Review Article

Impact of dietary fat on the serum lipid levels in human: a review

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Received on:19-07-2008; Accepted on :05-11-2008

ABSTRACT

Saturated fatty acids increase LDL and HDL cholesterol, whereas trans fatty acids increase LDL but not HDL cholesterol. Unsaturated fatty acids decrease LDL and HDL cholesterol, polyunsaturated more so than monounsaturated. Diet interventions that focus solely on lowering dietary cholesterol and saturated fat intake not only decrease LDL-C, but also high density lipoprotein cholesterol (HDL-C). There has been considerable interest in the potential benefit of major shifts in dietary macronutrients on weight loss and lipoprotein patterns. Additional efforts need to be focused on gaining a better understanding of the effect of dietary macronutrient profiles on established and emerging cardiovascular disease risk factors, mechanisms for changes observed and contributors to individual variability. There is need to allow reassessment of such data and, if necessary, modification of current recommendations. This brief review summarizes dietary interventions that affect the lipid profile.

Key words: Diet, trans fatty acids, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids.

1. Introduction

Carbohydrate, protein and fat are the primary energy-containing macronutrients consumed on a routine basis by humans. To meet the need for these macronutrients without increasing risk of chronic disease requires that people eat a balanced diet. Low-fat, high-carbohydrate diets might be harmful to people with a particular type of blood lipid profile, while diets high in fat could lead to obesity and its complications. Dietary reference intakes suggest that adults consume 45% to 65% of their total calories from carbohydrates, 20% to 35% from fat, and 10% to 35% from protein. These proportions are more flexible than previous proportions and will be useful for those planning diets to meet their unique needs [1]. The glycemic index (GI) of a particular food describes how quickly the glucose from that food enters the bloodstream. Unrefined carbohydrates high in dietary fibre have a low GI while foods such as sugar, white bread, and other highly processed foods have a high GI. Eating foods with a low GI might benefit those with type 2 diabetes because it will help to maintain an adequate balance between blood glucose and insulin levels [2]. Epidemiologic evidence [3-5] mostly supports the theory that foods with a low GI reduce risk of type 2 diabetes, but one study [6] found that GI was not associated with risk of diabetes. Increases in the relative proportion of carbohydrate result in dyslipidemia, characterized by high triglyceride and VLDL cholesterol concentrations, low HDL cholesterol concentrations, high total cholesterol-to-HDL cholesterol ratios, and, in some cases, small dense LDL particles [7,8]. Diets high in sugar relative to starch have been reported to increase rates of fatty acid synthesis [9]. In general, when the carbohydrate content of the diet declines, unless the decrease is limited to products made with highly refined foods, the fiber content of the diet also declines [10,11]. The sources of dietary protein are animal protein, primarily meat and diary; and vegetable protein, primarily grains and legumes. There are few work which shows beneficial effect on plasma lipoprotein concentrations relative to other types of protein, most commonly casein, have been more modest than originally thought [12,13]. During the past de-

cade have resulted in the generation of a considerable amount of data on how major shifts in the macronutrient content of the diet affect plasma lipoprotein patterns and to minimize the risk of developing cardiovascular disease (CVD). Myocardial infarction is the cause of death in more persons worldwide than any other disease [14,15]. Cardiac troponin I or cardiac troponin T, the only current biomarkers (a protein or other macromolecule that is associated with a biological process or regulatory mechanism) thought to be unique to the heart, the diagnosis of myocardial infarction has been veritably revolutionised [16,17]. Two accurate markers of heart failure have been validated in large observational and randomised controlled clinical studies. B-type natriuretic peptide (BNP) and the amino terminal fragment of proBNP (NTproBNP) [18-23]. Biomarkers reflecting and quantifying cardiac stress and cardiovascular homeostasis are powerful predictors of death in patients presenting with common systemic infections such as community-acquired pneumonia. Procalcitonin and C-reactive protein, are the established biomarkers in systemic inflammation [24-27]. Under these circumstances, the effect observed on plasma lipoprotein patterns can be attributable to either the addition of one macronutrient or the reduction of the other(s). If a single macronutrient is increased or decreased without compensatory adjustments in the amount of the other macronutrients, body weight will change and any effect on plasma lipoprotein patterns will result from changes induced by weight loss or gain, a shift in the relative energy distribution of each macronutrient, or some combination thereof [28,29]. The National Cholesterol Education Program (NCEP) recommends that prior to medication use; "TLC" (therapeutic lifestyle changes) should be instituted for metabolic syndrome. These include a diet that is low in saturated fat and cholesterol, and a diet that is hypocaloric to help induce weight loss. An increase in physical activity is also recommended, generally in the form of a walking program. This review emphasize on the studies assessing many aspects of effect of diet on plasma lipid profile.

