THE ROLE OF RENIN–ANGIOTENSIN–ALDOSTERONE SYSTEM ACTIVATION IN THE PATHOGENESIS OF OBSTRUCTIVE UROPATHY

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Abstract

Obstructive uropathy is a pathological condition characterized by partial or complete impairment of urinary flow, leading to progressive deterioration of renal function. Altered intrarenal hemodynamics, tissue hypoxia, oxidative stress, and inflammatory responses play critical roles in the pathogenesis of this condition. In recent years, activation of the renin–angiotensin–aldosterone system (RAAS) has been recognized as one of the central molecular mechanisms involved in the development of obstructive nephropathy. Through increased concentrations of angiotensin II and aldosterone, RAAS activation promotes vasoconstriction, inflammation, oxidative stress, and fibrogenesis. These alterations contribute to the development of tubulointerstitial fibrosis and chronic kidney disease. This study analyzes the molecular and cellular significance of RAAS activation in obstructive uropathy. Therapeutic strategies targeting components of the RAAS represent a promising approach for slowing the progression of obstructive nephropathy.

Keywords: obstructive uropathy, renin–angiotensin–aldosterone system, angiotensin II, aldosterone, oxidative stress, TGF-β1, fibrosis, chronic kidney disease.

Introduction. Obstructive uropathy develops as a consequence of anatomical or functional obstruction at various levels of the urinary tract and represents one of the major causes of renal insufficiency in both urological and nephrological practice

[1]. Depending on the severity and duration of obstruction, reversible or irreversible structural and functional alterations may develop within the renal parenchyma.

The early stages of obstruction are characterized by increased intrapelvic pressure and reduced renal blood flow. As the disease progresses, tissue hypoxia, cellular stress, inflammatory responses, and fibrotic mechanisms become increasingly dominant [2]. Among these pathological processes, activation of the renin–angiotensin–aldosterone system is of particular importance, as it not only aggravates hemodynamic disturbances but also promotes molecular remodeling within renal tissues [3].

Recent studies have demonstrated that, beyond its vasoconstrictive effects, angiotensin II plays a significant role in the regulation of inflammatory mediator expression, oxidative stress, and profibrotic signaling pathways [4]. Consequently, the RAAS is currently regarded as one of the central regulators of obstructive nephropathy pathogenesis.

The aim of this study was to analyze the molecular and cellular significance of renin–angiotensin–aldosterone system activation in obstructive uropathy.

Materials and Methods. The theoretical framework of this study was based on contemporary scientific evidence concerning the pathogenesis of obstructive uropathy and obstructive nephropathy. Particular attention was directed toward the activation of the renin–angiotensin–aldosterone system, intrarenal hemodynamic alterations, inflammatory mediators, oxidative stress, cellular signaling pathways, and mechanisms of fibrosis.

Information regarding the molecular effects of angiotensin II and aldosterone, TGF-β1/Smad signaling, NF-κB-mediated inflammatory responses, generation of reactive oxygen species, and the development of tubulointerstitial fibrosis was systematically analyzed and synthesized using comparative and analytical approaches.

Results. The reduction in renal perfusion caused by urinary tract obstruction stimulates renin secretion from the juxtaglomerular apparatus. Consequently, the production of angiotensin II increases, leading to alterations in afferent and efferent arteriolar tone and disruption of intrarenal hemodynamics [3,5].

Through activation of angiotensin II type 1 (AT1) receptors, angiotensin II promotes vasoconstriction and exacerbates tissue hypoxia. In addition, it activates the NF-κB signaling pathway, thereby stimulating the production of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6. These processes contribute to the establishment of a chronic inflammatory microenvironment within the renal interstitium [4,6].

RAAS activation is also closely associated with enhanced oxidative stress. Angiotensin II stimulates NADPH oxidase activity, resulting in increased generation of reactive oxygen species. Oxidative stress induces damage to cellular membranes, mitochondria, and nucleic acids, ultimately promoting apoptosis of tubular epithelial cells [7].

In obstructive nephropathy, increased expression of transforming growth factor-beta 1 (TGF-β1) represents one of the principal molecular drivers of fibrogenesis. Angiotensin II activates the TGF-β1/Smad signaling pathway, enhancing the synthesis of collagen type I, collagen type III, and fibronectin. This process leads to excessive extracellular matrix accumulation and the development of tubulointerstitial fibrosis [8].

Aldosterone also plays an independent role in the progression of fibrosis. Activation of mineralocorticoid receptors promotes macrophage infiltration, oxidative stress, and the production of inflammatory mediators. Consequently, irreversible structural alterations develop within the renal parenchyma [9].

Discussion. In obstructive uropathy, activation of the RAAS initially functions as a compensatory mechanism. Under conditions of reduced renal perfusion, angiotensin II helps maintain glomerular filtration to a certain extent.

However, prolonged activation of this system results in detrimental pathological consequences.

Chronic RAAS activation functions as a molecular network that simultaneously promotes inflammation and fibrogenesis. The biological effects of angiotensin II and aldosterone extend beyond hemodynamic regulation and involve extensive reprogramming of intracellular signaling pathways. In particular, activation of the NF-κB and TGF-β1 signaling pathways plays a critical role in the progressive course of obstructive nephropathy.

Enhanced oxidative stress and mitochondrial dysfunction contribute to disturbances in cellular energy metabolism. These alterations limit the regenerative capacity of tubular epithelial cells and create a favorable biological environment for fibrosis development. Therefore, obstructive nephropathy should not be regarded merely as a consequence of mechanical urinary tract obstruction but rather as a complex molecular and immunoinflammatory syndrome.

Therapeutic approaches aimed at pharmacological blockade of RAAS components have demonstrated promising results in both experimental and clinical studies. Nevertheless, the complex interactions among different RAAS-associated signaling pathways indicate that further investigations are required to fully evaluate the efficacy of these therapeutic strategies.

Conclusion. Activation of the renin–angiotensin–aldosterone system represents one of the principal molecular mechanisms responsible for renal injury in obstructive uropathy. Angiotensin II and aldosterone contribute to intrarenal hemodynamic disturbances, inflammatory responses, oxidative stress, and fibrogenesis.

The NF-κB and TGF-β1/Smad signaling pathways function as central regulators of RAAS-mediated pathological alterations. These mechanisms constitute the molecular basis for the development of tubulointerstitial fibrosis and chronic kidney disease.

RAAS-targeted therapeutic strategies may play an important clinical role in preserving renal function and slowing the progression of obstructive nephropathy.

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