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ISSFAL 2014 Debate: It Is Time to Update Saturated Fat Recommendations

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Key Words

Saturated fatty acids · Dietary recommendations · Dietary fat and coronary heart disease

Abstract

This paper summarizes a debate on whether to update recommendations for the consumption of saturated fatty acids (SFA); this debate was held at the 11th congress of the International Society for the Study of Fatty Acids and Lipids in Stockholm, Sweden, June 28–July 2, 2014. Recommendations to reduce SFA intakes are based largely on the premise that high intakes of SFA raise low-density lipoprotein (LDL)-cholesterol levels, which in turn increase the risk of coronary heart disease (CHD). Several systematic reviews question whether reducing SFA intakes lowers CHD risk. Arguing to revise SFA recommendations, Philippe Legrand noted that SFA are heterogeneous in structure and function, are synthesized *de novo* by humans and only certain SFA in excess have been linked to CHD risk. We cannot consider all SFA as a block. The effects of reducing SFA intakes depend on which nutrients replace them and on which biomarkers or endpoints are assessed, Ronald Mensink observed. The effects of reducing SFA on CHD risk vary with the nutrient of comparison, whether carbohydrates, monounsaturated or polyunsaturated fatty acids. Substitution of SFA with polyunsaturated fatty acids was associated with a lower incidence of cardiovascular disease, while the effects of substitution with monounsaturated fatty acids or high-glycemic index carbohydrates are less clear.

Two European experts on dietary fat and health debated the evidence for and against changing current dietary recommendations on saturated fat (SFA) intake at the biennial congress of the International Society for the Study of Fatty Acids and Lipids (ISSFAL), Stockholm, Sweden, June 29, 2014. The forum was held under the auspices of the International Union of Nutritional Sciences (IUNS) and the International Expert Movement to Improve Dietary Fat Quality (IEM, www.theiem.org).

Dietary advice to limit the consumption of saturated fatty acids (SFA) appeared as early as 1961 according to an American Heart Association report [1]. The rationale was based on evidence that high intakes of SFA raise serum cholesterol levels [2], which in turn increase the risk of atherosclerosis and coronary heart disease (CHD) [3]. However, the effectiveness of reducing SFA intakes in lowering the risk of CHD [4–6] has been called into question by weaknesses in the data [7, 8], the complexity of CHD [9], multiplicity of risk factors for the disease (e.g., genetics, smoking, age, sex, obesity, diabetes, hypertension, hyperlipidemia, physical inactivity, etc.), the inadequacy of a single biomarker to assess disease risk [10], certain reports and several systemic reviews [11, 12] that some SFA do not raise cholesterol levels [13]. Others have defended limits or reductions in SFA consumption [14, 15]. In 2008, the Joint Expert Consultation on Fats and Fatty Acids in Human Nutrition of the Food and Agriculture Organization and the World Health Organization concluded that convincing evidence supported partially

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replacing dietary SFA with PUFA for reducing the risk of CHD [16]. Similarly, several systematic reviews concluded that the partial replacement of SFA with PUFA decreased the risk of CHD, especially in men [17–19]. Together, these and other studies have rekindled arguments about the appropriate recommendations for SFA intakes in CHD risk reduction.

Urging that the time for new recommendations had arrived, Philippe Legrand, of the French National Institute for Agricultural Research, Rennes, France, emphasized that 'SFA are nutrients, not poisons'. They supply energy and some have specific physiological functions, for example, cell signaling [20] and protein-fatty acid acylation [21]. They are heterogeneous in structure and function [22] and humans can synthesize them de novo. There are important metabolic differences between various SFA [23]. For example, some SFA such as myristic acid are not stored, but are rapidly oxidized or converted to palmitic acid, which is stored [24]. Stearic acid, an 18-carbon SFA, is readily desaturated to oleic acid [25]. Besides supplying energy, some SFA have other important physiological effects as suggested by in vitro studies, for instance, suppression of colonic inflammation [26] and the regulation of apoptosis in cancer cells [27]. Certain SFA are also structural components of sphingolipids and ceramides, which are important components of cell membranes, skin and myelin. Thus, viewing all SFA as a single dietary block ignores the different effects of individual SFA. If anything, dietary advice should focus on SFA with 12 to 16 carbons, which, in excess, have been associated with increased CHD risk in some studies [28–30]. This focus is reflected in the updated nutritional recommendations in France, which distinguish between the consumption of total SFA at a maximum of 12% energy and intakes of lauric, myristic and palmitic acids, which are limited to no more than 8% energy [31].

