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Nutritional Management of Disturbances in Lipoprotein Concentrations

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1. Introduction

Atherogenic dyslipidemia includes increase in blood concentrations of LDL cholesterol, total cholesterol, triglycerides and decrease in high-density lipoprotein cholesterol, both of which are frequently associated with the development of cardiovascular diseases (CVDs) [1,2] .Treatment of dyslipidemia can reduce the risk of CVDs [3]. In both industrialized and non-industrialized countries, the prevalence of dyslipidemia is increasing (4-7), therefore management of dyslipidemia has become a mainstay of routine clinical practice for both public health and clinicians. Although the benefits of lipid-lowering therapy have been demonstrated most conclusively, the role of diet determinants in dyslipidemia needs to be further considered [8]. Diet plays an important role in the concentrations of lipoprotein and is the primary intervention for patients with dyslipidemia. Understanding the relationships between dietary determinants and dyslipidemia and the effect of diet on lipoprotein concentrations may help to identify the dietary changes needed to reduce health risks [2]. Dietary changes, including reduced intakes of saturated fat and cholesterol, increased intakes of polyunsaturated fatty acids, fish, fruits and vegetables, and reduced energy intakes may have beneficial effects on lipoprotein concentrations [9-12]. One important aspect of diet is dietary patterns that address the effect of the diet as a whole and thus may provide insight beyond the effects described for single nutrients or foods [13]. The effects of some dietary patterns including the Mediterranean diet, the dietary stop to hypertension (DASH) and traditional dietary patterns, on lipoprotein particles need to be discussed [14, 15, 16]. In addition, other aspects of diet, including herbal, phytochemical, and dietary supplement (plant stanols and sterols) also play important roles in the prevention and treatment of dyslipidemia and may improve lipoprotein concentrations [17]. We searched the medical literature for studies of the effects of diet and its component including macronutrient, dietary food groups, dietary patterns and herbal on disturbances of lipoprotein concentrations. The purpose of this chapter is to update current knowledge on

the role of the following dietary determinants in lipoprotein concentrations and dyslipidemia: including 1) macronutrients (total fat, saturated fatty acids, trans fatty acids, n-6 polyunsaturated fatty acids, n-3 polyunsaturated fatty acids, dietary cholesterol, carbohydrate and protein), 2) food groups (grains and cereal, fruit and vegetables, dairy products, nuts, beans and legumes, and meat, fish, poultry and eggs), 3) dietary patterns (Mediterranean diet, Dietary to Stop Hypertension, western **diet** and healthy diet), and therapeutic life style change (TLC), 4) dietary **supplements**, (plant stanols and sterols), herbal and phytochemicals.

2. Diet and lipoprotein

Lipoprotein concentrations are affected by both genetic and environmental factors. Among environmental factors such as physical activity and smoking, diet is an important component in preventing and improving dyslipidemia. Diet intervention is recommended by the National Cholesterol Education Program (NCEP) guidelines as first-line therapy for the management of disturbances in lipoprotein concentrations. Also the Third report of the NCEP recommended that if dietary therapy do not improve disturbances in lipoprotein concentrations, non-pharmacologic therapeutic factors such as viscous fiber and plant stanols and sterols should be recommended prior to advancing to drug therapy[18].

3. Macronutrient and lipoprotein

3.1. Total fat

The Nutrition Committee of the American Heart Association (AHA) emphasises on that diets providing up to 40% of dietary energy as primarily unsaturated fat (20% MUFA, 10% SFA, 10% PUFA and 1% TFA) were as heart healthy as low-fat diets (<30% of dietary energy) [19]. The effects of different dietary fatty acids on lipid profiles should be considered in the evaluation of strategies for controlling of disturbances in lipoprotein concentrations. Changes in dietary fat composition are clearly associated with changes in lipoprotein concentrations. Types of dietary fatty acids include saturated fatty acids (SFAs), monounsaturated fatty acid (MUFAs), polyunsaturated fatty acid (PUFAs) and dietary cholesterol, the effects of which on lipoprotein concentrations will be discussed.

3.2. Dietary saturated fatty acids (SFAs)

Among the dietary fatty acids only dietary SFAs and *trans* fatty acids increase LDL cholesterol concentrations [18]. The major sources of dietary SFAs are fast foods, processed foods, high-fat dairy products (whole milk, cheese, butter, ice cream, and cream), high-fat red meats, tropical oils such as palm oil, coconut oil, and palm kernel oil, baked products and mixed dishes containing dairy fats, shortening, and tropical oils. Dietary SFAs increase LDL and total cholesterol concentrations, in comparison with all dietary fatty acids except *trans* fatty acids [20-21], by inhibiting LDL receptor activity and enhancing apolipoprotein (apo) β-containing lipoprotein production [22]. Every 1 percent increase of total energy from

