S-D5

Cyclosporine에 의한 신독성 모델에서 항산화제가 Klotho-노화유전자 발현에 대한 영향

가톨릭대학교 서울성모병원 면역질환융합사업단, 장기이식연구소

박상국, 강석휘, 임선우, 정병하, 도경찬, 허성범, 양철우

Effect of Anti-oxidant on Klotho, Anti-aging Gene, Expression in an Experimental Model of Cyclosporine A Nephrotoxicity

Shang Guo Piao, Seok Hui Kang, Sun Woo Lim, Byung Ha Chung
Kyoung Chan Doh, Seong Beom Heo, Chul Woo Yang

Convergent Research Consortium for Immunologic Disease, Transplant Research Center
Seoul St. Mary's Hospital The Catholic University of Korea

Background: Previously, we reported that chronic CsA nephrotoxicity suppresses the expression of Klotho, and this is mediated by oxidative stress. This study was examined whether antioxidant, N-acetyl cysterine (NAC), protects the Klotho expression and kidney tissue damage against CsA induced nephrotoxicity.

Methods: Mice were divided 4 groups: vehicle group (VH, olive oil, 1 ml/kg/day), CsA group (30 mg/kg/day), NAC 300 group (300 mg/kg/day), and CsA+NAC 300 group, respectively. Under 0.01% sodium diet, mice received daily administrations of olive oil or CsA subcutaneously for 4 weeks. Mice also received drinking water with or without NAC. Degree of tubulointerstitial fibrosis (TIF) induced by CsA was expressed in TIF score. Oxidative stress was measured by urinary excretion of 8-hydroxy-2'-deoxyguanosine (8-OHdG). Immunoblot analysis was performed for Klotho protein expression.

Results: CsA treatment for 4 weeks was accompanied by typical striped interstitial fibrosis. Administration of NAC on CsA significantly decreased TIF level (NAC 300 group, 17±3% vs. 29±1%, $p<0.05$ vs. CsA group) compared to CsA group. Moreover, urinary 8-OHdG excretion was decreased in NAC treatment on CsA groups compared to CsA group (CsA±NAC 300 group, 187±49 ng/day vs. 409±149 ng/day, $p<0.05$ vs. CsA group). Amount of Klotho protein in CsA treatment was significantly decreased at 4-week compared to VH group (13±4% vs. 100±18%, $p<0.05$ vs. VH group). NAC 150 treatment on CsA was restored the Klotho protein expression (36±3% vs. 100±11%, $p<0.05$ vs. CsA group).

Conclusion: NAC may have protective effect in CsA-induced renal injury associated with oxidative stress. Up-regulated Klotho expression may be relevant to improvement against acute and chronic CsA nephrotoxicity.

Key Words: CsA, KLOTHO, N-acetylcyteine, Cyclosporine A, KLOTHO, N-acetylcyteine