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Cyclosporin-A에 의한 신독성 유발백서에서 cGMP phosphodiesterase 억제제 투여의 신보호 효과

연세대학교 원주의과대학 원주기독병원 신장내과

양재원 · 김비로 · 최정욱 · 한병근 · 최승옥

cGMP Phosphodiesterase Inhibitor (Sildenafil) Provides Functional Protection Against Ischemia-Reperfusion and Cyclosporine-Induced Renal InJury Rats

Jae Won Yang, BIro Kim, Jung Uk Choi and Byung Geun Han, Seung Ok Choi

Yonsei University Wonju college of medicine Nephrology

Introduction and Aims : Cyclosporin A (CsA)- induced nephrotoxicity is associated with oxidative stress and reduced nitric oxide availability. Many of the biologic actions if nitric oxide are mediated by cyclic3, 5 guanosine monophosphate (cGMP), which is rapidly degraded by phosphodiesterase (PDE). The aim of the present study is to analyze the renal function parameters and the expression of mediators of renal damage induced by CsA nephrotoxicity after cGMP phsphodiesterase inhibitor (Sildenafil).

Methods : Sparague- Dawley rats(N=30) performed right nephrectomy would be classified into 5 groups: (1) Control group (N=6); right nephrectomy only, (2) Ischemic- reperfusion (IR) group(N= 6); clamped left renal vascular pedicle for 45 minutes, (3) IR with sildenafil group(N=6); sildenafil (2.5 mg/day, P.O) would be administered for 7 days after IR injury, (4) IR with CsA group; CsA (15mg/kg/day, SQ) would be administered for 7 days after IR injury, (5) IR with CsA and sidenafil group(N=6); Cyclosporin A (15mg/kg/day) and sildenafil(2.5 mg/day) would be administered for 7 days after IR injury. After 7 days, serum BUN and creatinine were measured and then the kidney were removed. The expression of nitric oxide synthase was examined using confocal microscope and Image Analyzer.

Results :

Table 1. Renal Function in Each Group

	Controls	IR	IR+sildenafil	IR+CsA	IR+CsA+sildenafil
BUN (mg/dL)	24.4±1.6	30.1±6.1	25.0±1.6	56.8±26.9	29.5±8.1*
creatinine (mg/dL)	0.4±0.1	0.5±0.1	0.4±0.1	0.8±0.6	0.4±0.1*

p<0.01 vs CsA

The sildenafil treament groups were more srong expression of nitric oxide synthase than the ischemia-reperfusion injury group and CsA treatment group.

Conclusion : cGMP phosphodiesterase inhibitor (sildenafil) provides functional protection against cyclosporine induced renal injury in rats due to the attenuating effect of cGMP phosphodiesterase inhibitor on nitric oxide degradation.

Key Words : 급성신부전, 싸이클로스포린 A, Cyclic GMP
Acute renal failure, Cyclosporin- A, Cyclic GMP