

Cyclosporine A 신독성모델에서 Paricalcitol 보호효과

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The Renoprotective Effect of Paricalcitol on
Chronic Cyclosporine A Nephropathy

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Background: Vitamin D has protective effect on chronic kidney disease patients. We evaluated whether vitamin D has renoprotective effect of paricalcitol on cyclosporine (CsA)-induced renal injury using experimental model of chronic CsA nephropathy.

Methods: Male Sprague Dawley (SD) rats were divided 4 groups; vehicle, CsA, CsA+paricalcitol 50 ng/kg (P50) and CsA+paricalcitol 200 ng/kg (P200), respectively. CsA (15 mg/kg per day) was injected subcutaneously for 28 days and paricalcitol was injected as the concentration of 50 ng/kg per day (low) and 200 ng/kg per day (high) for 28 days. The responses of paricalcitol were evaluated by measuring renal functional parameters and the degree of the fibrosis by Masson's trichrome stain and the number of ED-1 positive cells. We also assessed the mechanism of the effect on renal pathology by analyzing the expression of β ig-h3, caspase-3 immunoblotting and 24-h urinary excretion and tissue expression of 8-hydroxy-2'-deoxyguanosine (8-OHdG).

Results: Four weeks treatment of CsA developed typical chronic CsA nephropathy, characterized by interstitial inflammatory cells infiltration and interstitial fibrosis. Quantification for tubulointerstitial fibrosis (TIF) revealed lower TIF score in the P200 group than CsA group ($15.5 \pm 2.3\%$ vs. $23.5 \pm 0.9\%$, $p < 0.05$). The number of ED-1 positive cells was also lower in the P200 group than CsA group ($36.8 \pm 1.59/0.5 \text{ mm}^2$, vs. $52.3 \pm 2.0/0.5 \text{ mm}^2$, $p < 0.05$). At molecular basis, increased β ig-h3 expression in the CsA group was significantly decreased in the P200 compared to CsA group ($9,750 \pm 101\%$ vs $6,897 \pm 465\%$, $p < 0.05$). Increased oxidative stress in the CsA group was significantly decreased compared to the P50 or P200 groups. Increased caspase-3 expression in the CsA group protein level for caspase-3 was decreased in paricalcitol groups. But lower paricalcitol dosage group (P50) did not show the significant difference with CsA group ($p > 0.05$).

Conclusion: Paricalcitol attenuates CsA-induced interstitial fibrosis and inflammation by decreasing oxidative stress, and the high dose is more effective than low dose in preventing CsA-induced renal injury.

Key Words: 사이클로스포린, Paricalcitol, 산화성 스트레스
Cyclosporine A, Paricalcitol, Oxidative stress