FATS: THE ROLE OF THE QUALITY OF DIETARY FAT ON ATHEROSCLEROTIC VASCULAR DISEASES

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In 2011, EHN concluded that a moderate amount of dietary fat with an emphasis on the quality of fat is significant for maintaining health and recommended the following: total fat less than 30 % of energy intake (E%), saturated fat (SFA) less than 10 E%, trans fat (TFA) less than 1 E%, polyunsaturated fat 6-11 E% including alpha-linolenic acid (ALA) 1-2 E%, and monounsaturated fatty acids 8-13 E%. This summary concentrates on the recent evidence on the field.

1. Introduction

Recently, there has been some debate regarding the significance of the amount and quality of dietary fat in the prevention and treatment of diseases, especially atherosclerotic vascular diseases (AVD), e.g. coronary heart disease (CHD).[1] There are meta-analyses confirming the current dietary recommendations that decreasing the intake of SFA is of benefit with regard to the prevention of AVD,[1] whereas some controversial meta-analyses show no benefit in this regard.[2] In particular, replacing SFA partly with polyunsaturated fatty acids (PUFA) has been shown to decrease the risk of AVD.[1,3–5] There are recent data, that individual SFAs may have different effects on the risk of diabetes.[6] It has been suggested that SFAs from some dairy products would not increase the risk of AVD or stroke,[7] but recent data do not support this, since individual SFAs present in dairy fat have been shown to be associated with AVD.[8] The results are similar for dairy fat in general.[9]

These controversies have gained a lot of publicity in the media and even the credibility of the current dietary recommendations has been questioned in some studies or comments. It is important to understand the basis of the current recommendations and understand the limitations of the controversial evidence.

2. The amount of fat and energy density

The evidence from many different analyses including prospective cohort studies indicates that total fat intake is not associated with the risk of AVD in Caucasian

[1] Throughout this paper we often refer to coronary heart disease (CHD), a term that is well recognised by general audiences. In this sub-chapter the term atherosclerotic vascular disease (AVD) is used. AVD includes, but is not limited to, CHD. The term is used in this sub-chapter in order to be precise about the research findings where the research was conducted on the broader range of conditions grouped together under the term AVD.

populations.[4] The original detailed analyses in Keys et al's Seven Country Study[10] made it clear that there was no relationship between the intake of total fat and the prevalence of heart disease in different communities and that the type of fatty acids in the dietary fat was the key to raising blood cholesterol concentration and thereby increasing the risk of heart disease.

With the escalating rates of obesity and diabetes with their longer-term effect in amplifying AVD rates there is a need for greater focus on the dietary factors that may promote excessive weight gain and this is where the importance of the total fat content has become apparent.

Progressive weight gain requires that the amount of dietary energy consumed exceeds the body's total use of energy both for normal body maintenance and physical activity thereby leading to an accumulation of energy in the body both as fat and lean tissue. So when physical activity declines it is necessary to reduce total food energy intake to maintain body weight. This then requires ether conscious reductions in food consumption or reliance on the recognised, but far from robust, satiety mechanisms of food intake control. Given the progressive and widespread reduction in physical activity in Europe as work and other physical demands on workers were mechanised, with computers often dominating the workplace, and with private car transport often satisfying general transport needs in much of Europe, it is perhaps not surprising that obesity has escalated over the last 30- 40 years. Furthermore, with the progressive fall in food costs and the increase in the general availability of attractive food, snacks and soft drinks throughout the day backed up by intense multiple forms of marketing it is easy to argue that these factors affecting food intake may be the primary determinants of weight gain (See Chapter 3).

Given this context of multiple factors affecting energy balance and the marked daily variation in food energy consumed as well as the usually more modest change in daily exercise, discerning significant changes in intake or output relevant to weight changes is not straightforward. We also cannot measure simultaneously both food intake and energy output with sufficient accuracy to discriminate the cause of a 0.3 to 1% (i.e. a 10 to 20 kcal change) in average intake or expenditure over say a month or more to reflect the energetic equivalence of the usual 0.5 to 1.0kg per year magnitude of weight gain in adults.

