

## STATIN-PARAOXONASE INTERACTIONS DURING STATIN TREATMENT

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Human serum paraoxonase-1 (PON1) protects lipoproteins against oxidation by hydrolyzing lipid peroxides in oxidized LDL, therefore it may protect against atherosclerosis. Changes in the ratio of HDL subfractions may alter the stability and antioxidant capacity of PON1. PON1 activity variations have been also related to some common polymorphisms in the coding and promoter regions. The PON1-192 polymorphism has the most significant impact on enzyme activity, and its prevalence can be estimated by phenotype distribution analysis.

The aim of the study was to examine the effect of atorvastatin treatment on the distribution of HDL subfractions, LDL size, cholesteryl ester transfer protein (CETP), lecithin:cholesterol acyltransferase (LCAT) and human serum paraoxonase-1 (PON1) activity, and to clarify the role of PON1 phenotypes on the effect of three different statins on paraoxonase activity and lipid parameters in patients with type IIa and IIb hypercholesterolemia.

Three months of 20 mg/day atorvastatin treatment significantly increased the HDL3 and decreased the HDL2a and HDL2b subfractions. The mean LDL size was significantly increased. The PON1 activity was augmented by the atorvastatin treatment. The CETP activity positively correlated with the HDL2b and negatively correlated with the HDL3 and HDL2a levels. Three months of statin (10 mg/day atorvastatin, 10/20 mg/day simvastatin and 80 mg/day extended-release fluvastatin) treatment significantly increased the paraoxonase activity in every statin-treated group. In patients with AB+BB phenotype the statin treatment was significantly more effective on paraoxonase activity than in the AA group. The statin treatment more effectively decreased the triglyceride levels in the AB+BB group compared to the AA group in the whole study population and in the simvastatin-treated group. The atorvastatin treatment was significantly more effective on apoB levels in patients with AB+BB phenotype than in the AA phenotype group.

These results confirm that atorvastatin normalizes lipid levels and preferentially increases HDL. Our data are consistent with the concept that changes in CETP and LCAT activities during statin treatment may directly alter the ratio of HDL subclasses. Data on PON1 activity and HDL subfraction alterations suggest that the increase in HDL3 ratio may also be responsible for the enhanced PON1 activity after atorvastatin treatment. Our results indicate that the PON1 phenotype may be a novel predictive factor for the effectivity of statin treatment on PON1 activity and serum lipid levels; however, different types of statins may exert different effects on these parameters.