Reduced natriuresis after oral sodium load in cholestatic rats: role of compartment volumes and ANP

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Abstract

The purpose of this study was to assess the participation of the atrial natriuretic peptide (ANP)-cGMP system in electrolyte and volume handling of cholestatic rats submitted to an acute oral sodium load. Cholestasis was induced by ligation and section of the common bile duct (n = 51). Control rats were sham operated (n = 56). Three weeks after surgery, 24-hr urinary volume, sodium, potassium, cGMP and creatinine excretion were measured. Three days later, animals received 10 mmol/kg NaCl (1 M) by gavage, and urinary excretion was measured for 6 hr. In parallel groups of rats, plasma volume, electrolytes and ANP concentration, extracellular fluid volume (ECFV), and renal medullary ANP-induced cGMP production were determined in basal conditions or 1 hr after oral sodium overload. As compared with controls, cholestatic rats had a larger ECFV and higher plasma ANP (67.2 +/- 5.2 vs 39.7 +/- 3.5 pg/ml), but lower hematocrit and blood volume, and were hyponatremic. Cholestatic rats showed higher basal excretion of sodium, potassium, and volume than controls, but equal urinary cGMP. After the NaCl overload, cholestatic rats showed a reduced sodium excretion but equal urinary cGMP. One hr after sodium overload, both groups showed hypernatremia, but whereas in control rats ECFV and ANP increased (50.7 +/- 4.1 pg/ml), in cholestatic rats ECFV was unchanged, and plasma volume and ANP were reduced (37.5 +/- 5.8 pg/ml). ANP-induced cGMP production in renal medulla was similar in cholestatic and control nonloaded rats (14.2 +/- 5.2 vs 13.4 +/- 2.6 fmol/min/mg). One hr after the load, medullary cGMP production rose significantly in both groups, without difference between them (20.6 +/- 3.1 vs 22.7 +/- 1.7 fmol/min/mg). We conclude that the blunted excretion of an acute oral sodium load in cholestatic rats is associated with lower plasma ANP due to differences in body fluid distribution and cannot be explained by renal refractoriness to ANP.