CYSTATIN and KIDNEY FUNCTION

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ABSTRACT

Currently, one of the most important problems of medical science and practice is the problem of diagnosis and treatment (both surgical and therapeutic profiles) of kidney diseases in children, which occupy one of the leading places in the structure of morbidity of children of the Russian Federation. The outcome of many kidney diseases is chronic renal failure, which is the most tragic pathological condition, often formed already in childhood. In this regard, it is for this age that the work on research and improvement of research methods used in clinical laboratory diagnostics and, first of all, the identification of the most diagnostically reliable markers of renal kidney function is relevant.

In modern nephrology, the filtration function of the kidneys is usually assessed by the level of endogenous creatinine or by using calculation formulas based also on creatinine concentration (in children's practice, the Schwartz formula was most widely used to calculate the glomerular filtration rate (GFR)). But, as you know, creatinine is not a specific marker for kidney damage, so in recent years pediatricians have increased interest in cystatin C as an alternative marker for assessing the state of renal functions.

Cystatin 3, more commonly called Cystatin C (Eng. Cystatin 3, CST3, Cystatin C, Gamma-trace) is a protein belonging to the second group of the genetic family of cystatins. Cystatin C is contained in blood plasma, and the function of protein excretion from the body is carried out by the kidneys. This protein has the following properties: firstly, it is synthesized at a constant rate by all cells of the body containing nuclei; secondly, it is freely filtered through the glomerular membrane; thirdly, it is completely metabolized in the kidneys; fourth, it is not secreted by the proximal renal tubules. All these properties suggested that cystatin C may be a marker of GFR. Studies conducted in patients undergoing hemodialysis showed that their cystatin C levels were 13 times higher than in healthy patients. Comparative experiments conducted to determine the dependence of serum cystatin C levels on GFR values allowed doctors to use the formula for calculating GFR for cystatin C in practice

Keywords: chronic kidney disease; glomerular filtration rate; cystatin C; type IV collagen

INTRODUCTION

Currently, serum creatinine is the most frequently studied marker of kidney function. It enters the blood from muscle tissue, so that the rate of entry into the blood and the individual plasma concentration of creatinine are relatively constant and depend on muscle mass, gender and age. Creatinine is not bound to plasma proteins, is freely filtered in the glomeruli and is almost not reabsorbed by the proximal tubules, but is secreted in small amounts into the urine by them. As the concentration of creatinine in plasma increases, its tubular secretion increases, which in the Rehberg test leads to a false overestimation of the glomerular filtration rate (GFR) in patients with moderate and pronounced decrease (< 50 ml per minute).

Cystatin C is a more sensitive indicator of a decrease in GFR than creatinine, even at normal creatinine levels (creatinine levels can remain within normal limits even with a 50% decrease in glomerular filtration rate).

Cystatin C is a protein from the family of cysteine proteinase inhibitors and is of interest as an early marker of decreased renal function. It is a protein that is synthesized at a constant rate by all cells containing nuclei, secreted into biological fluids: plasma, pleural, ascitic, cerebrospinal fluid, freely filtered through the glomerular membrane (due to its low molecular weight), fully metabolized in the kidneys, not secreted by the proximal renal tubules.

The inhibitory activity of cystatin C is vital for the regulation of normal physiological processes by inhibiting the activity of proteinases, which are the specific targets of its action. Being an inhibitor of cysteine proteases, it blocks their activity and thereby the degradation of the extracellular matrix carried out by them. Thus, it stimulates the synthesis or disintegration of extracellular structures: in the walls of blood vessels (atherosclerosis); in myocardial remodeling (heart failure, acute coronary syndrome); in the invasion of malignant tumors.

Normally, serum levels of cystatin C are due to:

1) a constant rate of its synthesis, practically independent of age, gender, weight;

2) the constant rate of its excretion from the body, which is determined mainly by real functions.

