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Diagnosis of Toxic Kidney Injury

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Annotation: The article is devoted to diagnostics of kidney damage in intoxications. It is revealed that there are no uniform criteria for assessing the degree and nature of kidney damage by nephrotoxins of different locations of action. The features of the mechanisms of nephron damage and predictors of both initial kidney damage and the potential severity of intoxication consequences are also not fully known and deciphered. Therefore, experimental approaches to the study of nephropathies of toxic genesis should include modeling, assessment of the degree of biological response to exposure and reversibility of changes, pathogenesis research for subsequent development of optimal prevention and diagnostics.

Keywords: kidneys, toxins, impact, diagnostic biomarkers, pathomorphological signs.

Introduction. Diagnosis of kidney damage in toxic nephropathies is based on a combination of clinical signs and laboratory urine test results. In toxic effects that initially trigger molecular changes, there is a delay in the excretion of phosphates and sulfates with the development of metabolic acidosis, the entry of biomarkers into the blood and urine, and the analysis of the dynamics of excretion of these markers has significant potential for the development of new methods for diagnosing damage, unattainable using routine tests (Smirnov A.V. et al., 2016; Fuentes-Delgado V.H., et al., 2018) [5,15].

In addition to measuring blood urea and creatinine levels (clinical tests for assessing the glomerular filtration rate), urine analysis should be performed, which is especially important for detecting tubular damage. Urine biomarkers include a number of enzymes that make up to 40% of the cytoplasmic content of the nephrothelium of different zones and sections of the nephrons (denBakker E., et al., 2018) [13]. To achieve clinical effectiveness and a definitive diagnosis, it is necessary to establish a cutoff value for biomarkers with high prognostic value. The cutoff values of NGAL in urine of 150 and 300 ng/ml demonstrated excellent specificity (92.4 and 97.1%, respectively) and negative predictive value (93.3 and 92.8%, respectively) to exclude severe damage (Coca S.G., et al., 2008) [11].

In addition, tubular dysfunction can be recognized by increased renal excretion of low molecular weight proteins, the presence of granular casts and renal tubular epithelial cells (RTEC) in the urine sediment (Chugunova O.L., et al., 2021) [8], hematuria, leukocyturia and proteinuria against the background of taking anti-inflammatory steroids and analgesics, and a general urine analysis in combination with microscopy made it possible to understand the localization and cause of damage (Parfenchik I.V., 2018; Crean D., et al., 2015) [2,12].

However, there are very few studies in the scientific literature evaluating the kinetics of marker excretion in urine for the diagnosis and prognosis of the course of toxic nephropathies. Four hours after the injection of sodium maleate, there was a significant increase in the concentration of monocyte chemotactic protein-1 in plasma as a biomarker of damage. In the work of Sivak K.V. et al. (2020), the effectiveness of an enzyme-linked immunosorbent assay was assessed using nine single-plex and two multiplex platforms in male and female rats. For some biomarkers, the differences between the platforms were up to 15 times (due to the use of different antibodies from different manufacturers), which, along with the general informational insufficiency of the results for females, indicates the need for further research (Sivak K.V., et al., 2020) [4].

Proteinuria as a consequence of tubular and glomerular damage is recognized as an independent risk factor for renal disease. Determination of the protein-to-creatinine ratio in urine allows one to "exclude" the presence of significant proteinuria, while qualitative tests for proteinuria and hematuria have low sensitivity. Electrophoretic separation is the most accessible method for determining the qualitative characteristics of proteinuria. Tubular proteinuria has been detected in various nephropathies, poisonings, and hypoxia (Chebotareva N.V., et al., 2022) [7].

Despite the current existence of a large number of kidney injury biomarkers, their common shortcomings are: low specificity in terms of distinguishing between acute and chronic kidney diseases, interstate differences in disease diagnostic standards, focus on assessing kidney function, and high cost. Future research should focus on studying the mechanisms of injury in order to expand knowledge about injury phenotypes based on their pathomorphology (Fastova O.N., 2014; Yagmurov O.D., 2011) [6,10].

Thus, biomarkers of damage are necessary for detailed diagnostics of this pathology in poisonings and in patients prescribed nephrotoxic drugs. The problem of using cytoprotectors is included in the strategic direction of modern emergency medicine, pharmacology and has not been finally solved. The use of the antihypoxant confumin allows avoiding overload of the circulating blood volume. The antioxidant 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl reduces the expression of nuclear factor-kappa B, cyclooxygenase-2 and tumor necrosis factor-α in kidney tissue with cisplatin-induced damage. In renal hypoxia, ischemia and inflammation, highly selective A3AR antagonists and A2AR agonists (Pavlova V.S., et al., 2020; Chugunova O.L., et al., 2023; Devarajan P., 2010) attenuate the progression of renal fibrosis and have a renoprotective effect [1,9,14].

The antiapoptotic activity of alpha-lipoic acid is a key mechanism for reducing cadmium nephrotoxicity, and correction of hypoxia is a promising strategy for blocking the transition from acute to chronic injury. Drugs with antioxidant activity, aminoglycoside reuptake inhibitors, excretion inducers, and calcium channel blockers have demonstrated significant nephroprotection. Inhibition of the necroptotic protein RIPK1 with necrostatin-1 attenuated gentamicin-induced renal necrosis, inflammation, and fibrosis in rats (Sivak K.V., et al., 2019) [3].

Conclusion. An analysis of existing approaches to the problem has shown that there are no uniform criteria for assessing the degree and nature of kidney damage caused by nephrotoxins with different locations of action. The features of nephron damage mechanisms and predictors of both initial kidney damage and potential severity of intoxication consequences are also not fully known and deciphered. This does not allow optimizing prevention, emergency and rehabilitation therapy of toxic nephropathies. The multifactorial nature of the etiology, pathogenesis of damage and functional heterogeneity of different nephron segments hinder the achievement of success. When studying new renoprotective strategies, it is necessary to take into account the morphophysiological heterogeneity of the kidneys. Therefore, experimental approaches to the study of nephropathies of toxic genesis should include modeling, assessment of the degree of biological response to exposure and reversibility of changes, pathogenesis research for the subsequent development of optimal prevention and diagnostics.

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