"ISOLATED" LOW HIGH-DENSITY LIPOPROTEIN CHOLESTEROL

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OBJECTIVE: To present information on the function, structure, and importance of high-density lipoprotein cholesterol (HDL-C) and to evaluate the current literature regarding the controversy of managing patients with an "isolated" low HDL-C concentration.

DATA SOURCE: A MEDLINE search was performed (1966–June 1996) to identify English-language clinical and review articles pertaining to HDL-C. Some articles were identified through the bibliography of selected articles.

STUDY SELECTION: All articles were considered for possible inclusion in the review. Pertinent information, as judged by the authors, was selected for discussion.

DATA EXTRACTION: Important historical lipid studies, recent review articles, and clinical trials involving therapy for HDL-C were evaluated.

DATA SYNTHESIS: The structure, function, and measurement of HDL-C and the state of an isolated low HDL-C are discussed for background. Lifestyle modification measures to increase HDL-C, medications to avoid, estrogen replacement, and lipid-altering agents used to raise an isolated low HDL-C are presented.

CONCLUSIONS: An isolated low HDL-C concentration poses a risk for coronary heart disease. The management of this state is controversial. The first step in management is in agreement with experts and includes lifestyle modification (e.g., weight reduction, diet, smoking cessation, aerobic exercise). Estrogen replacement therapy and discontinuance of drugs that secondarily lower HDL-C are additional treatment options. The use of lipid-altering agents has been used in some patients. Nicotinic acid appears to be an effective agent for an isolated low HDL-C. A large clinical trial evaluating the effect of treating an isolated low HDL-C for primary and secondary prevention of coronary events is needed.

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THE EXPERT PANEL on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults in 1994 issued their second report of the National Cholesterol Education Program's (NCEP's) recommendations for cholesterol management.[1] A notable change in the second report is that a greater significance is attributed to low concentrations of high-density lipoprotein (HDL) as a risk factor for coronary heart disease (CHD). The panel recommends that HDL-cholesterol (HDL-C) be measured through initial cholesterol testing, with a high HDL-C (≥60 mg/dL) considered a negative CHD risk factor. The panel also recommends that HDL-C concentrations be considered when selecting drug therapy for lipid disorders.

The link between HDL-C and CHD risk arises primarily from epidemiologic studies. The National Institutes of Health (NIH) Consensus Panel stated that among 19 prospective epidemiologic studies, 15 showed a significant and strong inverse relationship between HDL-C and CHD, 3 showed a direct relationship, and 1 showed no trend.[2] Many clinical trials designed to test the hypothesis concerning low-density lipoprotein (LDL) concentrations and CHD risk found evidence for the protective role of HDL on CHD. A review of the Framingham Heart Study, the Lipid Research Clinic's Mortality Follow-up Study and Coronary Primary Prevention Trial, and the Multiple Risk Factor Intervention Trial suggests that for every 1 mg/dL decrease in HDL-C concentrations, the risk of CHD is increased by 2–3%.[2-4]

Low HDL-C concentrations may be due to genetic or secondary causes (Table 1).[5-9] Strategies for managing decreased HDL-C focus on lifestyle modification, including smoking cessation, weight reduction, aerobic exercise, dietary modification, and alcohol consumption; discontinuance of medications that secondarily lower HDL-C; and estrogen replacement therapy.[10] In patients with existing CHD or a strong family history of CHD and low HDL-C, reduction of the LDL-cholesterol (LDL-C) fraction and an increase of the HDL-C remain therapeutic goals.

An "isolated" low HDL-C concentration is defined as less than 35 mg/dL with otherwise normal plasma lipids. A study[11] of 255 male outpatients in three Veteran Affairs Medical Centers suggested that 20% of men with CHD

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Table 1. Secondary Causes of Low High-Density Lipoprotein Cholesterol[5-9]

LIFESTYLE	DRUG THERAPY	DISEASE STATES
Cigarette smoking	anabolic steroids	hypertriglyceridemia
Sedentary lifestyle	non-ISA beta-blockers	obesity
Physiologic stress	isotretinoin	diabetes mellitus
Low-fat diet	progestins	nephrotic syndrome
High polyunsaturated-fat diet	thiazide and loop diuretics[a]	septic shock
	androgens	hyperthyroidism
	zinc supplementation	myocardial infarction
	parasympatholytic agents	liver disease
	probucol	acute illness
		syndrome X

ISA = intrinsic sympathomimetic activity.
[a]Reports include no change or a decrease in HDL cholesterol.

have isolated low HDL-C concentrations and 29% had HDL-C concentrations that were less than 40 mg/dL. More recently, prospective results were published from the Québec Cardiovascular Study,[12] which measured various lipoprotein fractions in 2103 men aged 45–76 years without ischemic heart disease. The authors report patients with isolated hypoalphalipoproteinemia had an adjusted odds ratio for developing ischemic heart disease of 2.2 (95% CI 1.2 to 3.9) and that the prevalence of isolated hypoalphalipoproteinemia was higher in men with ischemic heart disease than in men without it (17.5% vs. 13.4%).

This article reviews the structure, function, and measurement of HDL, as well as the lifestyle modification measures and drug therapy needed to increase HDL-C in patients with an isolated low HDL-C concentration.

High-Density Lipoprotein Characteristics

HDL consists of a heterogeneous group of particles classified either by size or by apolipoprotein content. Individual subfractions of HDL are attracting attention since research into these may offer insights to the protective effect of HDL and the relationship between HDL metabolism and atherogenesis.

Total HDL includes the larger, less dense HDL_2 and the smaller, denser HDL_3.[5,10,13] Even though the major proportion of HDL is normally present in HDL_3, individual variability in HDL concentrations usually reflects differences in HDL_2. HDL_2 is generally considered the more protective component of HDL than is HDL_3, although some data suggest that both HDL_2 and HDL_3 subfractions are strongly inversely related to myocardial infarction occurrence.[14]

Major HDL apolipoproteins include apolipoprotein A-I (apo A-I) and apolipoprotein A-II (apo A-II). Apo A-I is an essential protein component of HDL found in all HDL subfractions.[13] Apo A-I also functions as a coenzyme of lecithin cholesterol acyl transferase (LCAT), which catalyzes esterification of cholesterol within the HDL particle. Apo A-II is found most abundantly in HDL particles of intermediate density, but can be found throughout the density range of HDL particles. The function of apo A-II is undetermined. Apolipoproteins C (C-I, C-II, C-III) and E are minor but metabolically important HDL apolipoproteins.[6] HDL acts as a reservoir for apo E and C proteins. Apo E and C transfer onto triglyceride (TG)-rich lipoproteins and either provide a signal for the activation of lipolysis (apo C-II) or target information that allows uptake of lipolyzed remnant lipoproteins via liver receptors (apo E).

