Streszczenie w j. angielskim

In recent decades, hypertension in children and teens is an increasingly recognized health problem. This fact encourages to search for factors that will allow to better understand its pathogenesis, and thus to undertake new preventive and therapeutic interventions. One such newly discovered factor is the receptor for advanced glycation end products (RAGE), which plays an important role in the pathogenesis of diabetes and its complications, atherosclerosis, hypertension and hypercholesterolemia.

Soluble isoform of this receptor - sRAGE combining with AGEs prevents the activation of the receptor and leads to the reduction of oxidative stress.

What's more, the prevalence of metabolic syndrome in children and adolescents has raised significantly lately, which is undoubtedly related to an unhealthy diet. It has been proved that consumption of products containing glucose-fructose syrup leads to elevation in serum uric acid concentration. So far, the effect of hyperuricaemia on sRAGE concentration has not been evaluated.

Another factor that may contribute to the pathogenesis of hypertension in the paediatric population is renalase, which as an enzyme metabolizes catecholamines in the circulatory system. The results of the studies clearly indicate that renalase take part in the regulation of blood pressure. There is no data assessing the relationship between renalase and uric acid.

The aim of this doctoral dissertation was to assess the impact of elevated blood pressure and hyperuricaemia on the soluble receptor for advanced glycation end products (sRAGE) and renalase serum concentration in children and adolescents.

The study was conducted in two groups:

1 group - children and adolescents with primary hypertension and / or hyperuricemia aged 9.5-18 years hospitalized in the Department of Pediatrics and Nephrology in Bialystok

2nd group - age-matched normotensive, healthy children.

Informed consent was obtained from parents of all participants and from children older than 16 years of age. The protocol was approved by the Bioethics Committee of the Medical University of Bialystok in accordance with the Declaration of Helsinki R-I-002/327/2014 and R-I-002/493/2015.

All patients underwent anthropometric measurements and 24-hour blood pressure monitoring (ABPM). After overnight fasting, five milliliters of venous, peripheral blood were collected from each patient to obtain serum, in which the concentration of glucose, creatinine, urea, lipid profile and uric acid were evaluated. Serum sRAGE and renalase level were measured by commercial enzyme immunoassay ELISA (BioVendor, Czech Republic and USCN Life Science Inc., China respectively) according to the manufacturer's instructions and expressed in pg/ml and ug/ml respectively. Laboratory tests were carried out at the Department of Laboratory Pediatric Diagnostics of the University Children's Clinical Hospital in Bialystok. ABPM was performed using the oscillometric Spacelabs Medical. All statistical analyses were performed by using Statistica ver. 10.0 (StatSoft Inc., Tulsa, OK, USA). For all analyses, P values <0.05 was considered significant.

The results indicates statistically significantly higher sRAGE concentration in patients with hyperuricemia (median [IQR]) (167.57 [140.42-227.31]) pg/ml when compared to healthy children (median [IQR]) (129 [107.4-175.3]) pg/ml. No statistically significant differences in sRAGE concentrations was found between subgroups with NT (median [IQR]) (156.6 [127.3-211.0] pg/ml) and without (median [IQR]) (169.8 [148.3-231.1] pg/ml). In addition, a univariate analysis showed a positive correlation between the sRAGE and uric acid serum level ($r = 0.306$, $p <0.05$). There was no correlation between sRAGE concentration and blood pressure values.

The second study revealed higher renalase level (median [IQR]) (29.8 [26.1 - 35.8]) μg/mL in patients with NT compared to controls (median

[IQR]) (26.8 [22.96 - 29.4]) μg/mL; p <0.01. Additionally, renalase level was statistically significantly higher in patients with hyperuricaemia than without, both in hypertensive and normotensive children (p <0.01). In the study group a positive correlation was found between the concentration of renalase and uric acid (r = 0.37, p <0.01), body weight (r = 0.26, p <0.01) and Z-score BMI (r = 0.2, p <0.05). In patients with NT, renalase positively correlated with systolic (24H-SBP) and diastolic (24H-DBP) blood pressure measured for 24 hours and 24H-SBP and 24H-DBP Z-score (LMS), respectively (r = 0.4, p <0.01), (r = 0.36, p <0.05). The factors that were found to have significant correlation with the serum renalase concentration in the single regression analyses were used as explanatory variables to create the multiple regression models. In this model, three parameters (serum uric acid, BMI Z-score (LMS), and 24H-SBP Z-score) accounted for more than 25.28% of the variations in renalase levels (R=0.5, p<0.001).

Studies have shown that both the receptor sRAGE receptor and renalase seem to play an important role in the pathogenesis of primary hypertension and hyperuricaemia in children and adolescents.