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# ASSESSMENT OF VASCULAR ENDOTHELIUM CONDITION IN PATIENTS WITH RENAL NEPHROSCLEROSIS DUE TO CHRONIC PYELONEPHRITIS

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**Abstract:**
It is known that modern diagnostic methods allow visualization of the state of the kidney parenchyma, but each of the described examination methods has its own shortcomings. In addition, in patients with chronic kidney disease, some parameters of renal blood flow significantly change and are misinterpreted, which does not allow to reliably determine the presence and degree of sclerosis of the renal parenchyma.
The article covers information on determining the prognostic significance of markers for predicting the degree of damage to kidney structures during the treatment stages of patients with nephrosclerosis on the basis of chronic pyelonephritis.

**Keywords**: diagnostic methods, endothelial dysfunction, vasomotor, chronic pyelonephritis, thrombophilic, adhesive, renal fibrosis, angiogenicity.

## Introduction

Today, many studies have been conducted on the problem of signs of endothelial dysfunction in the development of kidney nephrosclerosis in chronic pyelonephritis, and it is noted that information on the pathogenesis and diagnosis of nephrosclerosis in many cases remains contradictory, and new sources of the disease are being identified. done These problems are related to the fact that the mechanisms of the formation of the main components of kidney nephrosclerosis in chronic pyelonephritis are not fully defined, as well as the difficulty of diagnosis in the early stages of the disease [1].
Modern diagnostic methods make it possible to imagine the state of the kidney parenchyma, but each of the described examination methods has its own shortcomings. In addition, in patients with chronic kidney disease, some parameters of renal blood flow significantly change and are misinterpreted, which does not allow to reliably determine the presence and degree of sclerosis of the renal parenchyma. Unfortunately, the results of such studies often depend on the subjective point of view and the skills of the specialist who performs them, and do not allow a full assessment of the degree of sclerosis and the effectiveness of treatment in dynamics [2].

Endothelial dysfunction is one of the most important links in the development of interstitial inflammation and fibrosis in progressive forms of kidney damage [3].

**Materials and Methods**

Endothelial dysfunction refers to the imbalance between the production of vasoconstrictor, prothrombotic and proliferative substances produced by the endothelium, on the one hand, and the production of vasoconstrictor, prothrombotic and proliferative factors, on the one hand.

There are four forms of endothelial dysfunction:

- vasomotor;
- thrombophilic;
- adhesive;
- angiogenicity.

The causes of endothelial dysfunction can be various factors: tissue hypoxia, age-related changes, damage by free radicals, dyslipoproteinemia, cytokine, hyperhomocysteinemia, hyperglycemia, hypertension, exogenous and endogenous intoxications [4].

Endothelial dysfunction can cause structural damage in the body: acceleration of apoptosis, necrosis, desquamation of endotheliocytes. However, functional changes in the endothelium usually precede morphological changes in the vascular wall [5].

Endothelial dysfunction may have prognostic value due to its early manifestation. Currently, this pathology is being studied by many foreign and domestic authors, including among patients with kidney pathology, it occupies one of the leading positions in the structure of morbidity.

Endothelial dysfunction is important among the mechanisms of development of renal fibrosis. Renal arteries have been shown to be highly sensitive to endothelin-1. The effect of endothelin-1 on the development and progression of renal fibrosis has been determined [6].

Recent studies have significantly changed the understanding of the role of the vascular endothelium in general homeostasis. Endothelial dysfunction is a central link in the pathogenesis of chronic diseases such as atherosclerosis, hypertension, diabetes, chronic kidney disease, etc.

At the same time, endothelial dysfunction has a systemic nature and occurs not only in large vessels, but also in the microcirculatory system. Endothelial dysfunction is one of the most important links in the development of interstitial inflammation and fibrosis in progressive forms of kidney damage.

Endothelial dysfunction plays an important role in the diagnosis of renal nephrosclerosis in patients with chronic pyelonephritis, in particular endothelin-1, Willebrand factor, plasminogen activator inhibitor, tissue plasminogen activator and fibronectin. In this regard, a deeper understanding of the cellular and molecular mechanisms of renal parenchymal fibrosis is very important and is necessary not only to form a new point of

view on the pathogenesis of the process, but also to develop appropriate treatment tactics.