Measuring total HDL-C provides important information regarding CHD risk. The measurement of subfractions either by size or apolipoprotein content may provide information concerning atherosclerotic risk and about the underlying physiologic mechanisms responsible for the risk.

High-Density Lipoprotein Functions

The antiatherogenic properties of HDL include the following proposed mechanisms: reverse cholesterol transport,[2-4,6,7,10,15,16] maintenance of endothelial function,[4,10,16] protection against thrombosis,[10] and the remnant hypothesis.[6,10] The problem with determining the function of HDL-C is that not all individuals with low HDL develop premature CHD. These differences may be related to the different HDL subfractions. Strategies of raising HDL-C concentrations have not been fully explored because lipoproteins may be modified without significantly altering their serum concentrations.[17]

Reverse cholesterol transport, one of the most important mechanisms of HDL, refers to the ability of HDL to remove intracellular cholesterol from atherosclerotic lesions and transport it back to the liver for excretion. By removing cholesterol from arterial walls, HDL may be able to slow the progression of atherosclerotic lesions. The maintenance of endothelial function suggests HDL has vascular actions. This activity interferes with the LDL aggregation step that facilitates the uptake of LDL by endothelial cells, competes with LDL for endothelial-localized LDL receptors, facilitates endothelial cell repair and proliferations, and maintains normal coronary vasoreactivity. The thrombosis protection includes HDL's enhanced fibrinolysis, decreased platelet aggregation, and increased prostacyclin production and stabilization properties. The remnant hypothesis suggests that decreased HDL-C is simply a marker for the accumulation of atherogenic lipoproteins, including chylomicron, very low-density lipoprotein (VLDL) remnants, and small dense apoprotein B-rich LDL.

Inherited Disorders of High-Density Lipoprotein

Low concentrations of HDL-C, or hypoalphalipoproteinemia, occur commonly in patients with premature coronary atherosclerosis and may be an isolated entity or be in conjunction with other dyslipidemias. Familial (primary) hypoalphalipoproteinemia, characterized by HDL-C concentrations below the 10th percentile compared with age- and sex-matched controls, has been linked to stroke and premature CHD.[7,10] Not all inherited disorders of HDL deficiency are characterized by premature atherosclerosis. Low HDL-C disorders caused by decreased production are associated with an increased CHD risk; those related to increased HDL catabolism are associated with a moderate CHD risk.[7,10] Tangier disease and LCAT deficiency are re-

lated to hypercatabolism of HDL and are not associated with an increased CHD risk; however, these disorders are also associated with low LDL concentrations. Genest et al.[18] reported that 54% of their patients with angiographically determined premature CHD (age <60 y) had a familial dyslipidemia. In those patients, hypoalphalipoproteinemia was present in 31% of the entire cohort and broken down as follows: 15% familial hypertriglyceridemia and hypoalphalipoproteinemia, 12% familial combined hyperlipidemia and hypoalphalipoproteinemia, and 4% familial hypoalphalipoproteinemia.

The link between hyperlipidemia and insulin resistance is well documented. However, until recently, it was not known whether an isolated deficiency in HDL-C was associated with an insulin-resistant state. Evidence suggests that low HDL-C and insulin resistance coexist independently of TG concentrations.[19] This finding suggests that the increased risk for CHD in patients with low HDL-C could also be explained by mechanisms that increase the degree of insulin resistance.

Measurement of High-Density Lipoprotein

Current NCEP screening guidelines recommend that HDL-C be measured with initial cholesterol testing in a nonfasting state.[1] Before initiating treatment based on this measurement, a fasting lipoprotein analysis should be done regardless of total cholesterol if HDL-C is less than 35 mg/dL. Accurate measurement of HDL is essential to determine the accurate diagnosis of the dyslipidemia as well as treatment goals. Several factors may contribute to spurious HDL-C concentrations: acute illness, acute infection, recent trauma, surgery, a change in usual diet, weight loss, and pregnancy. Following an acute myocardial infarction, HDL-C concentrations begin to decrease. At 5 and 7 days after onset of initial chest pain, the concentrations are 12–18% and as low as 32% below stable baseline concentrations, respectively. HDL concentrations may stay decreased from 30 days to up to 12 weeks following the infarct.[1,10]

When expressed as the coefficient of variation, the biologic and analytic variations in measuring HDL-C are 7–8% and 6%, respectively.[2] Variability depends on many factors, including prior alcohol intake, posture, prior exercise status, diet, time of day, medication or hormone administration, menstrual cycle, and sample collection. The NIH Consensus Panel suggests that at least two and preferably three fasting samples at least 1 week apart be analyzed for HDL-C and TG to enhance precision before treatment decisions are finalized. The NCEP defines a low HDL-C concentration as less than 35 mg/dL; this constitutes a coronary risk factor. If the HDL concentration is low, the analysis should be repeated before the patient is further advised.[20]

Lifestyle Modification

SMOKING

Cigarette smoking decreases HDL-C concentrations and is itself an important CHD risk factor. After adjustment for covariables in the Lipid Research Clinics Follow-up Study,[21] HDL-C concentrations were reduced by 5–9 mg/dL in smokers. In the Framingham Offspring Study,[22] the smoking relationship to HDL-C concentrations was confirmed in both men and women. After adjusting for alcohol consumption and obesity, 4 and 6 mg/dL HDL differences were found between men and women smokers versus nonsmokers, respectively. These data indicated that the number of years of smoking did not relate to HDL concentrations and that former cigarette smokers' HDL concentrations were not significantly different from nonsmokers. This lends support to smoking cessation in the management of low HDL-C.

In a group of women who smoked an average of 20 cigarettes per day for 5 years, their HDL-C increased to nearly that of the nonsmokers after 30 days of smoking cessation; however, the HDL-C concentrations decreased to their baseline 30 days after they resumed smoking.[23]

Passive smoke has been linked to heart disease in nonsmokers.[24] Moskowitz et al.[25] demonstrated that children with at least one smoking parent had HDL-C concentrations 3.8 mg/dL lower than children with nonsmoking parents.

