44) **cAMP Response to PGE₂ in Renal Medulla of Young Spontaneously Hypertensive Rats and the Early DOCA-salt Hypertension.**

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INTRODUCTION : It has been thought that renal prostaglandin (PG) E₂ plays an important role in the blood pressure control. The effect of PGE₂ is thought to be mediated by the specific receptor-adenylate cyclase system. However, little is known about the precise mechanism of this system in the pathogenesis of hypertension. In this study, we examined PGE₂-stimulated adenylylase cyclase activity in two types of experimental hypertension, young spontaneously hypertensive rats of Okamoto and Aoki strain (SHR) and the early DOCA-salt hypertension to clarify the role of PGE₂ receptor-adenylate cyclase-system in the pathogenesis of hypertension.

MATERIAL AND METHODS : Four-week-old male SHR and age- and sex-matched Wistar-Kyoto rats (WKY) were used. DOCA-salt hypertension was made in male Wistar rats weighing 152-178 g. The left kidney was removed and injected once a week with 10 mg deoxycorticosteroneacetate (DOCA) subcutaneously and given free access to 1% saline solution. The control groups were removed the left kidney and given tap water to drink. DOCA-salt hypertensive and control rats were killed 10 days after nephrectomy.

Renal medulla was homogenized and centrifuged at 400 x g for 10 min. The supernatant was centrifuged at 10,000 x g for 10 min and the supernatant was recentrifuged at 105,000 x g for 60 min. The pellet was washed and resuspended in the buffer containing 30μM indomethacin, 10mM MgCl₂ and 50mM Tris-HCl (pH 7.4). Adenylylase cyclase activity was measured in a reaction mixture in a total volume of 0.125ml, containing the following; membrane fraction (0.05mg of protein), 10μM GTP, 100μM PGE₂, 30μM indomethacin, 100μM ATP, 20μM creatine phosphate, 100U/ml creatine phosphokinase, 1mM 3-isobutyl-1-methylxanthine, 50mM Tris-HCl (pH 7.4) and 10mM MgCl₂. Incubation was carried out at 37°C for 2 min. The reaction was terminated by the addition of 0.125ml of 6% perchloric acid and cAMP content was measured by radioimmunoassay. The plasma membrane marker enzyme, 5'-nucleotidase activity was measured by the method of Emmelot et al. and the protein concentration was determined by the Lowry method. Data were shown as mean ± SEM.

RESULTS : The renal adenylylase cyclase response to PGE₂ was reduced in 4-week-old SHR (8.04 ± 0.59 pmoles/mg protein/min, n=8, p<0.05) compared with age-matched WKY (11.02 ± 1.03 pmoles/mg protein/min, n=8). Whereas, the adenylylase cyclase response to PGE₂ was increased in the early DOCA-salt hypertensive rats (9.22 ± 1.62 pmoles/mg protein/min, n=10, p<0.05) compared with unilaterally nephrectomized control rats (7.53 ± 0.17 pmoles/mg protein/min, n=8). The 5'-nucleotidase activity of renal plasma membrane fraction showed no significant change in SHR (5.90 ± 0.13 μmoles/mg protein/h, n=8) and DOCA-salt hypertensive rats (6.09 ± 0.21 μmoles/mg protein/h, n=11) compared with each control (WKY; 6.04 ± 0.48 μmoles/mg protein/h, n=10, unilaterally nephrectomized control rats; 5.86 ± 0.20 μmoles/mg protein/h, n=10).

DISCUSSION : PGE₂ increases the sodium excretion to the urine. The observed decrease in PGE₂-stimulated adenylylase cyclase activity in young SHR may contribute to the pathogenesis of hypertension through the decrease of sodium excretion to the urine. Whereas, the increase of adenylylase cyclase response to PGE₂ in the early DOCA-salt hypertension may be adaptational change to the sodium loading.