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The Role of Systemic and Gut Amino Acid Metabolism under Excessive Salt Intake to Control Fluid Balance and Kidney Function

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Summary

Background: Plasma amino acid analysis is starting to be applied for pathophysiological examinations. However, the effects of dietary salt intake on amino acid patterns in urine, plasma or feces and its species differences have not been assessed.

Methods: Urine, plasma and fecal amino acids were measured in Wistar-Kyoto rats (WKY), spontaneously hypertensive rats (SHR) and human subjects. Rats were fed normal-salt (NS: 0.3% NaCl) or high-salt (HS: 8% NaCl) chow for 7 days. In a clinical study, 23 healthy volunteers were placed on low-salt (LS: 3 g NaCl /day) then high-salt (HS: 20 g NaCl /day) diet for 7 days each. Oral lysine supplementation test (10 g/L in tap water for 4 weeks) was also performed in rats. Amino acid and metabolite concentrations were measured by LC/MS/MS.

Results: Salt loading increased the urinary excretion of most amino acids. In humans, urinary lysine concentration and excretion increased 1.9 and 3.1 folds respectively (both $P<0.01$) with HS, but its plasma lysine concentration decreased by 18% ($P<0.01$). In WKY, urinary lysine excretion increased while on HS diet, but its plasma concentration increased by 17% ($P<0.01$). Basal plasma lysine concentration of WKY was significantly higher than that of SHR. Fecal lysine concentration in SHR tended to be lower than that of SHR. Oral lysine administration to WKY and SHR increased fecal lysine concentration and increased urine volume in SHR without significant change in blood pressure.

Discussion: This study revealed for the first time that hypertensive and salt-sensitive strain, SHR, show lower plasma and fecal lysine concentrations compared to its normotensive control, WKY. The increase in plasma lysine in rats in contrast to its decrease in humans may contribute to the relative salt-resistance of rats compared to humans. Since lysine is reported to act on serotonin receptors to lower blood pressure, and some gut bacteria can synthesize lysine, differences in the production and absorption of lysine in the gut may contribute to the development of salt-sensitivity and hypertension.

Conclusions: Salt intake affects urine amino acid excretions in rats and human subjects. Lysine dynamics was different between WKY and human subjects, and plasma lysine concentration seem to be inversely related to blood pressure in rats. Further clinical studies are necessary to explore the diagnostic and therapeutic possibility of lysine in the future.