dietary SFAs raises the serum LDL cholesterol about 2 percent. Conversely, a 1 percent reduction in saturated fatty acids will reduce serum cholesterol by about 2 percent [23,24]. The LDL cholesterol–raising effect of dietary SFAs depends on the intake of dietary cholesterol and PUFAs. In high intakes of dietary cholesterol, dietary SFAs decreased LDL receptor activity and increased plasma LDL concentrations [25]. However, in the adequate of dietary PUFAs (5–10% of total energy), dietary SFAs have no effect on LDL clearance [22]. In addition different dietary SFAs have different effects on lipoprotein concentrations [29]. Short chain SFAs have been shown to have a stronger LDL cholesterol raising effect, such that lauric acid (12:0) raised LDL cholesterol the most, followed by myristic (14:0) and palmitic (16:0) acids. In contrast, stearic acid (18:0), as a long chain SFA, has no effect on LDL and HDL cholesterol or the TC: HDL cholesterol ratio, and even lowers serum cholesterol [27,28]. Finally, the effects of dietary SFAs can be modulated by the foods in which they are contained. Cheeses may have smaller effects on LDL cholesterol concentrations than butter, and fermented dairy foods, such as yogurt, have been associated with LDL reductions [29]. Reduced intakes of dietary SFAs and cholesterol are first steps for the purpose of achieving the LDL cholesterol goal (<100 mg/dl). To maximize LDL cholesterol lowering by reducing dietary SFAs, it will be necessary to lower intakes of dietary SFAs approximately to <7 percent of total energy [18]. However the replacement of dietary SFAs with other macronutrients is important. Although replacement of dietary SFAs with carbohydrate decrease total, LDL, and HDL cholesterol, it also increases triglycerides [20]; however replacement of dietary SFAs by PUFAs decreases concentrations of total, LDL, and the LDL/HDL cholesterol ratio by decreasing LDL cholesterol production and increasing LDL clearance [30]. Although replacement of dietary SFAs with PUFAs has been shown to decrease HDL cholesterol, it decreases LDL cholesterol even more substantially; thus, the HDL:LDL ratio is increased [23] and the TC:HDL cholesterol ratio is decreased [26]. Replacement of 5% of total energy from SFAs with PUFAs reduces CHD risk by 42% [31]. Replacement of dietary SFAs with MUFAs has also been associated with improving lipoprotein concentrations, although this effect is slightly less than when PUFAs are the replacement dietary fatty acid [23]. Replacement of dietary SFAs with both MUFAs and carbohydrate decrease LDL cholesterol; however replacement with MUFA was associated with lower reductions in HDL cholesterol and lower arises in triglyceride concentrations [32].

3.3. Trans fatty acids

Trans fatty acids contain at least one double bond in the *trans* configuration [40] and were the most harmful macronutrient that increase disturbances in lipoprotein concentrations [26,33,34]. Dietary *trans* fatty acids, produced during the hydrogenation of either vegetable or fish oils (industrial TFA**)**, are found in manufacturing products such as cookies, pastries, and salad dressings; *trans* fatty acids are also formed during anaerobic bacterial fermentation of unsaturated fatty acids that occurs in the rumen of polygastric animals such as cattle, sheep, and goats (natural trans fatty acids), and hence found in dairy products derived from the animals' milk and meat [33,35]. Industrial and natural *trans* fatty acids contain similar types of these fatty acids, but in different proportions. Industrial *trans* fatty

acids contain trans isomers of oleic acid, the major ones being C18:1 trans-9 (elaidic acid) and C18: 1 trans-10 [35]. Consumption of industrial *trans* fatty acids increases total, LDL cholesterol, and total to HDL cholesterol ratio and the LDL to HDL cholesterol ratio [33, 35-37] and decrease HDL cholesterol [40]. Data on the effects of natural *trans* fatty acids on plasma lipoproteins in humans are inconsistent. An equivalent of 1% natural *trans* fatty acids of daily energy, has no significant effect on total cholesterol, LDL cholesterol, apo B, triglyceride concentrations but may be associated with a reduction in plasma HDL cholesterol concentrations [38]. However high intakes of natural *trans* fatty acids, but not low intakes, have adverse effects [39]. Therefore both natural and industrial *trans* fatty acids have detrimental effects on lipoprotein concentrations and their intakes should be limited [40]. The effects of *trans* fatty acids on lipid profiles are also variable, depending on their chain length; long chain *trans* fatty acids may have more adverse effect on lipid profiles. Partially hydrogenated fish oil or *trans* alpha-linolenic acid had more detrimental effect on lipoprotein compared with isocaloric amount of partially hydrogenated soy bean oil [37,41]. Effect of *trans* fatty acids on lipoprotein concentrations is a current topic of debate. *Trans* fatty acid intake increases lipoprotein a and triglycerides when substituted for dietary SFAs [42,43]. Issues related to the potential change in lipoprotein a levels induced by *trans* fatty acid intake and risk for disease need to be clarified.

Dietary guidelines for American 2010 emphasize that consumption of *trans* fatty acids should be reduced as much as possible by limiting foods that contain sources of these fatty acids [43]. On the basis of these data, it should be attempts to substitute unhydrogenated oil for hydrogenated or SFAs in diet.

3.4. Monounsaturated fatty acids

Monounsaturated fatty acids have received increased attention as being potentially beneficial for their association with low rates of CHD in olive-oil consuming populations of the Mediterranean style diet [18]. The most common form of dietary MUFAs is oleic acid (18:1 n-9), which occurs in the cis form. Olive oil, canola oil, and sunflower oil are the main sources of dietary MUFAs. Oleic acid is an effective hypocholesterolemic factor when substituted for dietary SFAs. MUFA-rich oil consumption has been one of the strategies recommended for modulating the plasma lipid profile in humans. Diets containing high MUFA-rich foods reduce plasma total and LDL cholesterol levels and enrich LDL particles with cholesteryl oleate, a change in LDL particle composition that has been shown to confer atherogenicity [23, 45-48]. Also compared with diets rich in saturated fat, MUFA-rich diets lower apolipoprotein β concentrations along with declines in LDL cholesterol level [49,50]. Consumption of MUFA-rich diets also induces lower triglycerides and higher HDL cholesterol concentrations compared with low-fat, high-carbohydrate diets [51]. Long term MUFA-rich diets result in an earlier postprandial peak in plasma triglyceride and apo β-48 concentrations [52,53]; this mechanism is not clear, however oleic acid has been shown to be preferentially esterified into triglycerides in the enterocyte [54], which may be result a faster entry rate of chylomicrons into the circulation, reflecting accelerated rates of digestion and

absorption or upregulation of chylomicron synthesis and secretion [55]. However MUFA-rich diets increase clearance of plasma triglycerides compared with isocaloric SFA-rich or high complex carbohydrate diets and therefore decrease triglyceride concentrations [51,56,57]. MUFA substitution for dietary SFAs suggest an effective dietary strategy for improving disturbances of lipoprotein concentrations, which currently recommended in most national and international dietary guidelines [18].

