Objective: NO deficiency is associated with development of salt-sensitive hypertension. NO production is limited by the capacity of the kidney to regenerate endogenous arginine through the citrulline-NO pathway. High salt loading causes a deficiency in arginine availability which affects NO synthases in Dahl salt-sensitive (SS) rats. However, it is not clear why arginine in the kidney of SS rats reduced with high salt diet. Our previous research found that the activity of fumarase was lower in the kidney of SS compared with SS.13BN rats. The current study will determine whether decreased renal fumarase activity is associated with decreased endogenous arginine synthesis and whether aspartic acid supplementation has antihypertensive effects in SS rats.

Methods: The expression of the rate-limiting enzyme involved in the citrulline-NO pathway and the content of NO were measured by biochemical analysis. The level of amino acid in kidney was analysed by GC-MS. To determine whether decreased fumarase activity in SS rat kidney is associated with reduced endogenous arginine synthesis, the expression of fumarase was knocked down in HK-2 cells using siRNA.

Results: The results showed that the activities of fumarase, isocitrate dehydrogenase and ketoglutarate dehydrogenase were decreased in renal mitochondria of SS rats compared with SS.13BN rats. The production rate of ATP in SS was lower than that in SS.13BN rats (0.326 ± 0.030 in SS vs. 0.439 ± 0.050 μmol ATP/min/μg protein in SS.13BN medulla), and the ATP production rate were further decreased in SS rats with a high salt diet. Meanwhile, lower levels of purine nucleotides and higher levels of amino acids, including L-alanine, L-leucine, L-valine and DL-isoleucine were observed in SS rats’ mitochondria. Further dietary intervention experiments demonstrated that exogenous ATP supplements in the water significantly attenuated hypertension (126 ± 2 mmHg ATP + 8% NaCl vs. 136 ± 3 mmHg 8% NaCl) in SS rats after 10 days.

Conclusion: Those data indicated dysfunction of mitochondria in renal medulla and cortex in SS rats. And current research suggests that the decreased of renal mitochondrial energy metabolism may contribute to salt-induced hypertension in SS rats.