Professor Legrand concluded his presentation by drawing attention to the apparent inadequacy of the 'classical' risk markers to characterize saturates in terms of cardiovascular risk. Lauric acid strongly reduces the total-to-HDL-cholesterol ratio (TC:HDL-C), considered the most reliable predictor of heart disease [32], largely by increasing HDL-C levels [33]. Based on this indicator, lauric acid could be considered a heart-healthy saturate.

Mensink questioned the drive to change dietary SFA recommendations. He noted that several reviews [11, 34] concluded that the effect of lower SFA intakes on the risk of CHD depends on which nutrients replace them [35]. There is scientific evidence that a mixture of SFA increases LDL-cholesterol (LDL-C) compared with carbohydrates and unsaturated fatty acids [36] and that LDL-C is a risk factor for CHD. The question is, why are SFA intakes so weakly linked to CHD? Some explanation may relate to the inaccuracy and variability of dietary intake data and of SFA in particular. Confounding variables and the multifactorial nature of CHD risk also complicate the interpretation of existing data [37]. Presently, data are insufficient to establish a causal relationship between SFA and CHD. Sometimes, observational studies complement randomized trial data, but these two types of studies can also provide conflicting evidence. This discordance has been shown in CHD or cardiovascular disease studies on antioxidants, folic acid (homocysteine) and SFA.

Assessments of the effects of SFA on CHD risk depend in part on which biomarkers or endpoints are assessed: levels of plasma LDL-C, TC:HDL-C ratio or changes in HDL-C. These responses vary with the nutrient of comparison, whether it is carbohydrate, monounsaturated (MUFA) or polyunsaturated fatty acids (PUFA). TC:HDL-C is more sensitive and specific than either TC or LDL-C [33, 38], but the effects of dietary fats on TC:HDL-C may differ markedly from their effects on LDL-C. Mensink noted that we do not know what the best combination of lipid biomarkers is and we know little about the effects of SFA on other CHD-related risks.

The discussion shifted to the type of macronutrients that might replace dietary SFA if their intake is reduced [35, 39]. While there is abundant evidence that replacing SFA with PUFA reduces CHD risk [18], there is growing evidence that increased intake of highly refined carbohydrates – those with a high glycemic index – may be associated with a greater CHD risk [40–43]. Others reported that replacing SFA with carbohydrates has little or no effect on CHD [44] or mortality [17]. Diets high in carbohydrates have been associated with lipogenesis [45] and higher plasma levels of triglycerides, small, dense LDL particles, and lower levels of HDL particles [46] in plasma. It is of particular concern that carbohydrate-rich diets with a high glycemic index resulted in LDL particles of smaller size, which are more atherogenic, even in individuals at low-risk of CHD [47–49]. Plasma lipoprotein responses to dietary carbohydrate were also associated with an individual's genetically determined lipoprotein profile [50].

In contrast to the findings on high-carbohydrates in low-SFA diets, substitution of SFA with PUFA was associated with a lower incidence of cardiovascular disease [17]. Early trials of diets relatively low in SFA but high in vegetable PUFA reported significantly lower rates of

myocardial infarction, sudden death and cerebral infarction in men, but overall mortality was not always changed [51, 52]. Two other trials reported nonsignificant effects on cardiovascular disease of replacing SFA with PUFA [53, 54]. However, these early trials have been criticized because both SFA and *trans* fatty acid intakes were partially replaced with unsaturated fats that included both n-6 and n-3 PUFAs, which may affect CHD risk differently [55, 56].

