

Pathogenesis of edema: the kidney and beyond

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Nephrotic syndrome and liver cirrhosis are common clinical manifestations, and are associated with avid sodium retention leading to the development of edema and ascites. However, the mechanism for the sodium retention is still incompletely understood and the molecular basis remains undefined. We examined the changes of sodium (co)transporters and epithelial sodium channels (ENaCs) in the kidneys of experimental nephrotic syndrome and liver cirrhosis. The results demonstrated that puromycin- or HgCl₂-induced nephrotic syndrome was associated with 1) sodium retention, decreased urinary sodium excretion, development of ascites, and increased plasma aldosterone level; 2) increased apical targeting of ENaC subunits in connecting tubule and collecting duct segments; and 3) decreased protein abundance of type 2 11 β -hydroxysteroid dehydrogenase (11 β HSD2). Experimental liver cirrhosis was induced in rats by CCl₄ treatment or common bile duct ligation. An increased apical targeting of alpha-, beta-, and gamma-ENaC subunits in connecting tubule, and cortical and medullary collecting duct segments in sodium retaining phase of liver cirrhosis but not in escape phase of sodium retention. Immunolabeling intensity of 11 β HSD2 in the connecting tubule and cortical collecting duct was significantly reduced in sodium retaining phase of liver cirrhosis, and this was confirmed by immunoblotting. These observations therefore

strongly support the view that the renal sodium retention associated with nephrotic syndrome and liver cirrhosis is caused by increased sodium reabsorption in the aldosterone sensitive distal nephron including the connecting tubule and collecting duct, and increased apical targeting of ENaC subunits plays a role in the development of sodium retention in nephrotic syndrome and liver cirrhosis.

Key Words : Edema, Sodium retention, Epithelial sodium channel