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LOX-1, a new marker of risk and prognosis in coronary artery disease?

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Abstract The development of atherosclerosis is caused by the accumulation of lipid, inflammatory cytokine production, and the large amount of inflammatory cells in the arterial wall. It is now established that the presence of oxidized low-density lipoproteins (ox-LDL) has an important role in the pathogenesis of the disease. There are many scavenger receptors for ox-LDL, among which LOX-1 seems to be important for the induction of endothelial dysfunction and the other subsequent events that lead to the formation of atheromatous plaque. Our findings indicate the presence of a regulatory role induced by the presence of ox-LDL on LOX-1 through the amplification of IL-6 synthesis. This mechanism contributes to the upregulation of the ORL-1 gene expression in presence of risk factors. Many authors have shown the possibility to use LOX-1 as a good marker for the diagnosis and prognosis of coronary artery disease because it is easy to measure and more sensitive than other markers commonly used in the routine of laboratory medicine.

Keywords LOX-1 · Ox-LDL · Receptors · IL-6 · Inflammation · Atherosclerosis

Introduction

It is now accepted by the scientific community that the endothelial injury, associated to dysfunction, is the first step toward the development of atherosclerosis. In particular it occurs through the formation of fatty streaks, which are small sub-endothelial deposits of lipid-laden macrophages. Various risk factors for endothelial dysfunction and atherosclerosis, such as elevated low-density lipoproteins (LDL), hypertension, smoking, diabetes, elevated homocysteine, infections, hemodynamic forces such as high shear stress or their combinations, alter normal endothelium homeostasis causing production of reactive oxygen species (ROS) [1, 2].

Clinical investigations have demonstrated that well-known coronary risk factors, including diabetes, hyperlipidemia, hypertension, obesity and smoking, are associated with oxidative stress.

Once exposed to oxidative stress LDL particles, trapped in the vessel, are oxidized (ox-LDL) and trigger the development of fatty streak formation inducing the loss of constitutive nitric oxide synthetase (cNOs or eNOS). Oxidized LDL induces the production of a wide variety of inflammatory cytokines or chemokines by vascular cells; circulating monocytes roll along the activated endothelial layer and then move into the sub-endothelial region in response to chemotactic signals. Formed oxidized LDL is extensively accumulated into macrophages, resulting in the formation of foam cells [3].

Oxidation of lipoproteins, particularly of LDL, appears to play a primary role in initiating this pathological process [3] that causes endothelial dysfunction prerequisite for macrophage uptake and cell accumulation of cholesterol, inflammation, and proliferation of vascular smooth muscle cells in the subintimal space.

To investigate on the role of oxidized lipoproteins (ox-LDL), we examine their specific receptors available on endothelial cells.

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