3.5. N-6 Polyunsaturated fatty acids

Dietary n-6 PUFAs such as linoleic acid (18:2) are widely found in a variety of vegetables and vegetables oils [58]. Conjugated linoleic acid (CLA), a group of naturally occurring fatty acids that are mainly present in foods from ruminant sources, is a collective term used to describe positional and geometric derivatives of linoleic acid containing conjugated double bonds [59].

CLA have beneficial effects on lipoprotein disturbances. CLA reduced total, LDL and VLDL cholesterol, especially atherogenic apolipoprotein β-rich lipoproteins and triglycerides concentrations [60,61]. CLA increases the excretion of sterols and consequently decreases serum cholesterol concentration [86].

3.6. N-3 Polyunsaturated fatty acids

Dietary sources of n-3 PUFAs are limited. The shorter chain n-3 PUFAs FA, α-linolenic acid (ALA), is found in many plants, but the longer chains eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are produced almost exclusively by cold water algae, which are, in turn, ingested by fish. Humans cannot synthesize the n-3 double bond, but they do have the elongase and desaturase enzymes to convert ALA to EPA and DHA, a conversion, which however is an inefficient process. The conversion of ALA to EPA may be further reduced as a result of large amounts of n-6 FA in the diet, which compete for the same enzymes. Some studies however have found that ALA, irrespective of n-6 PUFAs, has a beneficial effect of lipid profiles [63]. Mechanism of actions of the medium- and long chain n-3 fatty acids appears to be independent. ALA exerts most of its effects by modulating lipoproteins, while EPA and DHA may reduce triglyceride synthesis [64]. Experts currently recommend the consumption of EPA and DHA, rather than ALA, to meet dietary goals for dietary n-3 PUFA [65]. Long-chain n-3 PUFA reduce triglyceride concentrations. An intake of 4 g EPA and DHA per day results in a 25–30% decrease of fasting triglyceride concentrations in both normolipidaemic and hypertriacylglycerolaemic subjects (66). Compares EPA and DHA, EPA-ethyl ester shows no change in triglyceride concentrations, suggesting that DHA is the active agent in fish oil, that decreases triglyceride concentrations. Therefore among long chain n-3 PUFAs, EPA may produce favourable effects on triglyceride and HDL cholesterol concentrations [67,68]. The hypotriglyceridaemic effect of long chain n-3 PUFAs, mediated by several mechanisms such as enhanced hepatic fatty acid oxidation [69], inhibition of fatty acid and triglyceride synthesis, reduced assembly and secretion of VLDL triglyceride concentrations [70], facilitates triglyceride rich lipoprotein removal through enhanced LPL

activity in plasma [71]. Significant increases in HDL have been observed after DHA supplementation [67,68,72,73]; it may be related to decreased cholesteryl ester transfer protein activity that reduces the exchange from HDL cholesterol ester and VLDL, resulting in larger, more cholesterol-rich HDL cholesterol particles [74,75].

Inconsistent effects of DHA on total and LDL cholesterol levels have been shown; some investigators found a LDL cholesterol-raising effect [68,76] or no significant changes in total cholesterol or LDL cholesterol concentration [77,78]. After supplementation with n-3 Long chain PUFA, limited amounts of triglycerides are available for packaging into VLDL, which results in VLDL particles with low triglycerides that are readily converted to LDL, increases LDL cholesterol concentrations [79]. N-3 PUFAs could increase production of LDL via conversion of VLDL to LDL by increased lipolysis of VLDL and/or increased lipolytic activity or decreased clearance of LDL, by decreases in LDL receptor binding activity or reduced LDL receptor expression [80]. ALA, an n-3 polyunsaturated fatty acid found mainly in plant sources, including flaxseed oil, canola oil, and walnuts, is a metabolic precursor of DHA and EPA and any risk reduction may be mediated through conversion to these fatty acids; ALA cannot be synthesized by humans, and therefore, it is an essential fatty acid in diet [58]. Although evidence indicates that consumption of long chain n-3 PUFAs from seafood reduces the risk factors of cardiovascular disease, the effect of ALA intake in these risk factors is less well established. Daily supplementation with ALA-rich flaxseed is reported to reduce total cholesterol, LDL-cholesterol [81,82]. Weight of the evidence favors recommendations for modest dietary consumption of ALA (2 to 3 g per day) for primary and secondary prevention of CHD [58]. The relationship between ALA intake and CHD risk was seen among participants who consumed very little seafood; among men with limited seafood intake, each 1 g per day ALA intake was associated with 50% lower risk of CVDs; in contrast among subjects with some seafood intake, ALA intake was not associated with CHD risk. If benefits of ALA are greatest when EPA and DHA intakes are very low, the consumption of plant sources of n-3 fatty acids may be particularly important for CHD prevention among individuals who do not regularly consume fish [58].

3.7. Dietary cholesterol

The main source of dietary cholesterol is eggs, which contribute about one-third of the cholesterol in the diet; intake of dietary cholesterol has increased in recent year. Other sources of dietary cholesterol include animal products, dairy, meats, poultry, and shellfish [83]. High cholesterol intakes increase LDL cholesterol and the degree of rise varies from person to person. On average, the response of serum cholesterol to dietary cholesterol as revealed is approximately 10 mg/dL per 100 mg dietary cholesterol per 1000 kcal [84,85]. A recent meta-analysis showed that dietary cholesterol raises the ratio of total to HDL cholesterol, adversely affecting the serum cholesterol profile [86].

