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Renoprotective role of fenoldopam pretreatment on microcirculation after kidney transplantation through heme oxygenase-1 expressions

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Objectives : Cytoprotective proteins, such as heme oxygenase-1 (HO-1), play a decisive role in ischemia-reperfusion injury during kidney transplantation. And it has been reported that donor preconditioning by fenoldopam is demonstrated to improve graft function in recipients. The aim of this study was to investigate the impact of heme oxygenase-1 on microcirculation and on ischemia-reperfusion injury in an isogenic kidney transplantation rat model.

Methods : Seventy Sprague-Dawley (SD) rats were distributed into three groups. In Group 1(control), the kidneys were only mobilized. In Groups 2 and 3, bilateral nephrectomy was performed, and a kidney from another SD rat was orthotopically transplanted on the left side. The donor animals in Group 3 intravenously treated with fenoldopam (5 μg/kg/min), Sch23390 (10 μg/kg/min), or fenoldopam + Sch23390 for 1 hour. Kidneys experiencing 24 hours of cold preservation were transplanted into syngeneic SD recipients. 24 hours after reperfusion graft function and morphology were examined. Microcirculation was investigated by in vivo microscopy of the renal surface 1 hours after reperfusion.

Results : Fenoldopam preconditioning significantly decreased the serum concentrations of sCR, BUN, IL-8, and TNF-α in recipients. Low apoptosis rate and reduced oxidative stress were found in these grafts. Increased HIF-1α activation and HO-1 expression were observed in fenoldopam pretreatment group. Sch23390 partly inhibited the effects of fenoldopam in the combination group. Fenoldopam preconditioning also led to significantly less histological damage and inducible nitric oxide synthase expression. Microcirculation was improved by a significant enlargement of the vascular diameter and an increase of the capillary flow.

Conclusions : Donor preconditioning by fenoldopam exerts renoprotection in grafts via HIF-1α activation and HO-1 expression. Treatment with fenoldopam improves microcirculation by induction of HO-1 and reduces ischemia-reperfusion injury after kidney transplantation.

Keywords : fenoldopam; heme oxygenase-1; microcirculation; ischemia-reperfusion injury