ABSTRACT

Charles University, Faculty of Pharmacy in Hradec Králové

Department of Biological and Medical Sciences

Title of Diploma Thesis: Effect of atorvastatin on endoglin expression and function in hyperlipidemia-induced endothelial dysfunction

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Aim: The aim of this thesis was to determine how atorvastatin affects the expression and function of endoglin and related biomarkers of inflammation/endothelial dysfunction at different concentrations and times in human endothelial cells from the aorta, in which hyperlipidemia was induced by using palmitic acid.

Methods: In the diploma thesis, we worked with human aortic endothelial cells. We premedicated them with atorvastatin/palmitic acid at different times and concentrations. Using flow cytometry, we measured the protein expression of endoglin. Furthermore, we used the qRT-PCR method to determine the level of mRNA expression of endoglin, its transcription factors and biomarkers of inflammation. Using the ELISA method, we detected the levels of soluble endoglin.

Results: We demonstrated that atorvastatin at a concentration of 5μM after 16 hours of premedication significantly increased the mRNA expression of endothelial nitric oxide synthase, and conversely decreased the expression of CCL2 (C-C motif chemokine ligand 2). Furthermore, we found that a 25μM concentration of palmitic acid after 24 hours of incubation led to a decrease in the protein expression of endoglin compared to the control. Using the ELISA method, we demonstrated a decrease in the level of soluble endoglin in a group of cells premedicated for 24 hours with 25μM palmitic acid and at the same time 5μM atorvastatin compared to the group premedicated only with 5μM atorvastatin. At the observed times and at the selected concentrations, atorvastatin, nor atorvastatin with palmitic acid had no significant effect on the mRNA expression of endoglin and its transcription factors, nor on the protein expression of endoglin.

Conclusion: The results showed that in cells in which was induced hyperlipidemia by palmitic acid, atorvastatin did not have a significant effect on the expression of endoglin or its transcription factors at the observed times and selected concentrations, but on the other hand, it significantly affected the mRNA expression of the related inflammatory biomarkers eNOS and CCL2.

Key words: endoglin, hyperlipidemia, endothelial dysfunction, atorvastatin