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Indoxyl sulfate modulates the activity of coagulation system and fibrinolysis in animal model of experimental arterial thrombosis

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Objective: Chronic kidney disease (CKD) is associated with higher risk for thromboembolic events compared with general population. Indoxyl sulfate (IS) is a potent uremic toxin associated with the appearance of cardiovascular disease prevalence. However, mechanism underlying IS association with thromboembolic events is not fully understood.

Material and methods: We evaluated the effect of IS on thrombotic process after acute treatment in electrical current-induced arterial thrombosis in Wistar male rats. IS doses: 3, 10, and 30 mg/kg of body weight were administered intravenously. We assessed IS influence on parameters of coagulation, fibrinolysis, collagen-induced platelet aggregation and blood morphology.

Results: IS doses: 10, 30 mg/kg increased thrombus weight in a dose-dependent manner ($p < 0.001$), whereas dose of 3mg/kg did not influence thrombus weight. From parameters of coagulation, two highest IS doses decreased activated partial thromboplastin time (APTT) ($p < 0.01$; $p < 0.0001$) and only IS dose of 30 mg/kg affected fibrinogen ($p < 0.01$), prothrombin time (PT) ($p < 0.05$) and thrombin time (TT) ($p < 0.01$). Moreover, IS exacerbated platelet aggregation in whole blood, what was reflected by decreased lag time of aggregation ($p < 0.05$; $p < 0.001$) and increased parameters like impedance ($p < 0.05$), slope ($p < 0.05$) and area under the curve (AUC) ($p < 0.001$). IS did not influence blood morphology parameters.

Conclusions: Data obtained from described experiments indicate that IS, in a dose-dependent way, affects the coagulation system, creating prothrombotic state. Thus, IS can be one of crucial factors responsible for thromboembolic events in CKD. This work was supported by funds from Leading National Research Centre 116/KNOW/15 and Polish National Science Centre 2015/17/N/NZ4/02334.

Biography

Malgorzata Karbowska graduated Jagiellonian University Medical College with a master degree in pharmacy and currently is a PhD student at Medical University of Bialystok. As a young scientist she received Scholarship from the Minister of Science and Higher Education for outstanding achievement. Presently she is managing project supported by Leading National Research Centre (The Centre for Innovative Research at Medical University of Bialystok) and is co-investigator of Preludium project supported by the Polish National Science Centre – both projects focus on nephrology.

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