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2K1C 쥐 모델에서 ACE/AT1R와 ACE2/MasR 축의 신장 내 발현에 관한 연구

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Intrarenal Expression of ACE/AT1R and ACE2/MasR Axis in 2K1C Rat Model

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Introduction: Recent studies showed ACE2/Antiogensin1-7 (ANG1-7)/Mas receptor (MasR) axis has opposing function to that of ACE/AngiotensinII (ANGII)/Antiogensin receptorI (AT1R) axis for renal and vascular homeostasis. But until now, there were no exact information about different intrarenal expression of ACE2/ANG1-7/MasR in clipped kidney (CK) and non-clipped kidney (NCK) in 2 Kidney 1 Clip (2K1C) hypertensive rat model. So, we are purposed to evaluate respective changes of CK and NCK for renal ACE/AT1 and ACE2/MasR axis in 2K1C rat model.

Methods: At 6 weeks of age, 19 male Sparague-Dawley rats (175-200 g) underwent clipping (n=10) of the left renal artery of sham (n=9) operation. Body weight and systolic blood pressure (SBP) of all rats were checked at 1-week interval and on 6 weeks after operation, we sacrificed rats. We carried out western blot and immunohistochemistry about ACE/AT1R, ACE2/MasR and renin components from renal cortex of NCK and CK, respectively.

Results: SBP were started to increase significantly in 2K1C group at 3 week after operation, at 6 weeks 2K1C and sham groups showed SBP of 164.71±34.57 and 120.33±2.52, respectively (p 0.005). The weights of CK were significantly lower (CK:NCK 0.80±0.37:1.74±0.44, p 0.007) than them of NCK and proteinuria (protein/creatinine g/gCr) was higher (119.3±56.88 vs 35.67±14.84, p 0.002) than control group. Generally renal ACE content was up-regulated, reciprocally renal ACE2 content was down-regulated but AT1R and MasR were almost same expression in 2K1C compared with sham. In 2K1C rats, renal ACE, ACE2, MasR and renin of CK were increased compared with NCK, but only ACE2 (CK:NCK 0.13±0.07:0.04±0.19 p 0.021) and renin (CK:NCK 0.41±0.21:0.02±0.01 p 0.014) has significance. Immunohistochemistry results proved strong staining of AT1R, ACE2, renin and MasR in cortical area of CK compared with NCK.

Conclusions: 2K1C rat revealed reciprocal intrarenal change of ACE/ACE2 expression. Intrarenal expression of ACE and renin are stronger in CK than NCK, in contrast MasR is stronger in NCK. Activated intrarenal renin resulted from ischemia might augment ACE, also lead to compensative rise of ACE2 expression in CK. In 2K1C model, physiologic change of renin-angiotensin system (RAS) have different regulatory mechanism in both kidneys.

Key Words: 레닌 안지오텐신 시스템, ACE, ACE2
Renin-angiotensin system, ACE, ACE2