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Effects of Iron Restriction on Salt Sensitive Hypertension

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Summary

Background: Iron accumulation is associated with the pathogenesis of cardiovascular disease and chronic kidney disease (CKD). Here, we investigated the effects of dietary iron restriction on salt sensitive hypertension in a rat model of CKD.

Methods and Results: CKD was induced by 5/6 nephrectomy in Sprague-Dawley rats. After operation, 5/6 nephrectomized rats were given iron-restricted diet from 1 day to 16 week for prevention protocol or from 8 week to 16 week for rescue protocol. Other CKD rats were given a normal diet. Sham-operative rats given a normal diet were served as a control. At 16 weeks after surgery, CKD rats developed hypertension, proteinuria, glomerulosclerosis, podocyte injury, and tubular dilatation. In contrast, dietary iron restriction prevented the development of hypertension and renal damage. Importantly, expression of cellular iron transport proteins, transferrin receptor 1 and divalent metal transporter 1 was increased in the CKD renal tubules, along with increased iron accumulation. On the other hand, late intervention with iron restriction did not remarkably ameliorate preexisting hypertension, while late intervention with iron restriction prevented further progression of preexisting renal damage in CKD rats. Of Interest, iron restriction led to increased urinary sodium and decreased urinary potassium excretions in CKD rats. Moreover, iron restriction attenuated renal expression of nuclear mineralocorticoid receptor (MR) and Rac1 activity in CKD rats.

Conclusions: Dietary iron restriction prevents the development of hypertension and renal damage, and further deterioration of preexisting renal damage. These beneficial effects of iron restriction seem to be associated with inhibition of renal MR signaling. Iron restriction could be an effective strategy for prevention of high salt-induced organ damage in salt-sensitive hypertensive patients.