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싸이클로스포린A에 의한 신장손상 모델에서 COMP-Ang1의 신장 보호 효과

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Protective Effect of COMP-Angiopoietin-1 on Cyclosporine-Induced Renal Injury

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Peritubular capillary injury induces chronic hypoxia in the renal tubulointerstitium and renal peritubular capillary dysfunction is an early event that contributes to tubulointerstitial fibrosis. Cyclosporine A (CsA) is a potent immunosuppressant and improves survival of renal allografts. However, the limitation of CsA use is chronic nephrotoxicity. A soluble, stable, and potent angiopoietin-1 (Ang1) variant, cartilage oligomeric matrix protein (COMP)-Ang1 has been developed. We investigated whether COMP-Ang1 ameliorates CsA-induced renal injury. Histologic examination showed that COMP-Ang1 significantly decreased CsA-induced tubular damage and tubulointerstitial fibrosis. CsA-induced increases in macrophage infiltration and expression of MCP-1 and ICAM-1 after CsA treatment were significantly reduced by COMP-Ang1. Treatment with COMP-Ang1 also decreased the CsA-induced increases in TGF-β1 and Smad 2/3 levels while increasing Smad 7 levels. Laser-Doppler sonographic findings and endothelial factor VIII staining revealed that COMP-Ang1 preserved the integrity of peritubular vasculature and intrarenal hemodynamic from the CsA-induced renal injury. COMP-Ang1 inhibited tubular cell apoptosis while increasing tubular cell proliferation in CsA-induced renal injury. These results indicate that COMP-Ang1 exhibited a protective effect on damaged peritubular capillaries, hemodynamic alteration, and inflammation in CsA-induced renal injury. Thus, COMP-Ang1 may be useful as a therapeutic and prophylactic agent for specific protection against endothelial dysfunction and inflammation.