EXERCISE

Patients with a low HDL should begin increased aerobic exercise. Regular exercise raises HDL-C concentrations, reduces VLDL concentrations, and, in some individuals, lowers LDL concentrations.[1] Intervention studies report a 10–20% increase in HDL-C concentrations in response to exercise dependent on the frequency, intensity, and duration of the exercise.[2] A regular exercise program may also attenuate or prevent the decrease in HDL-C often associated with a diet low in total fat, saturated fat, and cholesterol.

In the Framingham Offspring Study,[26] patients who participated in conditioning activities for 1 hour or more per week compared with those who participated less than 1 hour per week achieved an increase in HDL of 6–7 mg/dL in men and 7–8 mg/dL in women.

A threshold effect for exercise is required before HDL elevations are seen.[27,28] Exercise's effect on HDL became apparent when more than 6 miles were jogged weekly. Joggers who ran more than 10 miles per week for 10 months demonstrated a 10% increase in HDL-C concentrations that further increased as the miles jogged increased.[28] The elevation in HDL-C resulted from a rise in the HDL_2 subfraction, while the HDL_3 declined as the exercise increased.

A meta-analysis[29] of 66 studies on exercise, with 2068 sedentary subjects, showed a nonsignificant increase of 1.2 mg/dL in HDL-C concentrations. Eighty-five percent of the subjects were men. One positive result from this analysis was that individuals with the lowest HDL showed the greatest increase in postexercise HDL.

OBESITY

An inverse relationship between HDL-C concentrations and obesity exists. This relationship did not vary much with age or sex in the Framingham study.[30] However,

HDL-C concentrations tend to increase in men, but not always in women, when significant weight loss occurs. In a study of obese men and women, a 9- to 11-kg weight loss resulted in a 5% increase of HDL-C in the men but a 3.3% decrease in the women.[31] Weight loss alone can significantly increase HDL-C concentrations and when combined with regular exercise may increase HDL-C concentrations by 10–20%.[2] Many studies have shown that weight reduction increases HDL-C and lowers TGs.

A weight gain of 2.25 kg or one body mass index unit (1 kg/m^2) during an 8-year follow-up of the Framingham Offspring Study resulted in higher total, LDL, and VLDL cholesterol and a 5% decrease in HDL-C.[32] After adjusting for smoking habits, another study showed that for each body mass index unit increase, HDL-C decreased by 0.8 mg/dL.[33]

DIET

Dietary interventions may cause an elevation or decrease in HDL-C concentrations, depending on the individual, type of diet, and amount of weight loss.[1,4,15] Low-fat, high-carbohydrate diets tend to increase TGs and decrease HDL. However, individuals who consume high-carbohydrate, low-fat diets with high ratios of polyunsaturated to saturated fat tend to have relatively low concentrations of both HDL-C and LDL-C, with an overall low coronary risk. If body weight is kept constant, the substitution of polyunsaturated (i.e., corn oil) or monounsaturated (i.e., olive oil) fat for saturated fat affects HDL-C. Substitution of monounsaturated rather than polyunsaturated fat for saturated fat in the diet generally lowers LDL-C without lowering HDL-C. The mechanisms of diet-induced decreases in HDL are increases in the catabolic rate of HDL apolipoproteins as a result of increased carbohydrate intake and a decrease in their rate of synthesis when polyunsaturated fat intake is increased. Overall, patients should be placed on a step I or II diet,[1] with an emphasis on using monounsaturated instead of polyunsaturated fats for their substitution of saturated fat.

ALCOHOL

In patients with normal hepatic synthetic function, moderate alcohol consumption may result in higher concentrations of HDL-C, HDL_3, and apo A-I and A-II. Moderate alcohol intake may decrease the CHD risk ratio by 0.8.[10] Multivariate models suggest that 50% of alcohol's cardioprotective effects are related to the increased HDL-C concentration and 18% to a reduction in LDL-C concentrations.[34] However, the 18% reduction in risk attributed to the decreased LDL-C concentrations may be counterbalanced by a 17% increase in risk due to increased systolic blood pressure. Alcohol also mediates some favorable hemostatic changes including a reduction in fibrinogen, inhibition of platelet aggregation, and enhancement of prostacyclin formation or plasminogen activator secretion.[10] The amount of alcohol needed to increase HDL-C in men and women differs. Men need more than 30 drinks per month (i.e., 1 drink = 12 oz of beer, 5 oz of wine, or 1.5 oz of 80-proof liquor) and women can consume lower alcohol amounts (5–30 drinks/mo) to have a positive correlation of HDL-C with alcohol.[35]

It is important to note that chronic alcohol-induced liver injury is associated with decreases in HDL-C due to impaired hepatic synthetic function. Since alcohol has inherent problems and may elevate plasma TGs, the NIH Consensus panel does not recommend the use of alcohol to increase HDL-C concentrations.

Secondary Effects of Drugs on High-Density Lipoprotein

Screening a patient's profile for drugs that may be secondarily decreasing HDL-C concentrations is imperative.[8,36] Cholesterol is a precursor to androgens and progestins; therefore, these agents may affect lipid parameters. Anabolic steroids can cause a marked reduction in HDL-C, especially HDL_2. Progestins tend to decrease HDL-C, and in women using oral contraceptives, the agents lower in estrogen and higher in progestins cause significantly lower concentrations of HDL-C than do agents higher in estrogen and lower in progestin. The progestational agents, norgestrel and levonorgestrel, are more likely to lower HDL-C than is norethindrone, due to their androgenic activity. Decreased HDL-C concentrations by 5% and 16% have been reported for low (150 µg) and high (250 µg) levonorgestrel-dosed combination oral contraceptives, respectively.[37]

Beta-blockers without intrinsic sympathomimetic activity (ISA) lower HDL-C with little difference between selective and nonselective beta-blockers. Like the ISA beta-blockers, the alpha/beta-blocker labetalol has not been associated with lowered HDL-C concentrations. Although beta-blockers may reduce HDL-C concentrations, patients who have had a myocardial infarction should be allowed to use a beta-blocker. The Beta-Blocker Heart Attack Trial[38] showed that after adjusting for the effects on lowering the HDL-C, patients treated with propranolol at 6 months postinfarction had a tenfold treatment advantage.

Isotretinoin decreases HDL-C and HDL_2. Probucol may lower HDL-C concentrations up to 25%, mainly due to a decline in apo A-I.[10] Other medications that may decrease HDL-C are methyldopa, thiazide and loop diuretics,[9] parasympatholytic agents, zinc supplementation,[5] and benzodiazepines.

