Altered Regulation of Renal Nitric Oxide and Natriuretic Peptide Systems in Oxonic Acid-induced Hypertensive Rats

Eun Hui Bae[1], In Jin Kim[2], Chang Seong Kim[1], Joon Seok Choi[1]
Jeong Woo Park[1], Seong Kwon Ma[1], JongUn Lee[2], Soo Wan Kim[1]

Department of Internal Medicine[1] Chonnam National University Medical School
Department of Physiology[2] Chonnam National University Medical School

Although hyperuricemia may be associated with renal diseases, it is usually considered as a marker of renal dysfunction rather than a risk factor for progression. Recent studies have reported that mild hyperuricemia induced by a uricase inhibitor, oxonic acid (OA), results in hypertension in rats. The present study was aimed at examining whether an altered role of local renal hormones such as nitric oxides (NO) and natriuretic peptides (NP) may contribute to OA-induced hypertension. Hypertension was induced in Sprague-Dawley rats by administration of oxonic acid (750mg/kg per day), for 8 weeks. The amount of urinary NO metabolites was measured by calorimetric assay. The protein expression of endothelial, inducible, and neuronal NO synthase, soluble guanylyl cyclase (GC) and endopeptidase (NEP) was determined in the kidney by semiquantitative immunoblotting. The mRNA expression of components of NP system was determined by real-time polymerase chain reaction. The activities of soluble and particular GC (sGC, pGC) were determined by radioimmunoassay. In OA-treated rats, systolic blood pressure was increased compared with that in the control (125±1 vs. 151±9, $p<0.05$). The urinary NO metabolites did not differ between the two groups, while the expression of eNOS was decreased and iNOS was increased in the OA-treated rats. The protein expression and the catalytic activity of sGC were not changed in the glomerulus or papilla. The mRNA expression of ANP was increased in the kidney. The expression of NEP and the activity of pGC were both decreased in the glomerulus of OA-treated rats. Downregulation of eNOS may contribute to OA-induced hypertension. An increased expression of NP associated with downregulation of NEP may play a compensatory role against the hypertension through inducing a natriuresis.

Key Words: 고혈압, 요산, 산화질소
Hypertension, Uric acid, Nitric Oxide