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The effects of dietary salt on intrarenal immune cells and endothelial cells

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Objectives: Kidney immune cells and endothelial cells play important roles in kidney ischemia-reperfusion injury. We aimed to investigate the effect of dietary salt intake on kidney immune cells and endothelial cells using experimental models and allograft biopsy specimens.

Methods: C57BL/6 mice were fed with normal diet, low-salt diet, or high-salt diet, and kidneys were collected after 6 weeks of allocated diets. Kidney sections were stained for CD45. Glycosaminoglycan (GAG), a major sodium buffer, concentration was measured using exsanguinated whole kidney tissue. Kidney lymphocytes were isolated and analyzed with flow cytometry. Human renal allograft tissue obtained on 2 weeks after kidney transplantation was stained with CD45 and CD31 and analyzed according to donors' 24h urine Na levels. Induced pluripotent stem cell-derived endothelial cells (iPSC-ECs) from healthy individuals and end-stage kidney disease patients were cultured in different Na concentrations and the degree of proliferation was measured.

Results: High-salt diet group showed higher intrarenal leukocyte infiltration ($CD45^+$) compared to those with normal diet (1.9±0.3% vs 0.9±0.1%, P=0.043). GAG concentration was lower in high-salt diet group than low-salt group (41.0±3.1 vs 48.3±1.3ng/mg, P=0.004). Low-salt and high-salt diets increased effector-memory $CD4^+$ T cells (normal 44.2±2.6%; low-salt 57.1±3.5%, P=0.020; high-salt 62.1±2.5% of $CD4^+$ T cells, P=0.002) and mature B cells (70.0±1.5%; 79.1±1.4%, P=0.001; 76.7±1.6% of $CD19^+$ cells, P=0.015) in steady-state kidneys. Renal allografts from donors under low-salt diet showed reduced leukocyte infiltration ($CD45^+$, 0.3±0.1% vs 0.9±0.3%, P=0.019) and higher capillary density ($CD31^+$, 29.0±2.2% vs 16.1±1.8%, P=0.009) compared to those from donors under high-salt diet. iPSC-ECs with higher sodium concentrations exhibited reduced proliferation rates after hypoxia followed by reoxygenation.

Conclusions: Dietary salt induces changes in kidney immune cell numbers and compositions as well as endothelial cells. Reconstitution of renal microenvironment by modification of dietary salt intake could be a promising strategy to improve kidney transplantation outcomes.