P38

Altered Regulation of Renin-Angiotensin, Endothelin and Natriuretic Peptide Systems Following Unilateral Ureteral Obstruction in Rats

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Background : It has been known that angiotensin II (AngII) modulates cell growth and extra matrix synthesis. However, the classical view of renin-angiotensin-aldosterone system (RAS) has been challenged by the discovery of angiotensin converting enzyme2 (ACE2) and aldosterone synthase (CYP11B2). The present study was designed to investigate whether there is a role of local RAAS, endothelin (ET) and natriuretic peptides (NPs) in the development of renal fibrosis and progressive renal disease following ureteral obstruction.

Methods : Male Sprague-Dawley rats (180-200 g) were unilaterally obstructed of the proximal ureters by ligation for 14 days. Control rats were treated the same, except that no ligature was made. The mRNA expression of local RAS components, CYP11B2, ET-1 and NPs was determined in the cortex by real-time polymerase chain reaction.

Results : Following the ureteral obstruction, the expression of ACE1, ET-1 and transforming growth factor-β1 (TGF-β_1) was increased, while that of ACE2 decreased in the obstructed kidney. In the contralateral kidney, the expression of angiotensin II type 1 receptor was decreased, while that of TGF-β_1 remained unchanged. ANP, BNP and CNP increased and NPR-A decreased in the obstructed kidney.

Conclusion : The local RAS and ET-1 was upregulated, which may contribute to the development of progressive renal fibrosis in the obstructive kidney. On the contrary, the enhanced activity of NPs may play a compensatory role.