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Aldosterone or Angiotenisin II Inhibition Upregulates the Expressions of Heme Oxygenase-1 and ascular Endothelial Growth Factor in the Neonatal Rat Kidney

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Hypoxia is a vital physiological factor to control nephrogenesis, which is accompanied by the growth and development of the renal vascular system. We have recently demonstrated that aldosterone blockade in the developing rat kidney induces hypoxic response, and up-regulates the expressions of key mediators of hypoxia including hypoxia-inducible factor (HIF)-1α and Ets-1 whereas angiotensin II inihibiton do not affect hypoxia-related alterations in the developing kidney. In the present study, we investigated the role of other enzymes expressed in response to oxidative stress including vascular endothelial growth factor (VEGF) and heme oxygenase (HO)-1 in the enalapril- or spironolactone-treated kidney. We also investigated the expression of pimonidazole, a recognized marker of severe tissue hypoxia, to correlate the findings with the degree of hypoxia. Newborn rat pups were treated with enalapril (30 mg/kg/d) or spironolactone (200 mg/kg/d) for 7 d. Tissue hypoxia was assessed by the uptake of a hypoxyprobe, pimonidazole (200 mg/kg), and the expression of hypoxia-responsive genes. VEGF and HO-1 protein expressions were increased in both enalapril- and spironolactone-treated kidney ($p<0.05$). In the enalapril-treated group, VEGF and HO-1 expression were more strongly detected at dilated cortical tubules, compared to the controls. In the spironolactone-treated group, VEGF and HO-1 expression were also highly activated at cortical tubular epithelial cells and glomeruli. The immunoactivity of pimonidazole was not different from that of the controls in the enalapril group, whereas it was significantly increased in the spironolactone group. Our data indicate that aldosterone or angiotensin II inhibition in the developing rat kidney up-regulates renal HO-1 and VEGF expression irrespective of hypoxic conditions and may differentially modulate HO-1 and VEGF production. The novel pathway in the regulation of VEGF and HO-1 activation may be involved in the angiotensin II-inhibited neonatal rat kidney.

Key Words : 안지오텐신, 알도스테론, 저산소증
Angiotensin, Aldosterone, Hypoxia