Commentary on the supplement Trans fatty acids and coronary heart disease risk

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The health effects of partially hydrogenated oils have been debated for many years. As a result, such fats have been thoroughly scrutinized, but no toxic effects were detected even after massive doses were fed to various animal species for several generations.

Until recently the effect of trans fatty acids on serum cholesterol was equivocal: of the three studies that met certain quality criteria (1), two found effects of trans fatty acids intermediate between those of cis unsaturates and saturated fatty acids and one found no difference from cis monounsaturates. The issue was not pressing because concentrations of trans fatty acids in the diet are fairly low. However, we decided to reexamine the question. We found that the effect of trans monounsaturated fatty acids on total cholesterol was indeed intermediate between that of cis monounsaturates and saturates, but that this masked more drastic effects on high-density-lipoprotein (HDL) concentrations, which decreased, and on low-density-lipoprotein (LDL) concentrations, which increased (2). Several groups have investigated the matter since then (3–6).

PRESENT DATA ON TRANS FATTY ACIDS, LDL, AND HDL

Figure 1 summarizes the changes in LDL and HDL cholesterol that occurred when trans fatty acids replaced carbohydrates in recent trials. Actually, cis monounsaturates were used in the studies as a control treatment but we recalculated the raw data to a carbohydrate-rich diet (1) to ease comparison with the animal data in the International Life Sciences Institute (ILSI) report (7).

The figure shows that relative to carbohydrates trans fatty acids uniformly raised LDL cholesterol in humans. This is in contrast with the animal data in the ILSI report: in hamsters, trans fatty acids had a neutral effect on plasma LDL metabolism and concentration. Even replacement of saturated fatty acids by trans fatty acids does not always lower LDL in humans; in two studies (4, 6), LDL concentrations were the same with high-trans and high-saturated fatty acid diets, especially after minor differences in other fatty acids were corrected for. This is not to say that partially hydrogenated oils produce the same LDL concentration as do butter or tropical oils; the sum of saturated plus trans fatty acids in butter and tropical oils is much higher than that in products such as margarines. Therefore, an exchange of margarine for butter will still decrease LDL concentrations.

The effect of trans fatty acids on HDL shown in Figure 1 is small, but carbohydrates themselves lower HDL relative to fats (1). When trans fatty acids replace other fatty acids rather than carbohydrates the effect on HDL is sometimes quite marked, even though it varies between studies (8). I cannot agree with the authors of the ILSI report that these effects on HDL could be due to random variance. On the contrary, variability might obscure effects on HDL in studies with small numbers of subjects or low doses. I am also more concerned than the authors of the report about adverse effects of lowering HDL. In a recent angiographic trial, drug-induced decreases in HDL were significantly correlated with decreases in lumen volume of the femoral artery (9). In other trials, drug-induced increases in HDL reduced cardiovascular risk. When combined with the epidemiologic (10), genetic, and metabolic data on HDL this argues for some prudence.

LIPOPROTEIN(A)

Several trials have now reported that trans fatty acids raise serum lipoprotein(a) concentrations. The ILSI report argues that this may involve confounding through random fluctuations and assay artifacts; however, in a randomized, controlled trial, assay bias is equal for both treatments and will be eliminated.

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FIGURE 1. Effects of monounsaturated trans fatty acids (trans-18:1) on lipoprotein cholesterol concentrations relative to carbohydrates (circles, LDL; squares, HDL). Data are derived from six dietary comparisons between trans monounsaturates and other fatty acids, largely cis unsaturates fatty acids: Judd et al (6), Lichtenstein et al (5), Nestel et al (4), Zock and Katan (5), and Mensink and Katan (2). Values were recalculated to a comparison with carbohydrates and differences between diets in fatty acids other than trans and cis monounsaturates were adjusted for using regression coefficients from a meta-analysis of 27 controlled trials (1).

It would be uncommon for random fluctuations to produce an effect in three independent trials. On the contrary, variability might obscure the effect in a smaller trial with a lower dose, which may have happened in the negative trial (5). A recent Norwegian study also found that trans fatty acids from partially hydrogenated fish or soybean oil elevated lipoprotein(a) concentrations relative to butter (11). Trans fatty acids therefore appear to be one of the rare diet factors that influence lipoprotein(a) concentrations; however, the effect is modest compared with genetically determined differences.

EPIDEMIOLOGIC STUDIES

When saturated fatty acids are replaced by trans fatty acids, lipoprotein(a) goes up, HDL may be lowered, LDL changes little, and serum triacylglycerol concentrations—not discussed much in the report—also increase (12). It is this peculiar set of changes that makes epidemiologic studies of trans fatty acids and coronary disease of special interest. A weak point of such studies is that consumption of foods high in trans fatty acids may form part of a lifestyle that includes other factors affecting heart disease risk; such confounding is difficult to eliminate. On the other hand, the very crudeness of methods for measuring food intake should make us pay attention when an association makes itself heard above the noise. The poor precision of methods for determining intakes will cause associations between diet and disease to appear weaker than they are; this attenuation has in fact been the explanation for why no associations are seen between saturated fat intake and coronary heart disease within populations. The fact that the Nurses Health Study and other studies find a positive association between trans fatty acids and coronary heart disease therefore deserves attention. By themselves such data fall far short of proving that high intakes of trans fatty acids promote coronary heart disease, but the effects of trans fatty acids on plasma lipids and lipoproteins lend some credence to a causal link.

WHAT TO TELL THE CONSUMER?

For purposes of nutrition education I would favor summing trans and saturated fatty acid contents of foods to a single number. This avoids unnecessary emphasis on trans fatty acids, which are after all a minor food component; it inhibits the promotion of fats high in saturated fatty acids as replacements for partially hydrogenated oils, which from a public health point of view is undesirable; and it avoids sweeping assertions about health effects of trans fatty acids.

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REFERENCES