

싸이클로스포린에 의한 신독성 모델에서 시롤리무스의 투여 전환시점에 따른 효과

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Comparison of Early and Late Conversion to Sirolimus in Cyclosporine-induced Nephrotox

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Background : It is well known that combined treatment of calcineurin inhibitors (CNI) and sirolimus (SRL) causes synergistic nephrotoxicity. We performed this study to determine optimal time point of conversion of SRL in cyclosporine (CsA)-induced nephrotoxicity.

Methods : Three separate studies were performed in Sprague-Dawley rats. First, CsA was treated with or without SRL for 28 days. Second, CsA (15mg/kg per day) was treated for 7 days, and then switched to SRL (0.3 mg/kg per day) at 7 day (early conversion). Third, CsA was switched to SRL at 28 day (late conversion). The effect conversion from CsA to SRL was evaluated by renal function, histopathology (interstitial inflammation and fibrosis), inflammatory and fibrotic markers (osteopontin and beta-igh3), apoptotic cell death (TUNEL-positive cells and caspase 3).

Results : Combined treatment of CsA and SRL further deteriorated renal function, increased inflammation and interstitial fibrosis compared with the CsA or SRL groups. At molecular basis, osteopontin and beta-igh3 expressions were increased compared with the CsA or SRL groups. Early conversion from CsA to SRL improved renal function and decreased interstitial fibrosis and inflammation compared with CsA-treated rats. On the other hand, late conversion from CsA to SRL significantly decreased renal function and increased interstitial fibrosis and inflammation compared with CsA-treated rats.

Conclusion : Early conversion from CsA to SRL is an effective strategy for minimizing CsA-induced renal injury.

Key Words : 신독성, 싸이클로스포린, 시롤리무스
Nephrotoxicity, Cyclosporine, Sirolimus