Oxidation Of LDL :Role In Atherosclerosis
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Citation

Abstract
Atherogenesis is a multifaceted condition which has a complicated pathogenesis that is still being unraveled. Both systemic and local inflammation have been implicated in the development of atherosclerosis. Oxidative stress, or oxidation of LDL, is considered a marker of inflammation. This brief review focuses on the role of oxidation of LDL in development of atherosclerosis.

INTRODUCTION
Atherosclerosis is now thought to be a chronic low grade vascular inflammation. The ongoing search for markers of inflammation (1), which can be used as predictors of cardiovascular (CV) risk, has yielded many promising candidates.

These include C-reactive protein (CRP), cytokines such as interleukin -6 (IL-6), interleukin -18 and tumor necrosis factor –α (TNF – α), markers of hemostasis such as fibrinogen, plaminogen activator inhibitor -1 (PAI-1), D-dimer and von Willebrand factor (vWF), as well as total white blood cell count, especially neutrophil count.

Recently however, lipid –related biomarkers have been used as markers or surrogates for atherosclerosis. These include myeloperoxidase , a leukocyte –derived enzyme, lipoprotein –associated phospholipase A2, which is produced by monocytes, macrophages ,T lymphocytes, liver and mast cells, and adiponectin, an anti –atherogenic marker made in white adipose tissue (1).

One lipid –related marker, however, which, perhaps, has not got the attention it deserves, is oxidized LDL. This review focuses on the role of oxidized LDL (ox LDL) in the pathogenesis and risk stratification of atherogenesis.

FUNCTIONS OF OXLDL
LDL is modified by oxidation to produce an oxidized form of LDL (oxLDL) which promotes atherogenesis. This mechanism is known as the oxidative modification hypothesis (1).

Ox LDL acts by various mechanisms mediated through its multiple biological effects. These are summarized in Table 1.

OxLDL promotes foam cell formation, and attracts /traps/adheres monocytes, lymphocytes and macrophages, while causing vasoconstriction, and cell proliferation. These effects, coupled with increased apoptosis and plaque rupture, induction of pro-inflammatory genes, and antigenicity, lead to atherogenesis.

Ox LDL promotes the transition from stable plaques to unstable plaques. This is done by stimulating matrix metalloproteinase (MMP) -1 and MMP -3 in vascular endothelial cells as well as in monocyte –derived macrophages (2,3). OxLDL upregulates the expression of MMP-1 and MMP -3 in human coronary endothelial cells
Oxidative stress and low grade inflammation are well known predictors of coronary heart disease events when added to other risk factors. Concentration of oxLDL is higher in patients with severe acute coronary syndrome (myocardial infarction) than in those with angina. ox LDL has also been shown to correlate with the extent of coronary heart disease in heart transplant recipients.

Studies have demonstrated an association of ox LDL levels with subclinical atherosclerosis in asymptomatic general population and in members of familial combined hyperlipidemia families. Thus, ox LDL may be a useful marker, more sensitive than the Global Risk Assessment Score (GRAS) for identifying coronary artery disease.

CLINICAL STUDIES: PRESENCE OF ATHEROSCLEROSIS

Cross sectional studies have shown that patients of stable patients of stable coronary heart disease and acute coronary syndrome have higher plasma levels of of ox LDL than healthy controls. Concentration of oxLDL is higher in patients with severe acute coronary syndrome (myocardial infarction) than in those with angina. ox LDL has also been shown to correlate with the extent of coronary heart disease in heart transplant recipients.

Both cross sectional studies and prospective studies have demonstrated the importance of ox LDL concentrations as a means of diagnosing the presence of coronary heart disease, as well as predicting future cardiac events.

Oxidation of LDL, therefore, becomes not only a pathogenesis factor, but also a potential diagnostic and prognostic tool which can be used for risk stratification.

References


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