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허혈-관류 신손상 백서 모델에서 안지오텐신 II 수용체 차단제의 Toll-like Receptor 4 발현에 대한 효과

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Angiotensin II AT1 Receptor Blocker Reduces Toll-like Receptor 4 Expression in Experimental Ischemia-Reperfusion Renal Injury in Rats

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Introduction and Aims: Ischemia-reperfusion (IR) injury activates innate immunity through the engagement of Toll-like-receptors (TLR) by endogenous ligands. It has been suggested that renin-angiotensin system (RAS) plays an important role in IR renal injury.

Activation of innate immunity by angiotensin II was also reported, recently. We examined whether RAS inhibition by angiotensin II AT1 receptor blocker modulates the renal expression of TRL4 and its ligands and attenuates renal injury induced by IR injury.

Methods: Male Spargue-Dawley rat were divided into 4 groups; Sham group, losartan treated sham group, control IR group, and losartan treated IR group. IR injury was induced surgically by clamping of both renal arteries for 30 minutes under anesthesia. Losartan (40mg/kg) was injected intraperitoneally 60 minutes before IR injury. We evaluated the renal mRNA expression levels of TLR4, HMGB1, MCP-1, TNF-α, IL-6 by real-time RT-PCR 24 hrs after IR injury. We also evaluated the magnitude of renal mononuclear cell infiltration by immunohistochemistry.

Results: BUN and serum creatinine (s-Cr) levels in control IR mice were significantly increased compared to sham group (all. $p<0.05$). The levels of BUN and s-Cr of losartan treated IR group were significantly lower than those of control IR group (all, $p<0.05$).The levels of renal mRNA expression of TLR4 and HMGB1 in control IR group were significantly increased compared to sham operated mice (all, $p<0.05$). Losartan treated IR group showed significantly lower levels of renal TLR4 and HMGB1 mRNA expression than those of control IR group (all, $p<0.05$). Losartan decreased significantly renal mRNA expressions of TNF-α, MCP-1, and IL-6 (all, $p<0.05$). Losartan also reduced significantly infiltration of the ED1 positive cells in IR injured kidneys ($p<0.05$).

Conclusions: We thought that the inhibition of renin-angiotensin system by angiotensin II AT1 receptor blocker attenuated the renal injury induced by experimental ischemia-reperfusion in rats and at least in part, suppression of TLR4 may be involved in this mechanism.

Key Words: 급성신부전-섬유화-수용체
Acute renal failure-fibrosis-receptors