

KSN 2016 Abstract Submission

Clinical & Experimental CKD & Genetics

KSN2016ABS-1460

Sexual difference of intrarenal renin-angiotensin system (RAS) in Goldblatt hypertensive rats

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Background: Females are known to lessen the prevalence of hypertension compared with males. Several studies presented renin-angiotensin system (RAS) of female is differently regulated with that of male. We previously reported that classical pathway of RAS was elevated in 2 kidney 1clip male rats. Thus, the present study was designed to address sexual differences in intrarenal RAS expression and renal injury in 2K1C rats.

Methods: We inserted a 2.5mm sized clip into the left renal artery to male and female Sprague-Dawley rats, then measured systolic blood pressure (SBP) at one-week intervals. At 5 weeks after the operation, kidneys were harvested for molecular and pathologic analysis. Western blot was performed only in medulla to select only renal tubules.

Results: Systolic blood pressure increased in male 2K1C rats within one week following the clipping operation, but it was attenuated in female 2K1C rats. Left ventricular hypertension was observed only in male 2K1C rats. Tubulointerstitial inflammation and fibrosis was lessened in female 2K1C rats. Regardless of sexual difference, renin was similarly up-regulated in both kidneys of 2K1C. ACE was augmented in male 2K1C, but it was attenuated in female 2K1C. In contrast, ACE2 was elevated in female 2K1C and decreased in male 2K1C. AT1R was suppressed in both kidneys of 2K1C independent of sexual difference. MasR was more intensively expressed in female 2K1C kidneys than that of male.

Conclusion: Intrarenal RAS of female 2K1C showed low ACE and high ACE2/MasR compared with that of male 2K1C. Sexual dimorphism caused different occurrence of hypertension and intrarenal RAS expression and it might contribute to lessen renal injury in female.

Keywords: Goldblatt hypertension, renin angiotensin system, sexual difference