Oxidized LDL, a Predictive Marker for Development of Atherosclerosis

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Summary

- Oxidized LDL is the atherogenic form of LDL, directly involved in the initiation and progression of the atherosclerotic disease process.
- Oxidized LDL, measured by the Mercodia oxidized LDL ELISAs, has been found to be a predictive biomarker for the subclinical development of atherosclerosis and subsequent events.
- Monitoring circulating oxidized LDL levels may be important in patients with stable plaques since remaining high levels of oxidized LDL, by a continuous stimulation of the immune system, may contribute to the destabilization of growing plaques.

Introduction

It is today widely believed that the development and progression of atherosclerosis is caused by a chronic inflammation in the vessel wall. Due to the high blood pressure, plasma constituents seep continuously into the intima and at reasonable blood levels low density lipoprotein (LDL) particles can pass in and out of the intima. However, in excess LDL tends to get trapped in the matrix and subjected to modifications. The oxidatively modified LDL particles are considered by the cells as foreign and the immune system is activated. In several studies oxidized LDL has been found to be a predictive biomarker for the subclinical development of atherosclerosis and subsequent events.

Oxidized LDL measurements

Mercodia has developed oxidized LDL ELISAs, based on the mouse monoclonal antibody 4E6, developed by the professors Holvoet and Colfen at the University of Leuven, Leuven, Belgium. The monoclonal antibody 4E6 is directed against a conformational epitope in the apoB-Holvoet's monoclonal antibody, 4E6, which is specific ELISA procedure using the oxidized LDL-specific, is directly involved in the initiation and progression of Oxidized LDL is a unique plaque-specific protein mediator of accelerated development of atherosclerosis and subsequent events.

Studies of oxidized LDL as a predictive marker for CAD

In several studies, in which the Mercodia Oxidized LDL ELISAs were used, oxidized LDL was shown to be a sensitive and predictive biomarker for the subclinical development of atherosclerosis and subsequent event. By using the 4E6 antibody in a competitive ELISA Professor Holvoet et al. (1998) found elevated levels of circulating oxidized LDL in untreated patients with stable coronary artery disease (CAD) as well as in patients with acute coronary syndromes (fig. 3). These findings are important and suggest that this increase is independent of plaque instability. By using the 4E6 antibody in a similar assay (fig. 4) Tsimikas et al. found elevated levels of oxidized LDL only in patients with an acute myocardial infarction and were unable to demonstrate any elevated circulating levels of oxidized LDL in patients with stable coronary heart disease (CHD).

Clinical value of oxidized LDL measurements

Not only may oxidized LDL measurements be a powerful tool in monitoring patients with a developing cardiovascular disease from non-risk patients in a seemingly healthy population. Monitoring circulating oxidized LDL levels may also be important in patients with stable plaques since remaining high levels of oxidized LDL, by a continuous stimulation of the immune system, may contribute to the destabilization of growing plaques. The plaque stabilizing fibrin cap may subsequently be degradated by induced secretion of matrix metalloproteinases. If the weakened plaque ruptures, tissue factors, also induced during inflammation, will interact with clot-promoting elements in the blood, causing a thrombus to form.

By using the Mercodia Oxidized LDL Competitive ELISA Mesinger et al. (2005) showed that elevated blood levels of oxidized LDL are predictive for future CHD events, this in a study including 346 apparently healthy men. Compared to controls, baseline mean plasma levels of oxidized LDL were significantly higher in subjects who subsequently experienced an event. Plasma levels of oxidized LDL were the strongest predictor of future CHD events compared to a conventional lipoprotein profile and other traditional risk factors for CHD.

References

Mesinger et al. (2005) Plasma Oxidized Low-Density Lipoprotein, a Strong Predictor for Acute Coronary Heart Disease Events in Apparently Healthy, Middle-Aged Men From the General Population. Circulation 112: 651-657