Involvement of Vanin-1 in Renal Proximal Tubular Injury in Dahl-Salt Sensitive Rats

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[Background]In salt-sensitive hypertension, reactive oxygen species (ROS) play a major role in the progression of renal disease partly via activation of the mineralocorticoid receptor. Previously, we demonstrated that urinary vanin-1 is an early biomarker of oxidative renal tubular injury. However, it remains unknown whether urinary vanin-1 might reflect the treatment effect.
[Objective]This study aimed to clarify the treatment effect for renal tubular damage in Dahl salt-sensitive (DS) rats.
[Methods]DS rats (6 weeks old) were given one of the following for 4 weeks: high-salt diet (8% NaCl), high-salt diet plus superoxide dismutase mimetic, tempol (3 mmol/L in drinking water), high-salt diet plus eplerenone (100 mg/kg/day), and normal-salt diet (0.3% NaCl). After 4 weeks of the treatment, blood pressure was measured by the tail-cuff method and kidney tissues were evaluated. ROS were assessed by measurements of malondialdehyde and by immunostaining for 4-hydroxy-2-nonenal.
[Results]A high-salt intake for 4 weeks caused ROS and histological renal tubular damages in DS rats, both of which were suppressed by tempol and eplerenone. Proteinuria and urinary N-acetyl-β-D-glucosaminidase exhibited a significant decrease in DS rats receiving a high-salt diet plus eplerenone, but not tempol. In contrast, urinary vanin-1 significantly decreased in DS rats receiving a high-salt diet plus eplerenone as well as tempol. Consistent with these findings, immunohistochemical analysis revealed that vanin-1 was localized in the renal proximal tubules but not the glomeruli in DS rats receiving a high-salt diet, with the strength attenuated by tempol or eplerenone treatment.
[Conclusion]These results suggest that urinary vanin-1 is a potentially sensitive biomarker for ameliorating renal tubular damage in salt-sensitive hypertension.