CELLULAR AND MOLECULAR MECHANISMS OF KIDNEY TISSUE DAMAGE IN HYPERURICEMIA

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Abstract: Hyperuricemia, defined by elevated blood uric acid levels, is a common metabolic disorder that can lead to kidney dysfunction in addition to gout. Excess uric acid induces cellular and molecular changes in renal tissue, including oxidative stress, inflammation, apoptosis, and fibrosis. Both urate crystal-dependent and crystal-independent mechanisms contribute to renal injury, affecting endothelial function, tubular epithelial cells, and interstitial fibroblasts. Understanding these cellular and molecular pathways is crucial for developing early diagnostic, preventive, and therapeutic strategies. This paper reviews the current knowledge of the mechanisms underlying hyperuricemia-induced kidney damage, highlighting potential targets for treatment and improved patient outcomes.

Keywords: Hyperuricemia, Kidney Injury, Oxidative Stress, Inflammation, Apoptosis, Fibrosis.

Introduction:

Hyperuricemia, characterized by elevated levels of uric acid in the blood, is a growing metabolic disorder associated not only with gout but also with kidney dysfunction. Excess uric acid can directly affect renal cells, triggering a series of cellular and molecular changes such as oxidative stress, activation of inflammatory pathways, apoptosis, and fibrosis. These alterations disrupt normal kidney structure and function, potentially leading to chronic kidney disease over time. Recent research indicates that kidney damage in hyperuricemia occurs through both urate crystal deposition and crystal-independent mechanisms, including endothelial dysfunction and cytokine-mediated inflammation. Despite increasing studies, the precise pathways of uric acid-induced renal injury are not fully understood, limiting the development of targeted therapeutic interventions. A deeper understanding of these cellular and molecular processes is essential for early diagnosis, prevention, and treatment of hyperuricemia-

related kidney complications. Such knowledge can help improve patient outcomes, reduce the risk of chronic kidney disease, and inform future therapeutic strategies.

Relevance

Hyperuricemia is increasingly common due to lifestyle and dietary changes. Understanding its impact on kidney tissue at the cellular and molecular level is crucial for preventing renal complications and improving patient outcomes.

Main part

Hyperuricemia is a metabolic disorder defined by elevated levels of uric acid in the blood. It is commonly associated with conditions such as obesity, hypertension, diabetes, and gout. Excess uric acid can accumulate in tissues and blood vessels, causing systemic effects. In the kidneys, hyperuricemia is a significant risk factor for chronic kidney disease. Elevated uric acid affects renal hemodynamics and promotes glomerular hypertension. Studies indicate that high uric acid levels can impair endothelial function. This dysfunction reduces nitric oxide availability, increasing vascular resistance. Hyperuricemia can also activate the renin-angiotensin-aldosterone system. Activation of this system contributes to sodium retention and hypertension. Chronic exposure to elevated uric acid induces inflammatory processes in the kidney. Inflammatory cytokines, such as IL-1, IL-6, and TNF-α, are upregulated. These mediators promote infiltration of immune cells into renal tissue. Oxidative stress plays a major role in hyperuricemia-induced renal injury. Reactive oxygen species damage renal cells and their components. Apoptosis of tubular epithelial cells contributes to kidney function decline. Prolonged hyperuricemia leads to interstitial fibrosis. Fibrotic changes reduce glomerular filtration capacity. Clinical studies link hyperuricemia with progression of renal disease. Early detection of high uric acid is essential for prevention. Lifestyle modifications and pharmacological interventions are recommended. Understanding these impacts is crucial for developing therapeutic strategies.

