ASSOCIATION OF THE TRANSFORMING GROWTH FACTOR-B (*TGFB*) GENE *C(-460)T* POLYMORPHISM WITH URINARY EXCRETION OF KIDNEY INJURE BIOMARKERS IN PATIENTS WITH CHRONIC GLOMERULONEPHRITIS

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OBJECTIVES

Transforming growth factor-β (TGF-β) is upregulated in chronic kidney disease (CKD) and as a profibrotic cytokine TGF-β participates in the pathomechanisms of glomerular and tubulointerstitial sclerosis. In clinical trials high circulating or urinary TGF-β was associated with signs of kidney injury and CKD progression. Five polymorphisms of the TGF-β1 gene have been identified, but clinical data concerning their prognostic significance are limited and controversial.

The aim of the study was to estimate in chronic glomerulonephritis (CGN) patients the associations of *TGFB* gene *C(-509)T* polymorphism and urinary excretion of kidney injure biomarkers: neutrophil gelatinase-associated lipocalin (NGAL) and type IV collagen (COL4).

METHODS

65 CGN patients (mean age 42.7±16.8 yrs; 47.7% men) were examined. 92.3% patients developed arterial hypertension; nephrotic syndrome was revealed in 29.3%; $eGFR_{CKD-EPI}$< 60 ml/min/1.73 m^2 was found in 30.8% of the study patients. Mesangioproliferative GN was revealed in 34.6%, membranoproliferative GN – in 17.4%, minimal change disease – in 13.4%, focal segmental glomerular sclerosis – in 9.9%, membranous nephropathy – in 20.1%, diffuse nephrosclerosis – in 4.6%. Genotyping was performed by polymerase chain reaction-restriction length polymorphism. Morning urine samples were analyzed by ELISA to determine the excretion of NGAL and COL4.

RESULTS

The frequencies of genotypes were as follows: *CC*-41.5%, *CT*-44.6%, *TT*-13.8%. For further analysis patients with CGN were grouped according to *TGFB* gene *C(-509)T* genotypes in *CC, CT,* and *TT* group. *TGFB* gene variants were not associated with PU, $eGFR_{CKD-EPI}$, and other clinical signs of CGN activity as well as morphological changes. But we found statistically significant higher urinary excretion of NGAL and COL4 in patients with *TT*-genotype in compared with *CC* and *CT* genotypes (Table).

Table: eGFR, PU and urinary excretion of NGAL and COL4 according to *TGFB C(-509)T* genotypes

	***CC* genotype (n=26)**	***CT* genotype (n=29)**	***TT* genotype (n=9)**	**p value**
eGFR, ml/min/1.73 m^2	80.8 (53.1;104.0)	73.7 (55.8; 101.4)	91.5 (46.3;114.1)	> 0.05
PU, g/24h	0.9 (0.5;3.0)	1.6 (0.3;4.2)	1.3 (0.5;8.6)	> 0.05
NGAL, μg/l	0.9 (0.07;4.1)	0.9 (0;6.5)	17.1 (1.6;69.5)	CC vs.TT p=0.010 CT vs.TT p=0.026
COL4, μg/l	2.4 (1.8;3.3)	2.5 (1.6;3.3)	5.2 (2.9;16.1)	CC vs. TT p=0.019 CT vs. TT p=0.018

CONCLUSIONS

In this study we have found the significant associations between the *TGFB* gene *C(-509)T* polymorphism and urinary excretion of NGAL and COL4. Although there were no association of *TT*-genotype with traditional signs of CKD severity and progression so as PU and eGFR, the higher levels of NGAL and COL4 as the earliest biomarkers of kidney injury in CKD are of great interest and substantiate the need for prospective trials.

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