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Effects of Losartan Administration on Urate Transporters in Rat Kidney

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Purpose : Hyperuricemia is currently recognized as a risk factor for cardiovascular disease. It has been reported that losartan, an angiotensin II receptor blockade, decreases serum uric acid level through its uricosuric action. However, the mechanisms of the alteration of renal handling of uric acid by losartan have yet to be elucidated. This study was undertaken to investigate whether the expression of uric acid transporter proteins are affected by the administration of losartan in rat kidneys.

Methods : Three different sets of animal experiment were performed, randomly dividing male Sprague- Dawley rats into control and losartan- treated groups. Rats were fed regular rat chow containing 1% oxonic acid in Experiment I, 5% uric acid in Experiment II and 2% oxonic acid plus 5% uric acid in Experiment III, respectively. Losartan was orally given (3 mg/180 g BW/d) in Experiment I and Experiment II and subcutaneously infused (10 μg/kg/min) via osmotic minipumps in Experiment III for 7 days. Semiquantitative immunoblotting and immunohistochemistry of rat kidneys were carried out using polyclonal peptide- derived antibodies to URAT1, OAT1, MRP4, and Na/K- ATPase 1 subunit.

Results : After each of the animal experiments, neither serum uric acid nor urinary excretion of uric acid was significantly altered by losartan treatment. Semiquantitative immunoblotting revealed that the abundance of URAT1 protein in renal cortex was not significantly affected by losartan treatment. However, the OAT1 protein abundance in renal cortex was significantly increased by losartan treatment in Experiment I (100+8% vs. 179+25%, $p<0.01$), Experiment II (100+9% vs. 183+12%, $p<0.01$) and Experiment III (100+13% vs. 177+26%, $p<0.05$). Consistent with these results, OAT1 immunohistochemistry showed a remarkable increase in immunoreactivity in the basolateral membrane of proximal tubules with losartan treatment.

Conclusion : The abundance of URAT1 protein may not be affected by losartan treatment in rat kidney. The upregulation of OAT1 protein induced by losartan treatment may act to enhance urinary excretion of uric acid.

Key Words : 요산운반체, 로사탄, 근위세관
Uric acid transporter, Losartan, Proximal tubule