2. Methods

Methodological challenges associated with studies designed to assess the effect of diet composition on lipoprotein patterns in human. There is a tremendous degree of genetic heterogeneity among individuals, the significance of which is likely to be considerable but difficult at this time to adequately quantify or manage in humans. The amount of time humans can be subjected to strict diet control is limited, from the perspectives of cost, logistics, and subject cooperation, making it difficult to achieve a "steady state."

Metabolism varies by gender and age, and within each of these categories, multiple changes (e.g., hormonal and body composition) proceed at different rates, making them difficult to factor into the final analysis. With aging come comorbidities, which make it difficult to initiate an intervention in a well-matched cohort. And finally, but of utmost importance, ethical and humanitarian considerations limit the types and extremes of interventions and the invasiveness of the techniques that can be used to characterize and monitor outcomes. Nonetheless, data that have been generated in humans, within clearly defined contexts, have provided some of the most valuable and longstanding knowledge in the area of diet and plasma lipoprotein patterns. This is attributable to inherent differences in such factors as the physiology of gastrointestinal tracts, the characteristics of endocrine and immune systems, the pathways and nature of lipoprotein metabolism, and differences in body composition and metabolic rates. Hence, although critical data have emerged from animal and in vitro systems, particularly with respect to questions that cannot be adequately addressed in humans, these data need to be treated as pieces of the puzzle, critical but considered with caution when out of context.

2.1 Dietary Fat

2.1.1 Fat: The effect of the macronutrient content of the diet on plasma lipoprotein patterns, with specific emphasis on dietary fat and carbohydrate. There is an old evidence which shows that a diet very low in fat resulted in hypertriglyceridemia [29-33], and this effect was later attributed to increased rates of hepatic fatty acid synthesis [34,35] and the subsequent production of hepatic triglyceride-rich

Table 1: Very low fat diet lowers HDL accompanied by hypertriglyceridemia.

Studies	Baseline (HDL-C)	Low fat diet (HDL-C)	Baseline (Triglyceride)	Low fat diet (Triglyceride)
Lichtenstein et al [29]	48 ± 11 (mg/dl)	35 ± 7 (mg/dl)	110 ± 32 (mg/dl)	130 ± 32 (mg/dl)
Clevidence et al [30]	1.22 ± 0.04 (mmol/l)	1.11 ± 0.04 (mmol/l)	1.24 ± 0.09 (mmol/l)	1.32 ± 0.09 (mmol/l)
Schaefer et al [32] (Men)	1.29 ± 0.31 (mmol/l)	1.06 ± 0.23 (mmol/l)	1.23 ± 0.52 (mmol/l)	1.34 ± 0.58 (mmol/l)
Aro et al [33]	1.30 (mmol/l)	1.16 (mmol/l)	1.44 (mmol/l)	1.80 (mmol/l)
Omar et al [our study]	33.66 ± 10.63 (mg/dl)	31.16 ± 10.61 (mg/dl)	74 ± 36 (mg/dl)	110.33 ± 37 (mg/dl)