Endothelial dysfunction can cause structural damage in the body: acceleration of apoptosis, necrosis, desquamation of endotheliocytes. Due to the early manifestation of endothelial dysfunction, it is considered to have prognostic value. Early detection of the disease allows to slow down the development of nephrosclerosis and in some cases even prevent the loss of kidney function.

Endothelin-1 is a peptide consisting of 21 amino acids and is the most potent vasoconstrictor known to date, having a stronger and longer-lasting effect than angiotensin-2. The study of the role of endothelin-1 showed that it is the only isoform found in the endothelial cells of the aorta, and it is also present in other organs, including the brain, heart, lungs, and kidneys.

Previously, it was believed that endothelial-1 was only synthesized by endothelial cells. Renal epithelial cells, mesangial cells, leukocytes, macrophages, cardiomyocytes, and smooth muscle cells have been proven to have this ability. Its synthesis is regulated in an autocrine manner. The synthesis of endothelin-1 is regulated by physicochemical factors such as vascular pulsatility, blood pressure, pH, and hypoxia.

There are several types of endothelin-producing cells in the kidney, including endothelial cells, mesangiocytes, and epithelial cells that support its cumulative production.

Endothelial activation and damage are important in the development of a wide range of pathological conditions. It is clear that the evaluation of the condition of endothelial cells will be of great clinical importance for expanding the possibilities of diagnosing the activity of the immune-inflammatory process and predicting the development of complications.

Research in recent years shows the importance of changes in the functional activity of leukocyte cells, the structure and function of their membranes in the pathogenesis of nephrosclerosis, their changes can affect endothelial function, rheological properties of blood, hemostasis system, perfusion processes and hematopoietic metabolism, is important in determining the severity of the disease.

Our study of patients with renal nephrosclerosis due to chronic pyelonephritis revealed that endothelial function parameters differed from patients in the control group with significantly higher concentrations of annexin, fibronectin, endothelin-1, and cystatin C than in the control group. showed

The obtained result shows that this marker can be considered an earlier indicator of kidney function decline than creatinine. In our studies, the level of the apoptosis marker in patients with renal nephrosclerosis due to chronic pyelonephritis significantly increased from normal values.

In this regard, it was possible to assume that these indicators reflect the direct participation of programmed cell death at all stages of the development of chronic kidney disease.

At the same time, although there are many works that reveal various aspects of this problem in chronic kidney disease, in our opinion, the role of local and endothelial mechanisms of inflammation in kidney nephrosclerosis in patients with chronic pyelonephritis has not been comprehensively and multi-level studied. It is known that the level of proteinuria is more related to the dynamics of endothelin-1 level than other clinical and laboratory parameters.

Observation of the concentration of endothelin-1 in the blood of patients with renal nephrosclerosis, especially when this pathology is accompanied by chronic pyelonephritis, is the result of the loss of the protein from the body. Therefore, the data obtained on the dynamics of endothelin-1 in the blood show one of the mechanisms of the development of kidney fibrosis in chronic pyelonephritis.

Activated endothelium leads to violation of antithrombotic potential and with this feature participates in the process of coagulation and fibrinolysis. If the integrity of the vascular endothelium is violated, the adhesion and aggregation of platelets in the damaged area is disturbed, and it is observed that it causes the development of thrombosis. The procoagulant system of endothelial activation has a long-term effect, which activates plasminogen and its endogenous inhibitor in the blood (plasminogen activator inhibitor - PAI-1), as well as Willebrand factor.

**Results**

According to the obtained results, the study of its effectiveness in patients with renal nephrosclerosis due to chronic pyelonephritis significantly increased the level of PAI-1 compared to those in the control group (Table).

Similar results were observed for t-PA (tissue plasminogen inhibitor) and were found to be 52% higher than healthy individuals. At the same time, the level of antithrombin III was significantly reduced compared to the data of healthy individuals.

