ABSTRACT

Atherosclerosis, or sclerosis of arteries, is a degenerative disease of arteries. Sometimes it is called „the disease of the 20th century".

Double knockout mice (apoE/LDL – receptor double knockout) represent a new model for a study of atherogenesis which is capable of developing severe hyperlipidaemia and atherosclerosis.

Statins (or so-called competitive inhibitors of 3-hydroxyl-3-methyl-glutaryl-coenzym A-reductase) currently belong to the most efficient hypolipidemic drugs that are used all over the world. Statins have propitious effects on lipid plasma levels and cardiovascular mortality. They mainly decrease the levels of total cholesterol and LDL cholesterol.

The main aim of this diploma thesis was to evaluate whether atorvastatin possess the same antiatherogenic effects in apo/LDL-receptor deficient mice as were demonstrated in humans. Therefore we analyzed parameters of lipid spectrum in blood, the expression of inflammatory markers in atherosclerotic plaques and the size of atherosclerotic lesions.

All mice were fed with experimental diets in 8 weeks of age. Animals were randomly divided into 2 groups (a control and an atorvastatin group). The mice in the control group were fed only with an atherogenic diet, and the mice in the atorvastatin group had an atherogenic diet which was enriched with 10 mg of atorvastatin/kg of weigh a day.

The results of biochemical analysis showed that 8 weeks feeding with 10 mg atorvastatin/kg significantly decreased only total cholesterol levels. VLDL cholesterol, LDL cholesterol and TAG levels were decreased only slightly and non-significantly. On the contrary atorvastatin treatment resulted in a significant increase in HDL cholesterol levels.

Expression of VCAM-1 was studied in the control and the atorvastatin group. Large intensity was observed in vascular media under atherosclerotic plaques. Moreover strong intensity was observed in atherosclerotic plaque and in endothelium both over the lesion and outside it.

Stereologic analysis showed surprising yet non-significant increase in oil red area staining. On the other hand VCAM-1 expression area was slightly but only non-significantly decreased after atorvastatin treatment.

We conclude that apoE/LDL receptor deficient mice could be a good animal model for studying of effects of statins on atherogenesis. Eight weeks feeding of atorvastatin in dose 10mg/kg/day led to slight improvement in lipid profile in apo/LDL receptor deficient mice.

Other parameters were not significantly improved, thus we suggest, that higher dose of atorvastatin must be used to reach marked antiatherogenic effect in these mice.