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Depressor Effect of an Intervention in Renal Endogenous Acetylcholine Release on Salt-Sensitive Hypertension

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Summary

Background: We have already demonstrated that endogenous acetylcholine (ACh) release in the renal cortex is dependent on intracellular sodium concentration of cortical cells. This sodium-dependent ACh release may be impaired in Dahl salt-sensitive rats. Several pharmacological agents, such as rivastigmine, may suppress an elevation of blood pressure and improve the mortality in salt-sensitive hypertension through ACh-induced renal protective effects.

Purpose: To investigate the effects of rivastigmine on arterial pressure and mortality in Dahl salt-sensitive rats.

Methods: Male Dahl salt-sensitive rats at 6 weeks of age were fed 8% high salt diet for 8 weeks. An ACh esterase inhibitor, rivastigmine, was orally applied to the rats at a concentration of 50 μg/ml in drinking water. Systolic blood pressure was measured every week for 8 weeks by a tail-cuff method. Eight to nine weeks later, these rats were anesthetized with α-chloralose and urethane and the left kidney was extracted. The expression of epithelial Na^+ channel (ENaC) α-subunit mRNA (SCNN1a) in the renal cortex was measured using a droplet digital PCR. Histological examination with Periodic Acid Schiff's (PAS) staining was also performed.

Results: There were no deaths in the rivastigmine treated group, but 3 rats died in the control group (P=0.065 by a log-rank test). At first and 3^{rd} to 6^{th} week, systolic blood pressure was significantly lower in the rivastigmine-treated group. There were no significant differences in the expression of SCNN1a between the control and rivastigmine-treated groups. Histological examination demonstrated severer glomerular sclerosis in the control group.

Conclusions: An ACh esterase inhibitor, rivastigmine, significantly suppresses the elevation of blood pressure and tends to improve the mortality of Dahl salt-sensitive rats through renal protective effects. However, further investigations are needed to clarify the detailed mechanism.