**Table Description of indicators of endothelial dysfunction in patients with nephrosclerosis on the basis of chronic pyelonephritis**

| Indicators | Healthy people, n=24 | Patients who have not developed nephrosclerosis on the basis of chronic pyelonephritis, n =40 | Patients with developed nephrosclerosis due to chronic pyelonephritis, n =38 |
|---|---|---|---|
| Endotelin - 1, pg/ml | 33,72±2,78 | 54,89±5,21* | 132,64±9,73* |
| t-PA, ng/ml | 5,51±0,47 | 4,02±0,34* | 3,38±0,27* |
| PAI-1, ng/ml | 4,78±0,37 | 5,67±0,43* | 8,89±0,74* |
| Willebrand factor, % | 108,34±19,38 | 136,23±11,03* | 188,51±16,24* |
| Antitrombin III, % | 90,12±7,67 | 81,43±7,89* | 61,54±5,37* |

Note: * - R<0.05 is significant compared to healthy individuals

Since the vascular endothelium is a source of synthesis of not only anticoagulant factors, but also fibrinolysis factors (plasmin system), in patients with renal nephrosclerosis due

to chronic pyelonephritis, the decrease in the concentration of tissue plasminogen activator and the activation of its activator inhibitor not only cause endothelial dysfunction, but also fibrinolytic activity. also shows distortions in im.

According to the results, the synthesis and degradation of the main elements of the extracellular matrix and the mechanisms caused by fibrinolysis deficiency play an important role in the development of kidney fibrosis, and are regulated by the inhibitor of plasminogen activator, among other factors.

PAI-1 activation indicates increased fibrin thrombus formation in response to glomerular endothelial cell damage.

An increase in the level of PAI-1 in the blood plasma has been shown in many studies in patients with hemolytic uremic syndrome, and the level of this increase is related to the outcome of the disease.

It is known that endothelial dysfunction is one of the most important links in the development of interstitial inflammation and fibrosis in progressive forms of kidney damage. Endothelial dysfunction leads to structural damage in the body, i.e. acceleration of apoptosis, necrosis, desquamation of endotheliocytes.

An increase in the concentration of endothelin-1 in the blood of patients with renal nephrosclerosis is the result of the loss of the protein. Therefore, the results obtained on the dynamics of endothelin-1 in the blood show one of the mechanisms of the development of kidney fibrosis on the basis of chronic pyelonephritis.

Plasminogen activator inhibitor is known to control cell adhesion and migration and plays an important role in inflammation, wound healing, angiogenesis and tumor cell metastasis. When damaged or activated, the endothelium can change its antithrombotic potential to prothrombotic, its ability to adequately participate in coagulation and fibrinolysis is impaired.

Prothrombotic potential in endothelial cell damage is provided by secretion of Willebrand factor, tissue factor, inhibitor of tissue plasminogen activator. The procoagulant effect of endothelial activation can be measured by changing the balance of tissue plasminogen activator and its endogenous inhibitor in the blood, as well as Willebrand's factor.

**Conclusions**

According to the results of the study, we can see a significant increase in the level of PAI-1 in patients with renal nephrosclerosis due to chronic pyelonephritis compared to the control group.

In our studies, a significant decrease in the level of antithrombin III was noted. Since the vascular endothelium is the site of synthesis of not only anticoagulant factors, but also fibrinolysis factors (plasmin system), in patients with renal nephrosclerosis due to chronic pyelonephritis, the decrease in the concentration of tissue plasminogen activator and the activation of its activator inhibitor can cause not only endothelial dysfunction, but also fibrinolytic disorders. shows.

In turn, activation of PAI-1 indicates increased formation of fibrin thrombus in response to injury of glomerular endothelial cells.

Based on the obtained results, it can be said that in nephrosclerosis developed on the basis of chronic pyelonephritis, the activation and damage of endothelial cells occurs, as a result of which pathological reactions in the form of vasoconstriction, thrombosis, hypercoagulation with intravascular fibrinogen deposition, microrheological disorders appear.

Changes in the rheological properties of blood contribute to the reduction of adaptation in nephrons with damage and separation of the vascular endothelium, and then to the development of glomerular and tubulointerstitial fibrosis.

Signs of renal parenchymal sclerosis detected in the early stages allow a more reasonable approach to the issue of renoprotective therapy, thereby slowing down or preventing the development of renal sclerosis, as well as opening new directions and methods of treatment of patients with renal nephrosclerosis.

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