Estrogen Replacement Therapy

Postmenopausal women have an increased risk of CHD whether their menopause is natural, surgical, or premature. Prospective, uncontrolled studies suggest that in women without CHD a 50% reduction in CHD rates may be associated with oral estrogen replacement.[39-41] The protective action of estrogens is in part related to their impact on lipoprotein concentrations. Oral estrogen therapy lowers LDL-C, raises HDL, including HDL_2, and raises TGs. Transdermal estrogens have less effect than oral estrogens on lipid parameters, with relatively little effect on serum HDL-C and minimal effects on TGs.[42]

Overall, in postmenopausal women, oral estrogens (0.625 mg of conjugated estrogen or 2 mg of micronized estradi-

ol) increase HDL-C concentrations by up to 15%.[43-47] A study on ethinyl estradiol (1 μg/kg/d, average dosage 0.07 mg/d) administered for 28 days showed HDL-C and HDL_2 concentrations increased by 21% and 42%, respectively.[48] Progestins may decrease the beneficial effects of estrogens on the lipid profile. However, the effects can be minimized by adjusting the dosage of progestin and using a progestin with minimal androgenic effect.

Pharmacotherapy

Intensive efforts should be made with hygienic or lifestyle modifications for increasing isolated low HDL-C concentrations in individuals at risk. If these interventions are unsuccessful, pharmacotherapy may be needed. Figure 1[49] provides an algorithm to follow in managing the patient with an isolated low HDL-C concentration. Patients' medications need to be reviewed and those decreasing HDL-C concentrations should be discontinued and replaced, if possible. For example, practitioners could choose lipid-neutral antihypertensive agents (e.g., angiotensin-converting enzyme inhibitors, calcium-channel blockers) or an agent that may elevate HDL-C (e.g., $alpha_1$-adrenergic inhibitors such as doxazosin)[50] in patients with low HDL-C concentrations.

Patients with CHD, secondary prevention, and isolated low HDL concentrations should have a goal of reducing their LDL-C to 100 mg/dL or less. Nicotinic acid would be a good first choice since it not only lowers LDL-C effectively, but also increases HDL-C. Some feel that in addition to the aggressive lowering of LDL-C concentrations in patients with CHD, HDL-C concentrations should ideally be targeted to 45 mg/dL for men and 55 mg/dL for women.[51,52] These target HDL-C concentrations are based on relative risks established by the Framingham Heart Study.[52]

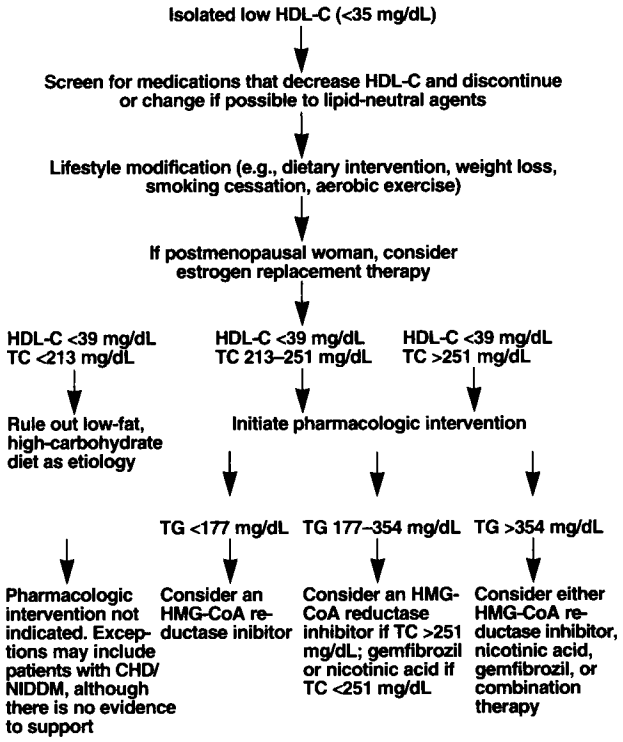

Figure 1. Algorithm for managing a patient with isolated low high-density lipoprotein cholesterol.[49] Pharmacotherapy of isolated low HDL-C has not been shown to prevent atherosclerosis, cardiovascular event rates, or mortality. CHD = coronary heart disease; HDL-C = high-density lipoprotein cholesterol; HMG-CoA = hydroxymethylglutaryl-coenzyme A; NIDDM = non-insulin-dependent diabetes mellitus; TC = total cholesterol; TG = trigylcerides.

In patients with isolated low HDL concentrations and other CHD risk factors without established CHD (primary prevention), the goal of therapy is to reduce LDL-C concentrations to less than 130 mg/dL.[1] In patients with a low risk for CHD due to a low LDL-C and absence of risk factors (i.e., a positive family history of premature CHD), pharmacotherapy for isolated low HDL-C concentrations is not recommended by the NCEP panel.[1] Primary hypoalphalipoproteinemia is frequently refractory to pharmacotherapy.[2,10]

Nicotinic acid, fibric acid derivatives (fibrates), and hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors are lipid-lowering agents that can be used if treatment for an isolated low HDL-C is initiated.[53] Recently, Kolovou et al.[54] demonstrated that HMG-CoA reductase inhibitors, gemfibrozil, and nicotinic acid all significantly increased HDL-C in patients who had HDL-C concentrations less than 39 mg/dL but not in patients with HDL-C greater than 39 mg/dL. Bile acid resins can raise HDL-C by 3–5%,[1] but are generally not used for this effect alone because they may also increase TGs. Nicotinic acid is the preferred agent, and if it cannot be tolerated, fibrates or HMG-CoA reductase inhibitors can be used. These two classes are approximately equivalent in HDL-C elevation in patients with isolated low HDL-C. Fibrates are more effective at lowering TGs, while HMG-CoA reductase inhibitors are more effective at lowering LDL-C.

