Trans Fatty Acids and Cardiovascular Disease Risk

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Abstract: *Trans* fatty acids (TFA) are fatty acids that contain at least one double bond that is in the *trans* configuration. TFA are consumed mainly with industrial partially hydrogenated vegetable fats that are used in the production of margarines and "shortenings". The consumption of ruminant TFA provide another source of TFA in European countries. TFA consumption generally increases total cholesterol and decreases high density lipoprotein cholesterol and is associated with increased risk of cardiovascular disease. The results of some large-scale epidemiological studies suggest that the increased cardiovascular disease risk with the consumption of TFA is possibly greater than would be predicted from changes in plasma lipid levels alone. The experience from different countries shows that the elimination of TFA is a cost effective and feasible public health intervention. Based on the scientific evidence, the consumption of TFA should be further targeted aiming to further reduce of TFA in fast food products and the implementation of newer industrial methods that produce vegetable oils with lower (or even zero) amounts of TFA.

Keywords: Trans fatty acids, fatty acids, lipids, diet, cardiovascular disease, cholesterol, hydrogenated oil.

Trans fatty acids (TFA) are fatty acids that contain at least one double bond that is in the *trans* configuration [1]. In human diets, TFA may arise from three sources [2]. The main source in most countries originates from the industrial partial hydrogenation of foods, which is an industrial process that reduces the unsaturation of fatty acids. This process results in solid vegetable fats that are used in the production of margarines and "shortenings", which in turn are used for cooking. TFA from partially hydrogenated oils can be found in margarine and other spreads, coffee creamer, baked goods such as cakes, cookies and pies, frozen pizza, snack foods such as microwave popcorn, and refrigerator dough products such as biscuits and cinnamon rolls. Indeed, margarines may contain from 1-2% (high-quality margarine) to 60% (low-quality margarine) TFA [3]. The second source is the biohydrogenation, which is observed in nature and mainly results from the enzymatic transformation of *cis*-fatty acids into TFA by the bacterial flora of the rumen of animals (e.g. cows, sheep, goats). Ruminant TFA provide up to 10 % of total fatty acids and consumed primarily with milk products (e.g. butter, cheese) and meats [4, 5]. The third source, which represents a minor source, is originated by extreme thermal treatments of food, which is observed, among others, in domestic processes such as long-time baking at high temperatures, dry pan frying or barbecue [6].

Several meta-analyses of controlled dietary interventions that examined the relationship between TFA intake and lipid levels consistently report a dose–related impairment of lipid levels [7-11]. TFA are associated with an increase of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) levels, a decrease of high-density lipoprotein cholesterol (HDL-C) levels, and in some studies an elevation of serum triglycerides (TG) concentration [12-16]. It seems that the substitution of TFA for *cis* unsaturated fatty acids results in elevation of TC and LDL-C levels, whereas the substitution for saturated fatty acids results in a decrease of HDL-C levels and increase of TG concentration and the TC/HDL-C ratio [12, 17, 18]. In a meta-analysis of 60 selected trials, the isoenergetic replacement of *trans* 18:1 constituting 1% of energy with saturated fatty acids decreased TC/HDL-C ratio by 0.019. The isoenergetic replacement with *cis* monounsaturated fatty acids decreased TC/HDL-C ratio by 0.048 and with *cis* polyunsaturated fatty acids by 0.054 [19]. When TFA constituting 1% of energy were isoenergetically replaced with a 1:1:1 mixture of carbohydrates, *cis* monounsaturated fatty acids, and *cis* polyunsaturated fatty acids, then the TC/HDL-C ratio decreased by 0.04. The detrimental effect of TFA is also demonstrated by the fact that the isoenergetic replacement of TFA constituting 1% of energy with carbohydrates has the same effect on TC/HDL-C ratio as with the isoenergetic replacement of saturated fatty acids constituting 7.3% of energy with carbohydrates [19]. The increase in TC/HDL-C ratio with the consumption of TFA is clinically important since it is associated with increased cardiovascular disease (CVD) risk [20].

These harmful effects of TFA on lipidemic parameters have been attributed to decreased rates of apolipoprotein B-100 catabolism, increased rates of

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apolipoprotein A-I catabolism, and increased activity of cholesteryl ester transfer protein. Evidence from animal studies indicate that TFA suppress hepatic LDL receptor activity [21]. *In vitro* studies also have implicated TFA with decreased lecithin:cholesterol acyltransferase activity [9, 22, 23]. Interestingly, prospective studies have shown that the actual incidence of CVD attributed to TFA intake is greater than that predicted by changes in serum lipids alone [9, 24-27]. Thus, effects of TFA on other additional risk factors have been proposed, such as the increase of lipoprotein (a) levels or the association with cardiac arrhythmias or sudden cardiac arrest [7, 9]. Additionally, TFA consumption has been associated with endothelial dysfunction and an increase of soluble inter-cellular adhesion molecule 1, soluble vascular-cell adhesion molecule 1, E-selectin, tumor necrosis factor-α, interleukin-6 and C-reactive protein [28].

It should be mentioned that in European countries TFA derived from milk and ruminant fat comprises a large proportion of total TFA consumption. Indeed, the ruminant TFA exceeds 50% of total TFA consumption in the Mediterranean countries [29]. There is a debate if the intake of TFA derived from ruminant fats has a similar association with CVD as with the intake of industrial hydrogenated fats [30-32]. However, in the Zutphen Elderly Study the intakes of both ruminant and industrially produced TFA predicted a higher risk of coronary artery disease [25]. Furthermore, a quantitative review of the literature concluded that TFA derived from any source increase the LDL-C/HDL-C ratio [33]. The consumption of ruminant TFA is low in most countries (<1% of energy), because ruminant fat contains low levels of TFA. Generally, the amounts of ruminant TFA that is actually consumed does not seem to provide a significant contribution to CVD risk compared with industrially-derived TFA [34]. In any case, the intake of ruminant TFA can be kept low by the consumption of skimmed dairy products and lean meat.

The experience from different countries shows that the elimination of TFA is a cost effective and feasible public health intervention. Recently, the United States Food and Drug Administration (FDA) made a preliminary determination that partially hydrogenated oils, the major dietary source of TFA in the processed food supply, are no longer Generally Recognized as Safe (GRAS) [35]. Before that announcement, the World Health Organization had recommended that TFA should be limited to less than 1% of daily caloric intake [36], and United States had mandated labeling of foods with more than 0.5 g of TFA content per serving [37]. In European Union, Denmark and Switzerland introduced laws strictly regulating the sale of many foods containing TFA, which limit TFA to <2% of fats and oils destined for human consumption. Based on the scientific evidence, the consumption of TFA should be further targeted. The fast food industry should be encouraged to decrease the amount of TFA content in their products. Furthermore, newer industrial methods should be employed in order to produce vegetable oils with lower (or even zero) amounts of TFA.

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