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Altered Regulation of Natriuretic Peptide System in the Kidney in Rats with PAN-induced Nephrotic Syndrome

전남대학교 의과대학 내과학교실[1], 생리학교실[2]

배은희[1] · 김인진[1] · 이종은[2] · 마성권[1] · 최기철[1] · 김수완[1]

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Eun Hui Bae[1], In Jin Kim[1], JongUn Lee[2], Seong Kwon Ma[1], Ki Chul Choi[1], Soo Wan Kim[1]

Departments of Internal Medicine[1] and Physiology[2], Chonnam National University Medical School

Purpose : Sodium retention is a hallmark of nephrotic syndrome. However, the molecular basis for the sodium retention and edema remains to be defined. We investigated changes of natriuretic peptide system in the kidney and heart at different stages (i.e., a sodium retaining stage and a compensatory stage) of nephrotic syndrome.
Methods: Male Sprague- Dawley rats were treated with PAN (180 mg/kg, i.v.). The control group was treated with vehicle only. Tissue levels of atrial natriuretic peptides (ANP) were determined in the kidney, plasma and heart. The mRNA expression of ANP, natriuretic peptide receptor (NPR)- A, and NPR- C was determined by real- time PCR. Neutral endopeptidase (NEP) was determined by immunohistochemistry.
Results: At day 6 (sodium retaining stage), PAN rats developed ascites, along with a positive sodium balance. Urinary sodium excretion was decreased. The mRNA expression of ANP in cardiac atrium and kidney was markedly increased, while that of NPR- A and NPR- C in the kidney was decreased. The ANP immunoreactivity in the atrium was significant increased in the PAN group. The expression of NEP in proximal tubule was decreased in PAN group. At day 13 (compensatory stage of sodium retention), while urinary sodium excretion was not changed compared with the controls, ANP mRNA expression in the kidney was increased in association with increased urine ANP immunoreactivity. The expression of NEP in proximal tubule was decreased.
Conclusion : The increased renal synthesis and decreased metabolism of ANP may play a compensatory role against the sodium retention in nephrotic syndrome. The decrease of NPR- A expression in the kidney may contribute to the ANP resistance in the sodium retaining stage of nephrotic syndrome. The subsequent recovery of NPR- A expression may promote sodium excretion in later stages of nephrotic syndrome.

Key Words : 신증후군, 이뇨호르몬, 부종
Nephrotic syndrome, Natriuretic peptide, Edema