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Statin의 말초혈액 단핵세포 내 cyclosporine A 축적효과에 대한 연구

인제대학교 부산백병원 신장내과학교실[1], 인제대학교 부산백병원 병리과학교실[2]

박석주[1], 강선우[1], 김태희[1], 강미선[2]

In vitro Effect of Statins on Intracellular Cyclosporine A Concentration in Human Peripheral Blood Mononuclear Cells

Seok Ju Park[1], Sun Woo Kang[1], Tae Hee Kim[1], Mi Sun Kang[2]

Department of Nephrology[1], In Je University, Busan Paik Hospital
Deparment of Pathology[2], In Je University, Busan Paik Hospital

Background: It was known that declining intracellular T-lymphocyte concentration of cyclosporine A precedes acute rejection in kidney transplant recipients. The aim of this study was to elucidate the impact of various statins on intracellular cyclosporine A concentration in the PBMC (peripheral blood mononuclear cell).

Method: PBMCs were isolated from 30 ml of freshly collected blood which were obtained from healthy 4 volunteers with informed consent. PBMC were incubated in the media with 0.1 ml of ND96 buffer containing 200 nm of cyclosporine A in the presence and absence of rosuvastatin (10 μm, 100 μm), simvastatin (10 μm, 100 μm), atorvastatin (10 μm, 100 μm), fluvastatin (10 μm, 100 μm), pitavastatin (10 μm, 100 μm) for 30 min at 37℃. The radioactivity was measured by a MicroBeta TriLux 96-well Scintillation/Luminescence detector (PerkinElmer). We also measured intracellular cyclosporine A concentration in the presence of the statins (100 μm) in the LLC-PK1 overexpressing P-glycoprotein cells.

Result: The intracellular concentration of cyclosporine A in the control and in the presence of verapamil was 30.5±6.2 fmol/min/^{2}×10^{5} and 55.8±6.4 fmol/min/2×10^{5} (p=0.008) respectively. The intracellular cyclosporine A concentration with simvastain (10μm, 100 μm) and with atorvastatin (10μm, 100 μm) showed significant higher value, 67.1±6.7 fmol/min/^{2}×10^{5} (p=0.002), 66.2±4.5 fmol/min/^{2}×10^{5} (p=0.001), 45±4.9 fmol/min/^{2}×10^{5} (p=0.03), 57.5±2 fmol/min/^{2}×105 (p=0.002),respectively. But the others were not (p>0.05). It also revealed higher intracellular cyclosporine A concentrations in the presence of verapamil, atorvastatin and simvastatin, 398.7±1.1 fmol/min/^{1}×10^{4} (p=0.0002), 108.3±0.6 fmol/min/^{1}×10^{4} (p=0.04), 222±0.8 fmol/min/^{1}×10^{4} (p=0.01), respectively, in the LLC-PK1 cells.

Conclusion: The intracellular cyclosporine A concentration could be affected variously with statins by p-glycoprotein mediated inhibition.

Key Words: 스타틴, 시클로스포린
Statin, Cyclosporine