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Altered regulation of local renal and vascular natriuretic peptide systems in obstructive uropathic rats

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The present study was aimed at investigating whether the regulation of local natriuretic peptide system is altered in the kidney and the vasculature in obstructive uropathy. Male Sprague-Dawley rats were bilaterally obstructed by ligation of proximal ureters for 48 hours. Control rats were treated the same, except that no ligature was made. The mRNA expression of various isoforms of atrial, brain, and C-type natriuretic peptide (ANP, BNP, CNP) and different subtypes of natriuretic peptide receptor-A, -B, and -C (NPR-A, NPR-B, NPR-C) was determined in the kidney and the thoracic aorta by reverse transcription polymerase chain reaction. The basal and stimulated activities of particulate guanylyl cyclase were also examined. Following the bilateral ureteral obstruction, the expression of ANP, BNP, and CNP was increased in the aorta as well as in the kidney. On the contrary, the expression of NPR-A, NPR-B, and NPR-C was decreased both in the kidney and the aorta. Accordingly, the guanylyl cyclase activity in response to natriuretic peptides was significantly decreased. ANP relaxed phenylephrine-precontracted aortic rings in a dose-dependent manner, the degree of which was significantly diminished. It is suggested that the local synthesis of natriuretic peptides is increased in the kidney and in the vasculature in obstructive uropathy.

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Upregulation of vascular renin-angiotensin and endothelin systems in rats inhibited of nitric oxide synthesis

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The present study was aimed at investigating whether the regulation of vascular renin-angiotensin and endothelin (ET) systems is altered in hypertension induced by a chronic blockade of nitric oxide (NO) synthesis. Male Sprague-Dawley rats were supplemented with N^G-nitro-L-arginine methyl ester in drinking water (L-NAME, 100 mg/L) for 4 weeks to inhibit the endogenous synthesis of NO. The mRNA expression of renin, angiotensin converting enzyme (ACE), type 1 angiotensin II receptor (AT1R), ET-1, ETA receptor, and neutral endopeptidase (NEP) was determined in the thoracic aorta by reverse transcription-polymerase chain reaction. Following the treatment with L-NAME, tissue levels of NO metabolites in the thoracic aorta were significantly decreased, along with increased blood pressure. The mRNA expression of renin, ACE, and AT1R was increased in the aorta. The protein expression of AT1R, as assessed by Western blot analysis, was also increased. The expression of ET-1 and ETA receptor mRNA was increased, whereas that of NEP mRNA decreased. The increased expression of components of renin-angiotensin and ET systems and the decreased expression of NEP may be causally related with the development of hypertension following a blockade of NO synthesis.