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Rosiglitazone Preserves Aquaporin Water Channels and Sodium Transporters in Deoxycorticosterone Acetate (DOCA)-Salt Hypertensive Rats

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Background : An antihypertensive effect of rosiglitazone (RGZ), a PPARγ agonist, has been reported in patients with hypertension. The molecular mechanisms underlying the therapeutic application of RGZ were investigated in DOCA-salt hypertension.

Methods : One week after left unilateral nephrectomy, rats were subcutaneously implanted with silastic DOCA (200 mg/kg) strips and supplied with 0.9% saline to drink. Two weeks later, the rats were either treated with RGT (10 mg/kg/day) or none for another 2 weeks. Systolic blood pressure was measured by tail cuff method. The protein expression of aquaporins (AQP), sodium transporters and neutral endopeptidase was determined in the kidney by semiquantitative immunoblotting and immunohistochemistry. The mRNA expression of atrial natriuretic peptide (ANP) and endothelin (ET)-1 was determined by real time PCR.

Results : DOCA-salt rats showed an increase of systolic blood pressure. Accordingly, the creatinine clearance and urine osmolality decreased, while urinary flow rate and sodium excretion increased. The expression of AQP1-3, Na,K-ATPase, NHE3, NKCC2 and NCC proteins decreased. The expression of ANP was increased, while that of neutral endopeptidase decreased. The expression of ET-1 mRNA was increased. Masson's trichrome stain demonstrated increased collagen deposition and glomerulosclerosis. Transforming growth factor β1 expression was also increased. RGT attenuated or prevented the dysregulation of these parameters, along with improvement of renal function and lowering the blood pressure.

Conclusion : The antihypertensive effect of RGT may be attributed to preservation of AQP and sodium transporters, along with the humoral mediators such as ET-1 and ANP systems in the kidney.

Key Words : DOCA-salt, 수분통로, 나트륨수송체, 이뇨호르몬
Rosiglitazone, DOCA-salt, AQP, sodium transporters, ANP