Diminished Chloride Channel Activity in Renal Juxtamedullary Microvessels from Spontaneously Hypertensive Rats (SHR). Takahiko Nagahama, Koichi Hayashi, Kiyoshi Oka, and Takao Saruta. Department of Internal Medicine, School of Medicine, Keio University, Tokyo, 160

It has been demonstrated that a chloride ion (Cl⁻) plays an important role in tubuloglomerular feedback and mesangial cell contractility. The role of Cl⁻ in renal microcirculation, however, has not been previously elucidated. Furthermore, it has not been determined whether Cl⁻ channel activity is altered in renal microvessels of hypertensive animals. In the present study, we examined the effects of a Cl⁻ channel blocker, IAA-94, on angiotensin (Ang) II-induced vasoconstriction of afferent (AFF) and efferent arterioles (EFF) from Wistar-Kyoto rats (WKY) and SHR. To directly visualize the renal microcirculation, we used the isolated perfused hydronephrotic rat kidney model. Ang II induced marked vasoconstriction of AFF (WKY, from 16.9±0.8 to 12.2±0.8 μm; SHR, from 16.4±0.9 to 12.0±1.1 μm) and EFF (WKY, from 13.9±0.8 to 10.5±1.0 μm; SHR, from 14.6±0.9 to 11.0±1.1 μm). The subsequent addition of IAA-94 (1, 3, 10, 30 μM) elicited dose-dependent vasodilation of AFF, with 72±9% reversal in WKY and 62±16% reversal in SHR by 30 μM IAA-94. In addition, EFF tended to exhibit a greater vasodilation than AFF in WKY, and exhibited a significantly greater dilation in SHR in response to 1 and 3 μM IAA-94 (1 μM, 31±10% vs. 2±4% reversal; 3 μM, 50±13% vs. 17±4% reversal). Furthermore, in WKY IAA-94 exerted vasodilation of both AFF and EFF, similar in magnitude in superficial and juxtamedullary nephrons. In striking contrast, in SHR AFF responses to IAA-94 tended to dilate less in juxtamedullary nephrons, and EFF of juxtamedullary nephrons manifested a markedly diminished vasodilator response to 10 μM (46±7% vs. 92±10%) and 30 μM IAA-94 (71±3% vs. 106±4%). In conclusion, the present study demonstrated that Cl⁻ channels contribute to Ang II-induced vasoconstriction of both AFF and EFF. The participation of Cl⁻ channels, however, differs in magnitude, with greater contribution in EFF. Furthermore, the present study suggests that in juxtamedullary EFF from SHR kidney, contribution of Cl⁻ channels to angiotensin II-induced vasoconstriction is reduced, and additional mechanisms would contribute to angiotensin II-induced EFF vasoconstriction. The preferential alteration in Cl⁻ channel activity in juxtamedullary EFF may be associated with the deranged glomerular microcirculation of juxtamedullary nephrons in SHR.