Diet and Exercise in the Management of Hyperlipidemia.

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Dietary factors that influence lipid levels include modification of nutritional components, consumption of specific foods, use of food additives and supplements, and major dietary approaches. The most beneficial changes result from reducing intake of saturated and *trans* fats; increasing intake of polyunsaturated and monounsaturated fats; fortifying foods with plant stanols or sterols; isocalorically adding tree nuts to the diet; consuming one or two alcoholic drinks per day; and adopting a Portfolio, Mediterranean, low-carbohydrate, or low-fat diet. Smaller but still beneficial effects result from reducing intake of dietary cholesterol, increasing intake of soluble fiber and soy protein, and eating fatty marine fish or taking marine-derived omega-3 fatty acid supplements. Red yeast rice supplements have effects similar to those of statin medications and are better tolerated in some patients. Regular aerobic exercise has beneficial effects on lipid levels, particularly if performed for at least 120 minutes per week. Brief physician counseling will have relatively small effects on unselected patients, so efforts should be concentrated on patients who are motivated and ready to make lifestyle changes.

Hyperlipidemia is a common risk factor for the development of cardiovascular disease. The Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program has for the past decade recommended nonpharmacologic treatment as initial therapy in most patients with hyperlipidemia.[1] The Therapeutic Lifestyle Changes (TLC) approach was based on the panel's review of the available evidence in 1999 that concluded that diet and exercise can have a beneficial effect on serum levels of total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides. The TLC diet recommendations include obtaining 25 to 35 percent of daily calories from fats, and restricting saturated fats to less than 7 percent of total calories and cholesterol to less than 200 mg per day. However, physicians and patients are often unsure of how much change in blood lipid levels can be expected when the TLC diet is prescribed, and wonder which lifestyle changes have the greatest effects. This article attempts to shed some light on these questions by examining recent literature that was not available at the time of the ATP III analysis. Because of the volume of published evidence in these areas, emphasis will be placed on meta-analyses, structured reviews, and randomized controlled trials (RCTs) that reported findings on serum lipid levels.

Dietary Factors

A large number of dietary factors may influence lipid levels. These include modification of nutritional components, consumption of specific foods, use of food additives and supplements, and major dietary approaches.

NUTRITIONAL COMPONENTS

Comprehensive reviews of the evidence for dietary influences on levels of serum lipids and cardiovascular disease have been published. Decreasing total fat intake and replacing saturated and *trans* fats with polyunsaturated and monounsaturated fats, along with limiting dietary cholesterol, lower total cholesterol, LDL cholesterol, and triglyceride levels. Compared with a baseline or Western diet, reducing saturated fat intake to 7 percent of total calories and limiting cholesterol to 200 mg per day reduce LDL

cholesterol levels by 9 to 12 percent. A meta-analysis of 224 studies of dietary interventions showed that changes in total cholesterol levels were affected primarily by changes in intake of saturated and polyunsaturated fats, and dietary cholesterol. A more recent meta-analysis of 60 controlled trials showed that replacing *trans* fats with polyunsaturated fats from unhydrogenated oils is the most effective measure for improving blood lipid profiles.

A meta-analysis of 67 controlled trials of dietary soluble fiber as a single intervention showed that the effects on total cholesterol and LDL cholesterol levels were modest. For example, the addition of three 28-g servings of oats per day decreases LDL cholesterol levels by 5 mg per dL (0.13 mmol per L).

Some persons have little change in lipid levels despite significant changes in fat and cholesterol intake. This observed variation may be explained by genetic factors[8] or insulin resistance.

SPECIFIC FOODS

Tree nuts are high in unsaturated fats and low in saturated fats. Recent reviews of published data conclude that consumption of tree nuts can reduce LDL cholesterol levels by 2 to 19 percent compared with lower-fat and Western diets. Nuts are calorie-dense and therefore should be isocalorically substituted for other foods. Recommended amounts range from 1 to 3 oz. per day, at least five days per week.

Soy protein can also be used to replace foods high in saturated fats and *trans* fats. A meta-analysis of 41 RCTs concluded that soy protein supplementation leads to small reductions in total cholesterol and LDL cholesterol levels (about 5 and 4 mg per dL [0.13 and 0.10 mmol per L], respectively), as well as small increases in HDL cholesterol levels (about 0.8 mg per dL [0.02 mmol per L]). The typical amount of soy protein used in studies has been 1.0 to 1.5 oz. per day.

