

Oxidized Lipoprotein (a) - a potent risk factor for Atherosclerosis

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A. Introduction:

Inflammation has been postulated to play an important role in the development of Atherosclerosis¹. Research in this field has been focused on the role of lipoprotein^{2,3,4}. Lp(a) first identified in 1963 by Kare & Berg. Since that time several case control and prospective studies have identified elevated levels of plasma Lp(a) as a risk factor for a variety of atherosclerotic disorders including coronary artery disease. Lp(a) is similar to LDL in lipid composition and presence of apoproteinB-100 but it is distinguished from LDL by the presence of additional glycoprotein moiety apo(a) which is covalently linked to apoB-100 by single disulfide bond^{5,6}. Apo(a) is composed of repeated loop-shaped units called kringle, the sequence of which is highly similar to a kringle motif present in fibrinolytic proenzyme plasminogen⁷; it competes for plasminogen receptors on endothelial cells⁸; so it may inhibit thrombolysis and fibrin clearance, further increasing the risk for cardiovascular disease^{9,10,11}. Oxidative modification of Lp(a) makes it even more potent risk factor for atherosclerosis which is supported by (1) It increases plasminogen activator inhibitor-1 (PAI-1) in endothelial cells¹² (2) Oxidized Lp(a) impaired endothelium dependent vasodilatation¹³ (3) Oxidized Lp(a) is taken up by macrophages via scavenger receptors. The biological effects of oxidized Lp(a) are more potent as compared to native Lp(a)^{12,13,14, 15,16}; but lack of suitable assay to detect serum oxidized Lp(a) has limited investigation of oxidized Lp(a) until now. Since the recent development of antibody against epitope of oxidized Lp(a)¹⁷ it is possible to measure oxidized Lp(a) in human, it is noteworthy to investigate the correlation of oxidized Lp(a) in pathogenesis of atherosclerosis.

B. Hypothesis:

Oxidized Lp(a) is potent risk factor for atherosclerosis.

C. Method & Study design:

This will be case control study. oxidized Lp(a) levels (normal 0.04nMol/L) will be measured by standardized assay from "United States Biological Corp" laboratories. The study will be divided into 2 groups (1) with disease (2) without disease where disease is defined as symptomatic cardiovascular disease with angiographic evidence of atherosclerosis of >50% in at least one segment of coronary artery.

D. Statistical Analysis :

All values are expressed as mean \pm SEM. Unpaired student's t-test will be used and values of $P < 0.05$ and power > 0.80 will be consider significant.

E. Sample size:

Using the unpaired t-test $n(\text{in each arm}) = 1 + 16(\text{Std-devn}/\text{effects})^2$. Sample size is calculated to detect 50% difference in oxidized Lp(a) levels among two group with significance level of 0.05 & power of 0.80. A total of 34 subjects will be enrolled, 17 in each group.

F. Subject Selection:

Subjects will be recruited from cath lab of Columbia Presbyterian Medical Center who are referred for angiography.

G. Inclusion/Exclusion Criteria:

People with well known risk factors for atherosclerosis like Diabetes Melitis (DM)-fasting glucose of >120, renal disease (creatinine >2), liver disease (AST/ALT >100), hyperlipidemia (NCEP-III guide lines), hypertension (>140/90), smoking, and positive family history will be matched in both groups. Subjects will be equally distributed in regards to gender, age and race. Women on oral contraceptive pills & hormone replacement therapy will be excluded. Peoples taking vitamins will be excluded.

H. Study Procedure:

Blood sample will be obtained during angiography and oxidized Lp(a) will be analysed by standardized assay.

I. Study drugs:

None.

J. Medical devices:

None.

K. Study Questionnaire:

A small study questionnaire will be given to all subjects (five minutes) about their past medical history.

L. Confidentiality of study data:

Every participant will be given a code number and all data will be stored in ICCR in a locked cabinet.

M. Location:

Study will take place at Columbia Presbyterian Medical Center.

N. Risks and Benefits:

There are no extra risks related to participate in the study. There might not be any immediate personal benefit of the study to the participant, however study result might be helpful to understand the co-relation of oxidized Lp(a) as a potent risk factor for atherosclerosis.

O. Alternative therapies:

None.

P. Compensation and costs to subjects:

None.

Q. Minors:

Anybody under the age of 18 years will not be included in the study.

R. Radiation or radioactive substances:

Will not be used.

S. References:

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