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Role of Angiotensin II and Angiotensin II Type 1 Receptor in Kidney Resistance Conferred by Ischemic Preconditioning

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Ischemic preconditioning (IPC) renders resistance to the kidney against subsequent injury. However, IPC results in undesirable fibrotic changes in the kidney. Angiotensin II (AngII) and its receptor are involved in the fibrotic changes. Here, we investigated the role of AngII and AngII type 1 receptor (AT1R) in the susceptibility of IPC kidneys to subsequent ischemia/reperfusion (I/R) insult. IPC of kidneys was generated by 30 minutes of bilateral renal ischemia and 8 days of reperfusion. Sham-operation was performed to generate control (non-IPC). To examine the roles of AngII and AT1R in susceptibility of IPC kidneys to subsequent I/R insult, IPC kidneys were subjected to either 30 minutes of bilateral kidney ischemia or a sham-operation with or without treatment with AngII, losartan (an AT1R blocker), or AngII plus losartan 10 minutes before operation. IPC kidneys showed fibrotic changes, decreased AngII expression, and increased AT1R expression. I/R dramatically increased plasma creatinine (PCr) concentrations in non-IPC mice, but did not do in IPC mice. AngII treatment in IPC mice resulted in enhanced morphological damage, oxidative stress, and inflammatory responses, with increased functional impairment, whereas losartan prevented these effects of AngII. However, AngII treatment in non-IPC mice did not change I/R-induced injury. AngII abolished the resistance of IPC kidneys to subsequent I/R insult via the enhancement of post-I/R increases in oxidative stress and inflammatory responses, suggesting that the resistance of injury-experienced fibrotic kidney is associated with AngII/AT1R signaling.

Key Words: Ischemia, Angiotensin II, ROS