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DOCA-salt 고혈압 흰쥐모델에서 sildenafil의 신보호 효과

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Renoprotective Effect of Sildenafil in DOCA-salt Hypertensive Rats

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Background: Sildenafil, the first selective inhibitor of phosphodiesterase-5 (PDE5), has cardioprotective effects in animal experiments. This study was designed to evaluate the possible renoprotective effects of sildenafil in deoxycorticosterone acetate (DOCA)-salt hypertensive (DSH) rats.

Methods: Rats were implanted with DOCA strips (200 mg/kg) on 1 week after unilateral nephrectomy. Rats received control diet with or without sildenafil for 2 weeks. The systolic blood pressure (SBP) was measured by tail cuff method, and urinary albumin excretion ratio (UAE) was calculated by urine microalbumin and creatinine. The glomerulosclerosis and tubulointerstitial fibrosis was determined by masson's trichrome stain. The expression of ED-1, COX2, HSP25, transforming growth factor-β (TGF-β), STAT3, AKT, Bax, Bcl-2 and caspase-3 was determined in the kidney by semiquantitative immunoblotting and immunohistochemistry. TUNEL stain was performed for detecting apoptic cell.

Results: In DSH rats, SBP was increased, which was attenuated by sildenafil treatment. Creatinine clearance was decreased while UAE was increased in DSH rats compared with controls, which were attenuated by sildenafil treatment. Glomerulosclerosis and tubulointerstitial fibrosis in DSH rats were also attenuated by sildenafil treatment. The expression of ED-1, COX2, TGF-β, HSP25, STAT3, AKT, Bax, and caspase-3 was increased, while Bcl-2 expression was decreased in the kidney of DSH rats. These changes werecounteracted by sildenafil treatment. The number of apoptic cells was increased in DSH rats, which was attenuated by sildenafil treatment.

Conclusions: Sildenafil is effective in preventing progression of renal injury in DSH rat, the mechanism of which is associated with anti-inflammatory, anti-fibrotic and anti-apoptotic effects.

Key Words: 사구체 경화, 고혈압, 실데나필
Glomerulosclerosis, Hypertension, Sildenafil