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Effects of angiotensinogen converting enzyme inhibitor and angiotensin II receptor blocker on ischemic acute kidney injury

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Objectives The usefulness of renin-angiotensin system (RAS) blockers has been well established in chronic kidney disease with proteinuria, but its role in acute kidney injury (AKI) remains unclear. Furthermore, despite the difference in sites of action, the effects of angiotensinogen converting enzyme inhibitors (ACEi) and angiotensin II receptor blockers (ARB) on susceptibility and the overall course of ischemic AKI have not been fully elucidated. We aimed to evaluate the effects of ACEi and ARB on ischemic AKI, focusing on changes in intrarenal immunological micromilieu and RAS.

Methods 9-week-old male C57BL/6 mice were treated with saline (control group), ramipril, or telmisartan that were intraperitoneally injected before (D-3 and D-1, pre-treated group), intraoperatively (D0, intraoperative-treated group) or after (D1 and D3, post-treated group) bilateral renal ischemic-reperfusion injury operation. Intrarenal leukocyte phenotypes, cytokines/chemokines, and ACE/ACE2 were analyzed.

Results Compared to the control group, D1 serum creatinine was higher in the ramipril and telmisartan pre-treated groups and telmisartan intraoperative-treated group. Blood pressures were comparable between groups. Ramipril pre-treated group had a higher proportion of activated CD4, activated CD8, and regulatory CD4 T cells and a lower proportion of total B cells and macrophages than the control group. Ramipril intraoperative-treated group had a higher proportion of total B cells. There were no differences in intrarenal leukocyte phenotypes among post-treated groups. Ramipril intraoperative-treated group had higher RANTES, and telmisartan intraoperative-treated group had lower IL-4 and higher VEGF than the control group. There was no difference in intrarenal cytokines/chemokines in pre- or post-treated groups. Intrarenal ACE and ACE2 concentrations were similar between groups regardless of treatment timings.

Conclusions ACEi and ARB showed different effects on intrarenal immunologic micromilieu after ischemic AKI according to the treatment timings. Further analyses including histopathologic findings or other intrarenal RAS components are required to clarify the clinical impact of RAS inhibitors in ischemic AKI.