Trans Fat and Cardiovascular Disease

Qi Sun, MD, ScD

Abstract

Cardiovascular disease remains the number one killer in the United States. According to the American Heart Association statistics, CVD accounted for 35.2% of total deaths in 2005 in the United States.¹ This is also true for developing countries, such as China and India: CVD has also become the first or second leading causes of death; it is responsible for around 30% of total deaths in developing countries.² Of many risk factors for CVD, dietary intake of fats received much attention and has been extensively studied due to the facts that blood cholesterol levels are a strong predictor for CVD³ and that dietary fats are a strong determinant for serum lipids.⁴ Although the effects of some fatty acids on coronary health are still a matter of debate, the relationship between trans fatty acids and risk of CVD has been established.⁵ [N A J Med Sci. 2008;1(1):34-35.]

Biochemistry of trans fatty acids

Fatty acids are categorized into different sub-groups according to the chain length of carbon-backbone and presence of unsaturated double bonds. Saturated fatty acids have a carbon-backbone of 4-24 carbons and no unsaturated double bonds. In contrast, unsaturated fatty acids have a carbon-backbone of 16-22 carbons and at least one unsaturated double bond. Trans fatty acids are a special kind of unsaturated fatty acid in that the hydrogen atoms are on opposite (trans configuration) sides of the double bonds, whereas for the rest of unsaturated fatty acids these hydrogen atoms are on the same (cis configuration) sides of the double bonds.⁵ It is because of this trans configuration, trans fat is similar to saturated fat in terms of physical properties and is semi-solid at room temperature. More importantly, it is because of this subtle structural difference, trans fatty acids are entirely different from other unsaturated fatty acids with respect to coronary effects.

History

Trans fatty acids are naturally produced in the rumen through bacterial fermentation; about 5% of ruminant fat is trans fat. However, most trans fats in the US diet are produced by the food industry via partial hydrogenation vegetable oils. Nobel Prize winner Paul Sabatier developed the methods of

Qi Sun, MD, ScD Department of Nutrition Harvard School of Public Health Boston, Massachusetts 02215, USA. Tel: 617-459-8638 Fax: 617-432-2435 email: qisun@hsph.harvard.edu hydrogenation in 1890s which enables the production of trans fats. Hydrogenation of oils is a process that adds hydrogen atoms to the unsaturated double bonds and thus unsaturated fatty acids are converted to saturated fatty acids. In partial hydrogenation, only a proportion of the double bonds are fully saturated and some double bonds are converted from cis to trans configuration. Partially hydrogenated oils first entered US food supply by 1920. But it is until 1950s-1960s the use of trans fats (primarily margarine) became substantial.⁶ Ironically, at that time, margarine was regarded as a healthy substitute of butter because of low saturated fatty acid content. Total consumption of trans fat was approximately 2-3% of total energy in the US.

Physiological Effects of Trans Fatty Acids

The evidence regarding adverse effects of trans fatty acids on blood lipids and other CVD risk factors is substantial. Of many potential mechanisms through which trans fatty acids may increase the risk of CVD, the effect of trans fatty acids on blood lipid profiles has been most extensively studied in clinical trials. Mensink et al. summarized results from 8 clinical trials that specifically examined the effect of 18:1 *trans* isomer intake in a meta-analysis.⁷ Results indicated that of all classes of fatty acids, trans fatty acids had a strong effect on raising serum LDL cholesterol (bad cholesterol) concentrations and were the only class of fatty acids that did not raise HDL cholesterol (good cholesterol) concentrations when replacing carbohydrates. As a result, trans fatty acids had the strongest effect on raising total cholesterol to HDL ratio, which is a stronger predictor of CHD risk than total cholesterol.8 Trans fatty acids may increase the risk of CVD through other pathways, including increasing lipoprotein(a),^{9,10} and blood triacylglycerol concentrations,⁴ and interfering with essential fatty acid metabolism and eicosanoid balance by inhibiting delta-6-desaturase.11,12 Furthermore, trans fat intake has been shown to be associated with systemic inflammation, endothelial cell dysfunction, and insulin resistance.^{5,13} By their incorporation into the phospholipids in cell membranes, trans fatty acids may also alter the membrane function and decrease the membrane fluidity in a way similar to saturated fat.¹⁴

Epidemiologic Evidence

Because of the clear adverse effects of trans fatty acids on blood lipids and inflammatory markers, it is unethical to conduct clinical trials that use the incidence of CVD as the outcome. Evidence from several well-designed prospective studies consistently showed a strong association between trans fatty acid intake and the risk of CVD. In a metaanalysis, 2% of total energy from trans fat was associated with a 23% increase of CVD risk.⁵ It is worth noticing that 2% of total energy is a small unit. These results were corroborated by several case-control studies that used trans fatty acid contents in human tissues as an indicator of trans fat intake. For example, in the Nurses' Health Study, women whose trans fatty acid levels in red blood cells were in the highest quartile had more than 3 times elevated risk of developing coronary heart disease than women in the lowest quartile.¹⁵ Data from developing countries were rare. In a Costa Rican population, trans fatty acids in adipose tissue were also associated with an increased risk of CVD.¹⁶

