CLINICAL SIGNIFICANCE OF PODOCYTE INJURY MARKERS EVALUATION IN PATIENTS WITH PRIMARY GLOMERULOPATHIES

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Objectives:

Podocyte injury is crucial in progression of glomerular diseases because of limited rate of podocyte proliferation. Thus early recognition of podocyte damage has a significant clinical value. A few years ago identification of podocyte injury biomarkers in urine was proposed as a method of early identification of podocyte structural changes. In our investigation we studied daily urinary exretion of nephrin, podocalyxin (PCX) and soluble tumor necrosis factor receptor type 1 (sTNF-R1) as a possible marker of podocyte apoptosis. The aim of our work was the assessment of relationship between biomarkers excretion level and clinical and pathomorphological signs of glomerular diseases.

Methods:

71 patients with byopsy proven primary glomerulopathies were included in the study. Patients with acute kidney injury, infectious diseases, heart failure, respiratory insufficiency and cancer were excluded. According to the results of light and electron microscopy 23 (32,4%) patients had IgA-nephropathy (mesangial proliferative glomerulonephritis), 14 (19,7%) - focal segmental glomerulosclerosis, 22 (31,0%) - membranous nephropathy, 12 (16,9%) - minimal change disease. Besides standart laboratory and instrumental investigations samples of serum and daily urine were obtained in the day of byopsy. Nephrin, PCX and sTNF-R1 levels were studied using ELISA-method. Glomerulosclerosis, tubulointerstitial sclerosis and tubular atrophy were estimated quantitatively and semi quantitatively.

Graphs and tables

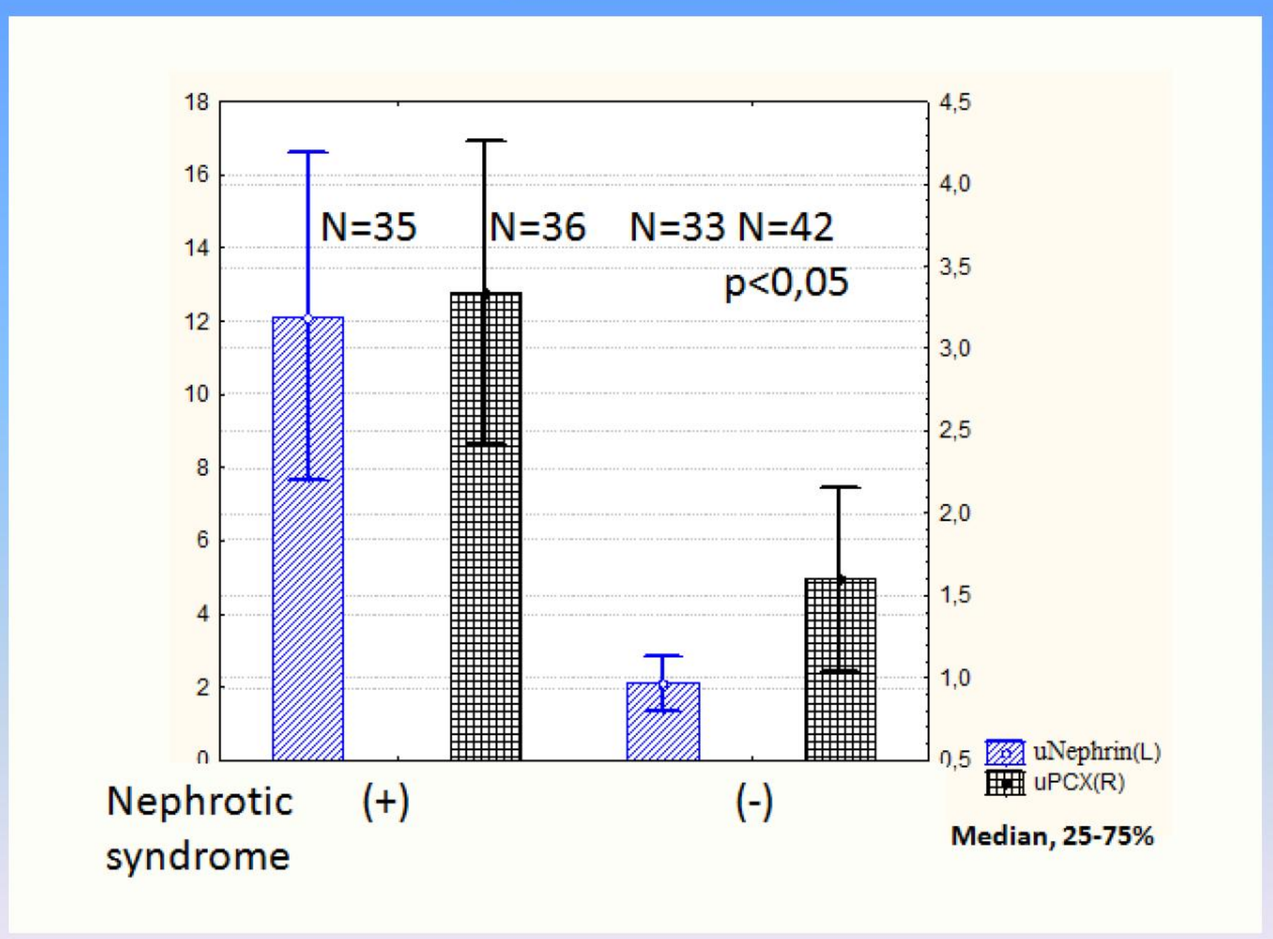

Figure 1: uNephrin and uPCX excretion in patients with and without nephrotic syndrome

Results:

Excretion of both nephrin and PCX correlated with level of daily proteinuria (r=0,67, r=0,43 respectively, p<0,05). The rates of nephrin and PCX were the highest in patients with nephrotic syndrome. Proteinuria and nephrinuria rates were lower in patients who received cyclosporine therapy. PCX excretion was higher in patients with history of arterial hypertension and there was a significant difference of podocalyxinuria depending on duration of arterial hypertension (more or less than 5 years, p<0,05). Urinary levels of sTNF-R1 correlated with rates of nephrin and PCX (r=0,40, r=0,41 respectively, p<0,05). There was no correlation between markers excretion and such morphological signs of kidney injury like glomerular, tubular sclerosis and tubular atrophy.

Conclusions:

Correlation between daily proteinuria and urinary podocyte injury markers excretion supports the conception that podocyte injury is crucial in development of high proteinuria and nephrotic syndrome. Reduction proteinuria and nephrinuria due to cyclosporine therapy also confirms this fact. PCX rate depends on course of arterial hypertension. sTNF-R1 marker can reflect apoptosis of podocytes as one of the earliest stage of their damage. There was no relation of markers levels with pathological changes on light microscopy. In our opinion excretion of podocyte injury biomarkers characterises the presence of ultrastructural changes which may be revealed only by electronic microscopy.

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