3.8. Carbohydrate

Recommendations to decrease fat and increase carbohydrate intake have come under scrutiny. Diets low in fat necessarily has a high proportion of carbohydrates, and high

carbohydrate diet increase triglycerides, reduce HDL cholesterol concentrations, and increase LDL cholesterol concentrations [87]. In addition to carbohydrate intake, the type of carbohydrate, according to glycemic index, most likely influences lipid profiles [88]. Glycemic index refers to the value obtained by feeding a carbohydrate load and measuring the level of blood glucose. Using the glycemic index, carbohydrates with a low glycemic index may decrease triglyceride concentrations and increase HDL cholesterol [89]. Also substituting low-GI foods for high-GI foods lowers triglyceride concentrations by 15 to 25% [138]. High-carbohydrate diets increase triglyceride concentrations, compared to high-fat diets [91] via enhance hepatic lipogenesis [92] and decrease the synthesis of lipoprotein lipase [93]. A high carbohydrate diet also increases glucose and insulin concentrations, the latter increasing lipogenesis, leading to increases in triglyceride concentrations, triglyceride-enriched VLDL particles, and increases the LDL cholesterol concentrations [94]. Therefore reductions in dietary carbohydrate have been associated with reduced concentrations of LDL cholesterol [95] and increase means LDL particle size [96].

High carbohydrate diets (>60 percent of total energy) are associated with lipoprotein disturbances; reduction in the content of carbohydrate have beneficial effects on lipid profiles. However substitution of carbohydrate with other macronutrients is important. When carbohydrates are substituted for SFAs, the fall in LDL cholesterol levels equals that with monounsaturated fatty acids, and however, compared with MUFAs, this substitution frequently causes a fall in HDL cholesterol and a rise in triglycerides [23,97]. When dietary carbohydrate is consumed along with high-fiber diets, however, the rise in triglycerides or fall in HDL cholesterol has been reported to be reduced [98,99]. Addition of n-3 PUFA to low-fat, high-carbohydrate diets decreases the adverse effects of carbohydrate on blood lipids [51,100]. Also refined- and whole grains, as sources of carbohydrate, have an essential role in the metabolism of lipid profiles, that will be discussed in the section on food groups. In a relatively short period of time, dietary consumption of fructose has increased several fold above the amount present in natural foods, because of the use of high fructose corn sweeteners and sucrose in manufactured foods [101]. In human diets approximately one-third of dietary fructose comes from fruit, vegetables, and other natural sources and two-thirds is added to beverages and food in the diet (e.g. soft drinks, fruit-flavored drinks, candies, jams, syrups, and bakery products). Although there is little evidence that modest amounts of fructose have detrimental effects on carbohydrate and lipid metabolism, larger doses have been associated with numerous metabolic abnormalities, suggesting that high fructose consumption adversely affects health. High levels of plasma triacylglycerols are a well-established consequence of dietary fructose intake [101]. Numerous mechanisms have been suggested to explain this phenomenon [102,103], e.g. enhanced hepatic lipogenesis, and therefore overproduction of VLDL [102,104].

3.9. Protein

Plant sources of protein are predominantly legumes, dry beans, nuts, and, to a lesser extent, grain products and vegetables, which are low in saturated fats and cholesterol. Animal sources of protein include dairy products, egg whites, fish, poultry, and meats. Dietary

protein in general has little effect on lipoprotein profiles. However, substituting plant protein including wheat gluten, soy proteins for animal protein decrease serum cholesterol [104,105]. Advice on the use of soy foods to displace animal products is consistent with the AHA advisory on soy [107], which states that 50 g/d soy protein consumption reduces approximate 3% LDL-C with no apparent dose-response effect [108]. Maximum reduction in LDL cholesterol was achieved when ~50 g of soy protein when was replaced meat or dairy protein [109]. Soy is a complex protein with a globulin fraction to which its cholesterol-lowering effect has been attributed; this fraction digested to peptides with inhibitory effects on cholesterol synthesis [110]. Isoflavones or the saponins found in soy, are also responsible for the cholesterol-lowering effect of soy [111,112]. Soy and other vegetable proteins also reduce oxidized LDL due to antioxidant activity [112,113].

4. Dietary food groups and lipoprotein

4.1. Grains and cereal

Based on evidence from both population and intervention studies, the recommended intake of whole grains of the 2005 Dietary Guidelines for Americans, is at least three ounces per day [114]. The Dietary Guidelines Advisory Committee (DGAC) 2010 Report emphasizes fiber-rich carbohydrate foods such as whole grains and vegetables, fruits, and cooked dry beans and peas, it specifically recommends that half of the grains consumed be whole grains, hence some whole grains should replace refined grains [115]. Similar recommendations are made by the American Heart Association [116] and the American Diabetes Association [117]. Whole grains are referred to as "complex" or "high-quality" carbohydrates, mainly due to their dietary fiber content [118], which has a beneficial effect on body weight, and lipid profiles because they are usually less energy-dense and more satiating than refined-grain foods [119] may be due to their high fiber content. Among whole grains, oat and barley have an advantage over wheat and brown rice in lowering serum lipids [120,121,122], contain viscous fibres, including β-glucacon [118] that lower serum cholesterol; 3.5 g of β-glucan from oats reduces LDL-C by 5% [123,124]. β-glucan interferes with reabsorption of bile acids and cholesterol by binding to bile acids, leading to increase bile acid excretion and lowering the bile acid levels in the liver and thereby increasing the conversion rate of cholesterol to bile acids. A viscous fiber intake of 10–25 g/d is recommended by the National Cholesterol Education Program's Adult Treatment Panel III as an additional diet option to decrease LDL cholesterol; an intake of 5–10 g/d lowers LDL-C by about 5% [126].

