Streszczenie w języku angielskim

People with congenital absence of one kidney (unilateral renal agenesis) or loss due to disease or kidney donation have decreased renal mass which is associated with compensatory increase in glomerular filtration rate (GFR) of the other kidney. The importance of the problem is evidenced by the fact that main causes of chronic kidney disease (CKD) in the pediatric population are congenital anomalies of the kidneys and urinary system, which account for approximately 50% of all cases. Due to the improvement of perinatal care and more effective treatment of children with CAKUT, more and more patients survive to adulthood and develop symptoms of CKD.

The tests assessing kidney function (serum creatinine concentration, endogenous creatinine clearance, GFR) available in routine diagnostics are still not perfect, and most importantly, they do not detect subclinical changes. Proper biochemical assessment of patients with kidney disease is extremely important from the clinician's point of view. That is why the search for new biomarkers with high sensitivity and specificity for the assessment of early renal impairment is ongoing.

Recent years, there has been a growing interest in the role of a protein important in the diagnosis of inflammatory and systemic diseases with multi-organ involvement, such as the tumor necrosis factor-like weak inducer of apoptosis (TWEAK).

In studies carried out on a mouse model, TWEAK, apart from causing a direct inflammatory reaction, also stimulated mesangial cells, endothelial cells and podocytes to secrete cytokines, including the monocyte chemoattractant protein-1 (MCP-1) and regulated on activation, normal T cell expressed and secreted chemokine (RANTES). TWEAK was also confirmed to be a promoter of non-inflammatory compensatory hypertrophy of the kidney after unilateral nephrectomy in mice.

Hence, the question whether, similarly to the mouse model, also in children with a solitary functioning kidney (SFK), the concentrations of the above-mentioned markers increase and whether there is a relationship between their levels and the progression of chronic kidney disease.

The aims of the studies included in this doctoral dissertation were: 1. Assess and compare serum TWEAK concentration and urinary excretion of MCP-1 and RANTES in patients with congenital and acquired solitary functioning kidney; 2. Test TWEAK and the cytokines MCP-1 and RANTES potential usefulness as biomarkers of renal impairment in children with solitary functioning kidney; 3. Determine probable cut-off points, which may be used in clinical practice in differentiation of SFK children with impaired renal function.

The study included 80 children and adolescents divided into 2 subgroups: with congenital (subgroup A - 54 patients) or acquired (subgroup N - 26 patients) solitary functioning kidney. In addition, patients from the study group (B) were divided into those with features of impaired renal function (albuminuria and/ or decreased eGFR <90mL/min/1.73m^2 and/ or hypertension) and those with normal renal function. The reference group (K) consisted of 40 children, appropriately matched according to sex and age, with normal ultrasound imaging of the urinary system.

Serum TWEAK concentration and urinary excretion of uMCP-1 and uRANTES were performed at the Laboratory of the Department of Pediatrics and Nephrology, University Children's Clinical Hospital of Bialystok.

The study was approved by the Bioethics Committee of the Medical University of Bialystok (RI-002/137/2018) and the Bioethics Committee at the Faculty of Medical Sciences of the University of Warmia and Mazury in Olsztyn (No. 27/2017).

Based on conducted research, significantly higher levels of serum TWEAK and urinary MCP-1 and RANTES excretion were found in the study group compared to the reference group ($p<0,05$).

The ROC analysis determined the cut-off point for TWEAK equal to 421.934 pg/mL to identify children with impaired renal function (albuminuria and/or decreased eGFR <90 mL/min/1.73m^2 and/or hypertension) among SFK patients. The analysis of classification trees showed that the most optimal cut-off point of patient differentiation is the TWEAK value of 395.628 pg/mL. It should be noted that in both analyses the proposed cut-off point was similar.

In the case of uRANTES, the ROC analysis determined the cut-off point equal to 10.734 pg/mL. Based on the classification trees analysis, the value of 10.332 pg/mL definitely differentiates patients into those with normal and impaired renal function. It is also very important that both the cut-off points in the ROC curve and classification trees are almost identical.

Conclusions:

This is the first study investigating serum TWEAK and urinary excretion of MCP-1 and RANTES together in children with SFK. Obtained results indicate that TWEAK and RANTES may serve as potential markers of renal impairment in SFK children.