S-B13(E)

만성사이클로스포린 신독성 동물모델에서 HMG-CoA 환원효소 억제제의 klotho 유전자의 발현 및 FoxO 경로 조절을 통한 항노화효과

가톨릭대학교 의과대학 내과학교실[1], 장기이식연구소[2]

윤혜은[1], 정현화[1], 신석준[1], 기정연[2], 박상국[2], 송지현[2], 양철우[2]

HMG-CoA Reductase Inhibitors Attenuate the Aging Process via Regulation of klotho Gene and FoxO Pathway, in an Experimental Model of Chronic Cyclosporine Nephrotoxicity

Hye Eun Yoon[1], Hyun Wha Chung[1], Seok Joon Shin[1]
Jung Yeon Ghee[2], ShangGuo Piao[2], Ji-Hyun Song[2], Chul Woo Yang[2]

Department of Internal Medicine[1], Transplant Research Center[2], The Catholic University of Korea

Background: The aim of this study was to evaluate the effect of HMG-CoA reductase inhibitor on cyclosporine (CsA)-induced nephrotoxicity in the aging process by using the expression of aging-associated markers.
Methods: Mice were daily treated with vehicle (VH; 1 mL/kg/day of olive oil) or CsA (30 mg/kg/day) with or without pravastatin (PRVT; 20 mg/kg/day in drinking water) for 4 weeks. The expressions of klotho, phosphorylated FoxO-3 (p-FoxO-3), and manganese superoxide dismutase (MnSOD) were evaluated as markers of aging process. Oxidative stress was evaluated by measuring urinary excretion of 8-hydroxy-2-deoxyguanosine (8-OHdG), and apoptotic cell death was evaluated by western blot of caspase-3 and deoxynucleotidyl transferase-mediated dUTP-biotin nick end-labelling (TUNEL) staining. Results. Treatment with CsA significantly decreased the expression of klotho and MnSOD, increased that of p-FoxO-3. However, the administration of PRVT increased the expression of klotho and MnSOD and decreased that of p-FoxO-3 with histologic improvement. The increased excretion of urinary 8-OHdG and expression of caspase-3 and TUNEL-positive cells by CsA treatment were decreased with the administration of PRVT.
Conclusion: HMG-CoA reductase inhibitors attenuate the aging process by upregulating the expression of klotho, activating FoxO pathway and decreasing oxidative stress in chronic CsA nephrotoxicity.

Key Words: 사이클로스포린, HMG 환원효소 억제제, 노화
Cyclosporine, HMG-CoA reductase inhibitor, Senescence