Alcohol consumption is associated with an increase in HDL cholesterol levels of as much as 9 to 13 mg per dL (0.23 to 0.34 mmol per L) when nondrinkers are compared with the highest consumers. In an eight-week controlled study of postmenopausal women, alcohol consumption (15 g per day, equivalent to one drink) lowered LDL cholesterol levels by 7.8 mg per dL (0.20 mmol per L), but HDL cholesterol levels only increased significantly when alcohol consumption was increased to 30 g per day.

ADDITIVES AND SUPPLEMENTS

A comprehensive review of plant stanols and sterols showed that these substances lower LDL cholesterol levels in persons at risk of coronary heart disease. This review included a meta-analysis of 41 trials showing that 2 g per day of either stanols or sterols reduces LDL cholesterol levels by 10 percent. These effects are additive with other diet or drug interventions. Fortified foods (e.g., Promise Active and Benecol spreads) typically have 0.5 to 1 g of sterol or stanol per serving. The approximate cost for the recommended 2 g of stanols or sterols from fortified foods is $0.60 to $1.20 per day.

Two marine-derived omega-3 fatty acids, eicosapentaenoic acid and docosahexaenoic acid, lower triglyceride levels in a dose-dependent fashion. However, their effects on cardiovascular mortality probably result more from their antiarrhythmic, anti-inflammatory, and other effects than from their effects on lipid levels. A systematic review showed that plant-derived alpha-linoleic acid has no effect on lipid levels.

Extracts of Chinese red yeast rice (a traditional dietary seasoning of *Monascus purpureus*) have several active ingredients, including naturally occurring lovastatin (as monacolin K, 5 mg to 10 mg per typical daily dose). A meta-analysis of 93 trials concluded that red yeast rice lowers total cholesterol, LDL cholesterol, and triglyceride levels. The magnitude of this effect is similar to that of statin medications. Safety and effectiveness are potential concerns because some preparations have been found to contain toxic byproducts of fermentation, and available products are not standardized. Red yeast rice is an option for patients who cannot tolerate statins because of muscle aches.

DIETARY APPROACHES

Both low-fat and low-carbohydrate diets affect lipid levels. In a meta-analysis of RCTs comparing these approaches, low-fat diets had the most favorable effects on total cholesterol and LDL cholesterol levels, whereas low-carbohydrate diets had the most favorable effects on triglyceride and HDL cholesterol levels. An RCT showed that the total-to-HDL cholesterol ratio was reduced by 20 percent in participants following a low-carbohydrate diet, compared with a 12 percent reduction in those following a low-fat diet; this was a statistically significant difference. The reduction in the total-to-HDL cholesterol ratio is similar to the reduction in LDL cholesterol levels, and the total cholesterol level is reduced primarily by changes in the LDL cholesterol levels. Meta-analyses of trials of low–glycemic index versus high–glycemic index diets have concluded that low–glycemic index diets have a weak effect on total cholesterol levels, but no effect on LDL and HDL cholesterol or triglyceride levels.

The Mediterranean diet is characterized by a high consumption of monounsaturated fats (primarily from olive oil) and low consumption of saturated fats. Other characteristics include limited consumption of red meat, dairy products, eggs, and poultry; increased consumption of fish, tree nuts, vegetables, and whole grains; and moderate consumption of wine. When two versions of a Mediterranean diet were compared with a low-fat diet, the Mediterranean diets lowered the total-to-HDL cholesterol ratio more than the low-fat diet.

The Portfolio Diet is a plant-based TLC diet that is a composite of four additional LDL cholesterol–lowering components: soluble fiber, soy and other vegetable proteins, plant sterols, and almonds. In controlled settings, the Portfolio Diet has been shown to reduce LDL cholesterol levels by 29 to 35 percent, comparable to a combination of a diet low in saturated fats and cholesterol plus 20 mg of lovastatin (Mevacor) daily.[2] Among persons eating self-selected Portfolio Diet foods, 32 percent achieved LDL cholesterol reductions of more than 20 percent after one year

