International Journal of Education, Social Science & Humanities.
Finland Academic Research Science Publishers
ISSN: 2945-4492 (online) | (SJIF) = 7.502 Impact factor
Volume-11| Issue-6| 2023 Published: |22-06-2023|

THE VALUES OF MARKERS OF DAMAGE TO THE DISTAL TUBULES IN METABOLIC SYNDROME IN POSTMENOPAUSAL WOMEN

https://doi.org/
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Purpose of the study

Evaluation of the information content of diagnostic laboratory biomarkers of damage to the distal tubules in metabolic syndrome in postmenopausal women.

Material and methods

We examined 82 women aged 40 to 65 years (54.0 + 4.8) with kidney damage in the metabolic syndrome in the postmenopausal period . n nephrosclerosis of the kidneys, combined with chronic pyelonephritis, who were treated in the department of nephrology, gynecology , endocrinology of the TMA multidisciplinary clinic. The control group consisted of 18 practically healthy individuals. ELISA , clinical and biochemical studies were carried out using automatic analyzers of the company. Mindray and diagnosticum Human , " BioKhimMak " Russia.

keyword : _ Lipocalin-2 (lipocalin -2 neutrophil gelatinase - assoriated lipocalin – NGAL -2) , chronic kidney disease (CKD) , kidney damage , acute kidney injury (AKI), pi - glutathione -S- transferase

Today, the search for new markers of kidney tissue damage, as well as the identification and refinement of the functional characteristics of known biomarkers with the aim of more objective and early kidney damage in women with metabolic syndrome (MS) in the postmenopausal period, is relevant in modern conditions.

Lipocalin-2 (NGAL -2 neutrophil gelatinase - associated lipocalin) enters the plasma from the secondary granules of activated neutrophils, but can be synthesized in different organs and in different cell types. NGAL human is a single polypeptide chain consisting of 178 amino acid residues and having a molecular weight of 22 kDa .

The glycosylated form has a molecular weight of 25 kDa . In neutrophils and in urine NGAL is present as a monomer with a small percentage of dimeric and trimeric forms. The main functions of NGAL are stimulating the proliferation of damaged cells, especially epithelial cells, and counteracting bacterial infections.

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NGAL blood serum entering the kidneys helps to restore damaged cells, and NGAL synthesized in the kidneys , which has a bacteriostatic effect (prevents the entry of iron into bacterial cells), prevents the subsequent development of urinary tract infections.

According to some authors, with damage to the renal tubules, an increase in the level NGAL both in serum (7-16 times) and in urine (25-1000 times). In an experiment on animal models of NGAL proved to be a highly sensitive biomarker gentamicin nephrotoxicity , but clinical studies of its use as a marker of acute kidney injury (AKI) in the treatment of gentamicin have been insufficient.

One clinical study suggests that NGAL may be predictive biomarker nephrotoxicity vancomycin . When studying nephrotoxicity immunosuppressant tacrolimus in patients after liver transplantation, it turned out that NGAL is the most sensitive among new biomarkers (MCP-1, L - FABP , IL -18, osteopontin , cystatin C and clusterin) - high levels of NGAL in urine have been associated with AKI in these patients. Several clinical studies have shown that an early rise in NGAL levels in urine helps to detect AKI and thus prevent cisplatin in patients nephrotoxicity .

Definition of N gal in urine detects DILI after the use of platinum preparations earlier than can be determined by the level of serum creatinine . Increasing the level of NGAL predicts the onset of cisplatin nephrotoxicity better than albuminuria and urinary cystatin C , it may be an early marker of cisplatin- induced DILI . In addition, NGAL in studies with various pathologies, it shows itself to be a good predictor of AKI and the severity of AKI, for example , in cardiac surgery, after shock wave lithotripsy . However, the possibility of using a biomarker NGAL for the diagnosis of AKI in clinical practice is limited.