In pathology, its level in the blood increases. The more severe the renal pathology, the worse cystatin C is filtered in the kidneys and the higher its level in the blood. In addition, serum levels of cystatin C increase with heart failure, violation of kidney function (chronic renal failure of any etiology; acute renal failure, including due to fungal toxins, pesticides, medications, etc.), acute urinary tract obstruction, diabetes mellitus (as a sign of diabetic nephropathy), kidney amyloidosis against the background of autoimmune diseases (rheumatoid arthritis, systemic lupus erythematosus, polymyositis), in chronic infectious diseases (tuberculosis), in the early stages of preeclampsia, in some oncological diseases and in Alzheimer's disease.

An increase in the level of cystatin From blood plasma may be associated with taking certain nephrotoxic medications.

- Antibiotics aminoglycosides (gentamicin, amikacin, tobramycin, kanamycin, streptomycin) (a sign of kidney damage!).
- Cephalosporin antibiotics (cefazolin, ceftriaxone, cefotaxime, cefpir, etc.) (a sign of kidney damage!).
- Angiotensin-2 receptor blockers – sartans (candesartan, irbesartan, valsartan, olmesartan, telmisartan, eprosartan).

An increase in creatinine levels when taking an angiotensin-2 receptor blocker is a sign of kidney damage!

- Diuretics (loop – etacric acid, furosemide) (a sign of kidney damage!).
- ACE inhibitors (captopril, enalapril, lisinopril, spirapril, trandolapril, quinapril, ramipril, moexipril, perindopril, benazepril, fosinopril, etc.). An increase in the level of cystatin C when taking an ACE inhibitor is a sign of kidney damage!
- Nonsteroidal anti-inflammatory drugs (almost everything, including paracetamol) (a sign of kidney damage!).
- Gold preparations (a sign of kidney damage!).
- Sulfonamides (including co-trimoxazole) (a sign of kidney damage!).

The more severe the kidney pathology, the higher the level of cystatin C in the blood.

Indications for the purpose of the study

- Routine examination of persons over 55 years of age to assess kidney function and related cardiovascular diseases.
- Assessment of kidney function in persons with arterial hypertension, metabolic syndrome and/or diabetes mellitus, with kidney diseases, after kidney and liver transplantation, with cardiovascular insufficiency, examination and assessment of the severity of kidney diseases in children; assessment of the risk of preeclampsia during pregnancy; monitoring of the effectiveness of treatment for kidney pathology. Reference values: from 17 to 65 years: 0.5–1.0 mg/l; over 65 years: 0.9–3.4 mg/l.

With age, GFR decreases and cystatin C levels increase, which best reflects the indicators of renal function, since its levels practically do not depend on muscle mass. After 50 years, reference cystatin levels increase. When determining GFR in the elderly using creatinine (MDRD equation), the results indicate the prevalence of stage three CKD in the elderly, which is not confirmed when determining GFR using cystatin C.

107 elderly patients with CKD were examined in our clinical diagnostic laboratory. GFR was determined by creatinine clearance (Cockcroft–Gault formula), serum creatinine (MDRD formula) and cystatin C (Hodges formula) and measured using 51SGADT ("gold standard"). The average clearance value was 47 ml/min/1.73 m2, the average serum creatinine level was 269 mmol/L, and cystatin C was 2.68 mg/l.

At the boundary level of GFR = 60 ml/min / 1.73 m^2, the determination of GFR by cystatin C was more accurate – the GFR indicators determined by the MDRD formula (91.6% vs. 84.1%, respectively), and more accurately than the GFR indicators calculated by the Cockcroft–Gault formula (91.6% vs. 88.3%). The results show that serum cystatin C is a reliable marker of GFR with very high diagnostic accuracy and the ability to detect patients with CKD and GFR below 60 ml/min/1.73 m^2.

Cystatin C levels increased with age and were higher in men than in women.

At the same time, cystatin C levels were positively associated: 1) with age (especially after 60 years);

2) with high BMI;

3) with smoking;

4) with hypertension;

5) with low

HDL levels;

6) with high triglycerides;

7) with high levels of C-reactive protein in the highly sensitive range (hsCRB).

In individuals aged 60-80 years, cystatin C levels were 40-50% higher than in younger people. Note that in this large-scale study, GFR indicators were not measured, and the measurement of cystatin C was a single one.

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