NICOTINIC ACID

Many experts believe nicotinic acid is the agent of choice in raising HDL-C concentrations due to its efficacy and low cost.[53,55] HDL-C concentrations may increase by 15–35%.[1] Nicotinic acid is also effective at decreasing LDL-C, total cholesterol, and TGs. As monotherapy for dyslipidemia, it is the only agent that has been proposed to reduce heart disease events and mortality from all causes.[56] Mechanisms for the HDL-C elevations include delayed HDL catabolism and decreased VLDL synthesis that reduces transfer of cholesterol ester from HDL to VLDL particles.[10]

Peptic ulcer disease, gout or hyperuricemia, diabetes mellitus, and liver disease are contraindications to nicotinic acid use. HDL-C elevations begin to manifest at low total daily doses of 1000 mg (range 1000–3000), which contrasts to the higher dosages needed for VLDL lowering.[10,53] Adverse effects often limit the use of nicotinic acid; these can be caused when physicians initially use too high a dosage and/or increase the dosage too rapidly. A slower upward titration of the dosage, careful monitoring, and the judicious use of aspirin may blunt some of the adverse effects. In addition, immediate-release nicotinic acid should be used instead of extended-release preparations, especially in light of recent reports of increased hepatotoxicity with extended-release nicotinic acid.[57]

In a 24-week, crossover study of 28 normolipidemic men with low HDL-C concentrations, King et al.[58] evaluat-

ed unmodified crystalline niacin's effects on basal lipids and lipoprotein and on postprandial increases in TGs due to lipemia after a fatty meal, which is often found in patients with a low HDL-C. Patients were assigned to the immediate-release niacin group for 12 weeks or no drug for 12 weeks and then crossed over to the alternate regimen. Fifteen patients completed the study. Patients had to tolerate at least niacin 1500 mg/d, with the goal dosage being 1 g tid, if tolerated. The mean baseline HDL-C was 31.7 ± 6.2 mg/dL. Significant increases of 30% in HDL-C, 100% in HDL_2, and 21% in HDL_3 occurred. HDL-C increased to 42 mg/dL, HDL_2 from 5 to 9 mg/dL, and HDL_3 from 27 to 33 mg/dL. Significant reductions occurred in TG and LDL-C parameters, as well as a 45% reduction in postprandial lipemia. Overall adherence to the regimen was 60%. The authors concluded that crystalline niacin effectively raises HDL-C, lowers LDL-C, and reduces postprandial lipemia in patients with an isolated low HDL-C. They found that many patients have difficulty tolerating niacin and that supervision is required to support patient compliance and avoid toxicity.

Lavie et al.[59] evaluated the effects of 3 months of extended-release niacin at an average dosage of 2.4 g/d (range 1000–3000 mg) in 36 men with known coronary artery disease and low concentrations of HDL-C (<35 mg/dL, with 82% having values <30 mg/dL). All the patients received 3 months or more of nonpharmacologic treatment (i.e., exercise, weight reduction) prior to starting niacin therapy. Nineteen of these patients had an isolated low HDL-C. Among this subgroup, the mean ± SD HDL-C at baseline was 25 ± 4 mg/dL and after 3 months of niacin was 32 ± 6 mg/dL, for a 27% increase that was statistically significant ($p < 0.002$). LDL-C in this group decreased by 5% and TGs increased by 10%; neither was statistically significant. Overall, 34 patients completed the study; there was a statistically significant decrease in total cholesterol ($p < 0.005$), LDL-C ($p < 0.01$), and the LDL/HDL ratio ($p < 0.0001$). Also, HDL-C increased by 30% from a baseline of 26 ± 4 to 33 ± 6 mg/dL ($p < 0.0001$). The authors concluded that extended-release niacin in patients with low concentrations of HDL-C should prove beneficial in primary and secondary coronary prevention. They stated that this study was short term, and that long-term safety concerns of extended-release niacin, especially in terms of hepatic dysfunction, must be considered.

Recently, Martin-Jadraque et al.[60] found low-dose crystalline nicotinic acid (1.5 g/d) caused an average HDL-C increase of 20% in both normolipidemic and hyperlipidemic patients with low HDL-C concentrations. This low dosage was well tolerated in 37 of 44 patients. The authors stated that although nicotinic acid's HDL-C-raising effects are dose-dependent, a moderate rise in HDL-C concentrations can be achieved with a low dosage and be well tolerated.

FIBRIC ACID DERIVATIVES

The major mechanism of gemfibrozil, a fibric acid derivative, is increased lipoprotein lipase activity, resulting mainly in TG lowering and, to a lesser extent, HDL-C elevation. HDL-C increases generally range between 10% and 15%.[1] LDL-C may be decreased or increased, depending on the dyslipidemia. Gemfibrozil may increase the lithogenicity of bile, leading to gallstones. It is not indicated in patients with established CHD.[1]

In a randomized, double-blind, placebo-controlled, crossover study, Miller et al.[61] evaluated the efficacy of gemfibrozil in 14 men with primary isolated low HDL-C concentrations. Patients were assigned to receive placebo or gemfibrozil 600 mg bid for 3 months, then a 1-month washout, and then the alternate treatment for 3 months. Total HDL-C increased by 9.2% ($p = 0.001$) and TGs decreased by 38% ($p < 0.01$). Patients with the highest fasting TGs (≥95 mg/dL) had a 14.6% ($p = 0.05$) HDL-C increase. Patients with fasting TGs less than 95 mg/dL had a 4.1% ($p > 0.05$) increase in their HDL-C. The authors concluded that gemfibrozil raises HDL-C and lowers TG concentrations similar to those seen in hyperlipidemic men in the Helsinki Heart Study[62] (HDL-C increase of 11%).

In a recent study of 23 patients with isolated low HDL-C (mean ± SD 35 ± 3 mg/dL), bezafibrate 400 mg/d once in the evening with dinner was evaluated.[63] After 6 months of therapy, bezafibrate increased HDL-C concentrations from 35 ± 3 to 40 ± 2.2 mg/dL ($p < 0.001$). Eight of 23 patients did not respond to bezafibrate. The study concluded that since most patients with low HDL-C concentrations have a defect in postprandial lipoprotein metabolism, bezafibrate reduces the concentrations of these atherogenic lipoproteins and increases HDL-C concentrations. Bezafibrate is recommended in high-risk patients with isolated low HDL-C concentrations.

HMG-CoA REDUCTASE INHIBITORS

The HMG-CoA reductase inhibitors include lovastatin, pravastatin, simvastatin, and fluvastatin. These agents inhibit HMG-CoA reductase, which is a key rate-limiting enzyme in cholesterol biosynthesis. As a class, these agents increase HDL-C an average of 5–15%.[1] Their main lipid-lowering activity is a 20–40% reduction of LDL-C.[1] These agents are well tolerated.

Vega and Grundy[64] compared lovastatin and gemfibrozil in 22 normolipidemic men with hypoalphalipoproteinemia. The study used a randomized, crossover design consisting of two phases of drug therapy that alternated with two placebo control phases. The lovastatin and gemfibrozil dosages were 20 mg and 600 mg bid, respectively. Overall, both lovastatin and gemfibrozil caused a small and statistically significant increase in HDL-C (9%) and lovastatin produced the best change in overall lipoprotein cholesterol and apolipoprotein B concentrations. The authors concluded that even though lovastatin does not appreciably raise HDL-C per se, it favorably modifies the lipoprotein profile in normolipidemic patients with low HDL-C concentrations and should mitigate any harmful effect of a low HDL-C concentration. They also stated that niacin is the preferable agent in patients with isolated low HDL-C and should be tried first.

