of energy from trans–
C18:1, but intakes of 2.5% did not cause a significant decrease in HDL
cholesterol. When the results of five dietary trials on the effects of trans–
C18:1 are combined it is clearly shown that the LDL cholesterol–raising
and HDL–lowering effect of trans–C18:1 relative to oleic acid is con-
centration dependent (22). Table 5 shows the estimated changes in se-
rum lipid and lipoprotein levels for a group of subjects when 1% of
energy from carbohydrates in the diet is replaced isocalorically by fatty
acids of a particular class (22, 23). Trans fatty acids elevate LDL choles-
sterol levels, although to a slightly less extent than a mixture of saturated
fatty acids do. Although the coefficient for the effect of trans–C18:1 on
HDL cholesterol levels was negative, it was not significantly different
from zero (P = 0.07), which suggests that trans–C18:1 and carbohy-
drates have similar effects HDL cholesterol levels. All other fatty acids,
however, increase HDL cholesterol levels as compared to carbohy-
drates. The ratio of HDL to LDL cholesterol will decrease if carbohy-
Table 5. Estimated changes in serum lipid and lipoprotein levels for a group of subjects when 1% of energy in the diet from carbohydrates is replaced isocalorically by a fatty acid of a particular class.\(^a\)

<table>
<thead>
<tr>
<th>Fatty acid</th>
<th>Total (mg/dL, mmol/L)</th>
<th>LDL (mg/dL, mmol/L)</th>
<th>HDL (mg/dL, mmol/L)</th>
<th>Ratio of HDL to LDL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saturates</td>
<td>1.51(^b), 0.039</td>
<td>1.28(^b), 0.033</td>
<td>0.47(^b), 0.012</td>
<td>0</td>
</tr>
<tr>
<td>Cis-monoenes</td>
<td>-0.12, -0.003</td>
<td>-0.24, -0.006</td>
<td>0.34(^b), 0.009</td>
<td>0.003(^b)</td>
</tr>
<tr>
<td>Trans-monoenes</td>
<td>0.97(^b), 0.025</td>
<td>1.16(^b), 0.030</td>
<td>-0.19, -0.005</td>
<td>-0.007(^b)</td>
</tr>
<tr>
<td>Cis-polyenes</td>
<td>-0.60(^b), -0.015</td>
<td>-0.59(^b), -0.014</td>
<td>0.28(^b), 0.007</td>
<td>0.005(^b)</td>
</tr>
</tbody>
</table>

Derived from references (22, 23).

\(^a\)Cis-monoenes refer mainly to oleic acid, trans-monoenes to trans-C18:1, and cis-polyenes to linoleic acid.

\(^b\)\(p < 0.05\).
Dietary Trans Fatty Acids and Serum Lipoproteins

Drates are replaced by trans-C18:1 or by any other fatty acid. Thus, it is predicted that replacement of 1% of energy from carbohydrates by trans-C18:1 will lead to a decrease in the HDL to LDL cholesterol ratio of 0.007. Replacement of cis-monounsaturated fatty acids for trans-C18:1 is predicted to cause a fall of 0.010 in this ratio.

One possible mechanism for the effect on the serum lipoprotein profile is that trans fatty acids increase the activity of the plasma cholesteryl ester transfer protein (CETP). CETP exchanges cholesteryl esters from HDL for triglycerides in LDL and very low density lipoproteins (VLDL). Indeed, Abbey and Nestel (24) showed that in vitro the activity of CETP was significantly higher after replacement of oleic acid for trans-C18:1. These results were confirmed by van Tol et al. (25), who also reported that the ratio of cholesteryl esters to triglycerides in HDL was decreased. This finding indicates that the increased CETP activity as observed in vitro truly changes lipid transfer reactions in vivo.

Trans-C18:1 also have an effect on serum lipoprotein (a) (Lp(a)), a strong risk factor for coronary heart disease (CHD). The Lp(a) concentration in the blood is largely under genetic control, and it has been stated that diet has only negligible effects on Lp(a) levels. However, it has been demonstrated that trans fatty acids increase Lp(a) levels in mildly hypercholesterolemic and normocholesterolemic subjects (26, 27).

Trans Fatty Acids and Risk for Coronary Heart Disease

Trans fatty acids increase levels of LDL cholesterol and Lp(a), and decrease those of HDL cholesterol relative to oleic acid. Therefore, high intakes of trans-C18:1 may be related to increased CHD risk. Willett et al. (28) calculated the intake of trans fatty acids for 85,095 apparently healthy women from dietary questionnaires. In the next eight years, 431 new cases of CHD were diagnosed. It was demonstrated that the intake of trans fatty acids was associated with CHD risk. It should be noted, however, that this was only evident for the women with the highest trans-fatty acid intake (median value: 3.2% of total energy). Ascherio et al. supported this conclusion (29). Aro et al. (30) compared in nine European countries the proportion of trans-C18:1 in adipose tissue from 671 men with acute myocardial infarction with levels from 717 healthy men. The proportion of trans-C18:1 in adipose tissue, which reflects dietary intake, varied in the controls from 0.4% in Granada...
(Spain) to 2.4% in Zeist (The Netherlands). The results did not suggest a higher intake in patients as compared to controls. The authors, however, did not exclude the possibility that trans-C18:1 may have a significant impact on cardiovascular risk in countries with high intakes. Roberts et al. (31) also reported that the amount of trans fatty acids in adipose tissue, obtained at necropsy from 66 cases who died of sudden cardiac death, was not significantly different from amounts in healthy controls. Thus, results from epidemiological studies are inconclusive. It should be realized, however, that only intervention trials can prove whether or not high intakes of trans fatty acids are causally related to cardiovascular risk.

Conclusions

The intake of trans-C18:1 should be as low as possible to optimize the serum lipoprotein profile. However, it would be a misconception to conclude that dietary fats high in trans fatty acids should now be replaced by butter and other fats with high amounts of saturated fatty acids and cholesterol. The role of saturated fatty acid and cholesterol in the development of CHD has been unequivocally established. Also, intakes of saturated fatty acids largely exceed those of trans-C18:1. It is therefore essential to decrease the intake of the cholesterol-raising saturated fatty acids and of trans-C18:1. This means that hard fats should be replaced by oils and soft margarines low in trans and saturated fatty acids. Also, it seems prudent to lower total fat intake to 30%–35% of total energy intake.

REFERENCES


3. Åkesson B, Johansson BM, Eng M, Svensson M, Öckerman PA. Content of trans-octadecenoic acid in vegetarian and normal diets