4.2. Fruit and vegetables

The 2010 Dietary Guidelines for Americans, recommend consuming sufficient amounts (5-13 servings, depending on energy needs) and a varieties of fruits and vegetables to reduce the risk of developing chronic diseases [115]; fruits, vegetables, or both should be emphasized at each meal, being major sources of vitamins C, E, and A, beta-carotene, other vitamins, fiber, flavonoids, and some minerals. Snacks and desserts that contain fruits and/or vegetables can

be low in saturated fat, total fat, and cholesterol, and are very nutritious [18]. Fruits and vegetable intakes do not significantly change HDL cholesterol concentrations, but do decrease total and LDL cholesterol [9,127-132]. The protective effect of fruit and vegetables against CVDs is from their water-soluble and also viscous fibers (e.g. pectins) [133]. Viscous fiber increases fecal bile acid losses [134] and chenodeoxycholic acid synthesis [135].

4.3. Dairy products

Dairy products are important sources of protein, calcium, phosphorus, and vitamin D. The recommendation for intakes of dairy products is 2-3 serving per day; fat-free milk or 1 percent fat milk, fat-free or low-fat cheese (e.g., ≤3g per 1 oz serving), 1 percent fat cottage cheese or imitation cheeses made from vegetable oils, and fat-free or low-fat yogurt are good choices. Fat-free milk and other fat-free or low-fat dairy products provide as much or more calcium and protein than whole milk dairy products, with little or no saturated fat [18].

Recent studies confirm that milk products were associated with lower small dense LDL, and triglyceride concentrations, and higher HDL cholesterol [136]. In the CARDIA study, obese subjects with more frequent consumption of dairy products showed a trend towards lower risk of dyslipidaemia [137]. Minerals (calcium, magnesium), protein (casein and whey) and vitamins (riboflavin and vitamin B-12) have the hypocholesterolaemic effect of dairy product. The possible hypolipidaemic mechanism of calcium includes decreased intestinal absorption of cholesterol, bile acids, or fat [138], decreased fatty acid synthesis, increasing lipolysis, all of which lead to decreased triacylglycerol stores [139]. Milk proteins (whey) [140] or peptides [141] may also play a role. Whey may act independently or synergistically with the calcium; attenuate lipogenesis, and accelerate lipolysis [142]. Dairy products contain SFAs that could affect the blood lipid profile. A recent meta-analysis of 21 prospective cohort studies showed that the harmful effects of SFAs on CHD are still controversial [143]. An inverse association was shown between milk-specific fatty acids in serum cholesterol esters with serum cholesterol and apolipoprotein β levels [144]. Consumption of fat-free dairy products might decrease plasma cholesterol levels, while whole milk has neither a hypo- nor hypercholesterolaemic effect [139]. SFAs in dairy products can adversely influence CHD, although the effect of SFAs on CHD risk depends on the source of calories by which it is substituted to maintain energy balance [145]. Different dairy products have different effects on the lipid profiles. The LDL-C-raising effect of cheese was less than that of butter at comparable intakes of total fat and saturated fat [146,147]. Butter fat may increase total and LDL cholesterol by down-regulation of LDL removal from the circulation [148]. Fermented dairy products may have a favourite effect on lipid profiles. The protective effect of yogurt [139,149], a fermented dairy product, was shown to reduce absorption of cholesterol and therefore prevent dyslipidemia; it is thought to increase calcium bioavailability through its high acidity [149]. Fermented milk products may decrease cholesterol levels more than non-fermented products [149-151]. Probiotic yogurt decreased total cholesterol by 4% and LDL cholesterol by 5% [149]. A meta-analysis of fermented dairy products has shown a possible cholesterol lowering property, through the high content of probiotic bacteria [152].

4.4. Nuts

Although nuts are high in fat, in most nuts the predominant fats are unsaturated. Studies over the last decade have demonstrated favourable effects of nuts in modifying lipid risk factors for CHD [153]. However, their use is not yet part of standard advice for patients with hyperlipidemia, despite recognized health benefits for the general population. Intake of nuts fits well with current American Heart Association guidelines [19] to replace dietary SFAs with unsaturated fats and with the National Cholesterol Education Program (NCEP) guidelines to increase intake of dietary MUFAs [153]. Less atherogenic plasma lipid profiles associated with long-term consumption of nuts [154,155]. Addition of nuts to the habitual diet of both normocholesterolemic and hypercholesterolemic subjects results in a significant reduction in plasma total and LDL cholesterol, whereas HDL remains unchanged or increases [155-158]. One-percent reductions in LDL cholesterol would be achieved with daily intakes of 4-11 g of walnuts, pecans, peanuts, macadamias, and pistachios [50,155,157-161]. There are several components in nuts i.e. high MUFA, high PUFAs : SFAs ratio, proteins (specially high arginin), plant sterols, fiber, and associated phenolic substances, which may all contribute to the cardioprotective effect of nuts [154,162]. Also replacement of dietary SFAs with MUFAs due to the high MUFA content of nuts and high content of vitamin E in nuts reduce susceptibility of LDL to oxidation, a key event in the development of CVDs [233]. Consumption of almonds, either as the whole nut or the oil, lower total and LDL cholesterol concentrations. Addition of 100 g of almonds to the diets reduces total cholesterol by 9-16% and LDL cholesterol by 12-19 % in hypercholesterolemic subjects [164]; in one study almond consumption also reduced fasting triglyceride concentrations by 14%, compared with baseline [165]. Macadamia is another nut that improve lipid disturbances, and its inclusion as part of a healthy diet favourably altered the plasma lipid profile, despite the nuts being high in fat; their consumption reduced plasma total and LDL cholesterol concentrations and increase HDL cholesterol without any change in the triglyceride concentrations [166]. These changes could contribute to high MUFA intake and lower intake of PUFA and SFA consumption of macadamia nuts. Of nuts, walnuts are unique in improving dyslipidemia because they are a rich source of PUFAs, especially α-linolenic acid and linoleic acid; 100 g of walnuts contain 65.2 g fat; mainly from PUFAs (47.2 g) including α-linolenic acid (9.1 g) and linoleic acid (38.1 g) [167]. In a meta-analysis, consumption of walnuts resulted in decrease in total and LDL cholesterol concentrations, whereas HDL cholesterol and triglycerides were not affected [168]. Despite favourable effects of nuts on dyslipidemia, the intake of nuts should fit within the calorie and fat goal [18].

