**SOME FACTORS OF FIBROGENESIS AND ANGIOGENESIS AS BIOMARKERS OF RENAL SCARRING IN CHILDREN WITH VESICOURETERAL REFLUX**

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Introduction and Aim. One of the most common forms of congenital obstructive uropathy in children is vesicoureteral reflux (VUR), which is observed in 1-2% of pediatric population, and its incidence in urinary tract infection is 70%. According to the International Committee for the Study of Reflux, the incidence of nephrosclerosis in VUR among children of the European population is 48% and it results in the development of the terminal stage of chronic renal failure in 25-60% of patients. Approximately 25% of children with renal scarring (RS) resulting from VUR require hemodialysis and kidney transplantation. The aim of the study was to improve the early diagnosis of the formation and progression RS in children with VUR and chronic pyelonephritis by assessing the urine levels of transforming growth factor beta1 (TGF-β1) and vascular endothelial growth factor (VEGF).

Material and Methods. The study involved 117 children (32 boys and 85 girls) aged from 6 months to 17 years with III-V degrees of VUR and chronic pyelonephritis. Taking into account the presence or absence of signs of the RS, the examined children were divided into groups: Group 1 (n = 78) included patients with III-V degree VUR without signs of the RS, group 2 (n = 39) – patients with III-V degree VUR and signs of the RS. The control group included 16 practically healthy children.

Urine concentrations of TGF-β1 and VEGF were measured with commercially available Platinum ELISA (catalog # BMS249/4 and BMS249/4TEN human TGF‑β1 # BMS277/2/ and BMS277/2TEN human VEGF, Austria), according to the manufacturer’s instructions. Renal ultrasound, 99mTc‑dimercaptosuccinic acid scintigraphy (DMSA) and voiding cystourethrography were carried out in all patients. Statistical analyses were performed with StatSoft STATISTICA Version 8 (Tulsa, OK). Non-parametric variables are given as median (interquartile range). Differences between groups were tested using Mann-Whitney test. The clinical studies from which materials were obtained for the current study were approved by the Medical Ethics Committee of the Kharkiv National Medical University and conducted in accordance with the guidelines of the Declaration of Helsinki. All participants and/or their parents gave written informed consent.

Results. Assessment of the results of the study of pro-fibrotic cytokines revealed a statistically significant increase in urinary excretion of TGF-β1 and VEGF in children with VUR and chronic pyelonephritis, regardless of the presence or absence of signs of the RS, indicating remodeling processes in vessels and renal parenchyma.

The urine TGF-β1 levels were increased in the patients of the 1st and 2nd groups, compared with controls (70.2 (28.7; 105.5) and 139.5 (117.2; 215.9), compared with 14.0 (3.1; 29.2) pg/ml, respectively) (P1-k = 0.0002; P2-k = 0.0001)). The level of urinary excretion of TGF-β1, as the main factor for the development of fibrosis, in children of the 2nd group was significantly higher than those of patients of the 1st group ((139.5 vs. 70.2), (P1-2 = 0.0010)). Indices of urinary excretion of VEGF in children of the 2nd group were significantly lower than those of patients of the 1st group (124.9 (104.9; 152.6) and 244.2 (189.3; 295.8)) (P1‑2= 0.0101), but were higher than those of control group children (124.9 (104.9; 152.6) and 40.9 (27.2; 59.3)) (P1-k = 0.0003), which further confirmed existing nephrosclerosis.

The conducted research allowed to propose non-invasive methods for early diagnosis of kidney damage in children with VUR and chronic pyelonephritis, namely urinary excretion rates: TGF-β1> 109.9 pg / ml, VEGF <207.6 pg / ml.

#### Conclusions. We found out significant differences in children with VUR and with or without RS uTGF-β1, uVEGF. The determination of uTGF-β1 and uVEGF levels can provide additional information about the status of the renal parenchyma status in children with VUR especially in places where other investigations are not available.