



Is the Association between Dietary Trans Fatty Acids and Insulin Resistance Remarkable in Japan?

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See article vol. 24: 1206-1214

Trans fatty acids (TFA) are unsaturated fatty acids with at least one unsaturated and nonconjugated double bond in the *trans* configuration. The main food sources of TFA are industrial products formed by partial hydrogenation of vegetable oils and natural ones formed by microbial action in the rumen, which are included in dairy products and the meat. Milk fat contains low amounts of TFA compared with partially hydrogenated oils^{1, 2}. The major industrial TFA is generally elaidic acid, while the main ruminal TFA is vaccenic acid.

Growing evidence has shown that TFA intake increases the risk of developing atherosclerotic cardiovascular diseases³. Recent cross sectional study in Japan has also demonstrated that serum TFA concentration is elevated in young patients with coronary artery disease⁴. Underlying mechanisms inducing atherosclerosis may involve a direct effect on vascular cells and the influence on the classical coronary risk factor such as dyslipidemia, abnormal glucose metabolism, hypertension, and adiposity. Among these, both controlled trials and observational studies revealed that TFA elevate low-density lipoprotein cholesterol (LDL-C) and lipoprotein (a) concentrations and reduce high-density lipoprotein cholesterol (HDL-C) concentration³.

Similarly, the effects of TFA on glucose metabolism and insulin sensitivity have been examined in relatively fewer studies. However, the conclusion is not yet fixed⁵. The reasons may be due to the varieties in the characteristics of subjects (young or old, obese or healthy, diabetic or healthy), and the differences in

trial duration, fat and carbohydrate percentages in total energy and fatty acid compositions in diets, or the estimation of TFA (dietary questionnaires or measurement of TFA in serum or phospholipids).

For instance, in randomized crossover design studies, Christiansen *et al.* showed that among 16 obese type II diabetic patients [mean age, 55 years; mean body mass index (BMI), 33.5 kg/m²; mean hemoglobin A1c, 7.7%] with a total fat of 30% of total energy intake (30%E) including either 20%E from saturated fatty acids (SFA), monounsaturated fatty acids (MUFA) or TFA provided for 6 weeks, postprandial insulin levels were 59% higher with the TFA diet than with the MUFA diet. There was no significant difference between SFA and TFA diets⁶. On the other hand, MUFA diet [oleic acid, 9%E in total fat of 30%E] for 4 weeks did not differ from SFA or TFA diet (palmitic acid, 8.4%E or elaidic acid, 7.3%E, respectively) in the effects on insulin sensitivity and secretion in 25 healthy young men and women (mean age, 28; mean BMI, 23.5 kg/m²; 18 subjects had BMI < 25 kg/m²; 7 were overweight with BMI of 25-30 kg/m²)⁷. In randomized, double-blind controlled trial for 4 weeks with 63 healthy women with abdominal obesity (waist circumference > 88 cm and BMI > 28 kg/m²), there was no difference in insulin sensitivities and parameters estimated by euglycemic hyperinsulinemic clamps among low TFA diet (mean, 0.23%E in total fat of 41.7%E), ruminant TFA-rich diet (vaccenic acid, 2.04%E in 41.6%E), or industrial TFA-rich diet (elaidic acid, 2.59%E in 43.5%E)².

Icho *et al.* reported that excessive TFA intake worsens insulin resistance in the analysis of the 75-g oral glucose tolerance test in a cohort of 454 native Japanese living in Hiroshima, Japan, but not in a cohort of 456 Japanese American living in Los Angeles, USA⁸. Participants in two Japanese cohorts shared identical genetic predispositions but had different lifestyles. In this paper, serum elaidic acid concentrations were significantly higher in the Japanese American population (median, 18.2 μmol/L) than in the native

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Received: May 16, 2017

Accepted for publication: May 22, 2017

Japanese population (median, 11.0 $\mu\text{mol/L}$). Serum elaidic acid concentrations in native Japanese with diabetes mellitus (DM) group (16.0 $\mu\text{mol/L}$) were significantly higher than those in the normal glucose tolerance (NGT, 10.8 $\mu\text{mol/L}$) and impaired glucose tolerance (IGT, 11.7 $\mu\text{mol/L}$) groups. In Japanese Americans, however, no significant difference was observed among NGT, IGT, and DM groups (18.4, 18.4, and 16.3 $\mu\text{mol/L}$, respectively). In the native Japanese, multiple linear regression analyses showed that serum elaidic acid concentrations were significantly positively associated with homeostasis model assessment for insulin resistance values after adjustment for various factors, except after adjustment for triglycerides. They previously reported that the intake of animal fat and simple carbohydrates were markedly higher in Japanese Americans than in native Japanese⁹⁾. Although they did not show the detailed diet composition in the two cohorts, they suggested that the effect of TFA intake on the development of DM is presumed to be relatively greater in the native Japanese, whose intake of animal fat and simple carbohydrate are lower. In other words, in Western diet with high fat and energy, the effect of TFA on glucose metabolism and insulin sensitivity may not be remarkable. Taken together, one can deduce that intake of adequate total energy and fatty acid is the most important and that at least reduction of industrial TFA is also significant issue.

Thus, although it is very difficult to clarify the contribution of TFA to worsening glucose metabolism, it is necessary to research this issue under matching total energy intake, total fatty acid intake and the balance of SFA, MUFA, and polyunsaturated fatty acids. Furthermore, although it has not been determined yet whether ruminant TFA affects atherogenesis, we should know how much we take TFA in our usual diet to reduce TFA intake.

In Japan, a recent cohort study demonstrated the significant associations of high-energy intake with all-cause and cancer mortality among men, and associations with CHD mortality among men and women¹⁰⁾. Data obtained from the annual "Specific Health Check and Guidance in Japan" showed that target level-attainment rates of blood pressure and LDL-C recommended by the Japanese Society for Hypertension and the Japan Atherosclerosis Society were improved from 2008 to 2011¹¹⁾. Actually, total risk management that focused on LDL-C, blood pressure, and HbA1c has a beneficial impact on the coronary plaque regression in diabetic patients with acute coronary syndrome¹²⁾. Thus, we should encourage total management of food intake including TFA.

Conflict of Interest

None.

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