4.5. Beans and legumes

Legumes include a variety of beans such as navy, pinto, kidney, garbanzo, lima beans and peas such as split green peas or lentils. The Dietary Guidelines for Americans suggest consuming 3 cups of legumes per week [18, 169]. Legumes are a rich source of soluble dietary fiber and vegetable protein and have long been known to be hypercholesterolaemic foods [170,171]. One-half cup of cooked beans or peas can provide a range of dietary fiber from 4.6 g in fava beans up to 9.6 g fiber in navy beans, with a half cup of chick peas

providing 6.2 g of total fiber, and 1.3 grams soluble dietary fiber [169]. In a meta-analysis both total and LDL cholesterol decreased, while HDL cholesterol did not change significantly, when diets uses supplemented with non-soy legumes [169]. The hypocholesterolaemic property of legumes is associated with the water-soluble fibre. Dietary fiber in legumes is not digested in the small intestine but be fermented in the colon and produces short chain fatty acids such as acetate, propionate and butyrate [172,173]; that inhibits hydroxy-3-methylglutaryl-CoA reductase, the limiting enzyme for cholesterol synthesis. Dietary fiber also decrease LDL cholesterol concentration by partially interrupting the enterohepatic circulation of bile acids via binding to bile acids in the intestines and preventing their re-absorption [174]. Consequently, an increase in the production of bile acids decreases the liver pool of cholesterol and increases uptake of serum cholesterol by the liver, decreasing thereby circulating cholesterol in the blood [175]. Another hypercholesterolemic component of legume is phytochemicals, which has been shown to reduce blood cholesterol levels and is present in small to moderate amounts in many types of legumes, such as chickpeas [176]. Dietary modification strategies that target the reduction of risk factors for CVDs should include an increase in legume consumption in addition to other strategies which have been of proven benefit [169].

4.6. Meat, fish, poultry and eggs

Recommendation for intakes of meat, fish and poultry are up to 5 oz per day from lean meats (beef, pork, and lamb), poultry, and fish [18]. To achieve NCEP dietary goals, individuals are often counselled to reduce the amount and frequency of red meat consumption because of its hypercholestromia effects [177-179]. Cholesterol raising effects of red meats appears to result from high contents of SFAs [177,179]. Therefore, lean red meats that provide small amounts of these fatty acids do not adversely influence the blood lipid profile, compared with lean white meats. In isoenergetic low-fat diets, lean meat, fish and, poultry had similar effects on blood lipid response in both hypercholesterolemic and normocholesterolemic subjects [178,180,181]. Data available suggest that meat protein, per se, is not hypercholesterolemic [177,181,182]. The blood cholesterol-raising potential of meat products appears to be a function of their SFA fat and cholesterol contents. Therefore, substituting lean for higher fat red meat should favourably influence serum total cholesterol and LDL-C levels. Incorporating lean beef, fish, or poultry into the AHA diet can be beneficial in lower disturbances of lipid profile in patients with hypercholesterolemia [178,183]. Therefore the hypercholesterolemic subjects known to be at high risk for CVDs, could be advised to include lean fish as well as lean beef or poultry without skin in an AHA diet to reduce their lipoprotein disturbances [184,185]; normolipidemic subjects can also incorporate lean fish in an AHA diet [184], althought it is not necessary to eliminate or drastically reduce intake of lean red meat consumption because it is a rich source of iron, zinc and vitamin B12. One of the dietary recommendations in the prevention of CVDs is to limit egg consumption, because they have been shown to be a major source of dietary cholesterol (One egg contains 200 mg/cholesterol) that increases both serum total and LDL-cholesterol concentrations [21,86,186]. Several epidemiologic studies however found no

relation between egg consumption and risk of coronary heart disease [187,188], may be because dietary cholesterol increases not only concentrations of total and LDL cholesterol but also concentrations of HDL cholesterol [21,186,189,190]. Egg intake has been also shown to promote the formation of large LDL particles, which is less atherogenic [191]. Therefore dietary recommendations aimed at restricting egg consumption should not be generalized to include all individuals [191].

