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만성 사이클로스포린 신 독성 모델에서 안지오텐신 II 차단이 Toll-like 수용체 및 수지상 세포의 활성화에 미치는 영향

가톨릭대학교 의과대학 신장내과연구실, 내과학교실*

안경옥 · 임선우 · 양현주 · 기정연 · 최범순* · 김용수* · 방병기* · 양철우*

Purpose : Cyclosporine A (CsA)-induced renal injury upregulates toll-like receptor (TLR) and induce maturation of dendritic cells (DC) (Lim SW et al, Transplantation, 2005). Angiotensin II is a major mediator of CsA-induced renal injury. We evaluate the role of renin-angiotensin system in regulating TLR expression and maturation of DC in chronic cyclosporine nephropathy.

Methods : Sprague-Dawley rats were used. Two experimental studies were performed. First experiment, angiotensin II (435 ng/kg/min) was infused to the rats for 14 days via minipump. Second experiment, losartan (10 mg/kg per day) was concurrent administered with CsA (15 mg/kg per day) to the rats for 28 days. The effect of angiotensin II on expression of TLR2 and TLR4 mRNA and protein, potential TLR ligands (HSP70, HSPG), costrimulatory molecule (CD80, CD86) and maturation of DC was evaluated.

Results : In the first experiment, angiotensin II infusion increased expression of TLR2 and TLR4 mRNA and protein, TLR ligands, costimulatory molecules, CD8-positive lymphocytes and maturation of DC in rat kidney. However, concomitant treatment of losartan decreased all parameters. In the second experiment, CsA-treated rat kidney showed increased expression of TLR2 and TLR4 and maturation of DC, but concomitant treatment losartan decreased these parameters.

Conclusion : This finding suggests that angiotensin II plays a pivotal role in activating TLR and maturation of DC in kidney, and blockade with angiotensin II decreases innate immune response caused by CsA-induced renal injury.