

Altered Expression of Major Renal Sodium Transporters in Rats with Chronic Renal Failure : Response to Angiotensin II AT1A Receptor Blockade

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In chronic renal failure (CRF), reduction in renal mass leads to an increase in the filtration rates of the remaining nephrons and increased excretion of sodium per nephron. We have previously demonstrated that remnant kidneys were associated with an altered expression of proximal tubule sodium transporters (NHE3, NaPi-2, and Na,K-ATPase) and compensatory increases of BSC-1 and TSC expression per nephron in distal tubular segments (Kwon et al. Am J Physiol 1999). In the present study, we aimed to examine the effect of angiotensin II AT1A receptor blocker on the expression of major renal sodium transporters in rats with CRF, where plasma levels of angiotensin II (AngII) and vasopressin are known to be increased. During two weeks after 5/6 nephrectomy or sham operation, both CRF rats (n=10) and sham-operated control rats (n=7) received a fixed amount of low sodium diet (0.13 meq/200g bw/day) and had free access to water. CRF rats (n=10) were divided into two groups which were either candesartan-treated (CRF-C, 1 mg/kg/day for 2 weeks, s.c., n=4) or vehicle-treated (CRF-V, n=6). Both CRF-C and CRF-V group demonstrated azotemia, decreased GFR (Ccr), polyuria, and decreased urine osmolality compared with sham-operated control rats. However, CRF-C was associated with higher BUN level (153.8±9.6 vs. 77.2±13.9 mg/dL) and lower remnant kidney weight (0.29±0.03 vs. 0.39±0.02 g/100 g bw) compared with CRF-V. Semiquantitative immunoblotting of whole kidney homogenates revealed that AQP2 expression was decreased in both CRF-C (54% of sham-operate control level) and CRF-V (57%) compared with sham operated rats, whereas BSC-1 expression was significantly increased in both CRF groups. Particularly, CRF-C was associated with higher BSC-1 expression (611% of control level) compared with CRF-V (289% of control level). In contrast, the expression of NHE3 and TSC was significantly decreased in CRF-C, whereas no changes of NHE3 and TSC were observed in CRF-V compared with sham-operated controls. In conclusion, 1) the decreased urine concentration is likely mainly due to the decreased expression of vasopressin-regulated AQP2; 2) the compensatory increase of BSC-1 was observed in CRF rats, and the higher BSC-1 expression in response to candesartan treatment in CRF could be associated with the increased delivery of sodium and water to the thick ascending limb possibly due to the decreased NHE3 in the proximal tubule; 3) the decreased expression of aldosterone-regulated TSC could be due to the candesartan-induced decrease of the aldosterone synthesis in the adrenal glands.

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