4.7. Dietary pattern

Using single nutrients or dietary food groups have some limitations in assessing their effect on lipid profiles separately because nutrients and foods are consumed in combination. To date, dietary patterns consider how foods are consumed in combination, and are used to evaluate the effects of overall nutritional habits on health status. There are two dietary patterns that demonstrate the beneficial effect on disturbances of lipoprotein concentrations; there include the dietary to stop hypertension (DASH) and the Mediterranean diet. The DASH dietary pattern, rich in fruits, vegetables, and low-fat dairy foods, emphasizes fish, poultry, and whole grains, and is reduced in total fat, SFAs and cholesterol, red meat, sweets, and sweetened beverages [192,193]; it lowers total, LDL and HDL cholesterols, without any adverse effects on triglyceride concentrations [194]; all of these coupled with decrease in blood pressure, reduce 10-year coronary heart disease risk of approximately 12% [194]. The Mediterranean dietary pattern consists of: (a) daily consumption: of non refined cereals and products (whole grain bread, pasta, brown rice, etc), vegetables (2 – 3 servings/day), fruits (6 servings/day), olive oil (as the main added lipid) and dairy products (1 – 2 servings/day), (b) weekly consumption: of fish (4–5 servings/week), poultry (3 – 4 servings/week), olives, pulses, and nuts (3 servings/ week), potatoes, eggs and sweets (3 – 4 servings/week) and monthly consumption: of red meat and meat products (4 – 5 servings/month). It is also characterized by moderate consumption of wine (1 – 2 wineglasses/day). Mediterranean diet is a diet poor in SFAs and PUFAs but rich in MUFA (oleic acid) provided by the olive oil. The ratio of MUFAs : SFAs fat ratio is high > 2 [195]. This diet pattern is associated with reduction in total and LDL-cholesterol, and also a significant effect on triglycerides and VLDL concentrations, and a small positive or no effect on HDL-cholesterol [196-199] and improves dyslipidemia in dislipidemic patients [200]. This diet also includes antioxidant vitamins and phenolic compounds, and therefore reduces levels of circulating oxidized LDL and increases total antioxidant capacity [201]. Beside these two dietary patterns, other dietary pattern such as the western, and healthy dietary patterns affect lipoprotein profiles. The western pattern is characterized by high consumption of food such as refined grains, french fries, and red meats that have detrimental effects on lipid profiles. The healthy pattern included non-hydrogenated fat, vegetables, eggs, and fish and was negatively associated with lipoprotein disturbances [202-205]. In addition of dietary patterns, therapeutic lifestyle change is another dietary approach that ATP III recommends to reduce risks for CHD. This dietary approach includes the following: 1) Reduced intakes of dietary SFAs (<7% of total calories) and cholesterol (<200 mg/d), 2) weight reduction, 3) increased physical activity, and 4) therapeutic options for enhancing LDL lowering such as plant stanols/ sterols (2 g/d) and increased viscous (soluble) fiber (10-25 g/d) [18].

5. Dietary supplement

5.1. Plant stanols and sterols

Dyslipidemia may be treated with dietary interventions, including the daily consumption of foods with added plant stanols or plant sterols. Plant sterols are isolated from soybean and tall pine-tree oils. Also some foods such as macadamia nuts are a rich source (1.28 mg/g lipid) of plant sterols. Plant sterols can be esterified to unsaturated fatty acids, creating sterol esters, to increase lipid solubility. Hydrogenating of sterols produces plant stanols. Plant stanols and sterols are available in commercial margarines. Daily consumption of 2 g plant stanols or plant sterols, expressed as free plant stanol or plant sterol equivalents improves dyslipidemia [18]. FDA confirms a daily dose of plant sterols and stanols of 2 g per day as safe, a dose which reduces LDL cholesterol by 10% [206], with little or no change in HDL cholesterol or triglyceride levels. There were no apparent added benefits at higher doses of palnts stanols and sterols. Plant stanols and sterols compete with absorption of dietary cholesterol and bile acid [8]. The consumption of plant stanols and sterols is an effective LDL cholesterol lowering strategy for patients who are undergoing statin therapy. The lipid-lowering response to combined plant stanols and sterols/statin therapy target both intestinal and hepatic cholesterol metabolism. Consumption of plant stanols and sterols reduces intestinal cholesterol absorption and reduces hepatic cholesterol synthesis. Consumption of statins simultaneously with plant stanols and sterols inhibit hepatic cholesterol synthesis and therefore reduce in LDL cholesterol concentrations [8]. Plant sterols/stanols reduce absorption of dietary carotenoids, and decrease levels of plasma betacarotene; therefore increased intakes of fruits and vegetables are recommended with consumption of plant stanols/sterols[18].

5.2. Herbal

There is a need to identify additional non-pharmacologic therapeutic options for cholesterol lowering. There is also a need to find products that are more practical for the consumer than viscous fiber and plant stanols and sterols to permit widespread adoption.

5.2.1. Flavonoid

Flavonoids have 2 aromatic rings that are bound by an oxygenated heterocyclic ring. On the basis of their chemical structure, they are divided into several subclasses: flavones, flavonols, flavanones, flavan-3-ols, anthocyanins and isoflavones. Flavones and flavonols are found in leaf vegetables and onion. Flavanones are mainly found in grapefruits and citrus fruits. Tea and cocoa are the richest sources of flavan-3-ols. Soy and soy products such as tofu, and miso are the main sources of isoflavones [207,208]. Although increased resistance of LDL to oxidation was observed after treatment with various synthetic pharmaceutical agents, an effort is made to identify natural food products which can offer antioxidant defense against LDL oxidation. Polyphenolic flavonoids are powerful antioxidants and their antioxidative capacity is related to their chemical structure [209].

Incubation of LDL with flavonoids protects the lipoprotein against oxidation [210]. Certain flavonoids such as quercetin could have a potentially protective role in suppression of LDL oxidation, regardless of the effect of antioxidant vitamins [211] via scavenging radicals and reduce total and LDL cholesterol concentrations, by reducing the hepatic lipogenesis [212].

