

만성 사이클로스포진 신독성 모델에서 지방세포 유래 줄기 세포에 의한 산화 스트레스 표지자의 증가

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Increase of Oxidative Stress Marker by Human Adipose Tissue Derived Mesenchymal Stem Cells in Chronic CsA Nephrotoxicity Rat Model

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It has been reported that human adipose tissue derived mesenchymal stem cells (hATMSCs) have beneficial effects on various animal models of renal injury. This study was performed to investigate whether hATMSCs have protective effect on renal injury caused by cyclosporine (CsA). CsA (7.5 mg/kg) and hATMSCs ($3 \times 10^6/5$ mL) were administered alone and together to the rats for 4 weeks. The effect of hATMSCs on CsA induced renal injury was evaluated by assessing renal function and pathology, mediators of inflammation and oxidative stress markers; and apoptotic cell death. Four weeks of CsA treatment caused renal dysfunction, interstitial fibrosis and inflammatory cell infiltration, and apoptotic cell death. Urine 8-OHdG levels was significantly increased compared to VH group. Treatment with hATMSCs did not improve renal function and histopathology (fibrosis and inflammation) compare to CsA group and significantly deteriorated compared to VH group. Inflammatory cell infiltration and apoptotic cell death showed increasing pattern in MSC+CsA group compared to CsA group even though it did not reach statistical significance. Of note, urine and serum 8-OHdG was significantly increased in MSC+CsA group ($p < 0.05$). To define the cause of no beneficial effect of hATMSCs on CsA-induced renal injury, we performed in vitro study. Addition of hATMSC conditioned media increased apoptosis of HK-2 cell under CsA treatment compared to CsA only treated condition. These data suggest that MSC treatment may be harmful in state of chronic CsA nephropathy because hATMSCs can aggravate CsA induced injury via induction of oxidative stress.

Key Words: 간엽줄기세포, 사이클로스포린, 신독성
Mesenchymal stem cell, Cyclosporin, Nephrotoxicity