particles, such as VLDL [36,37]. It was also observed that this hypertriglyceridemia was accompanied by lower HDL concentrations. Our study also favour the studies in which very low fat diet lowers HDL accompanied by hypertriglyceridemia (Table 1). Within the context of a stable body weight, replacement of dietary carbohydrate with fat resulted in lower triglyceride and VLDL cholesterol concentrations, higher HDL cholesterol concentrations, and a lower, more favorable total cholesterol-to-HDL cholesterol ratio [29,38,39]. Additionally, the more moderate the shifts in the fat-to-carbohydrate ratio of the diet, the more moderate the change in triglyceride concentrations [40]. Krauss et al [41] reported that moderate carbohydrate restriction and weight loss provide equivalent but non additive improvements in the atherogenic dyslipidemic pattern characterized by increased triglyceride concentrations and total cholesterol-to-HDL cholesterol ratios. The shortest-term markers of fat intake are proportions of fatty acids in chylomicrons. These reflect the dietary fat intakes that enter the enterohepatic circulation directly after a meal.

Other serum or plasma measures reflect the dietary intakes of the past few hours (triglyceride) or the past few days (cholesterol ester and phospholipid fatty acids) [42].

The next most immediate biomarker medium is the serum or plasma levels of individual fatty acids, which can reflect intake over the last few days or meals. Serum fatty acids levels were shown to be sensitive indicators of changes in the polyunsaturated fat intakes of the diet [43,44]. Red cell membranes and platelets are of interest as the biomarker media for fatty acid analyses because they reflect longer-term intake than circulating triglycerides but are still accessible through phlebotomy.

2.1.2 Dietary fatty acids: Fatty acids are the basic structural components of triglycerides and are also found in phospholipids and cholesterol esters. The fatty acid profile of the diet is the major determinant of plasma cholesterol concentrations [45]. When carbohydrate replaced from the diet, saturated fatty acids increase total cholesterol, polyunsaturated fatty acids decrease total cholesterol, and monounsaturated fatty acids have a neutral effect [46]. It is estimated that the total cholesterol increasing effect of saturated fatty acids is approximately twice the cholesterol-decreasing effect of polyunsaturated fatty acids, resulting in early dietary recommendations that stressed reductions in dietary saturated fat [47]. It is suggested that saturated fatty acids, particularly lauric (12:0), myristic (14:0), and palmitic (16:0) acids, increase LDL and HDL cholesterol, polyunsaturated fatty acids decrease LDL and HDL cholesterol, and monounsaturated fatty acids, to a lesser extent than polyunsaturated fatty acids, decrease LDL and HDL cholesterol concentrations [38, 46, 48]. The total cholesterol-to-HDL cholesterol ratio is similar and more favorable for polyunsaturated and monounsaturated fatty acids than for saturated fatty acids [38]. Data suggest polyunsaturated and monounsaturated fatty acid, relative to saturated fatty acids, intakes are associated with reduced CVD risk [49].

2.1.3 Saturated fatty acids: Not all saturated fatty acids had identical effects on plasma cholesterol concentrations. Shorter chain saturated fatty acids (6:0-10:0) and 18:0 have little effect on plasma cholesterol concentrations, whereas those with intermediate chain lengths (12:0-16:0) increase concentrations [45]. The minimal effect of the shorter chain fatty acids is attributed to their being absorbed directly into the portal circulation, and that of 18:0 is attributed to its high rate of conversion to 18:1, a monounsaturated fatty acid [50]. The LDL cholesterol-increasing effect of the intermediate chain saturated fat is attributed to a decreased fractional catabolic rate of plasma LDL, with little effect on production rate [51, 52]. The effect of alterations in the major dietary fatty acid subclasses, relative to carbohydrate, assumes that the plasma cholesterol-increasing effect of saturated fat is approximately twice the cholesterol decreasing effect of polyunsaturated fat. At this time, the predicative equations have factors for saturated, mono-unsaturated, and/or polyunsaturated fatty acids and do not take into consideration the differences among individual saturated fatty acids [48, 53, 54]. Given that each food contains a mixture of fatty acids and the difficulty in accurately assessing the fatty acid profile of the diet, this approach is reasonable at this time. Likewise, from a dietary perspective, it is difficult to formulate recommendations on the basis of the differential effects among saturated fatty acids and CVD risk. Hence, the focus has been to recommend restrictions of total saturated fat intake [55, 56]. Development of the technology for genetic modification of the fatty acid profiles of plants and animals, this approach may need to be revisited as these foods become commercially available on a large scale [57-60].

