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The Role of Anti-Inflammatory Cytokines in Patients With Kidney Nephrosclerosis in Chronic Pyelonephritis

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ABSTRACT

In recent years, the pathogenetic mechanisms of the formation of nephrosclerosis have been actively studied, since nephrosclerosis is formed in 30-60% of patients with impaired urodynamics. At the same time, the participation of many factors in the progression of kidney damage in nephrosclerosis has been proven.

KEYWORDS: *Anti-Inflammatory, Pyelonephritis.*

Work has been carried out to study the dependence of the activity of the inflammatory process in the kidneys on the concentration of various types of inflammatory mediators in the blood serum, as well as in the urine. However, the analysis of the literature did not reveal information about the cellular composition of urine and the balance of inflammatory mediators of kidney nephrosclerosis. Thus, the present study is aimed at identifying prognostic significant clinical and molecular markers of kidney nephrosclerosis, which are necessary for timely diagnosis and personalized treatment of this category of patients.

Purpose of the study: To assess the information content of diagnostic laboratory biomarkers of kidney nephrosclerosis in patients with chronic pyelonephritis.

Material and methods: We examined 78 patients with kidney nephrosclerosis, combined with chronic pyelonephritis, aged 22 to 58 years, observed in the department of nephrology, urology and endocrinology of the TMA multidisciplinary clinic. Of these, 40 patients with CRF without nephrosclerosis (1st group) and 38 with CRF nephrosclerosis (2nd group). The control group consisted of 24 practically healthy individuals. Immunoenzymatic, clinical and biochemical studies were carried out using automatic analyzers of the company "Mindray" diagnosticum "HUMAN".

In accordance with the tasks set, we determined the daily urinary excretion of cytokines and growth factor in patients with nephrosclerosis in chronic pyelonephritis. Determination of cytokines and growth factor was carried out by enzyme immunoassay. The daily urinary excretion of cytokines was determined: IL-1, IL-6, IL-8, IL-10; as well as growth factors; tumor necrosis factor-a (TNF-a). As is known, IL-1 is a mediator of acute and chronic inflammation; IL-6 induces the synthesis of acute phase proteins, enhances the production of IL-2 by T-helpers that recognize the antigen, and also, acting on brain cells, promotes the release of adrenocorticotropic hormone (ACTH).). IL-8 belongs to the group of chemokines, the main property of which is to provide chemotaxis to the area of inflammation of various cell types.

When comparing the results of daily urinary excretion of cytokines and growth factors in patients with chronic pyelonephritis without signs of nephrosclerosis, patients with nephrosclerosis in CRF found significant differences and a trend in the excretion of interleukins in the urine. Analysis of the daily urinary excretion of cytokines (IL-1, IL-6, IL-8, IL-10) and growth factors (TNF-a) indicates the predominance of the production and excretion of pro-inflammatory, prosclerotic cytokines and growth factor over anti-inflammatory ones, which confirms the prevalence process of fibrogenesis

over inflammation in chronic pyelonephritis. As can be seen from the presented research results, the content of IL-1 in the urine of patients with nephrosclerosis of concomitant chronic renal failure increases by 2.2 times relative to healthy individuals.

As is known, the main source of IL-1 production is phagocytic mononuclear cells of various tissue localization: macrophages and monocytes of peripheral blood and peritoneal exudate, Kupffer cells of the liver, Langerhans cells, microglial cells of the nervous tissue. At the same time, among the set of substances that cause the production of IL-1, the most active components of the bacterial cell wall and cytokines appearing in the focus of inflammation are responsible for the formation of a local inflammatory reaction and an acute phase response at the level of the body.

It should be noted that IL-6 induces the synthesis of acute phase proteins, and therefore, like IL-1 and TNF-a, it can be classified as an inflammatory cytokine. As is known, the secretion of IL-6 increases under the influence of stress and is regulated by catecholamines according to the principle of positive feedback. An increase in the level of IL-6 is observed in severe inflammatory processes, infections, and in violation of the secretion of vasopressin (antidiuretic hormone). A quick and pronounced reaction to this entire diverse group of endogenous and exogenous substances indicates that this cytokine belongs to the category of early mediators. This property is of particular importance in the rapid formation of the body's response to tissue damage.

Analysis of the presented research results showed that the concentration of IL-6 in the urine is also increased in the group of patients with renal nephrosclerosis combined with chronic renal failure. This cytokine prepares the proliferative response of T cells to a mutagen or antigen, provides an increase in the production of IL-2 by T helpers that recognize the antigen. In nephrosclerosis in patients with chronic renal failure, high values of IL-6 in the urine, in our opinion, suppresses the secretion of TNF-a and interleukin-1, while activating the production of acute phase inflammation proteins by the liver, and also stimulates the hypothalamic-pituitary-adrenal system, which in turn regulates the inflammatory process. In this sense, IL-6 can be considered as both an inflammatory and an anti-inflammatory cytokine. In this situation, high levels of IL-6, in our opinion, are produced by smooth muscle cells of blood vessels and are involved in the production of immunoglobulins by B-lymphocytes in response to the intake of antigens against the background of tissue damage.

Table 1. The content of urine cytokines in patients with nephrosclerosis in chronic pyelonephritis

Indicators	Healthy faces n=24	Patients with CRF without nephrosclerosis n=40	Patients with nephrosclerosis with CRF n = 38
ИЛ-1 пг/мл	11,88±0,25	18,01±1,65	26,13±2,01*
ИЛ-6 пг/мл	9,54±0,11	9,78±0,87	18,57± 1,64*
ИЛ-8 пг/мл	14,28±0,48	14,83±1,34	44,53± 3,67*
ИЛ-10 пг/мл	18,23±1,67	12,34±1,23	5,46±0,44*
ФНО-а пкг/мл	131,45±0,32	278,56±1, 09	1829,67±25,59*

Note: * - significance of differences P <0.05 relative to the comparison groups. The properties of IL-8 to cause cell migration and promote their adhesion determine it as an active participant in an acute inflammatory reaction at the sites of pathogen penetration. As can be seen from the presented research results, an increased level of IL-8 in the urine of patients with kidney nephrosclerosis is associated with chronic inflammatory conditions and correlates with tissue infiltration of neutrophils in kidney diseases.

Inflammatory cytokines also include TNF-a. TNF-α in the urine of patients with nephrosclerosis of the kidneys combined with chronic renal failure increased by 2.6 times, respectively, compared with healthy individuals. It should be noted that a prolonged and pronounced increase in TNF-a in the urine is apparently due to the consequence of inflammatory-destructive processes in the tissues of the kidneys and reflects the intensity of autoimmune processes. The factual material revealed in our studies, in particular, the increase in the level of the studied cytokines in the urine, may be associated with the degree of severity of destructive processes, i.e. the prevalence of fibrogenesis over inflammation in chronic pyelonephritis.

Thus, the features of the cytokine status in the urine allow us to expand the understanding of the pathogenesis of kidney nephrosclerosis in patients with chronic renal failure due to interstitial inflammation and tissue destruction with the participation of IL-1, IL-6, IL-8, TNF, as well as with the likelihood of immune aggression or immunosuppression. The obtained results show that the determination of the level of IL-1, IL-6, IL-8 and TNF-a in the urine are useful for the early diagnosis of nephrosclerosis in patients with chronic pyelonephritis.

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