LIPOPROTEIN (a) LEVELS IN ALCOHOL DRINKING AND ALCOHOL NON-DRINKING CORONARY ARTERY DISEASE PATIENTS

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ABSTRACT

This study examines the role of alcohol drinking on lipoprotein(a) [Lp(a)] levels in angiographically assessed coronary artery disease patients. A lower Lp (a) level was noted in the alcohol drinking group as compared to the alcohol non-drinking group.

KEY WORDS : Lipoproteins, Alcohol, Coronary Artery disease

INTRODUCTION

The clinical and experimental evidence has suggested that raised lipoprotein (a) [Lp (a)] levels may have atherogenic and thrombogenic potentials leading to the development of premature coronary artery disease (CAD) and stroke (1-3). Persons with Lp (a) levels greater than 30 mg/dl have a risk of myocardial-infarction (MI) 1.75 times more than subjects with Lp (a) levels lower than 30 mg/dl, specially in the younger age group. An overwhelming number of case control studies including those from our laboratory have shown increased Lp (a) levels in patients of atherosclerotic disorders as compared to matched controls (4-7).

A few recent prospective studies (8) have strongly supported the independent association between Lp (a) and atherosclerosis. Biochemical and immunological studies have demonstrated the presence of Lp (a) in arterial atheroma. Lp (a) concentration in serum has also been reported to be a predictor of vein graft occlusion after bypass surgery (9) further strengthening its role in atherogenesis. The exact function of Lp (a) is not known, though it is tempting to sepculate that its function is similar to LDL and hence its atherogenecity. Another school of thought is that probably apo (a) has some affinity for arterial intima and despite its much lower concentration than LDL manages to initiate and aggravate atherosclerosis (10,11).

Although Lp (a) has been suggested to act as an independent pathogen, its levels are not totally controlled by the apo (a) gene locus. Other factors like lipoprotein lipase, abetalipoproteinemia and LDL-receptor activity also affect Lp (a) levels including genes like apo-E; Apo-E2 has been associated with lower Lp (a) levels and apo-E4 allele with higher levels of Lp (a). Endothelial dysfunction and local inflammation is reported to alter the Lp (a) levels, as well as certain physiological and disease states including pregnancy, menopause, diabetes mellitus, liver and renal disease, hypertension, abdominal aortic aneurysms and seropositive rheumatoid arthritis (3).

The reported strict genetic control of plasma Lp (a) levels and its association with early myocardial infarction are of particular relevance to predictive medicine. However, no data is available on the status of plasma Lp (a) levels and/or apo (a) genotype polymorphism in Indian population. Hence the study of apo (a) genotypes would play an important role in understanding the specific apo (a) gene which is more prevalent in the patient population and its association with CAD.

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There are no clear environmental factors known which modulate Lp (a) activity in plasma. Recently a 30% rise in Lp (a) levels has been observed in people consuming trans-fatty acids (12). However, age, sex, alcohol, dietary fatty acids or dietary cholesterol are reported to have negligible effect on plasma Lp (a) levels (12). Low to moderate alcohol consumption is associated with a reduction in mortality from ischemic heart disease. However, it is not known whether alcohol drinking affects Lp (a) levels, thereby modulating the cardiovascular risk factors. Hence, the study of Lp (a) levels in alcohol drinking and alcohol nondrinking angiographically assessed CAD patients should help in understanding the putative contribution of Lp (a), as well as of alcohol in pathogenesis of CAD. We report here a preliminary study in this regard.

MATERIALS AND METHODS

The subjects consisted of 114 consecutive male patients (mean age = 51 ± 9 yrs) undergoing coronary arteriography for chest pain. Thirty CAD patients without evidence of atherosclerosis as assessed by coronary angiography served as controls (mean age = 50 ± 11 yrs). The patients and controls were divided into alcohol drinking and alcohol nondrinking groups based upon self-reports. Those reported to consume the equivalent of about 30 to 60 g pure alcohol/day at least three times a week were included into the alcohol drinking group. The duration of alcohol drinking varied from two to many years.