2.1.4 Unsaturated fatty acids: Dietary unsaturated fatty acids which are categorized by the length of their acyl chains, the degree of unsaturation (number of double bonds), the position of the double bond(s), and the conformation of the double bond(s). From the perspective of diet and CVD risk, all of these factors are important in dictating the biological effects of the individual unsaturated fatty acids on plasma lipoprotein patterns. With respect to chain length, the major dietary unsaturated fatty acids range from 18 to 22 carbons,

with shorter and longer chain unsaturated fatty acids occurring in relatively small amounts. Although there are multiple nomenclatures for denoting the position of the double bonds for categorical purposes, the distinction from a biological perspective is made on the basis of the location of the first double bond from the methyl end of the fatty acyl chain (as opposed to the carboxyl end). Two major dietary subclasses of polyunsaturated fatty acids are Omega-6 (or n-6) and Omega -3 (or n-3). These fatty acids can have an identical chemical composition but differ in the location of double bonds. They are referred to as positional isomers. In addition, the double bonds can occur in either the cis or trans configuration. Trans double bonds have a greater bond angle than cis double bonds; resulting in acyl chains with a more linear conformation, similar to a saturated than an unsaturated fatty acid. Fatty acids with an identical composition but double bonds differing in conformation are referred to as geometric isomers.

2.1.5 Omega-3 fatty acids: Omega-3 (n-3) fatty acids derive primarily from cold-water fish, but some plants are also rich in (n-3) fatty acids. The protective effect of very long-chain Omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), on CVD began in earnest in the 1970s [61, 62], which was supported by a considerable number of observational studies [63-66] and some interventional studies [67, 68]. A number of systematic reviews, meta-analyses of the relationship of dietary Omega-3 fatty acids and CVD events are available. Majority of them concluded that the inverse relationship between Omega-3 fatty acid intake and CVD events is significant for EPA and DHA but not for alfa-linolenic acid (ALA) [69-73]. The major dietary source of EPA and DHA is oily fish. A plant source of Omega-3 fatty acids, ALA, can be converted to EPA, albeit at very low rates (~5%) [74]. Major dietary sources of ALA are canola and soybean oils. It has been suggested that the inefficient conversion of ALA to EPA can be attributed to the limited incorporation of ALA into the hepatic phospholipid pool [75]. It has likewise been suggested that the inefficient conversion of EPA to DHA can be attributed to the low rate of conversion of EPA into docosapentaenoic acid, which is necessary for the subsequent conversion to DHA [75]. It is likely that the purported beneficial effects of the very long-chain fatty acids on CVD risk are multi-factorial [76]. The postulated mechanisms underlying the relationship include decreased arrhythmias, lower triglyceride concentrations in hypertrigyceridemic individuals, lower blood pressure, and decreased platelet aggregation [68, 77]. In individuals with increased triglyceride levels, Omega-3 fatty acids decrease plasma concentrations by decreasing hepatic production rates of VLDL, with little effect on fractional catabolic rates [78, 79] in some cases. An increase in LDL cholesterol concentration has been attributed to very long-chain Omega-3 fatty acids, in part as a result of an increased conversion rate of VLDL to LDL [78, 80]. Omega-3 fatty acids decrease postprandial plasma triglyceride concentrations by accelerating the fractional catabolic rate via increased lipoprotein lipase activity [81]. On the basis of the available data, the American Heart Association recommends that the general population consume at least two fish meals per week, individuals with established CVD consume 1 g of EPA plus DHA per day, and hypertriglyceridemic individuals consume 2-4 g of EPA plus DHA per day [68].