Time constraints did not permit the speakers to focus on total dietary patterns, although both recognized that several dietary patterns have been associated with lower CHD risk and events, LDL-cholesterol levels and blood pressure [57–59]. In particular, a Mediterranean-type diet has been most frequently associated with improved CHD risk, fewer CHD events, fewer coronary complications and improved survival, even though no uniform definition of this dietary pattern has been agreed [60–62].

In discussion with the audience, Joseph Hibbeln, National Institutes of Health, USA, questioned Mensink's suggestion that dietary recommendations should be 'conservative,' asking whether that means resistant to change or cautious interpretation? To continue the status quo recommendations, which were established in the 1970s, would be considered conservative. However, there is a paucity of substantial causal and associative data from the last 50 years to support these recommendations. Mensink commented that recommendations should be preventive and given the debate about SFA and CHD, one should wait for greater certainty before changing the recommendations.

William Lands, retired professor, asserted that talking about the predictive ability of LDL-C closely suggests causality, which is not evidence-based. LDL-C appears in the blood stream as a result of VLDL hydrolysis, which is accompanied by the release of huge quantities of non-esterified fatty acids [63]. That is the major concern, not LDL-C. Lotte Lauritzen, University of Copenhagen, Denmark, also challenged the focus on LDL-C, noting that the metabolic syndrome (MetS) is another marker for CHD and lifestyle diseases. The effects of SFA on markers of MetS may be quite different from those on LDL-C [64].

Mensink agreed that the focus should extend beyond LDL-C, but because the effects of SFA on other markers are not well known, it is too early to consider different SFA separately. We need to consider the entire evidence base, determine what is certain, what is less certain and what we do not know. Then we would have the basis to derive new evidence-based guidelines.

Chris Ramsden, National Institutes of Health, USA, noted the possibility of substantial publication bias in several earlier clinical trials that might not have occurred under current standards for clinical trial protocols. Concerns relate to confounding variables, failure to distinguish between n-3 and n-6 fatty acids and inadequate study design [55]. LDL is a complex molecule in which the core is esterified mainly to linoleic acid. Many oxidized linoleic acid products are major components of atherosclerotic plaque, as observed in smokers and those consuming oxidized vegetable oils [65]. Could potentially oxidized linoleic acid and other fatty acid products help account for the relationship between LDL and heart disease? Legrand suggested that the problem could occur in the case of excess linoleic acid, but we do not know how much is excess.

Susan Carlson, University of Kansas Medical Center in the United States, wondered what balance marker we are striving for. Is it more or less SFA, the 10–10–10 percents [of saturated monounsaturated and polyunsaturated fatty acids]? The real issue is balance in the diet and the [scientific] justification for it. In his reply, Legrand referred to the new French dietary recommendations, which advise an intake of no more than 12% energy intake from all SFA, with the consumption of lauric, myristic and palmitic acids combined limited to 8% energy or less [31].

Jagdave Bhullar, Protherapix, Malaysia, pointed out the paradox that in Thailand, people consume mainly coconut oil, which is 98% SFA, yet they have the third lowest incidence of heart disease in Southeast Asia [66]. Similarly in Kerala, India, and Sri Lanka, almost every food is based on coconut milk or coconut oil and rates of CHD are low [67]. Mensink commented that heart disease cannot be explained only in terms of SFA – there is much more to it than SFA. Some evidence suggests that virgin coconut oil diets in humans do not raise the TC:HDL-C ratio compared with olive or palm oil [68].

Andrew Sinclair, Deakin University, Australia, drew attention to the fact that in many nutritional debates there is a lack of scientific rigor in what is put forward. Discussants often just give opinions, not comments based on sound facts. The focus should be on well-defined issues.

In conclusion, Mensink noted three main needs: first, consideration of the other factors related to CHD, for example, systemic inflammation, blood pressure and endothelial function, because LDL-C is not the only risk factor; second, the determination of what should best replace SFA in the diet; and third, thinking in terms of foods and

dietary patterns rather than nutrients. Legrand concluded that it may be time to revisit the relationships between epidemiology and physiology; to determine if there is excess intake and if so, evaluate what is the best replacement for those foods or nutrients; and finally, to avoid describing foods and nutrients as 'good' or 'bad'. All agreed that dietary recommendations should also be food-based.

Disclosure Statement

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