URINARY EXCRETION OF PODOCYTE'S DAMAGE AND SELF-DEFENSE FACTORS IN PATIENTS WITH CHRONIC GLOMERULONEPHRITIS (CGN)

OLGA ESKOVA, NATALIA NEPRINTSEVA, NATALIA CHEBOTAREVA, IRINA BOBKOVA, LIDIYA KOZLOVSKAYA,

I.M. Sechenov First Moscow State Medical University, Nephrology department, Russia

INTRODUCTION

The imbalance between local injury factors and defense mechanisms determines the tissue damage in CGN. The most interest of recent studies was focused on the effector link of renal inflammation, but self-defense mechanisms of kidney cells, including podocytes (Pdc), are poorly studied.

THE AIM

The aim of the study was to evaluate in patients (pts) with different CGN courses the podocyturia (PdcU) level (as a marker of Pdc's injury), urinary excretion of proinflammatory interleukin-6 (IL-6) and heat shock protein-27 (HSP-27) (as a protective intracellular protein, which helps to keep structure of Pdc's actin cytoskeleton).

METHODS

73 CGN patients were studied: 20 - inactive CGN (I group), 23 - active CGN with proteinuria (PU) 1-3 g/d (II group), 30 active CGN with nephrotic syndrome (NS) (III group), including 16 patients with moderate NS (PU-3-5 g/d), 7 patients with severe NS (anasarca, PU – 6-12 g/d, hypoalbuminemia < 20 g/L), and 7 patients - with NS in combination with nephritic syndrome and impaired renal function. 8 healthy subjects were studied as control. PdcU was estimated by urinary flow cytometry, urinary IL-6 and HSP-27 levels were measured by ELISA.

RESULTS

The PdcU, urinary IL-6 and HSP-27 levels in active CGN were higher than in control. These indices in III pts group were significantly higher than in II and I groups (table 1).

In active CGN urinary HSP-27 excretion correlated directly with PU (Fig. 1) and negatively with serum albumin level (Rs=-0,22, p<0,05). In CGN with severe NS PdcU and urinary HSP-27 levels were higher than in CGN with moderate NS (168 [19; 782] cells/μl vs 7,87 [4,2; 30] cells/μl and 2,28 [0,93; 4,02] ng/ml vs 1,07 [0,71; 1,72] ng/ml respectively, p<0,01).

Urinary IL-6 excretion in progressive CGN course was significantly raised compared to patients with NS and normal renal function (22 [10,2; 92,5] ng/mL vs 8,27 [1,48; 16,35] ng/ml, p<0,05). Exactly in these patients urinary IL-6 correlated positively with serum creatinine level (Rs=0,53, p < 0,01) and a negatively - with GFR (Fig. 2).

We consider that revealed direct correlation between PdcU and urinary IL-6 (Fig. 4) reflects podocytes injury during a local immune inflammation. At the same time, correlation between the PdcU and urinary HSP-27 (Fig. 3) in NS indicates the reciprocal activation of mechanisms, which limit podocytes structural damage and glomerular permeability.

Table 1. Urinary excretion of heat shock protein-27 (HSP-27) , interleukin-6 (IL-6) and podocyturia level in patients with CGN (n=73)

Patients groups	N	HSP-27 urinary level (ng/ml)	Podocyturia (cells/μl)	IL-6 urinary level (ng/ml)
I. Inactive CGN	20	0,72 [0,65;0,98] *	6,2 [3,7;6,8] *	5,35 [0,41; 13,1] *
II. Active CGN with PU 1-3 g/d	23	0,76 [0,68;1,14] * °	6,77 [3,2;17,4] * °	5,44 [1,3; 12,8] * °
III. Active CGN with NS	30	1,1 [0,73; 1,83] °	16 [8;38,4] * °	9,97 [1,95;25,6] * °
Healthy control	8	0,73 [0,66;0,96]	0 [0;6]	2,05 [1,05;4,26]

* - p<0,05 vs «III patients group» °- p<0,05 vs «healthy control»

Fig 1. Correlation between urinary HSP-27 and PU level in pts with active CGN

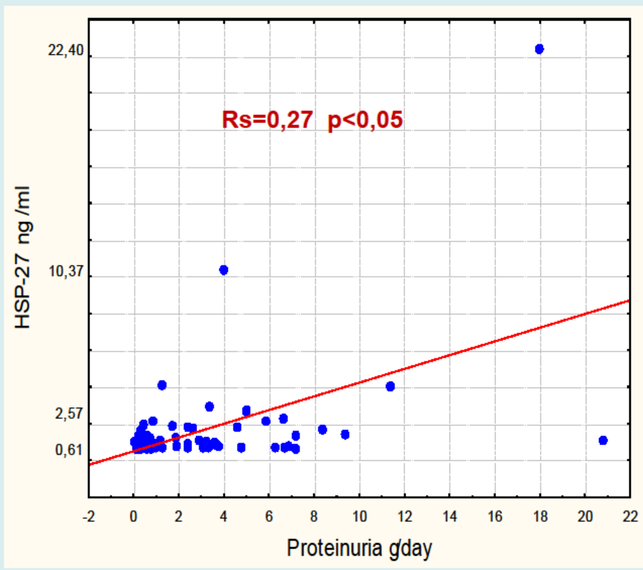


Fig 2. Correlation between urinary IL-6 and GFR in pts with progressive CGN course

