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Original Research Article

Serum Lipoprotein (A) In the Etiology of Acute Myocardial Infarction

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Abstract

Cholesterol and triglyceride fats are transported as part of lipoprotein particles in the bloodstream. The various lipoprotein classes Low Density Lipoprotein (LDL) that carry most part of the blood cholesterol, Very Low Density Lipoprotein (VLDL), which carry most of the blood triglycerides, High Density Lipoprotein (HDL) and Chylomicrons. LDL also found as serum cholesterol plays a significant role in coronary heart diseases. The role of these lipoproteins is quite independent of other risk factors and is quite predictive that could be easily assessed. The present article is focused on the estimation of plasma lipoprotein (a) [Lp(a)] level in AMI patients along with their cardiac Troponin-I levels to study the correlation between the two and to look into the possibility of dual marker approach to deal with complications associated with acute myocardial infarction. Lp(a) is a major risk factor of several cardiovascular diseases, namely atherosclerotic vascular diseases, aortic calcification, and perhaps also venous thromboembolic diseases and hence could be a prominent therapeutic target for primary and secondary prevention. This calls for the development of a safe and effective means of lowering Lp(a) that will provide an opportunity to conduct intervention trials to further decipher its contribution in the etiology of CHD.

Keywords: Serum Cholesterol, Acute myocardial infarction, Plasma lipoproteins, Lipoprotein (a).

INTRODUCTION

The clinical and therapeutic interest in lipoprotein(a) [Lp(a)] is mostly due to its role as a prominent cardiovascular risk factor. In several studies Lp(a) levels have been associated with cardiovascular disease although it is not considered an established risk factor [1]. There are various evidences of interaction between Lp(a) and other established and potential cardiovascular risk factors, such as low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and homocysteine [2]. LDL and Lipoprotein(a) has many features in common. However, across different geographical races the distribution of plasma Lp(a) levels is very skewed, ranging from 0.1 to 300 mg/dl in contrast to LDL [3]. The skewed distribution of Lp(a) and the fact that very few subjects have high levels of Lp(a) represent many challenges in firmly associating Lp(a) with any cardiovascular diseases.

Number of clinical trials have shown that an increased level of Lp(a) can be an independent risk factor for developing cardiovascular disease [4]. A meta-analysis of 5436 CHD subjects from 27 prospective studies found that individuals in the upper third of Lp(a) measurements were70% more likely to develop CHD than those individuals in the bottom third [5]. The commonly cited cut-off value for Lp(a) becoming a risk factor is 300 mg/L. Evidence from some other studies suggest that the risk of developing CHD from high Lp(a) level is exacerbated in the presence of other lipids such high levels of LDL and low HDL cholesterol levels, in combination with thrombogenic risk factors such as Factor V Leiden, protein C deficiency and antithrombin III deficiency [6,7]. From this perspective, it is proved that modifiable risk factors in individuals that also have elevated Lp (a) levels should also be considered along with the Lp(a) during treatment.

High levels of Lp(a) may also result into its deposition in human arteries affected by atherosclerosis. Studies have found the deposition Lp (a) being related to the extent of atherosclerosis by immuno-histochemical staining for Lp(a) in the aorta as well as coronary, cerebral and peripheral vessels [8, 9]. Although a number of possible functions have been proposed yet the physiological role of Lp(a) remains unknown because a considerable number of individuals have no detectable Lp(a) with no apparent consequence. Probably the most likely function for Lp(a) is a role in wound healing. This makes biological sense given apo(a)'s affinity for fibrin, its ability to promote cell

division and to carry a cholesterol load that could be used for wound repair. Most of the studies have uncovered an array of biological activities produced by Lp(a) that could explain its role in the development of CHD (Table 3).

MATERIAL AND METHODS

The present study was conducted in Department of Biochemistry, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, Uttar Pradesh, India. Total 50 subjects diagnosed with acute myocardial infarction (AMI) were enrolled for this study. These patients were detected with their cardiac Troponin-I level > 0.200ng/ml and other MI related symptoms as explained by the cardiologists. Samples collected from the patients was centrifuged at 3000 rpm and subjected to analyses using commercial kits. Cardiac Troponin–I and Lp(a) levels were analyzed by chemiluminescence method on AU-480 Beckmann Coulter. All samples were treated in accordance with the Helsinki Declaration.

