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Renal expression of ammonia transporters in response to angiotensin II receptor blocker in the rat with chronic kidney disease

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Objectives : Metabolic acidosis in chronic kidney disease (CKD) is associated with a urinary acidification defect and accumulation of acid according to the reduction nephron number. The study aimed at examining the changes in renal expression of the ammonia transporter family members, Rh C Glycoprotein (Rhcg) in response to angiotensin II receptor blocker in the rat with chronic kidney disease to identify the cellular and molecular mechanisms for the urinary acidification defect associated with chronic kidney disease.

Methods : Male Sprague-Dawley rats were subjected to 5/6 nephrectomy (CKD) and sham surgery. The 5/6 nephrectomy surgery was performed through surgical resection of the upper and lower thirds of the left kidney. Right nephrectomy underwent 1 week later. The 5/6 nephrectomy rats were treated with losartan(Cozaar®) for 2 weeks (CKD-ARB). Animals were placed in metabolic cages and urine was collected under mineral oil. Urinary ammonia concentration was measured using commercially available assays. Rhcg expression were evaluated with immunohistochemistry with quantitative morphometric analysis.

Results : The serum creatinine concentration was significantly increased in CKD and CKD-ARB rats compared with controls(CKD, 0.80±0.02 mg/dL; CKD-ARB, 0.78±0.05 mg/dL; C, 0.37±0.05 mg/dL; $p<0.05$). The serum bicarbonate concentration was significantly decreased in CKD rats compared with CKD-ARB and controls(CKD, 24.2±2.1 mEq/L; CKD-ARB, 26.4±2.1 mEq/L; C, 27.2±2.3 mEq/L; $p<0.05$). The serum potassium level was significantly increased in CKD-ARB rats compared with controls(CKD, 4.86±0.87 mEq/L; CKD-ARB, 5.42±0.39 mEq/L; C, 4.14±0.57 mEq/L; $p<0.05$). 24-hour urinary ammonia excretion were significantly changed in CKD-ARB rats (CKD, 0.17±0.15 mmol; CKD-ARB, 0.14±0.04 mmol; C, 0.33±0.11 mmol; $p<0.05$). Light microscopy and immunohistochemistry with quantitative morphometric analysis demonstrated that total Rhcg expression was increased in the cortical collecting duct and outer medullary collecting duct in CKD and CKD-ARB compared with controls.

Conclusions : The CKD rat treated with angiotensin II receptor blocker have changed in urinary ammonia excretion and Rhcg expression in the CCD and OMCD. These changes suggest that angiotensin II receptor blocker may influence in urinary acidification associated with ammonia transporters.

Keywords : Chronic Kidney disease; Acidosis; Ammonia; Kidney tubules; Collecting duct; Angiotensin II receptor blocker