Exercise

The effects of exercise on serum lipid levels have been studied extensively. Published data have been subjected to meta-analysis, demonstrating that one positive effect of regular aerobic exercise is to raise HDL cholesterol levels by an average of 1.9 to 2.5 mg per dL (0.05 to 0.06 mmol per L). Other effects include decreases in total cholesterol, LDL cholesterol, and triglyceride levels by an average of 3.9, 3.9, and 7.1 mg per dL (0.10, 0.10, and 0.08 mmol per L), respectively. The minimal amount of exercise needed to increase HDL cholesterol levels is 900 kcal of energy expenditure per week, or about 120 minutes of typical aerobic exercise. In

patients with cardiovascular disease who exercise aerobically, HDL cholesterol levels increase by an average of 9 percent (3.7 mg per dL [0.10 mmol per L]), and triglyceride levels decrease by 11 percent (19.3 mg per dL [0.22 mmol per L]), suggesting greater benefits in this high-risk group.[31] However, in a small study of younger men, those with initially lower HDL cholesterol levels (less than 40 mg per dL [1.04 mmol per L]) responded less to exercise than those with higher levels (increase of 1.9 mg per dL versus 5.1 mg per dL [0.05 versus 0.13 mmol per L]), possibly because of differences in triglyceride metabolism. There is a great deal of variability in HDL cholesterol responses to exercise, ranging in one study from decreases of 9.3 percent in the least responsive quartile to increases of 18 percent in the most responsive quartile. Improvements in HDL cholesterol levels seem to be related more to the amount of activity than to the intensity of exercise or improvement in fitness. Physical inactivity has profound negative effects on lipid metabolism, including increases in LDL cholesterol levels, but this can be prevented by modest regular exercise.

Combined Changes in Diet and Exercise

Because dietary approaches tend to lower total cholesterol, LDL cholesterol, and triglyceride levels, and exercise tends to raise HDL cholesterol levels and lower triglyceride levels, it seems logical to combine these approaches. Combinations of dietary interventions and exercise have been studied, and the resulting data have been critically reviewed. The two reviewed approaches were (1) exercise combined with a diet low in saturated fats, and (2) exercise combined with nutritional supplements (fish oil, oat bran, plant sterols). Exercise plus a low–saturated fat diet reduced LDL cholesterol levels by 7 to 15 percent and triglyceride levels by 4 to 18 percent, while increasing HDL cholesterol levels by 5 to 14 percent. Exercise plus nutritional supplements reduced LDL cholesterol levels by 8 to 30 percent and triglyceride levels by 12 to 39 percent, while increasing HDL cholesterol levels by 2 to 8 percent. Therefore, combining diet and exercise interventions seems additive, or at least synergistic.

Effectiveness of Counseling

Physicians have many challenges to address in encouraging lifestyle changes to improve blood lipid profiles and other cardiovascular risks in their patients. These include patients' health beliefs, motivations, and stage of change for new lifestyle behaviors. A Cochrane review showed that patients who received dietary advice had reductions in total cholesterol levels of 6.2 mg per dL (0.16 mmol per L), and in LDL cholesterol of 7.0 mg per dL (0.18 mmol per L), with no significant change in HDL cholesterol levels. An older systematic review of 19 RCTs showed that dietary advice can result in reductions in total cholesterol of only 3 to 6 percent, mainly because dietary targets were not achieved by participants. A Cochrane review of dietitian advice compared with physician advice or self-help material found that dietitians were more successful than physicians in the short to medium term (total cholesterol reduced an additional 9.7 mg per dL [0.25 mmol per L] compared with physician results), but not better than self-help resources.

Counseling to promote increased physical activity also seems to be minimally effective. Evidence reviewed by the U.S. Preventive Services Task Force indicates that the more intensive the counseling, the more change in behavior can be expected. Physicians tend to counsel briefly, though they may also refer patients to dietitians and other educators for in-depth counseling. Low-intensity counseling by physicians produces the greatest effects when patients are already interested in and planning changes in their behaviors.

Final Comment

The effectiveness of dietary changes and exercise on hyperlipidemia has been clearly demonstrated. However, many counseled patients will not make lasting changes, and responses to lifestyle changes vary among individual patients. It makes sense to help motivated patients learn which lifestyle changes are most likely to improve their lipid-related cardiovascular risk, and then measure the effects that occur as they make changes. Decreased intake of saturated and *trans* fats, increased intake of poly- and monounsaturated fats, moderate alcohol intake, supplementation with plant sterols or stanols, and isocalorically increased consumption of tree nuts are likely to produce the most beneficial changes in lipid levels. The Portfolio Diet and Mediterranean Diet are worth recommending as alternatives to an unenhanced TLC diet. Aerobic exercise confers additional benefits if done on a regular basis. Physicians should tailor advice to patients in the context of other health conditions and risks.