

Human Peripheral Blood Mononuclear Cells Incubated in Vasculogenic Conditioning Medium Dramatically Improve Ischemia/Reperfusion Acute Kidney Injury in Mice

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Abstract

Acute kidney injury (AKI) is a major clinical problem that still has no established treatment. We investigated the efficacy of cultured human peripheral blood mononuclear cells (PBMNCs) for AKI. Ischemia/reperfusion injury (IRI) was used to induce AKI in male nonobese diabetic (NOD/severe combined immunodeficiency) mice aged 7 to 8 wk. PBMNCs were isolated from healthy volunteers and were subjected to quality and quantity controlled (QQc) culture for 7 d in medium containing stem cell factor, thrombopoietin, Flt-3 ligand, vascular endothelial growth factor, and interleukin 6. IRI-induced mice were divided into 3 groups and administered (1) 1×10^6 PBMNCs after QQc culture (QQc PBMNCs group), (2) 1×10^6 PBMNCs without QQc culture (non-QQc PBMNCs group), or (3) vehicle without PBMNCs (IRI control group). PBMNCs were injected via the tail vein 24 h after induction of IRI, followed by assessment of renal function, histological changes, and homing of injected cells. Blood urea nitrogen and serum creatinine (Cr) 72 h after induction of IRI in the QQc PBMNCs group dramatically improved compared with those in the IRI control and the non-QQc PBMNCs groups, accompanied by the improvement of tubular damages. Interstitial fibrosis 14 d after induction of IRI was also significantly improved in the QQc PBMNCs group compared with the other groups. The renoprotective effect noted in the QQc PBMNCs group was accompanied by reduction of peritubular capillary loss. The change of PBMNCs' population (increase of CD34+ cells, CD133+ cells, and CD206+ cells) and increased endothelial progenitor cell colony-forming potential by QQc culture might be one of the beneficial mechanisms for restoring AKI. In conclusion, an injection of human QQc PBMNCs 24 h after induction of IRI dramatically improved AKI in mice.

Keywords

acute kidney injury, ischemia/reperfusion, CD34, mononuclear cell, QQc culture

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