Lipoprotein(a) Status in Coronary Heart Disease

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Abstract

Objective: To compare the magnitude of lipid, and lipoproteins, especially the lipoprotein(a) p(a)], in controls and patients with coronary heart disease (CHD).

Methods: Serum total cholesterol, triglyceride, HDL-C, LDL-C, VLDL-C, apo Al, apo B, and Lp(a) levels were determined in 37 patients with CHD and 25 age matched control subjects.

Results: A significant difference (P<0.001) in lipid and apolipoprotein ratios were found. Lp(a) and other lipid parameters were found significantly high (P<0.001) with the exception of HDL-C and aN B which were significantly low (P<0.001) in CHD patients.

Conclusions: Elevated levels of Lp(a) suggest not only its role in atherogenesis, leading to CHD, hut also that Lp(a) should be given due consideration while assessing CHD risk (JPMA 50:47, 2000).

Introduction

Coronary heart disease (CHD) is the leading cause of mortality in the United States, and is endemic in the developing world[1]. Coronary atherosclerosis results from multi-factorial progressive vascular alterations that lead to the development of plaque within the coronary arteries[2] The atherosclerotic plaque eventually results in decreased coronary blood flow reserve and subsequent myocardial ischemis[3].

CHO is diagnosed when there is documented evidence of myocardial infarction (recent or past) or documented evidence of angina with subsequent sudden death or congestive heart failure[4]. Hypertension, hypercholesterolaem ia, cigarette smoking[5,6], diabetes mellitus and high-fat diet are considered as important risk factors in the development of CHD[6], Elevated serum concentrations of cholesterol, low-density lipoprotein cholesterol (LDL-C), and low serum concentration of high-density lipoprotein cholesterol (HDL-C) are associated with an increased Fisk of acute coronary events and premature at hemscleros is[7,8]. A study shows that a combination of HDL-C, apolipoprotein Al (apo Al), apolipoprotein B (apo 13), atid lipoprotein (a) p(ajj are useful in predicting coronary artery disease risk[9].

Lp(a) is an additional evolving lipoprotein risk factor[10], discovered by Berg in 1963[11], that structurally resembles low-density lipoprotein (LDL). It consists of apolipoprotein(a) po (a)], which is attached to apolipoprotein B-100 by a disulphide bridge[12-16]. Apo(a) is structurally related to plasniinogen, although it has no plasminogen activity. Lp(a) is mainly synthesized by the liver[17] and its physiological role is so far not known. However it has been speculated that Lp(a) delivers cholesterol to cells at wound sites, and this function may become pathological when plasma levels of Lp(a) are high. Excessive uptake and catabolism of Lp(a) by very-low-density lipoprotein (VLI)L) receptors in vascular cells and in macrophages of atherosclerotic lesions, may lead to lipid accumulation by these cells, and may account in part for the atherogenecity of this lipoprotein[18]. The present study was undertaken to determine and compare the levels of Lp(a) and lipid profile in control subjects and in patients with GHD.

Materials and Methods

Sera were collected from 37 patients (35-65years) with CHD and 25 age matched control subjects who had fasted overnight. Mean body mass index was 26.3 (SEM. 0.5) and 24.2 (SEM. 0.34) for the patients and controls, respectively. Controls were physicians who had no evidence of cardio-vascular disease, recent or past, at the time of sample collection. Coronary heart disease patients, who had first attack of myocardial infarction within the last seven days, were selected. A number of agents, such as estrogen, tamoxifen, niacin, gemfibrozil, omega-3 fatty acids, N-acetylcysteine, prednisone and neomycin, have been reported to lower circulating Lp(a) levels[19]. Therefore, only those patients or control subjects, who were not taking any of the aforementioned drugs, were included in this study. Serum total cholesterol, HDL-C, and triglycerides were analyzed enzymatically, using the kits supplied by Bio-Systems, Spain. LDL-C was calculated by a modification[20] of the Friedwald formula[21]. Very-low-density lipoprotein cholesterol (VLDL-C) was calculated according to the formula proposed by Wilson[22]. Lipid ratios, [HDL-C]/[total cholesterol], [LDL-C] / [total cholesterol], [HDL-C]23, were also calculated. Apo Al and Apo B were quantified from serum by immuno turbidimetric method, using the kits obtained form Boehringer Mannheim GmbH, Germany. The serum Lp(a) concentrations were determined by an enzyme linked immunosorbent assay (Immuno-Diagnostics, USA).
Statistical Analysis: The results are expressed as mean + SEM and the differences in lipid profiles were tested by Student\'s t-test.

Results

Serum lipid and lipoprotein concentrations were measured in 25 controls and 37 patients with CHD. The control and CHD groups were comparable in age, with means and SEM of 50.2 + 2.1 years (control group) and 54.2+1.3 years (CHD group).
Lipid and lipoprotein concentrations in the control and CHD groups, showed a significant increase (P<0.001) in the magnitude of total cholesterol, triglycerides, LDL-C, VLDL-C, Apo V and Lp(a), however, a significant dectease (P<0.001) was observed in HDL-C and Apo Al concentrations (Table 1)

Table 1. Serum Lipid and Lipoprotein concentrations in control subjects and CHD patients.