Discriminating dietary factors that intrinsically affect intake therefore requires careful analysis where it is necessary to distinguish between other environmental factors that influence intake. The amount of fat in the food does tend to increase the sensory mouth feel of a food with an intake promoting effect and fat has less of an effect in inducing satiety than either protein (the most powerful inducer of satiety[11] or carbohydrate.[12] These effects suggest, therefore, that the total amount of fat may promote weight gain by permitting more calories to be consumed inadvertently. This was originally called passive overconsumption. There are now major studies with systematic reviews showing that total dietary fat does promote weight gain[13], but a series of meticulously controlled dietary studies shows that it is the high energy/gram content of fat which affects markedly the energy density of the diet[14,15] and it is the energy density of the diet which readily leads to unrecognised overeating. So the lower the physical activity level becomes, the lower the energy density of the diet needs to be to maintain energy balance and avoid weight gain. Thus, severe inactivity

requires a low fat (e.g. 20% of energy) low sugar diet to lower the energy density of the diet sufficiently to limit weight gain whereas if adults are very active e.g. cycling to work and in their daily activity then a 40% total fat (low sugar) diet can still allow energy balance to be maintained.[16] Crude analyses of national diets in relation to national obesity rates showed a clear positive relationship to a nation's dietary fat content.[17] Further trials where the subjects were again unaware of the real purpose of the assessments then showed that the key to maintaining weight and energy balance when inactive was not the total fat content *per se* but the reduction in the general energy density of the diet[14,15] and this could be achieved by lowering either the refined carbohydrate content e.g. as sugar, or by lowering the fat content but preferably both.[18] The consumption of a fibre-rich, unrefined carbohydrate, and vegetable and fruit rich diet also helps as now documented in many trials.[19] So unrecognised changes which increase the energy density of the diet proved to be an important determinant of weight gain[20] and more recently analyses of energy density in communities have also been related to the prevalence of weight gain or obesity.[21]

The choice of a level of fat intake for body weight maintenance is therefore affected both by the degree of physical activity in a community and the extent to which other factors affecting the dietary energy density are changed. Thus a high fibre, whole-grain-rich diet with vegetables and fruit together with a lower sugar intake allows a slightly higher fat intake to be consumed without weight gain Furthermore the diabetes prevention problems in Finland, which require appreciable weight loss, require a low fat diet (as well as appreciable and defined increases in physical activity). So the total fat goal is set at below 30%[22] and in practice about 25% with an explicit need to eat far more fibre-rich food and more vegetables and fruit. The DASH diet where a lower fat intake led to a fall in blood pressure involved a reduction in fat intake from 37% to 26%[23] and Ferro–Luzzi's integrated data on the fat intake of middle-aged Italian men on the Mediterranean in the EURATOM studies[24] in the early 1960s showed their intake to be 28% which also fits with the chemical analyses undertaken on the Mediterranean diet even in Greece (28% fat) as well as in Italy (26% fat) in the 1950s by Keys and colleagues as part of the Seven Country studies.[25] About a fifth of these middle-aged men were already overweight or obese despite heavy manual work.[26]

Thus, given the data from meticulous studies on limiting both hypertension and diabetes and the linear relationship between the fat intake and the propensity to weight gain,[13] a fat intake of 25% accompanied by at least a 60% fibre rich carbohydrate diet with over 400 g/d of vegetables and fruit is consistent with an appropriate reduction in the risk of weight gain and diabetes and therefore the longer term risk of CHD. This 25% fat value is also consistent with the reduced energy density of the diet required by those who have been obese and then manage to maintain their reduced weight long term.[27,28]

3. The quality of fat

Risk factors

The quality of dietary fat has major impact on serum total and LDL-cholesterol concentration.[4,29] Furthermore, modern genetic studies strongly suggest that LDL-cholesterol is causally related to atherosclerosis.[30–32] Partial replacement of SFA and TFA by cis-MUFA and PUFA decreases convincingly serum LDL cholesterol

concentration without affecting HDL-cholesterol concentration,[4,33,34] and the total-cholesterol to HDL-cholesterol ratio improves as well. If total fat intake is markedly reduced HDL-cholesterol concentration tends to decrease and the concentration of triglycerides tends to increase.[34] However, if a fibre-rich diet is eaten the overall lipid changes are beneficial in that total and LDL cholesterol concentrations as well as triglyceride concentrations are lower.

According to a summary by Mensink and colleagues[35] replacing 1 E% of TFA with 1 E% SFA, cis-MUFA, or PUFA decreases the total-cholesterol to HDL-cholesterol ratio by 0.31, 0.34, and 0.67 units, respectively. The effects of ruminant and industrially produced TFA do not seem to differ in their effects on serum lipid profile.[36,37]

There are data that the dietary fatty acid matrix may affect the hypercholesterolemic effect of dairy fat. Thus Tholstrup et al[38] showed a more remarkable increase in serum total and LDL-cholesterol concentrations by butter than cheese with standardised dietary amount of SFA.