5.2.2. Tea

The effect of tea on lipid profiles is uncertain. Although some studies have found no lipid-lowering effects from green or black tea consumption, most showed hypolipidemic effects for tea [213-218]. The association between tea drinking and lipid profile concentrations was linear for up to 10 cups per day, beyond which the association disappeared [219]. Daily consumption of 10 cups of green tea was associated with a reduction of approximately 2% in serum total cholesterol [219]. Tea also is a major source of flavonoids, the predominant ones in green tea being catechins. Theaflavins are polyphenol pigments present in black tea, formed from the polymerization of catechins during fermentation of green tea [220]. Catechins reduce intestinal cholesterol absorption [221], reduce hepatic cholesterol content [222] and increase fecal excretion of total fatty acids, neutral sterols, and acidic sterols [223] and up-regulate the LDL receptor in liver cells [224]. Polyphenol in black tea also increases fecal excretion of total lipids and cholesterol [225].

5.2.3. Chocolate

The beneficial effects of chocolate on healthy humans have been widely addressed in recent years. Supplementation of cocoa products affects lipid profiles in subjects with cardiovascular-related diseases such as hypercholesterolemia, glucose intolerance, and hypertension as well as healthy individuals [226-228]. Consumption of cocoa and dark chocolate increase the concentration of HDL cholesterol [229] and plasma antioxidant capacity, decrease the formation of lipid oxidation products, and inhibit the oxidation of LDL [230]. In a meta-analysis study, cocoa was associated with small decreases in total and LDL cholesterol, but not HDL cholesterol concentrations [231]. Cocoa products contain more polyphenols than teas. A particular group of flavonoids, namely, the flavan-3-ols was found in chocolate (flavanols) [232]. Moderate consumption of cocoa or dark chocolate, have potential health benefits [231], however, a high dose of polyphenols has been shown to exert cytotoxic effects on liver cells [233] and higher polyphenol supplementation may counteract its beneficial biological effects on lipid metabolism [234].

5.2.4. Fenugreek

Fenugreek (Trigonella foenum-graecum), an annual medicinal plant of the Fabaceae family is well documented for its pharmacological properties. Fenugreek seeds have been historically used for the treatment of various chronic diseases such as diabetes, dyslipidemia, and obesity [235,236]. The seeds of Fenugreek contain many nutrients including protein, carbohydrates, fat, vitamin, and minerals, fiber, saponins, choline and

trigonelline, polyphenolic flavonoids, steroid saponins, polysaccharides mainly galactomannans and 4-hydroxyisoleucine [237,239], the fiber and saponin components of the seeds have been shown to have hypocholesterolemic effect [240], and the beneficial effect of raw fenugreek seeds on elevated serum cholesterol levels has been well established [241]. Raw fenugreek seeds reduce serum total cholesterol, LDL cholesterol, VLDL cholesterol and triglyceride concentrations, without altering the HDL fraction [242]; intakes of 20–25 g in three divided doses yielded maximum benefit in the control of cholesterol concentrations [243]. Its use as a dietary adjunct however is limited because of its bitterness. Soaking and washing of fenugreek seeds in water overnight removes the bitterness to a certain extent and makes then edible [243,244].

5.2.5. Ginseng

The beneficial metabolic effects of ginseng on lipid profiles as a hypolipidemic agent were reported over 20 years ago [245-247]. Ginseng leads to reduction of cholesterol and triglyceride concentrations in liver and serum. Administration of red ginseng powder and extract reduces plasma total cholesterol, triglycerides, FFA, and increased HDL-C [248,249]. Ginseng saponins may decrease blood cholesterol concentrations by increasing cholesterol excretion through bile acid formation [249,250]. Ginsenoside, one of active components of ginseng saponins, may accelerate serum cholesterol turnover by increased cholesterol degradation and excretion in the feaces notwithstanding increased hepatic cholesterogenesis [250,251]. Ginseng saponins as ginsenosides increase LDL receptors by promoting the synthesis of LDL receptors[252].

5.2.6. Ginger

Ginger has been listed in the ''Generally Recognized as Safe'' by FDA [338]; fresh ginger rhizome contains polyphenolic compounds such as gingerols; zingerone, which is the major active component and gingerol, is one of the most abundant constituents in the gingerol series and also responsible for its characteristic pungent taste [253,254]. Ginger oleo-resin and dried ginger rhizome reduce hypercholesterolaemia. The speculated mechanism for these compounds is by disrupting cholesterol absorption from the gastro-intestinal tract [255], which may be due to the presence of niacin in ginger, and it causes increased clearance of VLDL, lowers triglyceride levels, increases hepatic uptake of LDL and inhibition of cholesterogenesis [256]. Ginger powder significantly reduces the extent of lipid peroxidation and improves plasma antioxidant capacity, which decreases plasma-free radicals [257]. Moreover, polyphenolic flavonoids present in ginger may prevent coronary artery disease by reducing plasma cholesterol levels or by inhibiting LDL oxidation [258]. Reduction in serum triglycerides is dose dependent; doses of 200 and 400 mg/kg of ginger are more effective as antihypercholesterolaemics than atorvastatin when given for 4 weeks and are equivalent to it when given for shorter period under the same conditions of diet and life style for the treatment of the same pathologic condition. The triglyceride lowering effect of ginger may be due to ginger's ability to enhance lipase activity [255].

5.2.7. Licorice

Licorice root, derived from the plant Glycyrrhiza glabra is used widely in Asia as a sweetener or a spice, contains flavonoids from the flavan and chalcone subclasses, and has a antioxidative properties [259]. Licorice-derived glabridin binds to the LDL particle and protects it from oxidation by its capacity to scavenge free radicals and its property to reduce the LDL aggregation [260,261].

6. Conclusion

Diet therapy is the initial recommended intervention for prevention of and managing disturbances of lipoprotein concentrations, prior to advancing to drug therapy. Further research on the association between dietary components and lipoprotein disturbances is recommended.

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