8. MECHANISMS OF DRUG-INDUCED NEPHROTOXICITY

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Introduction. Drug-induced nephrotoxicity or drug-induced renal disease (DRID) is a common clinical problem. It has been reported that the incidence of drug-induced renal disease in adults can range from 14-26% to 66% and up to 16% in children. Research reports on drug-induced nephrotoxicity have increased significantly from 80 articles in the years 1930–1969 to over 5000 in the years 2010–2018. Understanding the risk factors, phenotypes through clinical presentation, development mechanisms, prevention and mitigation strategies of nephrotoxicity is essential due to the number of drugs used in medical practice and the possibilities for researching nephrotoxicity.

Aim of study. The aim of the study was to analyze and elucidate the molecular mechanisms of drug-induced nephrotoxicity.

Methods and materials. The study was analytical and focused on the selection of articles published between 2018 and 2023 in the PubMed and Google Scholar databases using the keywords nephrotoxicity and drug-induced nephrotoxicity.

Results. The following phenotypes of drug-induced nephrotoxicity were highlighted: acute kidney diseases; glomerular dysfunctions; tubular injuries; and nephrolithiasis. These phenotypes can be achieved through different mechanisms, such as: alteration of renal intraglomerular hemodynamics, direct and/or indirect tubular toxicity, development of inflammation and immune processes (glomerulonephritis and interstitial nephritis), glomerular damage, nephropathy caused by crystals, nephrotic syndrome, and thrombotic microangiopathy. The biochemical and molecular mechanisms of nephrotoxicity lead to cellular death through apoptosis, autophagy, and necrosis. The exact mechanism depends on the type of cells involved, the dose and duration of exposure, patient-dependent factors (sex, age, comorbidities, etc.). At the same time, the nephrotoxic action can be reflected on several types of cells, as well as it can develop against the background of hypertension, obesity, liver, lung, heart diseases, or the abuse of exogenous substances (alcohol, cigarette smoke, drugs, etc.).

Conclusion. Drug-induced nephrotoxicity represents a significant challenge in clinical practice and requires a complex and thorough approach to the prevention of kidney damage, the differentiation between the damaging action of the drugs and the kidney disease itself, the selection of appropriate specific and early biomarkers. Understanding these compartments and the mechanisms underlying drug-induced renal injury will enable an appropriate and rational treatment approach, early monitoring to address nephrotoxicity issues in the reversible stages of the processes.