Summary

In recent decades hypertension (HT) has became a major health problem among children and adolescents. Therefore, it is extremely important to search for new etiological factors to better understand the pathogenesis of HT and take new preventive and therapeutic interventions. One of these novel factors could be fibroblast growth factor 23 (FGF23), which role in the regulation of the calcium-phosphate metabolism is quite well known, but it also seem to regulate arterial blood pressure, for example by affecting the activity of renin-angiotensin system (RAS). In recent years it has been proposed that the activation of intrarenal RAS, not systemic, plays a major role in the development of HT. It seems that renin and angiotensinogen (AGT) concentration in urine can reflect the intrarenal activity of RAS. At the moment we have very little knowledge about the role of FGF23 and intrarenal RAS in hypertensive children and adolescents.

The aim of this paper was to determine the role of FGF23 and intrarenal RAS in the pathogenesis od HT in young population. In the first research the relationship between urinary excretion of FGF23 and the value of blood pressure were checked. In the second research we made an attempt to evaluate the activation of the intrarenal RAS in hypertensive children and adolescent by assessing the urine concentration of renin and AGT.

The study was conducted in two groups:

The first group (study group) - the hypertensive children and adolescents aged 4-18 years who were admitted to the Department of Pediatrics and Nephrology, Medical University of Bialystok,

The second group (reference group) - the normotensive peers without chronic diseases.

All participants underwent anthropometric and blood pressure measurements. In the hypertensive group, after 12 - hours overnight fasting, the blood samples were taken for the measurement of serum concentrations of: glucose, creatinine,

electrolytes, alkaline phosphatase, parathyroid hormon and vitamin D3 levels. First morning urine samples were obtained to perform urinalysis and assess the concentration of creatinine, FGF23, renin and AGT. Additionally, the 24-hours urine collection was carried out to assess the excretion of sodium, calcium and phosphorus. The urine concentration of FGF23 (Intact) was measured using an enzyme-linked immunosorbent assay kit (Immutopics Inc., San Clemente, CA, USA) and expressed in RU/mL The urine concentration of renin was measured using a The Human Renin Quantikine ELISA Kit (R&D Systems, Minneapolis, MN) and expressed in pg/mL. The urine AGT concentration was measured using ELISA Kit for Angiotensinogen (Cloud-Clone Corp., Houston, TX) and expressed in ng/mL. These measurements were normalized by urine concentration of creatinine (cr.).
The laboratory tests were carried out at the Department of Laboratory Pediatric Diagnostics of the University Children's Clinical Hospital in Bialystok. Data analysis was performed using a computer program Statistica 10.0 PL (StatSoft, Tulsa, OK, USA). Value of $p<0.05$ was considered statistically significant. Before the study, the written consent was obtained from parents/legal guardian, all participants older than 16 years old. The study had approval of the Local Committee of Bioethics, Medical University of Bialystok.

Analysis of the results showed that the hypertensive participants had significantly higher urine FGF23/cr. and urine renin/cr. compare to the reference group. In terms of urine AGT/cr. there was no difference between hypertensive and reference group. In all participants we found significant positive correlations between urine FGF23/cr. and systolic blood pressure expressed as a standard deviation score (SDS) ($r=0.281$, $p=0.022$) and a significant negative correlation between urine FGF23/cr. and serum 25(OH)D level ($r=-0.322$, $p=0.036$) and urinary phosphorus excretion ($r=-0.711$, $p<0.001$). What is more, in hypertensive children and adolescent we observed a significant positive correlations between urine renin/cr. and 24 hours ABPM diastolic blood pressure expressed as SDS ($r=0.419$, $p=0.0002$) and between

renin/cr. and urine AGT/cr. (r=-0.266, p=0.044). In a reference group there were no significant correlations between examined parameters.

In addition, we also marked the plasma level of FGF23 in children and adolescents participating in the study. However, there was no statistically significant difference in plasma FGF23 concentration between hypertensive and reference group (p = 0.85). There was also no statistically significant correlation between plasma FGF23 and blood pressure or intrarenal RAS markers. These results have not been published so far.

The study has shown that both FGF23 and intrarenal RAS activation seem to play an important role in the pathogenesis of primary HT in children and adolescents. However, there was no obvious relation between these two mechanism in our study. It should also be noted that the role of FGF23 in the pathogenesis of HT is unclear. It was found that the hypertensive children and adolescent had significantly higher urine excretion of FGF23 compared to their healthy peers, however similar observation has not been made in case of serum FGF23 levels.