2.1.6 Trans fatty acids: It contain at least one double bond in the trans configuration and can be either monounsaturated or polyunsaturated. Since the early 1990s, considerable attention has been focused on the effect of trans fatty acids on plasma lipid and lipoprotein concentrations [82]. The major source of dietary trans fatty acids is partially hydrogenated fats and products formulated with these fats, such as commercially prepared baked and fried foods. A smaller proportion of dietary trans fatty acids comes from ruminant animal fats found primarily in meat and full fat dairy products. As do saturated fatty acids, trans fatty acids increase LDL cholesterol concentrations [82-84]. In contrast to saturated fatty acids, they do not increase HDL cholesterol concentrations. Relative to unsaturated fat, both saturated fat and partially hydrogenated fat result in higher LDL cholesterol concentrations attributable to lower fractional catabolic rates, with little change in production rates [52]. Hydrogenated fat results in lower HDL cholesterol concentrations attributable to higher fractional catabolic rates, with little change in production rates [52]. Collectively, these changes result in a less favorable total cholesterol or LDL cholesterol-to-HDL cholesterol ratio when trans fat is compared with saturated fat [38, 85, 86]. In some cases, trans fatty acids have also been reported to increase triglyceride concentrations [38, 83].

2.2 Dietary cholesterol

Dietary cholesterol and increased plasma cholesterol concentrations and atherogenesis were originally made in the early 20th century in rabbits [87]. Although the major determinant of LDL cholesterol concentrations in humans is saturated fat [53], dietary cholesterol has nonetheless been positively associated with CVD risk and both LDL and HDL cholesterol concentrations [46, 88]. Estimating the absolute effect of dietary cholesterol on plasma lipoprotein concentrations has been difficult because of the high degree of variability in response among individuals [89].Nonetheless, in carefully con-

trolled studies performed in healthy young males and females, it was demonstrated that for every additional 100mg of dietary cholesterol, fasting plasma total cholesterol concentrations increased by 1.47 and 0.73mg/dl, respectively, with parallel increases in LDL cholesterol and apoprotein B concentrations [90, 91]. Increased levels of the cholesteryl ester transfer protein were observed at the highest levels of dietary cholesterol in males but not females. One mechanism by which dietary cholesterol alters plasma lipoprotein concentrations is by down regulating cell surface LDL receptor activity, thereby decreasing VLDL and LDL clearance from plasma and increasing the conversion rate of VLDL to LDL [92]. Consistent with these data, dietary cholesterol has been reported to decrease LDL fractional catabolic rates and increase LDL production rates [93]. The identification of genetic polymorphisms that alter rates of cholesterol absorption is likely to shed new light in this area [94-96].

3. CONCLUSIONS

The available data confounded by changes in body weight and alterations in the intake of two or more macronutrients necessitated to minimize body weight changes. High degree of variability in response among individuals, specific recommendations for dietary fat to optimize plasma lipoprotein patterns need to be made on a case-by-case basis, taking into consideration a realistic anticipated level of compliance. A considerable amount is known about the effect of fatty acid subclasses, and in some cases individual fatty acids, on plasma lipoprotein patterns and the metabolic basis for these effects. Additional efforts need to be focused on gaining a better understanding of the effect of the macronutrient content of the diet on established and emerging CVD risk factors other than lipoprotein patterns, understanding the mechanisms associated with diet induced changes in lipoprotein patterns and contributors to individual variability in response, and then to reassess and if necessary modify current recommendations.

ACKNOWLEGMENTS:

The study was performed at Department of Pharmacology, Faculty of Pharmacy, Jamia Hamdard, in collaboration with the Clinical Pharmacology Unit, Ranbaxy Research Lab., Majedia Hospital, Jamia Hamdard, New Delhi-110062, India. We thanks to the Ranbaxy staff for their nice cooperation during the study.

FUNDING:

Primarily the study was performed at Department of Pharmacology, Faculty of Pharmacy, Jamia Hamdard, but financially supported by the Clinical Pharmacology Unit, Ranbaxy Research Lab., Majedia Hospital, Jamia Hamdard, New Delhi-110062, India.

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Source of support: Clinical Pharmacology Unit, Ranbaxy Research Laboratories, Sec-62, Noida, U.P., India.

Conflict of interest: *I declare that there was no any issue of this article was published elsewhere.