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Letter to Editor

Angiotensin 1-7 receptor blockade attenuates renal clearance and urine flow in reno-vascular hypertensive rats

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Dear Editor

Hypertension is known as a risk factor of chronic renal disease with higher prevalence in male (Sullivan and Gillis, 2017). Systemic and intrarenal renin-angiotensin system have fundamental roles in the progression of hypertension and renal injury (Yim and Yoo, 2008). As a pilot study, the effect of angiotensin (Ang) 1-7 receptor (MasR) antagonist, A779, on renal perfusion pressure (RPP), urine flow (UF) and creatinine clearance (CrCl) in male and female renovascular hypertensive rats was investigated.

The renovascular hypertensive rats were obtained by two kidneys, one clip model via implement a small U-shaped silver clip (0.2 mm internal diameter) around renal artery. After 28 days, rats were anesthetized with urethane (1.7 g/kg, IP; Merck, Germany) and were tracheostomized. The vessels catheterization was applied for measurement of systolic arterial pressure, RPP and drug infusion using Power Lab system (AD Instruments, Australia). In addition, polyethylene catheter was inserted into the bladder for urine collection. After surgical procedure and equilibrium achievement in blood pressure, the animals received MasR antagonist (Bachem Bioscience Inc., King of Prussia, PA, USA) or vehicle for 30min. A779 was infused as a bolus dose of 50 µg kg^{-1} followed by continuous infusion of 50 µg kg^{-1} h^{-1} (Safari et al., 2012). The urine was collected during antagonist or vehicle infusion and the blood sample was obtained. Finally, the rats were killed humanly, and the right and left kidneys were removed and weighed immediately. RPP was normalized with base and analyzed using ANOVA for repeated measures. UF and CrCL were compared using Student's t-test.

The animals' systolic blood pressure was 152±2.3 mmHg. No significant difference was detected in normalized RPP between male and female rats during saline or A779 administration (Figure 1). The significant reduction of UF and CrCL were detected by A779 infusion in male and female rats when compare vehicle treated rats.

This study indicated that female has more UF and CrCL than male, and A779 attenuate CrCL and UF and abolish sex difference in hypertensive rats. Possibly, the sex difference in UF and CrCL is related to renin-angiotensin system receptors distribution in the kidneys (Sampson et al., 2012). Higher renal MasR distribution in female than male was detected (Sampson et al., 2012; Hilliard et al., 2013). Also renal MasR distribution increases in renovascular hypertensive female (Lee et al., 2019) which reinforces our findings. A779 eliminated MasR diuretic effect (Patel et al., 2017), so induced lower UF and CrCL. More over A779 equalized UF and CrCL in male and female due to higher reduction in UF and CrCL in female, may be because of higher MasR

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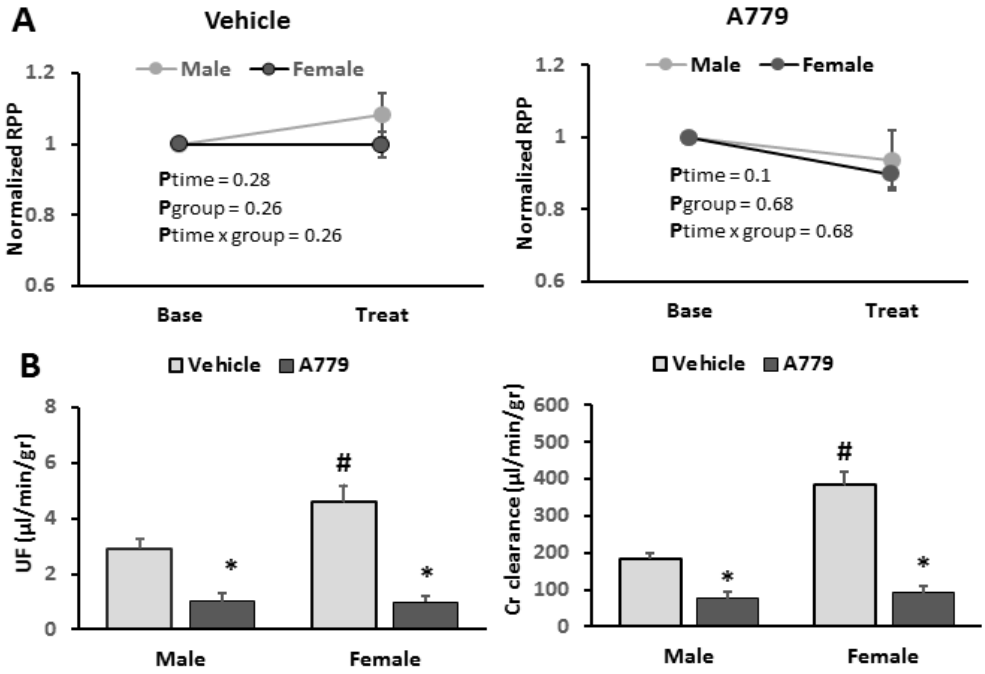

FIGURE 1. A: The effect of vehicle and A779 on normalized renal perfusion pressure (RPP). The difference between-subjects factor (group), within-subjects factor (time) and their interaction indicated by Pgroup, P_{time} and $P_{time\ \&\ group}$, respectively. **B**: UF and Cr clearance stand for urine flow rate/total kidney weight and Cr clearance/total kidney weight. *indicated significant differences from male or female vehicle groups. #significant difference between male and female in each treatment Student's t-Test. $P \leq 0.05$ was considered statistically significant.

activity in female hypertensive rats (Lee et al., 2019). It is concluded that MasR antagonist may attenuate CrCl and UF in renovascular hypertensive rats.

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