Food Sources and Customers' Choices

On January 1, 2006, US Food and Drug Administration (FDA) ruled that nutrition labels for all foods and supplements must indicate the content of trans fatty acids. At the end of 2006, New York City passed a trans fat ban at restaurants. Currently, more and more cities have passed or are considering to pass such a ban in the US and worldwide. This is probably the first time that, without clinical trial evidence, a nutrient is being eliminated from the food supply in the US. Traditionally, primary food sources of trans fatty acids are fast foods and bakery products, including French fries, breaded fish burgers, breaded chicken nuggets, pies, sweet rolls, doughnuts, cookies, cakes, brownies, and muffins. This is not at all a complete list. Consumers are recommended to read the food labels. It is necessary to point out those foods containing less than 500 mg trans fatty acids per serving are allowed to be labeled as zero trans fat content. Therefore, several servings of such foods can still provide substantial trans fatty acids.

Conclusions and Future Implications

Based on the evidence from basic research, clinical trials, and epidemiologic studies, it is safe to conclude that trans fatty acid intake bears no benefit to human health and can bring substantially harmful effects to overall coronary health. In developed countries, actions have already been taken to eliminate trans fats from the food supply. In contrast, data regarding trans fat content in food is lacking in third worl countries. In China, unpublished data showed that among a small middle-aged population, trans fatty acid content in plasma was 20% of that of US population. However, given the dramatic lifestyle and nutrition transition that is currently undergoing in China, whether younger Chinese populations also have low trans fat content in their bodies is questionable. It is important to shed more light on this issue. Governments of developing countries should seriously not hesitate to ban trans fat use for the sake of their people's health.

References

- Rosamond W, Flegal K, Furie K, et al. Heart disease and stroke statistics--2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2008;117(4):e25-146.
- **2.** The World health report: 2003: shaping the future. Geneva, Switzerland: World Health Organization; 2003.
- Kannel WB, Dawber TR, Friedman GD, Glennon WE, McNamara PM. Risk Factors in Coronary Heart Disease. An Evaluation of Several Serum Lipids as Predictors of Coronary Heart Disease; the Framingham Study. Ann Intern Med. 1964;61:888-899.
- 4. Katan MB, Zock PL, Mensink RP. Trans fatty acids and their effects on lipoproteins in humans. *Annu Rev Nutr.* 1995;15:473-493.
- Mozaffarian D, Katan MB, Ascherio A, Stampfer MJ, Willett WC. Trans fatty acids and cardiovascular disease. N Engl J Med. 2006;354(15):1601-1613.
- **6.** Willett WC. Trans fatty acids and cardiovascular diseaseepidemiological data. *Atheroscler Suppl.* 2006;7(2):5-8.
- 7. Mensink RP, Zock PL, Kester AD, Katan MB. Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am J Clin Nutr.* 2003;77(5):1146-1155.
- 8. Shai I, Rimm EB, Hankinson SE, et al. Multivariate assessment of lipid parameters as predictors of coronary heart disease among postmenopausal women: potential implications for clinical guidelines. *Circulation*. 2004;110(18):2824-2830.
- **9.** Nestel P, Noakes M, Belling B, et al. Plasma lipoprotein lipid and Lp[a] changes with substitution of elaidic acid for oleic acid in the diet. *J Lipid Res.* 1992;33(7):1029-1036.
- Sundram K, Ismail A, Hayes KC, Jeyamalar R, Pathmanathan R. Trans (elaidic) fatty acids adversely affect the lipoprotein profile relative to specific saturated fatty acids in humans. *J Nutr.* 1997;127(3):514S-520S.
- Hill EG, Johnson SB, Lawson LD, Mahfouz MM, Holman RT. Perturbation of the metabolism of essential fatty acids by dietary partially hydrogenated vegetable oil. *Proc Natl Acad Sci U S A*. 1982;79(4):953-957.
- **12.** Kinsella JE, Bruckner G, Mai J, Shimp J. Metabolism of trans fatty acids with emphasis on the effects of trans, trans-octadecadienoate on lipid composition, essential fatty acid, and prostaglandins: an overview. *Am J Clin Nutr.* 1981;34(10):2307-2318.
- **13.** Lopez-Garcia E, Schulze MB, Meigs JB, et al. Consumption of trans fatty acids is related to plasma biomarkers of inflammation and endothelial dysfunction. *J Nutr.* 2005;135(3):562-566.
- 14. Roach C, Feller SE, Ward JA, Shaikh SR, Zerouga M, Stillwell W. Comparison of cis and trans fatty acid containing phosphatidylcholines on membrane properties. *Biochemistry*. 2004;43(20):6344-6351.
- **15.** Sun Q, Ma J, Campos H, et al. A prospective study of trans fatty acids in erythrocytes and risk of coronary heart disease. *Circulation*. 2007;115(14):1858-1865.
- 16. Baylin A, Kabagambe EK, Ascherio A, Spiegelman D, Campos H. High 18:2 trans-fatty acids in adipose tissue are associated with increased risk of nonfatal acute myocardial infarction in costa rican adults. J Nutr. 2003;133(4):1186-1191.