

ROLE OF LCAT AND HDL IN RELATION TO OXIDATIVE STRESS IN MYOCARDIAL INFARCTION AND ISCHEMIC HEART DISEASE

SHANKAR MANOHAR PAWAR*¹, E PRABHAKAR REDDY, CHITRA NETARE¹ AND T. MOHANA LAKSHMI²

Department of Biochemistry, Sri Lakshmi Narayana Institute of Medical Sciences, Puducherry - 605 002

¹Department of Pathology, Sathya Sai Medical College Hospital, Chengalpet - 603 108

²Department of Microbiology Sri Lakshmi Narayana Institute of Medical Sciences, Puducherry - 605 002

E-mail: dr_pawarsmbio@yahoo.co.in

KEY WORDS

LPO – Lipid Peroxidation
Myocardial Infarction
Ischemic Heart Disease

Received on :

16.12.2010

Accepted on :

12.02.2011

*Corresponding author

ABSTRACT

Lipids are the most susceptible for free radicals attack; it has been found that there is a significant correlation between oxidative stress and HDL cholesterol and LCAT activity. Decrease in ratio between LCAT and HDL to lipid peroxidation has been a diagnostic marker for management of MI and IHD and will be a good marker.

INTRODUCTION

It is widely accepted that age, sex, high blood pressure, smoking, dyslipidemia, and diabetes are the major risk factors for developing cardiovascular disease (CVD) (Cupples and Agostino, 1987). It also is recognized that CVD risk factors cluster and interact multiplicatively to promote vascular risk (Jackson *et al.*, 2005). Researchers also have developed disease-specific formulations to predict risk of developing specific CVD events such as CHD events or stroke (Anderson *et al.*, 1991; Wolf *et al.*, 1991; Murabito *et al.*, 1997; Wilson *et al.*, 1998; Kannel *et al.*, 1999; Assmann *et al.*, 2002; Ferrario *et al.*, 2005). The present investigation is based on the premise that although the impacts of risk factors vary from one specific CVD type to another, there is sufficient commonality of risk factors to warrant generating a single general CVD risk prediction instrument that could accurately predict global CVD risk and the risk of individual components. Individuals with a high global CVD risk require more aggressive risk factor modification. The goal of therapy of dyslipidemia, diabetes, and hypertension should be linked to the global CVD risk. Although atherosclerotic disease-specific profiles are available, a multivariable risk formulation for global CVD made up of standard risk factors is particularly relevant for primary prevention of atherosclerotic CVD because it is intuitive that measures taken to prevent any one CVD outcome can be expected to also prevent risk of the other CVD outcomes. Therefore, use of a general CVD risk score is an attractive option in office-based primary care practices. Serial assessment of global CVD risk could be used to monitor progress of patients on treatment and improvement in their multivariable

risk scores. Other risk factors not included in the general risk profile must be taken into account in evaluating risk and selecting the most efficacious treatment. These include abdominal obesity, ECG evidence of left ventricular hypertrophy and indications of insulin resistance, triglycerides, and a strong family history of premature CVD. Obesity is not included because its influence is largely attributable to its promotion of insulin resistance and its attendant CVD risk factors.

Free radicals are an unstable and extremely reactive chemical species, which have unpaired electrons in their structure. The most important free radicals are the radical's derivatives of oxygen species. These free radicals are by products of energy generation and are formed during oxidation. Lipids are the most susceptible for free radical attack. Acute myocardial infarction (MI) is one important clinical condition in which this free radical mediated endothelial damage is said to play a role. LCAT is a specific enzyme of plasma and acts primarily on the plasma HDL and LDL cholesterol esters found in human plasma. MI is irreversible injury in which necrosis occurs as a consequence of prolonged ischemia. MI occurs as a result of segmental plaque formation in the coronary vessels. This plaque is due to atherosclerotic changes in the intima of coronary arteries (Jain *et al.*, 2000). Therefore this study is undertaken to review status of LCAT and HDL in relation to lipid per oxidation.

MATERIALS AND METHODS

40 patients aged 40-60 years with MI and IHD diagnosed by team of hospital physicians were studied in Rayachur Medical

Table 1: Activity of LCAT, LPO, Cholesterol and lipoprotein levels

Group	LPO nmole/mL Mean± SD	LCAT mg % Mean± SD	Total chol mg % Mean± SD	HDL-C mg % Mean± SD	LDL mg % Mean ±SD	VLDL-C mg % Mean± SD
Healthy	3.40±0.52	9.40±2.35	188.5±27.3	50±8.25	132.2±31	31.8±3.81
MI	6.28±0.63**	3.92±2.01*	245±30.51**	30±5.52	150±8.38*	43.4±4.21
IHD	5.47±0.45**	4.89±2.19	255±25.37*	32±9.72	145±5.78*	45.58*±5.62

* Significant; ** Highly significant

College. All patients gave informed consent for the study and the study was approved by the hospital ethical committee. Results obtained were compared with 40 years age sex matched controls. All parameters were evaluated on serum samples. Lipid per oxidation was measured in terms of Malonaldehyde and pileggi method (Satoh, 1978). Total cholesterol and HDL cholesterol was measured by Wybenga and pileggi method (Whybenga and Piliggi, 1967). LCAT activity was measured by Vivekanandan's method (John, 1971).