More recently, the Scandinavian Simvastatin Survival Study randomized 4444 patients with CHD to receive sim-

vastatin or placebo.[65] Simvastatin 10–40 mg/d was shown to induce greater mean changes in total cholesterol, triglycerides, LDL-C, and HDL-C. The simvastatin group also had a 3.3% lower mortality rate and 6.7% fewer major coronary events compared with placebo.

Summary

The NCEP's second report attributed a greater significance to a low HDL-C concentration on CHD risk. HDL-C concentrations should be measured with initial cholesterol screening. The exact protective mechanisms of HDL-C on atherosclerosis is not fully understood, but appears to involve at least reverse cholesterol transport.

Lifestyle modifications, including smoking cessation, dietary intervention, weight loss, aerobic exercise, and moderate alcohol intake, have favorable effects on HDL-C. Screening patients' medication profiles for medications that secondarily lower HDL-C and switching to lipid-neutral agents are important. Estrogen replacement therapy in postmenopausal women is advocated. The use of lipid-altering agents to raise an isolated low HDL-C may be needed in patients with established CHD or risk factors. Treatment of HDL-C lower than 39 mg/dL is recommended in subjects in whom the plasma total cholesterol is higher than 193 mg/dL.[49] However, familial hypoalphalipoproteinemia is usually refractory to pharmacotherapy. If pharmacotherapy is to be used, nicotinic acid appears effective at increasing an isolated low HDL-C concentration. Besides trying to increase HDL-C, a reduction in LDL-C remains a major therapeutic goal, especially in patients in whom prevention of secondary morbidity and/or mortality is a goal. A trial involving pharmacotherapy in a large number of patients with isolated low HDL-C concentrations is needed to determine whether raising HDL-C translates to a reduced incidence of CHD. ≏

References

1. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. National Cholesterol Education Program: second report of the expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel II). Circulation 1994;89:1329-445.
2. NIH Consensus Conference. Triglyceride, high-density lipoprotein, and coronary heart disease. JAMA 1993;269:505-10.
3. Gordon DJ, Probstfield JL, Garrison RJ, Neaton JD, Castelli WP, Knoke JD, et al. High-density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies. Circulation 1989;79:8-15.
4. Grundy SM. Atherogenic dyslipidemia: lipoprotein abnormalities and implications for therapy. Am J Cardiol 1995;75:45B-52B.
5. Miller M, Kwiterovich PO Jr. Isolated low HDL-cholesterol as an important risk factor for coronary heart disease. Eur Heart J 1990;11(suppl H):9-14.
6. Tall AR. Plasma high density lipoproteins metabolism and relationship to atherogenesis. J Clin Invest 1990;86:379-84.
7. Frohlich JJ, Pritchard PH. The clinical significance of serum high density lipoproteins. Clin Biochem 1989;22:417-23.
8. Stone NJ. Secondary causes of hyperlipidemia. Med Clin North Am 1994;78:117-41.
9. Houston MC. New insights and new approaches for the treatment of essential hypertension: selection of therapy based on coronary heart disease risk factor analysis, hemodynamic profiles, quality of life, and subsets of hypertension. Am Heart J 1989;117:911-51.
10. Rosenson RS. Low levels of high-density lipoprotein cholesterol (hypoalphalipoproteinemia) an approach to management. Arch Intern Med 1993;153:1528-38.
11. Rubins HB, Schectman G, Wilt TJ, Iwane MK. Distribution of lipid phenotypes in community-living men with coronary heart disease. Arch Intern Med 1992;152:2412-6.
12. Lamarche B, Després JP, Moorjani S, Cantin B, Dagenais GR, Lupien PJ. Prevalence of dyslipidemic phenotypes in ischemic heart disease (prospective results from the Québec Cardiovascular Study) Am J Cardiol 1995;75:1189-95.
13. Silverman DI, Pasternak RC. High-density lipoprotein subfractions. Am J Med 1993;94:636-45.
14. Stampfer MJ, Sacks FM, Salvini S, Willett WC, Hennekens CH. A prospective study of cholesterol, apolipoproteins, and the risk of myocardial infarction. N Engl J Med 1991;325:373-81.
15. Gordon DJ, Rifkind BM. High-density lipoprotein — the clinical implications of recent studies. N Engl J Med 1989;321:1311-6.
16. Drexel H, Amann FW, Beran J, Rentsch K, Candinas R, Muntwyler J, et al. Plasma triglycerides and three lipoprotein cholesterol fractions are independent predictors of the extent of coronary atherosclerosis. Circulation 1994;90:2230-5.
17. Gotto AM. Dyslipidemia and atherosclerosis a forecast of pharmaceutical approaches. Circulation 1993;87(suppl III):54-9.
18. Genest JJ Jr, Martin Munley SS, McNamara JR, Ordovas JM, Jenner J, Myers RH, et al. Familial lipoprotein disorders in patients with premature coronary artery disease. Circulation 1992;85:2025-33.
19. Karhapää P, Malkki M, Laakso M. Isolated low HDL cholesterol: an insulin-resistant state. Diabetes 1994;43:411-7.
20. Leighton RF. Management of the patient with low HDL-cholesterol. Clin Cardiol 1990;13:521-32.
21. Criqui MH, Cowan LD, Tyroler HA, Bangdiwalas S, Heiss G, Wallace RB, et al. Lipoproteins as mediators for the effects of alcohol consumption and cigarette smoking on cardiovascular mortality: results from the Lipid Research Clinics Follow-up Study. Am J Epidemiol 1987;126:629-37.
22. Garrison RJ, Kannell WB, Feinleib M, Castelli WP, McNamara PM, Padgett SJ. Cigarette smoking and HDL-C; the Framingham Offspring Study. Atherosclerosis 1978;30:17-25.
23. Moffatt RJ. Effects of cessation of smoking on serum lipids and high density lipoprotein-cholesterol. Atherosclerosis 1988;74:85-9.
24. Glantz SA, Parmley WW. Passive smoking and heart disease: epidemiology, physiology, and biochemistry. Circulation 1991;83:1-12.
25. Moskowitz WB, Mosteller M, Schieken RM, Bossano R, Hewitt JK, Bodurtha JN, et al. Lipoprotein and oxygen transport alterations in passive smoking preadolescent children; the MCV twin study. Circulation 1990;81:586-92.
26. Dannenberg AL, Keller JB, Wilson PWF, Castelli WP. Leisure time physical activity in the Framingham Offspring Study: description, seasonal variation, and risk factor correlates. Am J Epidemiol 1989;129:76-88.
27. Thompson PD, Cullinane EM, Sady SP, Flynn MM, Chenevert CB, Herbert PN, et al. High density lipoprotein metabolism in endurance athletes and sedentary men. Circulation 1991;84:140-52.
28. Wood PD, Haskell WL, Blair SN, Willigas PT, Krauss RM, Lindgren FT, et al. Increased exercise level and plasma lipoprotein concentrations: a one-year, randomized, controlled study in sedentary, middle-aged men. Metabolism 1983;32:31-9.
29. Tran ZV, Weltman A, Glass GV, Mood DP. The effects of exercise on blood lipids and lipoproteins: a meta-analysis of studies. Med Sci Sports Exerc 1983;15:393-402.
30. Kannell WB, Gordon T, Castelli WP. Obesity, lipids and glucose intolerance: the Framingham study. Am J Clin Nutr 1979;32:1238-45.
31. Brownell KD, Stunkard AJ. Differential changes in plasma high-density lipoprotein cholesterol levels in obese men and women during weight reduction. Arch Intern Med 1981;141:1142-6.
32. Anderson KM, Wilson PWF, Garrison RJ, Castelli WP. Longitudinal and secular trends in lipoprotein cholesterol measurement in a general population sample: the Framingham Offspring Study. Arterioscler Thromb Vasc Biol 1983;3:273-81.
33. Berns MA, DeVries JH, Katan MB. Increase in body fatness as a major determinant of changes in serum total cholesterol and high density lipoprotein cholesterol in young men over a 10-year period. Am J Epidemiol 1989;130;1109-22.