	Control (n=25)	Coronary Heart Disease (n=37)
Gender (Male/Female)	12/13	28/9
AGE (Years)	50.2 ± 2.1	54.2 ± 1.3#
Cholesterol (mg/dl)	177.32 ± 3.1	267.51 ± 6.81**
Triglycerides (mg/dl)	105.36 ± 4.2	174.24 ± 3.22**
HDL-C (mg/dl)	55 ± 1.3	36.02 ± 0.7**
LDL-C (mg/dl)	94.14 ± 3.31	187.02 ± 7.04**
VLDL-C (mg/dl)	21.07 ± 0.83	34.59 ± 0.71**
Apo A-1 (mg/dl)	104.52 ± 2.41	87.59 ± 1.22**
Apo B (mg/dl)	81.36 ± 2.51	143.1 ± 4.25**
Lp (a) (mg/dl)	23.73 ± 0.87	31.92 ± 0.99**

** P <0.001 as compared to control subjects.
# p value non-significant as compared to control subjects.

in CHD group, as compared to control subjects. The control and CHD group when compared showed a significant difference (P<0.001) in the lipid and apolipoprotein ratios (Table 2).

Table-2. Serum lipid and Lipoprotein ratios in control subjects and CHD patients.

	Control (n=25)	Coronary Heart Disease (n=37)
HDL-C/Cholesterol	0.3 + 0.01	0.1 + 0.01**
LDL-C/Cholesterol	0.5 + 0.02	0.7 + 0.02**
Apo A1/Apo B	1.3 + 0.03	0.6 + 0.02**
LDL-C/Apo B	1.2 + 0.04	1.3 + 0.02*
LDL-C/HDL-C	1.7 + 0.1	5.3 + 0.2**

** P <0.001 as compared to control subjects.
* P <0.05 as compared to control subjects.

Discussion

Epidemiologic and prospective studies have shown that the elevated levels of Lp(a) are related to CUD and Lp(a) deposits have been shown in atherosclerotic plaques of native arteries and in arterial bypass grafts[24-28]. However, among other studies, the Helsinki Heart Study[29] and the Physcians Health Study[30] have failed to show a relationship between serum Lp(a) and CHD. The reason for these observations is unclear. Bostom and colleagues[31] provided the first prospective evidence that elevated Lp(a) determined at baseline examination, is an independent risk factor for the development of premature CHD. Numerous studies have now demonstrated that Lp(a) concentrations are increased in patients with established CHD[13,20,32,33]. Our results also show significantly increased concentrations of Lp(a) in CUD patients.

Hargreaves et al[34] reported no relation of serum total cholesterol concentration to CHD. He noted no significant difference in the total cholesterol levels of subjects with and without CUD whereas, the LDL-C concentrations were significantly higher and HDL-C concentrations were significantly lower in patients with CUD as compared to those without CUD. He showed that both, raised LDL-C and low HDL-C are contributory to the development of CUD. Wu and associates9 found no significant difference in total cholesterol, triglycerides and LDL-C concentrations in Cl-ID patients and in control subjects. However, they reported lower HDL-C and apo A I, and higher levels of apo B and Lp(a) in CHD patients. In the United States, the Framingham Heart Study[35] has shown that tile incidence of CHD is positively associated with raised serum total cholesterol levels.

Serum cholesterol has been widely accepted as a risk factor for CUD, although high and low concentrations of cholesterol in LDL and HDL fractions respectively are more predictive of CUD. On the other hand, a clear association between increased concentrations of apo B and decreased amounts of apo A I and CHD has been reported. Furthermore, individuals with increased concentrations of Lp(a) have a greater risk of developing CUD[33]. Epidemiological studies have established a strong inverse

association of HDL-C concentration with CHD[36,37]. However, a study[38] reported the investigation of 5 healthy subjects with very low HDL-C concentrations and having no evidence of an early onset of CHD. Sandkamp and co-workers[20] reported significantly increased concentrations of total cholesterol, LDL-C, apo B and Lp(a) and decreased concentrations of HDL-C and apo M in CHD patients than in control subjects. Our results are in agreement with the observations of Sandkamp and coworkers[20]. Ratios between various serum concentrations of lipids or apolipoproteins have been proposed as risk markers of CUD. Best ratios for the detect ion of risk of CUD are DL-C] / DL-C] and [HDL-C]/[cholestrol] (23). Buring et al.29 have also emphasized that [LDL-C]/[HDL-c] is particulary a strong predictor of the presence and severity of the coronary heart disease. Munster Heart Study40 reported elevated [LDL-C]/[HDL-C] ratio in group of patients with CHD as compared to those without CHD. This 8 years follow-up study also showed a lineara increase in CHD events with increasing [LDL-C]/[HDL-C] ratios, with a steep increase at a ratio of 5. The findings of the present study revealed elevated ratios of [LCL-C]/[HDL-C] and decreased ratios of [HDL-C]/[choiesterol] in CHD patients as compared to the control subjects.

In conclusion, our study demonstrates a significant relationship between elevated levels of Lp(a) and CHD. The elevation of serum Lp(a) can also prove as a useful tool in the prediction of onset of CHD.

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