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Aldosterone Blockade Modulates Mitogen-activated Protein Kinase Family Expressions in the Neonatal Rat Kidney

Hyung Eun Yim, Kee Hwan Yoo

Department of Pediatrics College of Medicine Korea Univesity

Purpose : Our recent efforts have been focused on the mechanisms responsible for renin-angiotensin system (RAS)- induced renal injury in the developing kidney. Aldosterone plays a role in the pathophysiology of various renal diseases. Here, we investigated the role of endogenous aldosterone in renal development including cell proliferation & apoptosis, and the expression of mitogen-activated protein kinase (MAPK) family.

Methods : Newborn rat pups were treated with spironolactone (200 mg/kg/d) in olive oil or normal saline for 7 d. To identify cellular changes, kidneys were examined for apoptotic cells by TUNEL stain and proliferating cell nuclear antigen (PCNA) by immunohistochemical (IHC) stain. Immunoblot, IHC stain and RT-PCR for MAPKs, phospho- MAPKs, and p53 gene were performed.

Results : Spironolactone treatment resulted in decreased body weight, decreased PCNA-positive proliferating cells and increased TUNEL-positive apoptotic cells, especially renal cortical epithelial cells ($p<0.05$). In the spironolactone-treated group, c-jun N terminal kinase (JNK)-2 and phospho-JNK-2 protein expressions were significantly increased, whereas extracellular signal regulated kinase (ERK)-2 and p38 protein expressions were significantly decreased compared with the control group in immunoblot ($p<0.05$) and IHC stain. Expressions of ERK-1, phospho-ERK-1 and 2, and p53 were not changed by spironolactone. In RT-PCR, ERK-2 and p38 mRNA expressions were significantly increased in the spironolactone-treated group ($p<0.05$).

Conclusion : The present study demonstrates that aldosterone blockade in the developing rat kidney decreases cellular proliferation, increases apoptosis, and modulates the expressions of JNK-2, ERK-2, and p38. MAPK family may play differential roles in aldosterone-related intracellular signaling pathways during renal development.