34. Langer RD, Criqui MH, Reed DM. Lipoproteins and blood pressure as biological pathways for effect of moderate alcohol consumption on coronary heart disease. Circulation 1992;85:910-5.
35. Weidner G, Connor SL, Chesney MA, Burns JW, Connor WE, Matarazzo JD, et al. Sex differences in high density lipoprotein cholesterol among low-level alcohol consumers. Circulation 1991;83:176-80.
36. Henkin Y, Como JA, Oberman A. Secondary dyslipidemia. Inadvertent effects of drugs in clinical practice. JAMA 1992;267:961-8.
37. Godsland IF, Crook D, Simpson R, Proudler T, Felton C, Lees B, et al. The effects of different formulations of oral contraceptive agents on lipid and carbohydrate metabolism. N Engl J Med 1990;323:1375-81.
38. Byington RP, Worthy J, Craven T, Furberg CD. Propranolol-induced lipid changes and their prognostic significance after a myocardial infarction: the Beta-Blocker Heart Attack Trial experience. Am J Cardiol 1990;65:1287-91.
39. Stampfer MJ, Colditz GA. Estrogen replacement therapy and coronary heart disease; a quantitative assessment of the epidemiologic evidence. Prev Med 1991;20:47-63.
40. Barrett-Connor E, Bush TL. Estrogen and coronary heart disease in women. JAMA 1991;265:1861-7.
41. Grady D, Rubin SM, Petitti DB, Fox CS, Black D, Ettinger B, et al. Hormone therapy to prevent disease and prolong life in postmenopausal women. Ann Intern Med 1992;117:1016-37.
42. Belchetz PE. Hormonal treatment of postmenopausal women. N Engl J Med 1994;330:1062-71.
43. Cauley JA, LaPorte RE, Kuller LH, Bates M, Sandler RB. Menopausal estrogen use, high density lipoprotein cholesterol subfractions and liver function. Atherosclerosis 1983;49:31-9.
44. Fahraeus L, Wallentin L. High density lipoprotein subfractions during oral and cutaneous administration of 17 beta-estradiol to menopausal women. J Clin Endocrinol Metab 1983;56:797-801.
45. Jensen J, Nilas L, Christiansen C. Cyclic changes in serum cholesterol and lipoproteins following different doses of combined postmenopausal hormone replacement therapy. Br J Obstet Gynaecol 1986;93:613-8.
46. Krauss RM, Perlman JA, Ray R, Petitti D. Effects of estrogen dose and smoking on lipid and lipoprotein levels in postmenopausal women. Am J Obstet Gynecol 1988;158:1606-11.
47. Granfone A, Campos H, McNamara JR, Schefer MM, Lamon-Fava S, Ordovas JM, et al. Effects of estrogen replacement on plasma lipoproteins and apolipoproteins in postmenopausal, dyslipidemic women. Metabolism 1992;41:1193-8.
48. Applebaum-Bowden D, McLean P, Steinmetz A, Fontana D, Matthys C, Warnick GR, et al. Lipoprotein, apolipoprotein, and lipolytic enzyme changes following estrogen administration in postmenopausal women. J Lipid Res 1989;30:1895-906.
49. Barter PJ. Management of low HDL cholesterol. Aust Fam Physician 1995;24:2066-74.
50. Pool JL, Taylor AA, Nelson EB. Review of the effects of doxazosin, a new selective alpha-adrenergic inhibitor, on lipoproteins in patients with essential hypertension. Am J Med 1989;87(suppl 2A):57-61.
51. LaRosa JC, Cleeman JI. Cholesterol lowering as a treatment for established coronary heart disease. Circulation 1992;85:1229-35.
52. Castelli WP. Cardiovascular disease and multifactorial risk: challenge of the 1980's. Am Heart J 1983;106:1191-200.
53. Kreisberg RA. Low high-density lipoprotein cholesterol: what does it mean, what can we do about it, and what should we do about it? Am J Med 1993;94:1-6.
54. Kolovou GD, Fostinis YP, Bilionou HI, Cokkinos DV. Response of high-density lipoproteins to hypolipidemic drugs according to their initial level. Am J Cardiol 1995;75:293-5.
55. Schulman KA, Kinosian B, Jacoboson TA, Glick H, William MK, Kofler H, et al. Reducing high blood cholesterol level with drugs. Cost-effectiveness of pharmacologic management. JAMA 1990;264:3025-33.
56. Canner PL, Berge KG, Wenger NK, Stamler J, Friedman L, Prineas RJ, et al. Fifteen year mortality in coronary drug project patients: long-term benefit with niacin. J Am Coll Cardiol 1986;8:1245-55.
57. McKenney JM, Proctor JD, Harris S, Chinchili VM. A comparison of the efficacy and toxic effects of sustained- vs. immediate-release niacin in hypercholesterolemic patients. JAMA 1994;271:672-7.
58. King JM, Crouse JR, Terry JG, Morgan TM, Spray BJ, Miller NE. Evaluation of effects of unmodified niacin on fasting and postprandial plasma lipids in normolipidemic men with hypoalphalipoproteinemia. Am J Med 1994;97:323-31.
59. Lavie CJ, Mailander L, Milani RV. Marked benefit with sustained-release niacin therapy in patients with "isolated" very low levels of high-density lipoprotein cholesterol and coronary artery disease. Am J Cardiol 1992;69:1083-5.
60. Martin-Jadraque R, Tato F, Mostaza JM, Vega GL, Grundy SM. Effectiveness of low-dose crystalline nicotinic acid in men with low high-density lipoprotein cholesterol levels. Arch Intern Med 1996;156:1081-8.
61. Miller M, Bachorik PS, McCrindle BW, Kwiterovich PO Jr. Effect of gemfibrozil in men with primary isolated low high-density lipoprotein cholesterol: a randomized, double-blind, placebo-controlled, crossover study. Am J Med 1993;94:7-12.
62. Frick MH, Elo O, Haapa K, Heinonen O, Heinsalmi P, Helo P, et al. Helsinki Heart Study: primary-prevention trial with gemfibrozil in middle-aged men with dyslipidemia. N Engl J Med 1987;317:1237-45.
63. Weintraub MS, Grosskopf I, Charach G, Mor R, Rubinstein A, Wollman Y, et al. Bezafibrate therapy in patients with isolated low high-density lipoprotein cholesterol levels may have a beneficial effect in prevention of atherosclerosis. Metabolism 1995;44:1401-9.
64. Vega GL, Grundy SM. Comparison of lovastatin and gemfibrozil in normolipidemic patients with hypoalphalipoproteinemia. JAMA 1989;262:3148-53.
65. Scandinavian Simvastatin Survival Study Group. Randomized trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994;344:1383-9.

