Lipid lowering treatment substantially reduces the risk of cardiovascular diseases. The effects of lipid lowering go far beyond limiting the extent of atheroslcerotic lesions and decreasing the severity of atherosclerotic stenoses. Recently recognised effects of cholesterol on plaque stability, endothelial function, thrombosis, and plaque inflammation have been subject to intensive research during the past two decades. The effect lipid lowering treatment on the various aspects of the plaque development are being investigated in search of novel therapies to reduce the risk of ahterosclerosis. In this work, we examined cell adhesion molecules, microvascular reactivity and metalloproteinase PAPP-A in patients with hypercholesterolemia and investigated the effect of lipid lowering with atorvastatin and LDL-apheresis.

Leukocyte and endothelial adhesion molecules mediate leukocyte recruitment into subendothelial space, contributing thus to plaque inflammation. PAPP-A is a protease which has been related to plaque instability and acute coronary events; it's role in stable atherosclerotic lesions hasn't been studied yet Microvascular reactivity is supposed to reflect endothelial function in the microvascular bed; the knowledge of the effect of hyperlipidemia on microvasculature is currently limited.

Patients with severe hypercholesterolemia, who were free of vascular disease, were examined at the baseline and after 10 weeks of atorvastatin treatment. Patients with hypercholesterolemia and coronary artery disease were examined before and after the treatment with LDL-apheresis. Both patient groups were compared to healthy normolopidemic controls. Expression adhesion molecules on blood leukocytes was measured by flow cytometry, and serum endothelial markers and PAPP-A were measured by immunometric assays. Skin microvascular reactivity was examined by laser-Doppler flowmetry.

In patients with hyperlipidemia, there was an increased leukocyte expression of most cell adhesion molecules studied, which was considerably decreased after the atorvastatin treatment. In contrast, there was nearly no effect of hypercholesterolemia and/or atorvastatin on the serum endothelial molecules. Leukocyte molecules may therefore be a more sensitive marker of atherogenesis than endothelial molecules. Our results support the role of increased leukocyte adhesiveness in the development of atherosclerosis.

PAPP-A levels were elevated in hypercholesterolemic subjects without clinical signs of atherosclerosis. PAPP-A may therefore not only reflect plaque instability (as suggested earlier), but also serve as a marker of total atherosclerotic burden in asymptomatic subjects with hyperlipidemia. However, PAPP-A levels were not influenced by atorvastatin treatment.

Microvascular reactivity was normal in otherwise healthy subjects with hyperlipidemia; on the contrary, it was impaired in patients with hyperlipidemia and coronary heard disease. There was no effect of atorvastatin or LDL-apheresis on microvascular reactivity. These results suggest that microcirculation is not involved in the early vascular dysfunction induced by HLP and that MVR rather reflects changes which appear later in the course of the atheroslcerotic disease.