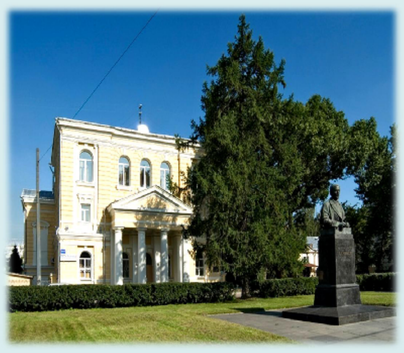
URINARY LEVELS OF INFLAMMATORY, PROFIBROGENIC AND KIDNEY SELF-DEFENSE FACTORS IN PATIENTS WITH CHRONIC GLOMERULONEPHRITIS (CGN)



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INTRODUCTION AND AIMS

During CGN, a number of mediators are released from infiltrating and resident cells, leading to kidney inflammation, apoptosis and fibrosis. Many protective molecules are produced in response to injury and play an important role in the kidney self-control of damage. The balance between offence and defense factors determines CGN regression or progression. Our study aim was to assess urinary excretion of inflammatory, profibrogenic and kidney self-defense factors in patients (pts) with different CGN course.

METHODS

53 active CGN pts were studied: 23 - with proteinuria (PU) 1-3 g/d (I group), 30 - with nephrotic syndrome (NS) (II group), including 7 pts with severe NS (anasarca, PU to 12 g/d, hypoalbuminemia < 20 g/L), and 7 pts - with NS and impaired renal function. Urinary level of inflammatory interleukin-6 (IL-6), a main profibrogenic growth factor TGF-β, apoptosis biomarker caspase-9 (CSP-9), anti-inflammatory factors IL-10 and IL-1 receptors antagonist (IL-1Ra), vessel endothelial growth factor (VEGF) and protective heat shock proteins (HSP-27 and HSP-70) were measured by ELISA.

RESULTS

Urinary excretion of IL-6 and TGF-β in pts with NS was significantly increased compared to I CGN group (tab.1). In severe NS urinary levels of these cytokines were higher than in moderate NS. Exactly in CGN with NS we revealed elevated CSP-9 in the urine, reflecting local renal apoptosis activation (tab.1).

Table 1. Urinary excretion of IL-6, TGF-β and caspase-9 in patients with CGN

CGN pts group	IL-6 (ng/ml)	TGF-β (pg/ml)	CSP-9 (ng/ml)
I . PU 1-3 g/d (n=23)	5,44 [1,3; 12,8]	1,1 [0,4; 2,2]	31,4 [31,3; 32,35]
II. NS (n=30)	9,97 [1,95; 25,6]*	1,65 [0,7; 2,4]*	33,1 [32,0; 34,1]*
Moderate NS	9,21 [0,45; 16,38]	1,3 [0,7; 2,3]	32,5 [31,8; 33,9]
Severe NS	11,2 [2,61; 82,9]**	3,0 [2,2; 4,6]**	33,7 [32,0; 34,4]
*p<0,05 compared to I group; **p<0,05 compared to moderate NS			

With offense factors in NS (especially severe) was increased the urinary excretion of anti-inflammatory IL-1Ra (tab.2). But in progressive CGN course (NS and renal failure) their levels were decreased (0,4 [0,11; 0,73] ng/ml p<0,05), they negatively correlated with serum creatinine (Rs= -0,22, p<0,05). In active CGN without NS we revealed only trace quantities of urinary IL-10, in pts with NS its level was undetectable.

Protective HSP-27 and HSP-70 urinary levels were significantly higher in pts with NS compared to I group (tab.2). These indices correlated directly with urinary IL-6 (Rs=0,44, p<0,05 and Rs=0,59, p<0,05) and PU (Rs=0,27, p<0,05 and Rs=0,26, p<0,1) and negatively with serum albumin (Rs= -0,22, p<0,05 and Rs= -0,42, p<0,05). In CGN pts with severe NS urinary excretion of HSP were higher than in moderate NS (tab.2).

Urinary level of VEGF (as survival factor that reflecting the glomerular permeability) was raised in CGN with NS compared to I group. It was the highest in severe NS (tab.2) and directly correlated with PU (Rs=0,673, p<0,01). But in progressive CGN course its level significantly decreased, negatively correlated with serum creatinine (Rs= -0,763, p<0,05).

Table 2. Urinary excretion of protective factors in patients with CGN

CGN pts group	IL-1Ra (ng/ml)	IL-10(ng/ml)	HSP-27 (ng/ml)	HSP-70 (ng/ml)	VEGF (pg/ml)
I . PU 1-3 g/d (n=23)	0,46 [0,08; 0,82]	0,1 [0; 1,1]	0,76 [0,68; 1,14]	0,43 [0,41; 0,45]	185,7 [163,8; 259,8]
II. NS (n=30)	1,22 [1,16; 2,85]*	0	1,1 [0,73; 1,83]*	0,46 [0,43; 0,50]*	300,15 [224,5; 547,3]*
Moderate NS	0,5 [0,07; 3,32]	0	0,84 [0,71; 1,81]	0,43 [0,41; 0,51]	260,5 [183,95; 279,2]
Severe NS	1,34 [0,34; 2,27]**	0	1,35 [0,93; 4,02]**	0,6 [0,5; 2,5]**	939,6 [824,2; 1049,5]**
*p<0,05 compared to I group; **p<0,05 compared to moderate NS					

CONCLUSION

Determination of disturbances between injurious and glomerular self-defense factors in the urine may be useful to assess CGN activity and prognosis.

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