Impact of Timing Administration of Mesenchymal Stromal Cells on Serum Creatinine Following Renal Ischemia/Reperfusion in Rats

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Experimental models of renal ischemia/reperfusion (I/R) have suggested protective effects of mesenchymal stromal cells (MSC) therapy. Still, parameters of MSC injection, including volume, route and timing of cell administration, remain largely debated. Particularly, MSC infusion in mouse has been shown to be beneficial “a priori” but deleterious “a posteriori” of renal I/R injury. In order to further investigate the influence of the timing of MSC administration, we used 10-week-old Lewis rats categorized in 4 groups. Groups 1 (MSC D-7, n = 10) and 2 (MSC D + 1, n = 7) received caudal i.v. injection of MSC (1.5 x 10^6 in 1 ml of saline) 7 days before or 1 day after renal I/R, respectively. Control groups 3 (saline D-7, n = 6) and 4 (saline D + 1, n = 6) received equal volume of saline at similar time points. Left renal ischemia (by clamping of the renal pedicle) lasted 45 min. Right nephrectomy was simultaneously performed. Blood sample was collected from inferior vena cava at 48 h post reperfusion. MSC phenotype was confirmed by FACS analysis. In groups 1 and 3, serum creatinine (SCR) reached 1.4 ± 0.7 versus 2.4 ± 0.8 mg/dl, respectively (p < 0.05). In groups 2 and 4, SCR was 4.9 ± 0.7 versus 3.3 ± 0.9 mg/dl, respectively (p < 0.001). Furthermore, SCR levels were statistically worse when MSC were administered after renal I/R in comparison to a priori infusion (p < 0.0001). In conclusion, MSC administration 7 days prior to renal I/R attenuates kidney injury in comparison to (i) saline infusion or (ii) MSC infusion 1 day after renal I/R. Conversely, on the basis of SCR levels, MSC therapy performed after renal I/R worsens kidney injury in rats.