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Involvement of Relaxin in Salt-Sensitive Hypertension

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Summary

Although potent anti-fibrotic and vasodilatory properties of relaxin(RLX) are recently reported, the involvement in salt-sensitive hypertension has not been elucidated. Since anti-fibrotic effects of RLX were observed in salt-sensitive hypertensive kidneys, we examined renal RLX-receptor in the kidney of Dahl salt-sensitive (DS) and Dahl salt-resistant (DR) rat. Specific binding of RLX in kidneys was observed and the binding sites of RLX were similar to LGR-7 (RLX receptor) immunostaining. Next, we examined RLX and RLX receptor (LGR7) mRNA in kidneys of Dahl salt-sensitive (DS) and Dahl salt-resistant (DR) rats by RT-PCR. DS rats showed an increased expression of RLX mRNA in the cortex compared to DR rats. LGR7 mRNA was slightly decreased in DS rats compared to DR rats. Then, we examined effects of RLX treatment on apoptosis and TGF-ß activation in DS and DR rats placed on an 8% NaCl diet. The administration of RLX (4 microg/h) to male DS rats for 8 weeks significantly reduced systolic blood pressure. Histologic studies revealed the amelioration of tubulointerstitial fibrosis (-21.8%), in rats received RLX. RLX-treated kidneys showed significantly decreased apoptosis (-40.8%), and phosphorylated Smad2 (-71.0%) expression in tubules compared to saline control. Finally, Since RLX is expressed in the kidney, we hypothesized that chronic inhibition of endogenous RLX turns salt-resistant into salt-sensitive in Dahl salt-resistant (DR) rats. DR rats with and without RLX neutralizing antibody and DS rats were placed on an 8% NaCl diet for 30 days. DR rats showed significantly lower blood pressure (125 mmHg) than DS rats (147 mmHg) on day 30. However, DR rats receiving RLX antibody showed an elevation of blood pressure (138 mmHg), which was not significantly different from the pressure of DS rats.

These results suggest the counterbalance of intrarenal RLX-RLX receptor axis in the progression of salt-sensitive hypertension and kidney fibrosis.