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**REDUCED NITRIC OXIDE BIOAVAILABILITY AS A FACTOR OF
ENDOTHELIAL DYSFUNCTION IN RENAL ARTERIOLES UNDER
HYPERURICEMIA**

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Annotation: This work examines the role of reduced nitric oxide (NO) bioavailability as a key factor in the development of endothelial dysfunction of renal arterioles under hyperuricemic conditions. Elevated serum uric acid promotes oxidative stress, inflammation, and inhibition of endothelial nitric oxide synthase, leading to NO inactivation. The resulting endothelial dysfunction causes persistent vasoconstriction, impaired microcirculation, and increased intraglomerular pressure, contributing to renal ischemia, interstitial fibrosis, and progression of chronic kidney disease. Understanding these molecular mechanisms is crucial for developing targeted therapeutic strategies to prevent vascular and renal complications associated with hyperuricemia.

Keywords: Hyperuricemia, Nitric oxide (NO) bioavailability, Endothelial dysfunction, Renal arterioles, Oxidative stress, Vasoconstriction.

Introduction

In recent years, hyperuricemia has been considered not only as a metabolic disorder associated with the development of gout, but also as an independent risk factor for cardiovascular and renal diseases. Elevated serum uric acid levels exert a direct effect on the vascular wall, initiating a cascade of molecular and cellular alterations. Renal arterioles are particularly vulnerable in this context, as they play a crucial role in the regulation of glomerular filtration and systemic blood pressure. One of the central mechanisms of vascular injury in hyperuricemia is the reduction in nitric oxide (NO) bioavailability. NO is synthesized by endothelial cells through the activity of endothelial nitric oxide synthase and is essential for maintaining vascular tone, inhibiting platelet aggregation, and providing anti-inflammatory protection. In hyperuricemia, suppression of nitric oxide synthase activity, increased production of reactive oxygen species, and formation of peroxynitrite lead to NO inactivation and the development of endothelial dysfunction. Endothelial dysfunction of renal arterioles is accompanied by persistent vasoconstriction, impaired microcirculation, tissue hypoxia, and activation of the renin–angiotensin–aldosterone system. In the long term, these changes contribute to vascular remodeling, intimal thickening, and progression of chronic kidney disease. Contemporary studies demonstrate that even moderate hyperuricemia is capable of inducing these pathological processes.

Main part

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Hyperuricemia is therefore regarded as an important pathogenetic factor in renal vascular damage. Increased serum uric acid directly injures endothelial cells, disrupting their barrier, metabolic, and vasoregulatory functions. Afferent renal arterioles, in particular, are essential for maintaining glomerular filtration and systemic hemodynamics, making their functional integrity critical for preserving kidney function. Under hyperuricemic conditions, pro-inflammatory cytokines are activated, adhesion molecule expression is enhanced, and chronic vascular inflammation develops. These processes are associated with impaired production of vasoactive mediators, altered smooth muscle tone, and structural remodeling of the vascular wall. Progressive medial thickening, narrowing of the arteriolar lumen, and reduced renal blood flow follow. Microcirculatory disturbances result in cortical ischemia and nephron injury. Thus, hyperuricemia initiates a complex set of morphofunctional changes that underlie endothelial dysfunction in renal arterioles.

The key mechanism of vascular impairment in hyperuricemia is the reduction of nitric oxide bioavailability, which is the principal endothelial vasodilator. Under physiological conditions, NO is synthesized by endothelial nitric oxide synthase and promotes relaxation of vascular smooth muscle cells, inhibits platelet aggregation, and exerts anti-inflammatory effects. In hyperuricemia, endothelial nitric oxide synthase activity is suppressed, while the production of reactive oxygen species is increased. Enhanced oxidative stress facilitates the rapid interaction of NO with superoxide anions, leading to the formation of peroxynitrite and subsequent inactivation of nitric oxide. Additionally, NADPH oxidase is activated, and inflammatory signaling pathways are amplified, including activation of the nuclear transcription factor NF- κ B. There is also increased synthesis of endothelin-1, a potent vasoconstrictor, which further aggravates the imbalance of vascular tone. Mitochondrial dysfunction in endothelial cells contributes to cellular energy deficiency and progression of endothelial impairment. Collectively, these molecular alterations result in a marked reduction of NO bioavailability and the development of sustained vasoconstriction in renal arterioles.

Reduced NO bioavailability and endothelial dysfunction in renal arterioles have significant clinical implications. Impaired vasoregulation leads to persistent elevation of intraglomerular pressure and the development of glomerular hypertension. Activation of the renin–angiotensin–aldosterone system further enhances vasoconstriction and contributes to the progression of arterial hypertension. Chronic renal tissue ischemia stimulates fibrotic processes and interstitial remodeling. Gradually, glomerular filtration rate declines, and chronic kidney disease develops. Clinical studies indicate that even moderate elevations in serum uric acid are associated with an increased risk of nephropathy and cardiovascular complications. Early correction of hyperuricemia improves endothelial function and slows the progression of renal damage. Therefore, reduced nitric oxide bioavailability in hyperuricemia represents a critical link in the pathogenesis of vascular and renal complications and requires further investigation to develop effective pathogenetically targeted therapeutic strategies.

Conclusion

In summary, reduced nitric oxide bioavailability is a key mechanism in the development of endothelial dysfunction of renal arterioles in hyperuricemia. Elevated uric acid levels induce oxidative stress, suppress endothelial nitric oxide synthase activity, and promote nitric oxide inactivation, leading to persistent vasoconstriction and impaired renal microcirculation. These changes contribute to increased intraglomerular pressure, activation of the renin–angiotensin–aldosterone system, and progressive renal damage. Therefore, early management of hyperuricemia is essential to preserve endothelial function and prevent the progression of chronic kidney disease.

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