Editorial

See corresponding articles on pages 1437 and 1532.

A changing view on saturated fatty acids and dairy: from enemy to friend[1–3]

Arne Astrup

Almost all national dietary guidelines recommend a reduction in SFAs as a key intervention to reduce incidence and mortality of cardiovascular disease (CVD). This has been translated into advice to reduce the intake of the major sources of SFAs, that is, dairy produce, meat products, and eggs. However, recent meta-analyses of both observational studies and randomized controlled trials not only have raised doubts about the scientific substantiation for this advice but have actually undermined it. It has become clear that there is a need for a completely different approach, with advice that is based on foods rather than on nutrients.

The evidence to support reducing SFAs rests on a 2-step argument: "A strong body of evidence indicates that higher intake of most dietary SFA (A) is associated with higher levels of blood total cholesterol and low-density lipoprotein (LDL) cholesterol (B). Higher total and LDL cholesterol levels (B) are risk factors for CVD (C)" (1).

Most would interpret the statement above as evidence of a causal relation between intake of SFAs (A) and CVD (C), but it is actually an assumption that increased concentrations of LDL cholesterol (B) will always increase the risk of CVD (C). The relation between dietary fats (and other dietary components) and CVD is, however, much more complex, and this assumption does not take into account the importance of LDL-cholesterol particle size, effects on HDL cholesterol, and other mediators of the atherosclerotic, thrombotic, and thrombolytic processes (2).

SFAs AND CVD

More recent meta-analyses of high compared with low intakes of SFAs fail to find any increased CVD risk. Siri-Tarino et al. (3) compared extreme quantiles of SFA intake and found RRs not different from 1.0. However, it has become obvious that the different fatty acids derived from different foods do not have the same biological effects, and that the food matrix within which they are delivered modifies their effect. So the health effects of any food matrix rich in SFAs cannot be predicted on the basis of the content of "total SFAs" given on the nutrient content label. There is a need to view the health effect of "whole foods" and to use biomarkers to improve the validity of the habitual food intake registered in observational studies and adherence in RCTs.

Chowdhury et al. (4) examined the effect of SFAs based on a meta-analysis of 17 observational studies with fatty acid biomarkers and 27 randomized controlled trials (RCTs) of fatty acid supplementation. In the observational studies, RRs for coronary disease were no different for SFAs, n–6 PUFAs, and MUFAs when the top and bottom thirds of baseline dietary fatty acid intake or circulating fatty acids were compared. The meta-analysis of RCTs with hard CVD endpoints reached the same conclusion. Another meta-analysis of RCTs even suggested that replacement of SFAs with pure n–6 PUFAs might increase CVD risk and mortality (5).

DAIRY AND RISK OF CVD AND TYPE 2 DIABETES

In recent years, a substantial body of research has investigated the effects of dairy and dairy fat on risks of CVD, type 2 diabetes, and obesity. A dose-response meta-analysis of prospective studies indicates that milk intake is not associated with total mortality but may be inversely associated with overall CVD risk (6).

Reliance on self-reported dietary intakes poses substantial problems with validity, and the development of objective biomarkers to distinguish between different food-derived fatty acids represents a major advantage; pentadecanoic acid (15:0), heptadecanoic acid (17:0), and *trans* palmitoleic acid (*trans* 16:1n–7) can be used as biomarkers for dairy intake. The literature has generated mixed results with regard to risk of stroke, but the most comprehensive study from 2 large U.S. cohorts (Health Professionals Follow-Up Study: 51,529 men; Nurses' Health Study: 121,700 women) using biomarkers of dairy fat (pentadecanoic acid, heptadecanoic acid, and *trans* palmitoleic acid) reports results for stroke in this issue of the Journal (7). After relevant adjustments, no significant associations with total stroke were seen for any of the 3 biomarkers. The results were similar for ischemic and hemorrhagic stroke subtypes, and the results remained in sensitivity analyses.

SFAs have also been associated with increased risk of type 2 diabetes, which is a major risk factor for CVD. However, meta-analyses of observational studies based on self-reported dietary intake failed to find that dairy increases the risk of type 2 diabetes (8, 9). In a meta-analysis of 17 cohort studies, there was a modest but significant inverse relation between intakes of total dairy products, low-fat dairy products, and cheese and risk of type 2 diabetes (9).

[1] From the Department of Nutrition, Exercise, and Sports, Faculty of Science, University of Copenhagen, Frederiksberg, Denmark.

[2] No financial support was received for this editorial.

[3] Address correspondence to A Astrup, Nørre Alle 51, Copenhagen, Denmark, DK-2200. E-mail: ast@nexs.ku.dk.

First published online October 29, 2014; doi: 10.3945/ajcn.114.099986.