NGAL levels have been shown to may increase with CKD, arterial hypertension, infections, anemia, hypoxia, and malignant neoplasms already present in patients. There are experimental and clinical data demonstrating the dependence of NGAL excretion with urine from the level of proteinuria. In addition, the NGAL level increases in the cells of the proximal renal tubules in response to ischemia-reperfusion.

Another acute phase the reactant synthesized by the epithelial cells of the proximal tubules of the kidneys in response to ischemic injury is lipocaine-2. This 25 kDa protein exists as a monomer in urine and neutrophils and is bound by metalloproteinase-9. Another indicator of damage to the proximal tubules of the kidneys is a reactive protein, lipocalin-2. In urine, lipocalin-2 is a marker of chronic tubulointerstitial injury in the kidney.

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As mentioned above, in women with MS in the postmenopausal period, the content of lipocalin-2 in the urine tends to increase, on average, to 7.86±0.61 ng/mg versus 5.01±0.43 ng /mg of healthy people. (tab.1)

Table 1
Some indicators of markers of damage to the distal tubules
in women with MS in the postmenopausal period

Index	Comparison group, n =18	Women with MS in postmenopausal, n =82
Lipocalin-2 in urine ng /ml	5.01 ± 0.43	7.86 ± 0.61*
pi - glutathione - S - transferase in urine mcg/ l	11.12 ± 1.29	36.28 ± 1.85*

Note: * - significance of differences P < 0.05 relative to the indicator of the comparison group

As mentioned above, the kidneys play an important role in the conjugation and excretion of various metabolites, drugs and organic anions from the body. For this, in the distal tubules of the nephron, there is an enzyme - piglutathione - S - transferase , which performs two important functions: the conjugation of halogenated aliphatic and aromatic hydrocarbons and their excretion by the kidneys; binding and regulation of the influx from plasma to the kidneys of large amounts of organic anions (SO_4^{-2} , RO_4^{-3} steroids, drugs, urobilicogen) . p - glutathione - S - transferase , located in the distal tubules, unlike alpha- glutathione - S - transferase , is sodium dependent. Therefore, an increase in the level of this enzyme in the urine indicates damage to the cells of the distal tubules of the kidneys.

The results of the study showed that the content of piglutathione - S - transferase in the urine of women with MS in the postmenopausal period increased by 3.3 times and amounted to 36.28 ± 1.85 μg/l (at a rate of 11.12 ± 1.29 μg /l).

Thus, according to the content of glutathione transferase , one can judge the damage not only to the proximal sphere of the tubules, but also to the distal tubules in patients with chronic pyelonephritis. Humoral regulators appear to include endothelial cytokines, nitric oxide, proximal tubular epithelial cytokines, and hormones.

Conclusion

One of the main tasks of clinical laboratory diagnostics is the identification of biomarkers that indicate the pathology of organs, tissues and body systems. In this regard, it is very relevant in modern conditions to search for new markers of kidney tissue damage, as well as to identify and refine the functional characteristics of known biomarkers in order to more objectively and early assess kidney damage. In women with metabolic syndrome in the postmenopausal period, dysfunction of the enzyme systems of the proximal and distal tubules, as well as dysfunction of endothelial cells of the glomerulus, is noted, which is one of the reasons for the violation of not only glomerular filtration, but also the processes of reabsorption and excretion in the kidneys of the examined persons. The observed changes in the functional system of the kidneys contribute to the disruption of not only the homeostasis of the body of women, but is also one of the causes of functional disorders of the regulatory system (hormonal) of the body of patients with metabolic disorders. The invention relates to medicine and is intended for diagnosing the initial stage of chronic kidney disease. In the patient's blood, the level of lipocalin-2 and albumin is determined, the ratio of lipocalin-2 to albumin is calculated, and if the value is greater than 0.27, chronic kidney disease is diagnosed. EFFECT: method allows diagnosing kidney damage at an early stage, without subjecting patients to additional urinalysis and invasive diagnostic methods.

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