Partial replacement of SFA or carbohydrates by cis-MUFA may have favorable effect on insulin sensitivity and fasting plasma insulin concentration.[4] Furthermore, recent observational studies show that the high amount of PUFA (e.g. linoleic acid) in different plasma fatty acid fractions is associated with better insulin sensitivity.[39,40]

The effect of the quality of dietary fat on blood pressure may depend on the total amount of dietary fat. In a randomised long term trial those with lower intakes of SFA from infancy had lower blood pressure.[41] However, in a study with 40 E% fat no difference between MUFA and SFA was found[42], whereas in the KANWU study a beneficial effect of MUFA on blood pressure was more pronounced in subjects with a fat intake below 37 E%.[43] However, in a recent systematic review, no conclusion could be drawn regarding the effect of the quality of dietary fat on blood pressure.[4]

One of the striking features of metabolic studies is the substantial, i.e. 4-5 fold differences, between individuals in their blood total and LDL cholesterol concentration responses to a standardised change in intake of the key SFAs. This means that although blood cholesterol concentrations are related to future CHD in cohort studies with a clear relationship to the development of heart disease whereas cohort dietary studies of SFA intakes rarely show this relationship. It is not just the errors in dietary assessment but the intrinsic differences in individuals' responsiveness that obscure the importance of reducing SFA intake for the whole population and explain why the relationships found across societies with very different SFA intakes show such a clear relationship to heart disease as originally observed by Keys and colleagues. Modest reductions in SFA intake achieved in community trials will induce only a modest effect on the average blood cholesterol concentration of the group so may not lead to a clearly evident reduction in CHD.

Atherosclerotic Vascular Diseases (AVD)

In a meta-analysis of 28 cohort studies and 16 RCTs SFA did not affect the risk of AVD independent of the intake of unsaturated fat or a healthy dietary pattern.[44] However, in RCTs where unsaturated fatty acids, especially PUFA, were substituted for SFA, AVD events were reduced by 14-19% corresponding to about 10% reduced

risk for each 5 E% increase in PUFA intake.[1,3] As expected, the effect was more pronounced in longer studies (>2 years) and in men and in younger subjects where the relative risks are higher. In a pooled analysis of prospective cohort studies there was a 20% decreased risk of AVD in both men and women when 5 E% of PUFA was substituted for SFA.[45] In a pooled analysis of different types of studies a substitution of 1 E% PUFA for SFA reduced the risk of AVD by ≥2–3%.[46] In a systematic review it was concluded that there is convincing evidence that partial replacement of SFA with PUFA decreases the risk of AVD, especially in men.[4] Recent data from prospective cohort studies show that those on a higher intake of unsaturated fats, especially PUFA, and/or high quality carbohydrates compared with those on a higher SFA intake had a lower risk of CHD.[5]

The effect of replacing SFA with carbohydrates seems to depend on to the quality of carbohydrates. In general, replacement of SFA with carbohydrates has shown no beneficial effect on the risk of AVD.[45] Replacement of SFA with carbohydrates with high glycaemic index was associated with an increased risk of myocardial infarction whereas there was no association when SFA was replaced with carbohydrates with low glycaemic index.[47] The importance of the quality of carbohydrates has been confirmed by recent evidence.[5] Diets that are rich in dietary fibre, i.e. with complex unrefined carbohydrates in the diet, are associated with lower rates of heart disease.[19] This led the UK government expert SACN committee to recommend a major increase in dietary fibre intake and implies that lower fat, higher carbohydrate diets need to be fibre rich to obtain a reduced risk of CVD. High fibre diets were also found to reduce the risk of type 2 diabetes and so will also reduce the long-term risk of CVD. When diets are also relatively rich in the beta–glycan components of fibre then dietary trials demonstrate a lowering of total cholesterol, LDL cholesterol and triglyceride concentrations in the blood consistent with the effects in lowering CVD.[19]

Regarding individual SFAs (C12:0-C18:0) there are minor differences in their association with AVD. Zong et al. (2016) have reported that 1 E% decrease in the intake of C12:0-C18:0 was associated significantly with reduced risk of CHD with PUFA, whole grain carbohydrates and plant protein as the replacements.[8] A similar decrease in the intake of C16:0 and an increase in the intake of MUFA were also significantly associated with reduced risk of AVD. There is some evidence from case-control studies that plasma levels of odd-chain fatty acids pentadecanoic acid (C15:0) and heptadecanoic acid (C17:0) are inversely associated with the risk of cardiovascular disease.[48,49] These fatty acids are often thought to be biomarkers of dairy fat intake but the association with dairy fat intakes is not always clear.[50] Levels of these acids may be associated with intake of fat from fish[50], other type of animal origin [51] and/or may be synthesised in the body from dietary fibre.[52]