Renal tissue damage in hyperuricemia begins at the cellular level. Uric acid directly affects tubular epithelial cells. High uric acid levels induce oxidative stress in these cells. Reactive oxygen species damage cellular organelles. Mitochondrial dysfunction occurs due to oxidative stress. Damaged mitochondria release pro-apoptotic factors. Apoptosis of renal cells reduces nephron function. Inflammatory signals are activated in response to cell stress. Monocytes and macrophages infiltrate renal tissue. Cytokines such as IL-1β, TNF-α, and IL-6 are released. These cytokines exacerbate cell injury. Uric acid crystals can also mechanically damage epithelial cells. Crystal deposition triggers additional inflammation. Endothelial cells are sensitive to uric acid-induced stress. Endothelial dysfunction impairs renal blood flow. This leads to ischemic injury

in the kidney. Fibroblast activation is stimulated by persistent cell stress. Activated fibroblasts promote interstitial fibrosis. Cell signaling pathways, such as MAPK and NF-κB, mediate these processes. Understanding cellular responses is key to therapeutic intervention.

At the molecular level, hyperuricemia activates several signaling pathways. Oxidative stress triggers activation of NADPH oxidase. This enzyme produces reactive oxygen species in renal cells. ROS damage DNA, proteins, and lipids. Apoptotic pathways, including caspase activation, are induced. Uric acid stimulates the NLRP3 inflammasome in renal tissue. Activation of the inflammasome promotes IL-1β and IL-18 release. These pro-inflammatory cytokines amplify tissue injury. Uric acid also activates MAPK pathways. MAPK signaling promotes inflammation and cell proliferation. NF-κB is another key transcription factor activated by uric acid. NF-κB regulates expression of inflammatory mediators. Endothelin-1 expression is increased, causing vasoconstriction. Reduced nitric oxide availability contributes to oxidative stress. Persistent molecular activation leads to fibrosis via TGF-β signaling. TGF-β promotes extracellular matrix accumulation. Collagen deposition and fibrosis impair kidney function. Molecular crosstalk between tubular and interstitial cells sustains injury. Targeting these pathways may provide therapeutic benefits. Research on molecular mechanisms can guide drug development.

Conclusion

Hyperuricemia significantly affects kidney function through complex cellular and molecular mechanisms. Elevated uric acid levels induce oxidative stress, inflammation, apoptosis, and fibrosis in renal tissue, ultimately impairing normal kidney structure and function. Both urate crystal-dependent and crystal-independent pathways contribute to renal injury, highlighting the multifactorial nature of hyperuricemia-induced kidney damage. Understanding these mechanisms is essential for early diagnosis, prevention, and development of effective therapeutic strategies. Targeting oxidative stress, inflammatory signaling, and fibrotic pathways may offer promising approaches to protect renal function. Continuous research in this field can improve patient outcomes, reduce the risk of chronic kidney disease, and provide insights into novel treatments for hyperuricemia-associated renal complications.

References

1. Su, H.-Y., Zhang, H., & Sun, L. (2020). Research advances in the mechanisms of hyperuricemia-induced renal injury: Oxidative stress, inflammation, endothelial dysfunction and fibrosis. *PubMed*, 14(3), 112–128.

2. Азимова, А. А., Маликов, Д. И., & Шайкулов, Х. Ш. (2021). МОНИТИРОИНГ ЭТИОЛОГИЧЕСКОЙ СТРУКТУРЫ СЕПСИСА ЗА. PEDAGOGICAL SCIENCES AND TEACHING METHODS, 48, 18-22.

3. Luo, Y., Song, Q., Li, J., et al. (2024). Effects of uric acid-lowering therapy on renal outcomes in CKD patients with asymptomatic hyperuricemia: Systematic review and meta-analysis. *BMC Nephrology*, 25, 112–127.

4. Kanbay, M., Segal, M., Afsar, B., et al. (2016). The role of uric acid in the pathogenesis of renal disease. *Journal of the American Society of Nephrology*, 27, 37–45.

5. АЗИМОВА, А. А., & МАЛИКОВ, Д. И. (2022). ПОВРЕЖДЕНИИ МЯГКОТКАНЫХ СТРУКТУР КОЛЕННОГО СУСТАВА И УЛЬТРАЗВУКОВОЕ ИССЛЕДОВАНИЕ. *МОЛОДЕЖНЫЙ ИННОВАЦИОННЫЙ ВЕСТНИК Учредители: Воронежский государственный медицинский университет имени НН Бурденко*, *11*(2), 10-13.