Myeloperoxidase as a risk marker for atherosclerosis

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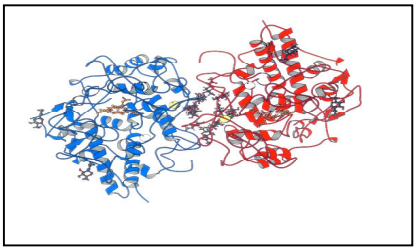
In several studies elevated blood levels of myeloperoxidase (MPO) have been associated with the development of atherosclerosis and cardiovascular disease. Atherosclerosis is today considered to be an inflammatory disease and oxidants produced during inflammation are thought to contribute to the progression of atherosclerosis by being involved in lipid peroxidation reactions. Lipid hydroperoxides fragment into reactive aldehydes that may substitute lysine residues of the ApoB-100 protein part of the low-density lipoprotein (LDL) particle to generate oxidized LDL. By being recognized by the cells as foreign and thereby activating the immune system, oxidatively modified LDL is believed to be atherogenic. MPO, released from activated leukocytes at sites of inflammation, is one candidate enzyme involved in the generation of oxidants and hence regarded to play an important role in the atherosclerotic disease process.

Background

During inflammation a variety of cells (vascular endothelial cells, smooth muscle cells, fibroblasts, neutrophils, monocytes, macrophages) produce inflammatory mediators such as oxidants and free radicals as defense against disease-causing agents (virus, bacteria, parasites, tumors, harmful substances). Atherosclerosis is today considered to be an inflammatory disease and oxidants and free radicals are believed to contribute to the development and progression of the disease process. Myeloperoxidase (MPO), an enzyme released from activated neutrophiles and monocytes as a result of inflammation, catalyzes reactions in which free radicals and oxidants are formed. Hence, MPO is believed to play an important role in the progression of atherosclerosis.



The MPO subunit is composed of an alpha and a beta chain.

Involvement of MPO in LDL oxidation

Myeloperoxidase (MPO) is an iron containing glucoprotein composed of two covalently linked subunits, each consisting of an alpha and a beta chain. MPO catalyzes a hydrogen peroxide mediated halogenation reaction in which hypochloric acid is formed. Hypochloric acid attacks and oxidizes lysine residues of the ApoB-100 protein moiety of the low-density lipoprotein (LDL) particle to generate oxidized LDL. MPO is also involved in LDL oxidation by the production of free radicals that may react with lipids of the LDL particle. Hydroperoxides of LDL lipids fragment into reactive aldehydes that may substitute lysine residues of ApoB-100 and thereby generating oxidized LDL. Native (unmodified) LDL lacks inflammatory properties whereas the oxidatively modified LDL particles are interpreted by the cells as foreign and the immune system is activated.

Myeloperoxidase, a predictive marker for atherosclerosis

In 2001 Zhang and colleagues studied subjects with and without coronary artery disease (CAD) and they found elevated MPO activity in patients with CAD compared to subjects without CAD. In several additional studies blood MPO levels have shown to be predictive for developing atherosclerosis and subsequent events. Brennan *et al.* (2003) found MPO to be predictive for cardiovascular events in patients with chest pain. Baldus *et al.* (2003) demonstrated an increased risk for myocardial infarction in patients with blood MPO levels above 350 µg/L. In a more recent study Exner *et al.* (2006) found elevated MPO levels to be associated with progression of carotid atherosclerosis in patients with high-density lipoprotein levels below 49 mg/dl.

Mercodia MPO assay

Mercodia has developed an ELISA assay for quantitative determination of MPO in serum and plasma. The Mercodia MPO ELISA is a solid phase two-site immunoassay based on two specific monoclonal antibodies directed against separate epitopes on the MPO molecule. Measuring blood MPO levels may become a useful complementary biomarker in the diagnosis of atherosclerosis progression and plaque vulnerability.

References

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