ABSTRACT

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Title of diploma thesis: The influence of LDL-apheresis on aggregation of blood platelets, blood coagulation and the effect of standard drugs

LDL-apheresis is a method that removes LDL-cholesterol (LDL-C) from the blood. It is used to treat familial hypercholesterolemia (FH), a genetic disorder causing high LDL-C levels and an early development of cardiovascular diseases. Blood platelets and coagulation system play an important role in these diseases and their activity is also affected by lipids.

The aim of this thesis was to analyze possible differences in platelet aggregation and blood coagulation in patients suffering from FH. Two methods of treatment in this group were compared – lipid apheresis and PCSK9Ab (proprotein convertase subtilisin/kexin type 9 monoclonal antibodies). The observed parameters were also compared with age-matched healthy volunteers.

Our cohort consisted of 15 patients and 15 healthy donors. Six patients were treated with lipid apheresis and also PCSK9Ab, six subjects only with PCSK9Ab. Platelet aggregation was measured with an impedance aggregometer using 7 different inducers and 3 clinically used antiplatelet drugs. Subsequently, standard coagulation tests (prothrombin time and activated partial thromboplastin time) were performed. LDL-apheresis decreased the platelet aggregation but significant differences were found only in two inducers – collagen and ristocetin. The response to most inducers, except TRAP (thrombin receptor activating peptide), was the same in both groups of patients. There were no differences in coagulation between these groups in both tests. The antiplatelet effect of ASA and vorapaxar was stronger in FH patients, whereas ticagrelor acted in patients and healthy donors equally. The coagulation and response to some of the used anticoagulants was also different in patients compared to healthy subjects. A correlation analysis revealed a relationship between higher levels of triglycerides and the platelet

aggregation. The platelet response to ristocetin was higher not only to increasing triglycerides, but also cholesterol.

In conclusion, despite some limitations, such as the chronic use of antiplatelet and anticoagulant drugs in analyzed patients, this study suggested that PCSK9Ab might completely replace LDL-apheresis in some cases. However, more studies are needed to confirm lower platelet aggregation and coagulation in patients with FH.