

## **Inhibition of NaCl Reabsorption with Furosemide Decreases Renal Cortical Interstitial Calcium While Stimulating Plasma Renin Activity**

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*In vitro*, low extracellular calcium (Ca) increases renin secretion. The basolateral membranes of the renin secreting juxtaglomerular cells are in contact with the renal cortical interstitium. Thus, decreasing cortical interstitial Ca could increase renin secretion *in vivo*. Furosemide increases renin secretion. This has been attributed to a macula densa-mediated mechanism. However, furosemide also decreases Ca reabsorption, which may decrease renal cortical interstitial Ca. We hypothesized that furosemide increases plasma renin activity (PRA) in part by reducing renal cortical interstitial Ca and increasing urinary Ca. We measured PRA and renal cortical interstitial, plasma and urinary Ca in anesthetized rats. Interstitial Ca was collected using *in situ* microdialysis. These parameters were measured before and after a 5 mg/kg i.v. bolus of furosemide. Plasma and urinary Ca were measured to determine whether changes in cortical interstitial Ca were due to changes in plasma or urinary Ca. Furosemide increased Ca excretion from  $0.11 \pm 0.02$   $\mu\text{mol/hr}$  to  $1.77 \pm 0.39$   $\mu\text{moles/hr}$  ( $p < 0.05$ ,  $n=4$ ) in response to furosemide, while plasma Ca did not change. Furosemide administration significantly decreased renal cortical interstitial Ca by  $0.13 \pm 0.03$  mM ( $p < 0.01$ ,  $n=9$ ), while the vehicle had no effect on cortical interstitial Ca ( $-0.03 \pm 0.04$  mM, n.s.). Furosemide increased PRA from  $12.64 \pm 2.4$  ng Ang I/ml/hr to  $33.82 \pm 8.0$  ng Ang I/ml/hr ( $p < 0.05$ ,  $n=9$ ), while the vehicle had no effect. Our data indicate that inhibiting thick ascending limb NaCl reabsorption with furosemide increased urinary Ca excretion, decreased renal cortical interstitial Ca and increased PRA. The stimulatory effects of furosemide on PRA may be due in part to changes in renal cortical interstitial Ca.

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