RESULTS AND DISCUSSION

Cardiovascular disease (CVD) continued to be growing and major leading cause of morbidity and mortality. It has been predicted that CVD will be one of the most important cause of mortality in India by the year 2015 (Gupta *et al.*, 1995). The diagnosis and management of patients in heart disease is based upon many biochemical tests. Recent studies have shown high prevalence of cardiovascular disease in both urban and rural population. There is also need to study various risk factors with biochemical changes associated with concentration of lipid peroxidation, HDL, LDL, VLDL cholesterol and enzyme LCAT activity. A crucial step in pathogenesis of myocardial infarction and ischemic heart disease is believed to be the oxidative modification of low density lipoproteins and high density lipoproteins played by the free radical process known as lipid peroxidation (LPO) (Steingerg *et al.*, 1990).

The results shown in (Table 1), reveal increased oxidative stress in both MI and IHD. As shown in the table, activity of LCAT is significantly decreased, this result in the decreased esterification of cholesterol, therefore unesterified cholesterol of LDL has been markedly increased, this leads to increased formation of aldehydes. This amounts to surplus oxidative stress. Above data reveals, correlation between ratio of [HDL] and [LCAT] as shown in group 1 and ratio of [HDL] and [LCAT] to lipid Peroxidation.

The present study was carried out to demonstrate the correlation ratio between LCAT and HDL in relation to lipid peroxide which reveals decreased ratio of [HDL] [LCAT] LPO will be a good diagnostic marker for MI and IHD.

REFERENCES

Anderson, K. M., Wilson, P. W., Odell, P. M. and Kannel, W. B. 1991. An updated coronary risk profile: a statement for health professionals. *Circulation*. **83**: 356–362.

Assmann, G., Cullen, P. and Schulte, H. 2002. Simple scoring scheme for calculating the risk of acute coronary events based on the 10-year follow-up of the Prospective Cardiovascular Munster (PROCAM) Study. *Circulation*. **105**: 310–315.

Cupples, L. A., D. and Agostino, R. B. 1987. Section 34: some risk factors related to the annual incidence of cardiovascular disease and death in pooled repeated biennial measurements. In: Kannel WB, Wolf PA, Garrison RJ, eds. *Framingham Heart Study: 30 Year Follow-Up*. Bethesda, Md: US Department of Health and Human Services.

Ferrario, M., Chiodini, P., Chambless, L. E., Cesana, G., Vanuzzo, D., Panico, S., Sega, R., Pilotto, L., Palmieri, L. and Giampaoli, S. 2005. Prediction of coronary events in a low incidence population: assessing accuracy of the CUORE Cohort Study prediction equation. *Int J. Epidemiol.* **34**: 413–421.

Gupta, R., Prakash, H., Majumdar, S., Sharma, S. and Gupta, V. P. 1995. prevalence of coronary heart disease and coronary risk factors in an urban population of Rajasthan Ind. *Heart J.* **47**: 331–338.

Jackson, R., Lawes, C. M., Bennett, D. A., Milne, R. J. and Rodgers, A. 2005. Treatment with drugs to lower blood pressure and blood cholesterol based on an individual's absolute cardiovascular risk. *Lancet*. **365**: 434–441.

Jain, A. P., Mohan, A., Gupta, O. P., Jajoo, U., Kalantri, S. P. and Shrivastava, L. M. 2000. Role of oxygen derived free radicals in causing endothelial damage in Acute myocardial Ischemia. *J. Assoc Physicians*. **48(5)**: 478–480.

John, D. P. 1971. Role of LCAT activity. *J. Clin investigation*. **50**: 259.

Kannel, W. B., D'Agostino, R. B., Silbershatz, H., Belanger, A. J., Wilson, P. W. and Levy, D. 1999. Profile for estimating risk of heart failure. *Arch. Intern. Med.* **159**:1197–1204.

Murabito, J. M., D'Agostino, R. B., Silbershatz, H. and Wilson, W. F. 1997. Intermittent claudication: a risk profile from the Framingham Heart Study. *Circulation*. **96**: 44–49.

Satoh, K. 1978. Serum lipid peroxide in cerebrovascular disorders determined by a new colorimetric method. *Clin Chim. Acta*. **90**:37–43.

Steingerg, D., Parthasarathy, S., Carew, T. E., Khou, T. C. and Witztum, J. L. 1990. Beyond Cholesterol. Modification of low density lipoprotein that increases its atherogenicity. *N. Eng. J. Med.* **320**: 915–924.

Whybenga, and piliggi, V. J. 1967. Quantitative determination of 3 Methoxy 4 hydroxymandelic acid (VMA) in clinical chemistry. *Acta*. **16**:147–154.

Wilson, P. W. D., Agostino, R. B., Levy, D., Belanger, A. M., Silbershatz, H. and Kannel, W. B. 1998. Prediction of coronary heart disease using risk factor categories. *Circulation*. **97**: 1837–1847.

Wolf, P. A., D'Agostino, R. B., Belanger, A. J. and Kannel, W. B. 1991. Probability of stroke: a risk profile from the Framingham study. *Stroke*. **22**: 312–318.