EXTRACTO

OBJETIVO: Presentar información sobre la función, estructura, e importancia de la lipoproteína de densidad elevada (LDE) y evaluar la literatura actual con relación a la controversia del manejo de pacientes con un nivel bajo "aislado" de LDE.

FUENTES DE INFORMACIÓN: Se realizó una búsqueda en MEDLINE (1966 al juino 1996) para identificar artículos clínicos y de repaso en el idioma inglés, pertinentes a LDE. Algunos artículos fueron identificados a través de la bibliografía de artículos seleccionados.

SELECCIÓN DE FUENTES DE INFORMACIÓN: Todos los artículos se consideraron para posible inclusión en el repaso. Información pertinente, según juzgada por los autores, fue seleccionada para discusión.

MÉTODO DE EXTRACCIÓN DE INFORMACIÓN: Estudios sobre lípidos, de importancia histórica, artículos de repaso recientes, y pruebas clínicas incluyendo tratamiento para LDE fueron evaluados.

SÍNTESIS: La estructura, función, medición de LDE, y el estado de un nivel bajo aislado de LDE fueron discutidos como trasfondo. Medidas para la modificación del estilo de vida para aumentar LDE, medicamentos a evitar, reemplazo de estrógeno, y agentes que alteran los lípidos, utilizados para aumentar un nivel bajo aislado de LDE son presentados.

CONCLUSIONES: Un nivel bajo aislado de LDE presenta un riesgo de enfermedad cardíaca coronaria. El manejo de este estado es controversial. El primer paso en el manejo está en acuerdo con los expertos e incluye modificación en el estilo de vida (reducción de peso, dieta, dejar de fumar, y ejercicio aeróbico). La terapia de reemplazo de estrógeno y el descontinuar fármacos que secundariamente bajan LDE son otras opciones de tratamiento. El uso de agentes que alteran los lípidos ha sido utilizado en algunos pacientes. El ácido nicotínico parece ser un agente efectivo para LDE baja aislada. Una prueba clínica extensa evaluando el efecto de tratar LDE baja aislada para la prevención primaria y secundaria de eventos coronarios es necesaria.

BRENDA R MORAND

RÉSUMÉ

OBJECTIF: Illustrer le rôle, la structure, et l'importance du cholestérol contenu dans la fraction lipoprotéique de densité élevée (LDE) et évaluer la littérature actuelle pertinente à la controverse du traitement des patients ayant un cholestérol LDE bas.

REVUE DE LITTÉRATURE: Une recherche dans la banque informatisée MEDLINE de 1966 à juin 1996 a été effectuée afin d'identifier les articles de langue anglaise traitant du cholestérol LDE. Quelques articles ont été identifiés à partir de la bibliographie de certains autres articles.

SÉLECTION DES ÉTUDES: Tous les articles ont été considérés pour inclusion dans cette revue. L'information pertinente, selon le jugement des auteurs, a été sélectionnée pour discussion.

SÉLECTION DE L'INFORMATION: Les études passées faisant autorité sur les lipides, les articles de revue récents, et les essais cliniques sur le traitement du cholestérol LDE ont été évalués.

RÉSUMÉ: La structure, le rôle, et la mesure du cholestérol LDE, ainsi que le LDE bas comme seule modification des fractions lipoprotéiques sont discutés. Les mesures de modification des habitudes de vie afin d'augmenter le cholestérol LDE, les médicaments à éviter, l'estrogénothérapie de remplacement et les médicaments pouvant augmenter le cholestérol LDE seul sont présentés.

CONCLUSIONS: Un cholestérol LDE bas sans modification des autres fractions lipoprotéiques est un facteur de risque de maladie coronarienne. La conduite à tenir dans ce cas est controversée. La première étape, selon les experts, consiste en la modification des habitudes de vie (perte de poids, diète appropriée, cessation de fumer, et exercice physique). L'estrogénothérapie de remplacement et l'arrêt des médicaments diminuant secondairement le cholestérol LDE sont des options additionnelles de traitement. L'emploi de médicaments élevant le cholestérol a été fait chez quelques patients. L'acide nicotinique semble efficace pour les cas de cholestérol LDE bas isolé. Une étude clinique d'envergure afin de mesurer l'efficacité du traitement du cholestérol LDE bas en prévention primaire ou secondaire des événements coronariens est souhaitable.

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