

Abstract

The molecular mechanisms of mesenchymal stem cell therapy to ameliorate renal fibrosis induced by Cyclosporine A on Wistar rat Ninik Soemyarso

Introduction. Renal fibrosis is still a major problem that may progress to end stage renal disease (ESRD). The current ESRD management of supportive therapy is very costly and unable to reduce or ameliorate the renal fibrosis. Mesenchymal stem cell (MSC) can be used to overcome renal fibrosis. However the mollecular mechanisms are still unclear.

Purpose. To investigate the mollecular mechanisms of allotransplantation MSC therapy to ameliorate renal fibrosis induced by Cyclosporine A on Wistar rat.

Methods. The experimental study was conducted using Wistar rat. Renal fibrosis was induced by intravenous cyclosporine A for 3 weeks. The study included four groups: O1 (n=4) were normal rats; O3 (n=8) were renal fibrosis rats that were immediately sacrificed after 3 weeks of cyclosporine A induction; O4 (n=8) were renal fibrosis rats with free serum medium therapy; O5 (n=8) were renal fibrosis rats with intravenous MSC therapy. The variables of KCP, E-cadherin, Smad7, FSP1, collagenI, Hsp72 and TGF- β 1 from renal tissue were examined using immunohistochemistry (IHC) method. Allotransplantation mesenchymal stem cell therapy intravenously was administered with the dose 2×10^5 , every two weeks for three doses. Renal fibrosis was examined by Axio vision software. Statistical analysis used one-way Anova or Kruskal-Wallis tests.

Results. KCP and E-cadherin increased significantly ($p=0.005$ & $p=0.000$), collagenI and TGF- β 1 decreased significantly ($p=0.005$ & $p=0.000$) when group O5 was compared to O4. Renal fibrosis was reduced significantly ($p=0.001$) as well. Smad7 increased significantly ($p=0.037$) in group O5 when compared to O1. Group O3 could not be examined by IHC because the renal tissue was severely damaged.

Conclusion. Allotransplantation MSC therapy reduced renal fibrosis by paracrine effects, inducing KCP microenvironment as BMP-7 agonist. Smad7 may reduce renal fibrosis by inhibiting TGF- β 1-Smad dependent pathway.

Key w ords: renal fibrosis, mesenchymal stem cell, KCP, BMP-7, E-cadherin, Smad7.