Recombinant LCAT rescues defective HDL mediated endothelial protection in acute coronary syndrome

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The vasoprotective effects of HDL are impaired during an acute coronary syndrome (ACS). Lecithin:cholesterol acyltransferase (LCAT) is the enzyme responsible for cholesterol esterification in plasma, and plays a key role in HDL maturation and remodeling. Very few studies have suggested that LCAT activity is decreased in ACS patients, but the possible link with HDL dysfunction observed during ACS has never been investigated. Aim of this study was to evaluate changes in LCAT concentration and activity in ACS patients, to investigate if these changes are related to the compromised capacity of HDL to promote endothelial nitric oxide production, and to assess if recombinant human LCAT (rhLCAT) can rescue the defective vasoprotective HDL function.

Thirty STEMI patients were enrolled and plasma was collected at hospital admission, 48 and 72 hours thereafter, at hospital discharge, and at 30-day follow-up. Plasma LCAT concentration and activity were measured and related to the capacity of HDL to promote nitric oxide (NO) production in cultured endothelial cells (ECs). In vitro studies were performed in which STEMI patients' plasma was added with rhLCAT and HDL vasoprotective activity assessed by measuring NO production in ECs. The plasma concentration of the LCAT enzyme significantly decreases during STEMI with a parallel significant reduction in LCAT activity. HDL isolated from STEMI patients progressively lose the capacity to promote NO production by ECs, and the reduction is related to decreased LCAT concentration. In vitro incubation of STEMI patients' plasma with rhLCAT increases HDL ability to promote endothelial NO production, possibly related to significant modification in HDL phospholipid classes.

Impairment of cholesterol esterification may be a major factor in the HDL dysfunction observed during ACS. rhLCAT is able to restore HDL-mediated NO production in vitro, suggesting LCAT as potential therapeutic target for restoring HDL functionality in ACS.