Blood samples were collected in EDTA containing tubes. Plasma was snap-frozen in liquid nitrogen within an hour of blood collection.

Plasma Lp (a) was assayed by ELISA technique using a commercial kit (Boehringer Mannheim).

Total cholesterol and cholesterol content of the various lipoprotein subfractions (LDL & HDL), separated by selective chemical precipitation, were assayed by using enzymatic kits of Randox, U.K. Triglycerides were estimated by fully enzymatic kits obtained from Boehringer Mannheim.

RESULTS AND DISCUSSIONS

The Lp (a) levels in the study subjects are presented in Table 1. They were considerably higher (24.1 ± 17.8 mg/dl) in CAD patients as compared to the controls (16.5 ± 14.8 mg/dl). A

Table 1. Plasma levels of Lp (a), lipids and lipoproteins (mg/dl) in alcohol drinking and alcohol non-drinking CAD patients

Group	Lp (a)	Cholesterol	LDL	HDL	VLDL	Triglycerides
CAD Patients (N=114)	24.29 ± 21.2	196.9 ± 47.8	113.5 ± 33.2	38.8 ± 5.9	47.9 ± 14.2	173.7 ± 73.9
Drinkers (N=59)	22.6 ± 15.5	201 ± 53	113.3 ± 31.7	38.1 ± 5.8	46.7 ± 12.4	175 ± 68.6
Nondrinkers (N=55)	26.1 ± 26	192.5 ± 41.5	113.8 ± 35	39.6 ± 5.9	49.3 ± 16	172.4 ± 80
Controls (N=30)	16.88 ± 15.2	201.2 ± 37.4	114.1 ± 29.5	40.7 ± 4.6	44.5 ± 14	151.8 ± 49.9
Drinkers (N=14)	14.8 ± 11.7	203.9 ± 47.6	120 ± 37.6	40.6 ± 3.6	43.3 ± 14.4	151 ± 59.6
Non-drinkers (N=16)	18.7 ± 17.9	198.9 ± 26.9	109 ± 20	40.9 ± 5.4	45.6 ± 14	152.5 ± 41.7

Values are mean ± SD

difference in Lp (a) levels was observed between drinking and non-drinking groups. Alcohol drinking subjects (patients or controls) showed lower levels than alcohol non-drinkers although this difference was not statistically significant. Alcohol drinking patients with a positive family history of CAD showed a lower level ($p < 0.05$) as compared to patients with a negative family history (Table 2).

Table 2. Plasma levels of Lp (a) in CAD patients with a positive or a negative family history (FH) for CAD.

Group	Lp (a) levels (mg/dl)	
	Positive FH	Negative FH
Drinkers (N=39)	18.6 ± 14.4	26.8 ± 22.4
Nondrinkers (N=38)	28.7* ± 20.1	26.2 ± 24.3

* $p < 0.05$ (Drinkers vs non-drinkers)

Moreover, no significant difference in serum lipids (total cholesterol, LDL-cholesterol, VLDL-cholesterol, HDL-cholesterol or triglycerides) was observed amongst any of the groups (Table 1).

Among the CAD patients and controls, although there was positive correlation seen between alcohol drinking, smoking habits and intake of non-vegetarian diet, yet the alcohol drinking subjects showed lower LP (a) levels (Table 1 & 2) than non-drinkers.

There are few studies available on the effect of alcohol abuse and withdrawal on the level of Lp (a) in sera of healthy subjects and CAD patients (13-16). Our results might mean that alcohol consumption either reduces Lp (a) synthesis in the liver and/or increases catabolism of Lp (a). It has been suggested that acetaldehyde could accelerate the rate of Lp (a) catabolism in a similar manner as reported for LDL (17).

The results of the present study support the widely accepted view that high Lp (a) level is an independent risk factor for atherosclerotic disorders but the direct effect of alcohol consmption and its withdrawal on Lp (a) levels need further detailed studies which are being carried out.

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