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Effects of Increased Uric Acid Intake on the Abundance of URAT1 and Organic Anion Transporter Proteins in the Rat Kidney

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Purpose : Renal handling of uric acid mainly occurs in the proximal tubule, and bidirectional transport of urate may involve apical absorption via the urate-anion exchanger (URAT1) and basolateral uptake via organic anion transporters (OAT1 and OAT3). We investigated in rat kidneys whether the protein abundance of URAT1, OAT1 and OAT3 is affected by the increase in uric acid intake.

Methods : Male Sprague-Dawley rats were randomly divided into control (n=6) and uric acid-supplemented (n=6) groups. Control rats were fed regular rat chow 15 g per 180 g BW per day, and uric acid-supplemented rats were additionally given 0.75 g of uric acid per 180 g BW per day for 8 days. Drinking water was freely accessible to both groups. After the animal experiment kidneys were harvested, and semi-quantitative immunoblotting was carried out from cortical homogenates using polyclonal peptide-derived antibodies to URAT1, OAT1, and OAT3.

Results : Throughout the study period, both control and uric acid-supplemented rats showed a steady increase in body weight, and there were no differences in body weight and daily urine output between the two groups. After the uric acid supplementation serum uric acid level showed an increasing tendency (p=0.055) in uric acid-supplemented rats (2.60±0.27 mg/dL) compared with control rats (1.97±0.29 mg/dL), whereas urinary uric acid excretion was not significantly different between uric acid-supplemented rats (3.27±0.40 mg/d) and control rats (2.61±0.34 mg/d). Creatinine clearance showed no difference between the two groups. URAT1 protein abundance in cortical homogenates was not significantly different between uric acid-supplemented rats (132±14%) and control rats (100±7%). However, OAT1 protein abundance was significantly (p=0.037) increased in uric acid-supplemented rats (148±13%) compared with control rats (100±8%). OAT3 protein abundance was not significantly different between uric acid- supplemented rats (131±12%) and control rats (100±17%).

Conclusion : Among the uric acid transporters in the rat kidney, OAT1 may have a regulatory role in response to the increase in uric acid intake. The up-regulation of OAT1 would exert to stimulate urinary uric acid excretion and might contribute to protection from hyperuricemia.