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만성 사이클로스포린으로 유도된 신독성 모델에서 대식세포의 역할

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The Role of Macrophage in the Pathogenesis of Chronic Cyclosporine-induced Nephropathy

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Background : Macrophages play diverse roles in tissue injury. We evaluated their role in cyclosporine (CsA)-induced renal injury by depletion with liposomal clodronate (CL).

Methods : Male Sprague Dawley rats were treated with CsA with or without CL treatment for 28 days. We assessed responses from the pathology and by measuring renal functions and levels of a proinflammatory cytokine (osteopontin), a profibrotic cytokine (□ig- h3), innate immune response markers (toll- like receptor 2 and MHC class II molecules), apoptotic cell death (deoxynucleotidyl transferase- mediated dUTP- biotin nick end- labeling staining and caspase 3 expression) and oxidative stress (8- hydroxy- 2- deoxyguanosine, 8- OHdG).

Results : Macrophage depletion improved renal function and histopathology compared with the CsA- treated rats. Osteopontin and □ig- h3 levels increased significantly in CsA- treated rat kidneys, but CL treatment decreased both markers. Enhanced innate immune response and apoptotic cell death in CsA- treated rat kidney were decreased with CL. The increased rates of urinary 8- OHdG excretion and the tubular expression of 8- OHdG produced by CsA treatment were reversed with CL treatment.

Conclusion : Infiltrating macrophages were involved in both nonimmunologic and immunologic injury and led to apoptotic cell death in this rat model of chronic CsA nephropathy.

Key Words : 사이클로스포린, 클로도로네이트, 대식세포
Cyclosporin A, Clodronate, Macrophage