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The Effect of Rosiglitazone on the L-NAME Induced Hypertensive Nephropathy in Spontaneously Hypertensive Rat

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Background : The peroxisome proliferator activator-gamma (PPAR-γ) agonist has a protective effect against various types of kidney injury. Anti-fibrotic and anti-inflammatory effect, vascular protective effect and anti-oxidant effect were proposed. This study was designed to investigate the PPAR-γ agonist prevent hypertensive renal injury during prolonged nitric oxide synthesis inhibition with NG-nitro-L-arginine methyl ester (L-NAME) in spontaneously hypertensive rats (SHR).

Methods : For 4 weeks, we studied three groups of 12-week-old male SHR : a control group, a L-NAME group (50 mg/L in drinking water), and a group treated with L-NAME and rosiglitazone (RGTZ, 3 mg/kg/day). Cortical mRNA expression of PPAR-γ and MCP-1 were assessed by RT-PCR. Renal expression and distribution of TGF-β protein and ED-1 positive cell infiltration were analyzed by immunohistochemistry.

Results : L-NAME rats developed severe hypertensive damage with significantly elevated blood pressure, increased urinary protein excretion and plasma creatinine levels, and more severe arteriolar injury and glomerular sclerosis. Levels of MCP-1 and TGF-β expression and the infiltration of ED-1 positive cells were significantly increased in L-NAME rats compared with control SHR. Addition of RGTZ significantly lowered blood pressure, urine protein excretion and plasma creatinine level. On the histological examination, arteriolar injury score and glomerulosclerosis score and interstitial fibrosis score were significantly lower in the RGTZ group than the L-NAME group (respectively, $p<0.05$). The number of ED-1 positive cells, renal MCP-1 and TGF-β expression were also decreased in the RGTZ treated group as compared with L-NAME only group.

Conclusion : RGTZ prevents glomerular and arteriolar damages and renal functions, through lowering blood pressure as well as anti-inflammatory and anti-fibrotic mechanism. PPAR-γ agonist may be useful in the prevention of hypertensive nephropathy.