

Enhanced Expression of NHE3 and Nitric Oxide Synthase in the Kidney in Rats with Maleic Acid-induced Metabolic Acidosis

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Background : The present study was aimed to determine whether there exists an altered regulation of tubular transporters and nitric oxide system in the kidney in maleic acid induced metabolic acidosis.

Methods : Male Sprague-Dawley rats were treated with maleic acid (2 mmol/kg, every 24 hours, intraperitoneally) for 2 days. Control rats were injected with saline. At 24 hours after the second injection of maleic acid, rats were killed by decapitation. Plasma HCO_3^- and anion gap were measured. The protein expression of type 3 Na^+/H^+ exchanger (NHE3), $\text{Na}^+:\text{HCO}_3^-$ cotransporter (NBC1), and aquaporin (AQP)-1 in the cortex of the kidneys was determined by Western blot analysis. In addition, the expression of isoforms of nitric oxide synthases (NOS) was determined. Nitric oxide metabolites (nitrite/nitrate, NOx) were also measured in the urine by colorimetric assay.

Results : Plasma concentrations of HCO_3^- were significantly decreased following the treatment of maleic acid, while plasma anion gap was did not differ between the experimental and control groups. In the experimental group, the protein expression of NHE3 was significantly increased in the cortex of the kidney, although that of NBC1 was not altered significantly. The expression of inducible NOS, endothelial NOS, and neuronal NOS was significantly increased in the cortex of the kidney. Accordingly, urine NOx contents were increased. The expression of AQP1 was not altered.

Conclusion : These results indicate that upregulation of NHE3 and nitric oxide system may play a role in the regulation of acid-base balance.