Abstract

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Title of Thesis: Effect of sunitinib on the expression of P-selectin in normotensive and hypertensive rats

Background: The objective of this thesis was to prove the P-selectin expression as a potential predictive marker of ongoing endothelial dysfunction. The experiments based on the application of cytostatic sunitinib were carried out on the aorta of spontaneously hypertensive rats (SHR) as well as normotensive rats (WKY).

Methods: Two groups of rats were subject of testing in this experiment - male SHR and WKY rats – both groups were divided into two subgroups. While the first subgroup of rats was fed by sunitinib from the beginning of the experiment, the second subgroup (a control group) was fed by placebo. The scheme of application of sunitinib to the SHR strain consisted of 8 weeks of application - 5 days without application - 8 weeks of application. In the case of WKY rats, the last stage of the scheme was shortened due to toxicity, thus 8 weeks of application - 5 days without application - 2 weeks of application. We applied imunohistological analysis ABC of the aortic endothels using DAB as a chromogen.

Results: Expression of P-selectin was not proven in endothelium cells of both types of animals. There were no significant differences between these 2 groups of animals; P-selectin was detected neither in SHR nor in WKY strain.

Conclusions: The experiment did not prove any signifiant increase of P-selectin expression in aortic endothel of the rats as a reaction to application of sunitinib. Probably the inflammatory atherosclerotic changes did not occure in endotelium cells of tested rats neither after administration of sunitinib nor after administrativ of placebo. The occurence of inflammatory atherosclerotic changes in vessels can not be excluded. Sunitinib certainly affects the vascular endothelium. Further experiments have to be carried out for proving its vascular toxicity by testing other markers of endothelial dysfunction.

KEYWORDS: Hypertension, P-selectin, sunitinib