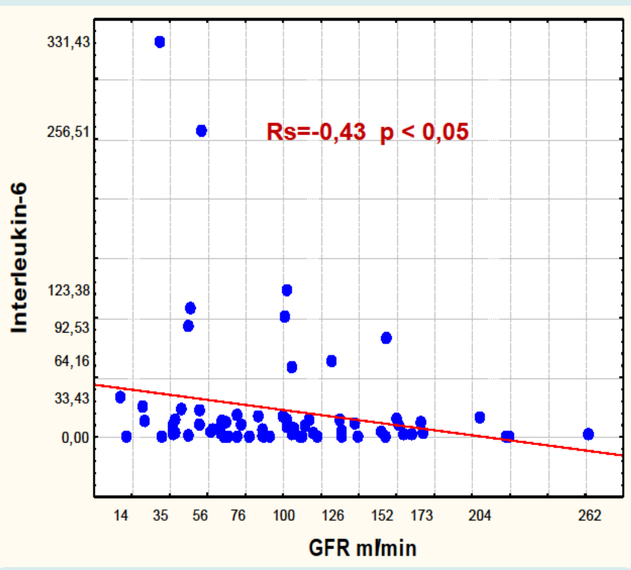


Fig 3. Correlation between urinary HSP-27 and PdcU level in CGN pts with NS

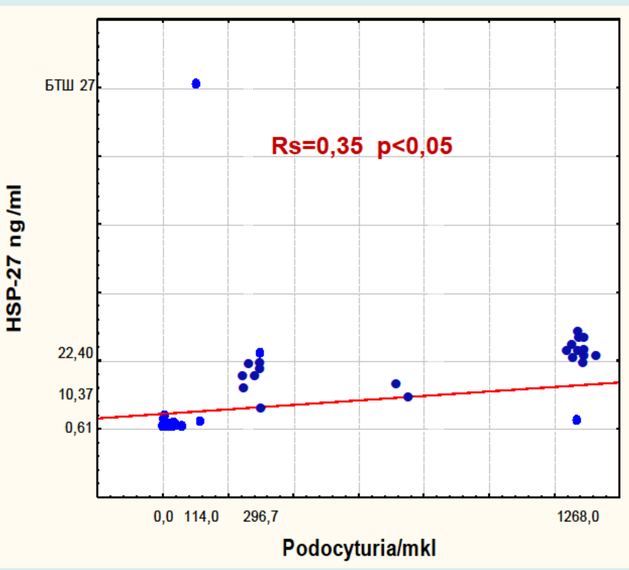
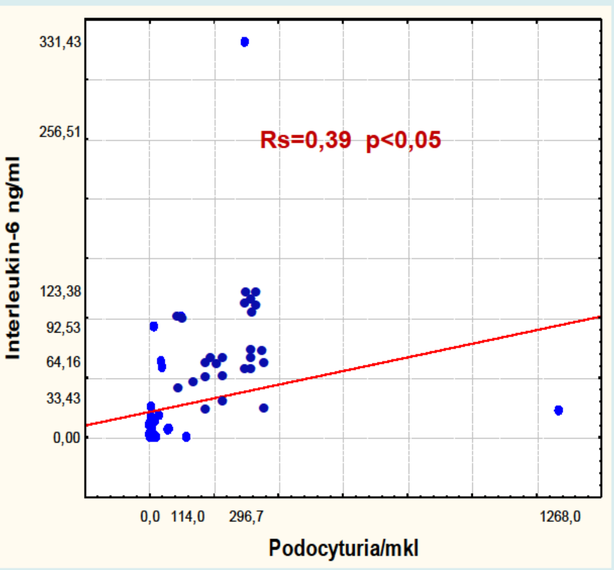


Fig 4. Correlation between urinary IL-6 and PdcU level in CGN pts with NS



CONCLUSION

Active podocytes damage in proteinuric forms of CGN and activation of local synthesis of intracellular protective molecules in response to environmental perturbation, inflammation and podocytes injury can be proposed according to our data.

Insufficiency of some kidney self-defense mechanisms can be considered as a risk factor for CGN progression.

REFERENCES

1. Kitamura M., Fine M.G. Concept of glomerular self-defense. Kidney. Intern. 1999; 55: 1639-1671
2. Tsagalis G.C., Nikolopoulou N., Sotsiou F., Hadjiconstantinou V. The Expression of heat shock proteins 27 and 70 in lupus nephritis. Hospital Chronicles. 2006; 1(3):125-129
3. Vogelmann S.U., Nelson W.J., Myers B.D., Lemley K.V. Urinary excretion of viable podocytes in health and renal disease. Am J Physiol Renal Physiol. 2003; 285: F40-F48
4. Yu D., Petermann A., Kunter U., Rong S., Shankland S.J., Floege J. Urinary podocyte loss is a more specific marker of ongoing glomerular damage than proteinuria. J Am Soc Nephrol. 2005; 16: 1733-1741