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Rigorous Thesis – Abstract

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Atorvastatin and its effects on atherogenic process in the genetically modified mouse model of atherosclerosis I

Statins (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors) represents golden standard in dyslipidemia treatment in humans. However, its effects in animal models of atherosclerosis are very inconsistent. Thus, the aim of this study was to evaluate whether statins has hypolipidemic and inflammatory effects in apoE/LDLR deficient mouse model of atherosclerosis. The aim of this rigorous thesis was to verify whether atorvastatin posses similar effects in apoE/LDL receptor double knockout mice that are common in human medicine.

Female ApoE/LDL receptor-double-knockout mice at 8 weeks of age were randomly divided into 2 groups. The control group of animals (n=8) was fed with the atherogenic (western type) diet for another 8 weeks. The same atherogenic diet and treatment period was used in other two groups where atorvastatin was added to the diet at the dosage of 100 mg/kg per day. Biochemical analysis of blood cholesterol fractions, ELISA analysis of monocyte chemoattractant protein-1, vascular cell adhesion molecule-1 levels in blood, and stereological analysis of atherosclerotic plaque size in aortic sinus was performed.

The eight week atorvastatin treatment in the dosis of 100mg/kg/day led to significant improvement of the lipid profile in the apoE/LDL receptor double knockout mouses. This hypolipidemic efficiency was accompanied by significant anti-inflammatory effects. The plasma levels of MCP-1 and the expression of VCAM-1 in atherosclerotc lesionwere reduced.

In conclusion, this study demonstrates that atorvastatin has hypolipidemic and anti-inflammatory affects in apoE/LDLR deficient mice as was described in humans. Thus, these mice might represent suitable animal model for the study of statins effects in experimental atherogenesis.