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Role of Sodium-Dependent Renal Acetylcholine Release in Acute Kidney Injury

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Summary

Acute kidney injury (AKI) is a condition in which renal function declines rapidly in a short period of time, and water and electrolyte disturbances occur due to the accumulation of creatinine and urea nitrogen in the blood. In AKI, an increase in serum creatinine of as little as 0.3 mg/dl has been shown to contribute significantly to patient mortality. Therefore, it is essential to establish an effective treatment for AKI. However, there are no drugs that act directly on the kidney, and infusions and vasoactive drugs are the mainstay of treatment.

In our previous study, which was supported by the Salt Science Research Foundation, we reported that the release of acetylcholine (ACh) in the renal cortex was non-neuronal and dependent on intracellular and extracellular sodium ion gradient. We also reported that this sodium-dependent renal ACh release was impaired in Dahl salt-sensitive rats and that an acetylcholinesterase inhibitor could reduce renal injury. Therefore, the purpose of this study is to evaluate the role of sodium-dependent renal ACh release in AKI and to develop drugs that can directly act on the kidney.

First, we examined renal ACh release in a prerenal AKI model. To induce prerenal AKI, we ligated the left renal artery of rats under general anesthesia. We implanted a microdialysis probe into the renal cortex of the rats and monitored dialysate ACh concentration using high-performance liquid chromatography. Contrary to our expectations, this experiment demonstrated that renal ischemia significantly increased dialysate ACh concentration. To investigate the mechanism of this renal ACh release, we tested an epithelial sodium channel inhibitor, Benzamil. However, Benzamil was unable to fully suppress this ischemia-induced renal ACh release. Next, we tested the contrast-induced AKI model. After intravenous injection of iopamidol, renal ACh release tended to decrease. These results suggest that the dynamics of renal ACh differ depending on the causes of AKI.