When the sources of fat are considered then recent data from three US cohort studies show that intakes of vegetable sources of fat and PUFA rather than animal fat including dairy fat, are associated with a lower risk of CVD.[9]

In observational studies, TFA is associated with increased risk of AVD.[44,53] This is also in line with the marked effect of TFA on LDL cholesterol concentration and on the LDL-cholesterol/HDL-cholesterol ratio.[36,37,54] The source, i.e. natural vs. industrially produced, does not seem to have an impact on the metabolic effects.[36,37]

Furthermore, it is important to keep in mind that the most abundant sources of TFA are also rich in SFA.[45]

The role of MUFA in affecting the risk of CVD has been unclear. In general epidemiological studies subjects eating more MUFAs rather than SFAs did not seem to have a lower risk of AVD,[45] whereas in long-term prospective cohort studies MUFA mostly associates with a decreased risk of AVD when compared with SFA or high glycaemic index carbohydrates richer diets.[34,55] In a recent systematic review the apparent favourable effect of cis-MUFA on AVD was considered unlikely to reflect a direct effect of MUFA intakes rather than the benefit of not eating SFAs.[4] In a recent analysis of large USA cohort studies of medical professionals, isocaloric differences of 5 E% MUFA rather than SFA was associated with a 13 % lower total mortality and a 27% lower mortality for 5% higher PUFAs rather than SFAs was 27%.[56] Population analyses giving variable results regarding MUFA may relate to MUFA intakes being also strongly linked to SFA intakes in many 'Western' countries, where olive oil is not used in abundance,[57] and in earlier studies the additional effect of TFAs also confused the picture.[45]

There are no data on the optimum ratio of n-6-to-n-3 PUFA, but it has generally been considered prudent to avoid replacement of SFAs with n-6 PUFA only (LA), and to include some n-3-PUFA (e.g. ALA) as well.[58] Nevertheless, some data do not suggest that avoiding LA is beneficial.[56] The role of n-6 PUFA has been considered controversial, but a recent systematic review concluded that the proportion of total PUFA, n-6 PUFA, and linoleic acid (LA, C18:2n-6) in plasma lipids has a favourable association with the risk of AVD.[4]

Regarding n-3 fatty acids, i.e. eicosapentaenoic acid (EPA, C20:5n-3) and docosahexaenoic acid (DHA, C22:6n-3) of mostly animal origin and ALA (C18:3n-3) of plant origin, they have favourable associations with the AVD risk.[4] An intake of 200–250 mg/d of EPA + DHA has been shown to be associated with some benefit whereas higher intakes are associated with no additional observed benefit.[59] A very low intake (<0.06 g/d) of EPA+DHA is associated with an increased risk of AVD in one study.[60] Regarding the source of these fatty acids it may be important whether they originate from fish or from supplements.[61] ALA intake has been shown to be associated with a decreased risk of AVD.[44,62–64]

4. Conclusions

There is convincing evidence that partial replacement of SFA with unsaturated fat, especially PUFA, and complex carbohydrates decreases the concentrations of both total and LDL cholesterol and the risk of AVD. Based on experimental and many observational studies a high intake of TFA is considered very deleterious regarding the serum lipid profile and the risk of AVD. Replacing SFA with simple carbohydrates has unfavorable effects as well but lower-fat, high-fibre diets are associated with consistent benefit. The dietary recommendations for reducing the levels of important risk factors, mainly LDL-cholesterol concentration, and the subsequent incidence of AVD highlight the value of limiting intakes of SFA and minimising intake of TFA, partly through eliminating industrially produced TFA, and having a moderate intake of unsaturated fat [65,33,66] within the context of healthy dietary pattern including fibre–rich carbohydrates.

Based on the current evidence it is important to emphasise the value of moderating the total amount of fat, i.e. to about 25 E%, to avoid the risks of weight gain related to too high an intake of dietary fat, e.g. excess energy intake and usually a lower than recommended intake of dietary fibre. This amount of total fat is sufficient to enable an adequate intake of essential fatty acids, namely LA and ALA, as well as vitamin E. There is a general consensus regarding the intake of SFA, i.e. it should be less than 10 E% for the general population and less than 7 E% for a population at high risk for AVD. There is also a wide consensus regarding the intake of TFA, i.e. it should be as low as possible. Due to this high level of consensus there is no reason for EHN to make an exception regarding these aims. In addition, it is important to emphasise the need for long term energy balance and avoiding weight gain and obesity. This re-emphasises the importance of the overall quality of the diet including a low sugar intake (i.e. a healthy dietary pattern), as in current recommendations.[33,65,66]

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