04C2-06C2

Possible Role of the Tubuloglomerumular Feed Back System in the Pathogenesis of Salt-Sensitive Hypertension

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Summary

We investigated the possible contributions of renal interstitial fluid (RIF) ATP and tubuloglomerular feedback (TGF) mechanism to the development of salt-dependent hypertension. Dahl salt-sensitive (DS) rats were maintained on low (L: 0.3% NaCl) or high salt (H: 8% NaCl) diet for 4 weeks. Using an intravital tapered-tip lens-probe videomicroscopy with a CCD camera system, superficial afferent arteriolar diameter (AAD) was measured before and during TGF activity enhanced with acetazolamide (2 mg/kg, bolus + 4 mg/kg/h, infusion, i.v.) in anesthetized rats. RIF ATP levels were measured by a microdialysis method. At 1 and 4 weeks after high salt treatment, DS/H rats showed smaller basal AAD and higher RIF ATP levels and blood pressure, as compared to DR/S rats. Acetazolamide significantly decreased AAD in DS/L rats, but did not alter AAD in DS/H rats. Acetazolamide increased RIF ATP levels in DS/L rats, whereas ATP levels were not altered by acetazolamide in DS/H rats. Treatment with suramin (20 mg/kg/day, i.p.), a non-selective P2 receptor antagonist, markedly attenuated the development of hypertension in DS/H rats. Suramin also significantly increased basal AAD in DS/H rats. However, AAD and RIF ATP levels did not change during the administration of acetazolamide in suramin-treated DS/H rats. These results suggest that augmented TGF activity associated with increases in RIF ATP levels contributes to the increased afferent arteriolar tone and the development of salt-dependent hypertension. Future studies in human will be necessary.