고혈압 병인에서 신장의 역할

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Hypertension

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The experimental model of spontaneously hypertensive rats (SHR) has been used to investigate the renal involvement in the pathogenesis of essential hypertension in humans. Altered renal functions have been suggested to play a role in the pathogenesis of essential hypertension. This has been documented by the development of high blood pressure in normotensive rats after renal cross-transplantation between normotensive and hypertensive strains where the genetic predisposition of hypertension is transferred with the donor kidney from the hypertensive strains. Moreover, this was demonstrated not only in adult rats with established hypertension, but also in young prehypertensive rats. These data therefore support the hypothesis that altered renal functions contribute significantly to the development and maintenance of primary hypertension. The renal defects could range from the altered glomerular hemodynamics to abnormal regulation of renal tubular sodium and water transport.

In models of genetic (primary) hypertension, the renal involvement may be presented, at least in part, by inappropriate sodium and water retention. The excessive retention of sodium in SHR may be resulted from either a reduced glomerular filtration rate (GFR) or an enhanced tubular reabsorption, or both. The activities of Na,K-ATPase and Na/H exchanger in the proximal tubule was found to be significantly higher in young SHR compared to age matched Wistar-Kyoto rats (WKY) and these changes may account in part for the increased ECF volume expansion in SHR. We have demonstrated that the protein abundance of β- and ɣ-subunits of ENaC was increased in the cortex and outer stripe of the outer medulla (cortex/OSOM), and inner stripe of the outer medulla (ISOM) in SHR, while αENaC abundance was increased in ISOM. Immunoperoxidase microscopy confirmed the increased labeling of β ENaC and ɣENaC subunits in the late distal convoluted tubule (DCT2), connecting tubule, and cortical and outer medullary collecting duct segments. In contrast, subcellular localization of αENaC, βENaC and ɣENaC was not changed. Expression of NHE3, NKCC2, and NCC was not altered in SHR. AQP2 level was increased in the ISOM in SHR, and immunoperoxidase microscopy demonstrated an increased apical labeling of AQP2 in the inner medullary collecting duct in SHR. These findings suggest the increased protein abundance of ENaC subunits, Na, K-ATPase as well as the increased apical targeting of AQP2 may contribute to the retention of sodium and water, and the development of hypertension in SHR.