RESULT AND DISCUSSION

In table 1and 2 of our study we found higher levels of Troponin-I and plasma Lipoprotein (A) in subjects with AMI, indicating that these markers are associated with the etiology of cardiovascular disorders. Lp(a) in considerable number of individuals have undetectable level with no apparent consequence. Most of the research on Lp(a) has centered around elucidating its role in promoting atherosclerosis (table 3). These studies have uncovered an array of biological activities produced by Lp(a) that could explain its role in the development of CHD.

It has been well studied that impaired lipid metabolism plays an prominent role in the pathogenesis of cardiovascular disease and since lipoproteins are the primary constituents of this metabolism, their serum levels tends to be easy biomarker tools that reflect the lipid metabolic pattern and thus can be used for risk stratification and AMI prognosis. A high LDL level is a risk factor for AMI, hence reduction in the LDL level is strongly associated with favorable outcomes in the treatment of AMI patients [10].

Table-1: Levels of Cardiac Troponin-I and Lp(a) in the AMI patients

	Cases (n=50)	**Control (n = 30)**
Age (yrs)	49.5 (35-75)	53.75 (35.6- 75.6)
Troponin-I (ng/ml)	16.14 (18.97- 47.10)	Non-detectable

Table-2: Comparison of plasma lipoprotein A values between cases and controls

	Controls (n=30) Median (IQR)	Cases (n=50) Median (IQR)	p-value
Serum LpA (mg/dl)	11.95 (2.9)	100.85 (90.2)	< 0.001

** The Troponin I was correlated significantly with plasma LpA levels ($r = 0.509$; $p < 0.001$ on Spearman's correlation).

Table-3: Pathogenic Activities of Lipoprotein (a)

Atherogenic Activity	**Thrombogenic Activity**
↑ Permeability of EC layer	↓ Plasminogen activation
↑ Vascular adhesion molecule expression	↑ PAI-1 expression
↑ Chemotaxis of monocytes	↓ TFPI activity
↑ Foam cell formation ↑ SMC proliferation and de-differentiation	↑ Platelet aggregation

EC, endothelial cell; SMC, smooth muscle cell; PAI-1, plasminogen activator inhibitor-1; TFPI, tissue factor pathway inhibitor.

All these facts have shown that knowing a patient's Lp(a) level can lead to some clinical utility. High Lp(a) levels aggravate the risk mediated by conventional risk factors and therefore can help to make treatment decisions to be more intensive hypolipidemic drug treatment and talso will help in starting the treatment quite earlier [11]. High Lp(a) levels can be the reason for reduced LDL-C lowering upon statin treatment because the cholesterol of Lp(a) contributes to the measured or calculated LDL-C but is not targeted by statins [11]. Lp(a) should be considered as an etiological factor not only for atherosclerotic cardiovascular disease but also of venous thromboembolic events, especially in patients where the early onset, progression and recurrence of events in the disease are not well explained by the classic risk factors [12]. In patients with progressing or refractory cardiovascular disease despite possible control of conventional risk factors, high plasma levels of Lp(a) also may serve as the indication to initiate Lp(a)- or LDL-targetted therapeutics and perhaps in the

development of anti-apo(a) antisense oligonucleotides in near future [12, 13].

To infer with, Lp(a) can be seen as a significant risk factor and hence therapeutic target for primary and secondary prevention of several cardiovascular diseases especially atherosclerotic vascular diseases, aortic calcification, and perhaps also venous thromboembolic diseases. Decades of research on Lp(a) have seen it emerge as a clinically important molecule. Several evidences has been there to show the involvement of Lp(a) in the development of CHD to such a point that recommendations can be made for routine measurement of Lp(a) in patients at risk. But the one major challenge that still remains is in developing a therapeutic agent to specifically lower Lp(a) levels. The development of a safe and effective means of lowering Lp(a) will provide the opportunity to conduct intervention trials to further decipher Lp(a)'s contribution to the development of CHD.

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