BIOMARKERS OF DAIRY AND DIABETES RISK

A case-cohort analysis was conducted based on the European Prospective Investigation into Cancer and Nutrition–InterAct study in 12,403 individuals with incident type 2 diabetes, and fatty acids were measured in plasma phospholipids (10). Whereas even-chain SFAs were positively associated with incident type 2 diabetes, the odd-chain SFAs pentadecanoic acid and heptadecanoic acid were inversely associated with incident type 2 diabetes (HRs: 0.79 and 0.67, respectively). However, whereas this study adds further to evidence of a diabetes-protective effect of dairy products, it does not present any mechanism nor does it provide information about whether it is the SFAs or other components within the food matrix of dairy that mediate the effects. In contrast, also in this issue of the Journal, Santaren et al. (11) confirm that serum concentrations of pentadecanoic acid were associated with a 27% risk of diabetes (OR: 0.73; $P = 0.02$), and the association remained after adjustment for BMI and waist circumference. This suggests that the effect is independent of body fatness, an important cause of type 2 diabetes. Santaren et al. also used frequently sampled intravenous glucose tolerance tests to measure insulin sensitivity (S_I) and β cell function (Disposition Index), and they found that concentrations of pentadecanoic acid were positively associated with both measures in fully adjusted models. These associations were substantially weakened by adjustment for obesity indexes. The authors correctly state that the mechanism underlying the inverse relation of pentadecanoic acid with diabetes risk is not known, and that it could be either an effect of fatty acid or attributable to other beneficial components within the dairy matrix.

CONCLUSIONS

The totality of evidence does not support that dairy SFAs increase the risk of coronary artery disease or stroke or CVD mortality. In contrast, lean dairy is clearly associated with decreased risk of type 2 diabetes, and this effect is partly independent of any effect of body fat loss. In addition, lean dairy does not increase body fatness but tends to preserve lean body tissue. There is no evidence left to support the existing public health advice to limit consumption of dairy to prevent CVD and type 2 diabetes. Cheese and other dairy products are, in fact, nutrient-dense foods that give many people pleasure in their daily meals.

The Department of Nutrition, Exercise and Sports at the University of Copenhagen receives research support from numerous Danish and international food companies/organizations, including The Danish Dairy Research Council, Arla Foods AS, and the Global Dairy Platform. AA currently serves as consultant/member of advisory boards for the Global Dairy Platform, USA; McCain Foods Ltd., USA; and McDonald's, USA. He is recipient of honoraria and sponsorship of congress attendance as a speaker for a wide range of Danish and international concerns.

REFERENCES

1. USDA; U.S. Department of Health and Human Services. Dietary guidelines for Americans, 2010. 7th ed. Washington: U.S. Government Printing Office; 2010.
2. Astrup A, Dyerberg J, Elwood P, Hermansen K, Hu FB, Jakobsen MU, Kok FJ, Krauss RM, Lecerf JM, LeGrand P, et al. The role of reducing intake of SFA in the prevention of cardiovascular disease: where does the evidence stand in 2010? Am J Clin Nutr 2011;93:684–8.
3. Siri-Tarino PW, Sun Q, Hu FB, Krauss RM. Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease. Am J Clin Nutr 2010;91:535–46.
4. Chowdhury R, Warnakula S, Kunutsor S, Crowe F, Ward HA, Johnson L, Franco OH, Butterworth AS, Forouhi NG, Thompson SG, et al. Association of dietary, circulating, and supplement fatty acids with coronary risk: a systematic review and meta-analysis. Ann Intern Med 2014;160:398–406.
5. Ramsden CE, Zamora D, Leelarthaepin B, Majchrzak-Hong SF, Faurot KR, Suchindran CM, Ringel A, Davis JM, Hibbeln JR. Use of dietary linoleic acid for secondary prevention of coronary heart disease and death: evaluation of recovered data from the Sydney Diet Heart Study and updated meta-analysis. BMJ 2013;346:e8707.
6. Soedamah-Muthu SS, Ding EL, Al-Delaimy WK, Hu FB, Engberink MF, Willett WC, Geleijnse JM. Milk and dairy consumption and incidence of cardiovascular diseases and all-cause mortality: dose-response meta-analysis of prospective cohort studies. Am J Clin Nutr 2011; 93:158–71.
7. Yakoob MY, Shi P, Hu FB, Campos H, Rexrode KM, Orav EJ, Willett WC, Mozaffarian D. Circulating biomarkers of dairy fat and risk of incident stroke among U.S. men and women in 2 large prospective cohorts. Am J Clin Nutr 2014;100:1437–47.
8. Gao D, Ning N, Wang C, Li Q, Meng Z, Liu Y, Li Q. Dairy products consumption and risk of type 2 diabetes: systematic review and dose-response meta-analysis. PLoS ONE 2013;8:e73965.
9. Aune D, Norat T, Romundstad P, Vatten LJ. Dairy products and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis of cohort studies. Am J Clin Nutr 2013;98:1066–83.
10. Forouhi NG, Koulman A, Sharp SJ, Imamura F, Kröger J, Schulze MB, Crowe FL, Huerta JM, Guevara M, Beulens JWJ, et al. Differences in the prospective association between individual plasma phospholipid saturated fatty acids and incident type 2 diabetes: the EPIC-InterAct case-cohort study. Lancet Diabetes Endocrinol 2014 Aug 6 (Epub ahead of print; DOI: 10.1016/S2213-8587(14)70146-9).
11. Santaren ID, Watkins SM, Liese AD, Wagenknecht LE, Rewers MJ, Haffner SM, Lorenzo C, Hanley AJ. Serum pentadecanoic acid (15:0), a short-term marker of dairy food intake, is inversely associated with incident type 2 diabetes and its underlying disorders. Am J Clin Nutr 2014;100:1532–40.