Angiotensin II(ANG II) Promotes Growth and Inhibits Apoptosis in the Neonatal Rat Kidney with Unilateral Ureteral Obstruction(UUO)

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Renin-angiotensin system(RAS) of neonate is activated than that of adult. ANG II is necessary for normal embryonic and postnatal kidney development. In vitro, ANG II stimulates renal cell growth-increases DNA synthesis in tubular epithelial cells, increases rapid cell division in LLCPK1 cells, and stimulates renal proximal tubular cell hypertrophy and proliferation. In the contrary to these findings, chronic UUO in the neonate markedly activates the RAS, but impairs growth and development, and increases apoptosis of the obstructed kidney.

To determine renal growth, maturation and apoptosis in response to ANG II in the neonatal rat with chronic UUO, 40 Spraugue-Dawley rats were subjected to UUO, 27 to sham operation within the first 48 h of life. Animals received intraperitonal time release pellets containing ANG II(2.5 ng/min) or vehicle(controls), and sham, obstructed, and opposite kidneys were removed after 3 days for histologic scoring of glomerular maturity, quantitation of cellular proliferation by PCNA staining, DNA and protein measurement, and identification of apoptotic cells by flow cytometry and TUNEL technique. As modulators of apoptosis, renal bcl-2 and clusterin were localized by immunocytochemistry and clusterin mRNA was quantitated.

ANG II increased kidney/body weight ratio, glomerular maturation, cellular proliferation, and renal DNA content in the obstructed kidney($p< 0.05$). In addition, ANG II increased tubular epithelial cell bcl-2 nuclear staining, while preventing the increase in apoptosis resulting from UUO ($p<0.05$). Clusterin mRNA expression and tubular staining were also increased in the obstructed kidney by ANG II.

We conclude that ANG II can stimulate growth and development of the obstructed kidney and inhibits apoptosis, possibly by enhancing expression of bcl-2 and clusterin. Thus ANG II modulates renal growth not only by stimulating proliferation, but by reducing programmed cell death. So, we speculate that upregulation of the RAS in the neonatal obstructed kidney may constitute a response to factors leading to reduced cell proliferation and increased cell destruction.