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Component in Common Dairy Foods May Cut Diabetes Risk, Study Suggests

Scientists at the Harvard School of Public Health (HSPH) and collaborators from other institutions have identified a natural substance in dairy fat that may substantially reduce the risk of type 2 diabetes. The compound, trans-palmitoleic acid, is a fatty acid found in milk, cheese, yogurt, and butter. It is not produced by the body and so only comes from the diet.

Reporting in the December 21, 2010, issue of *Annals of Internal Medicine*, investigators led by Dariush Mozaffarian, Associate Professor in the Department of Epidemiology at HSPH and Division of Cardiovascular Medicine, Brigham and Women's Hospital and Harvard Medical School, and Gökhan S. Hotamisligil, J.S. Simmons Professor of Genetics and Metabolism and Chair of the Department of Genetics and Complex Diseases at HSPH, explain that trans-palmitoleic acid may underlie epidemiological evidence in recent years that diets rich in dairy foods are linked to lower risk of type 2 diabetes and related metabolic abnormalities. Health experts generally advise reducing full-fat dairy products, but trans-palmitoleic acid is found in dairy fat.

The HSPH researchers examined 3,736 participants in the National Heart, Lung, and Blood Institute-funded Cardiovascular Health Study, who have been followed for 20 years in an observational study to evaluate risk factors for cardiovascular diseases in older adults. Metabolic risk factors such as blood glucose and insulin levels, and also levels of circulating blood fatty acids, including trans-palmitoleic acid, were measured using stored blood samples in 1992, and participants were followed for development of type 2 diabetes.

At baseline, higher circulating levels of trans-palmitoleic acid were associated with healthier levels of blood cholesterol, inflammatory markers, insulin levels, and insulin sensitivity, after adjustment for other risk factors. During follow-up, individuals with higher circulating levels of trans-palmitoleic acid had a much lower risk of developing diabetes, with about a 60% lower risk among participants in the highest quintile (fifth) of trans-palmitoleic acid levels, compared to individuals in the lowest quintile.

"This type of observational finding requires confirmation in additional observational studies and controlled trials, but the magnitude of this association is striking," said Mozaffarian, lead author of the study. "This represents an almost three-fold difference in risk of developing diabetes among individuals with the highest blood levels of this fatty acid."

In contrast to the types of industrially produced trans fats found in partially hydrogenated vegetable oils, which have been linked to higher risk of heart disease, trans-palmitoleic acid is almost exclusively found in naturally-occurring dairy and meat trans fats, which in prior studies have not been linked to higher heart disease risk.

"There has been no clear biologic explanation for the lower risk of diabetes seen with higher dairy consumption in prior studies. This is the first time that the relationship of trans-palmitoleic acid with diabetes risk has been evaluated," said Mozaffarian. "We wonder whether this naturally occurring trans fatty acid in dairy fats may partly mimic the normal biologic role of its cis counterpart, cis-palmitoleic acid, a fatty acid that is produced in the body. In animal experiments, cis-palmitoleic acid protects against diabetes."

"Unfortunately, with modern diets, synthesis of cis-palmitoleic acid is now driven by high amounts of carbohydrate and calories in the diet, which might limit its normal protective function. We wonder whether trans-palmitoleic acid may be stepping in as a "pinch hitter" for at least some of the functions of cis-palmitoleic acid," said Mozaffarian.

Hotamisligil, the study's senior author, also emphasized the magnitude of the risk reduction. "This is an extremely

strong protective effect, stronger than other things we know can be beneficial against diabetes. The next step is to move forward with an intervention trial to see if there is therapeutic value in people.”

Because trans-palmitoleic acid, also known as trans-palmitoleate, is a natural compound, Hotamisligil said that conducting clinical trials should be possible. “This study represents the power of interdisciplinary work bridging basic science with population studies to realize exciting translational possibilities,” he said.

Support for the study was provided by the National Heart,

Lung, and Blood Institute and National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health and the National Institutes of Health Office of Dietary Supplements and National Institute of Neurological Disorders and Stroke. A subset of additional fatty acid measurements were supported by a Searle Scholar Award.

Dariusz Mozaffarian, Haiming Cao, Irena B. King, Rozenn N. Lemaitre, Xiaoling Song, David S. Siscovick, and Gökhan S. Hotamisligil. Trans-Palmitoleic Acid, Metabolic Risk Factors, and New-Onset Diabetes in U.S. Adults. *Annals of Internal Medicine*, December 21, 2010