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Impact of repeated intravenous bone marrow mesenchymal stem cells infusion on myocardial collagen network remodeling in a rat model of doxorubicin-induced dilated cardiomyopathy

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Abstract Bone marrow mesenchymal stem cells (MSCs) transplantation improved cardiac function and reduced myocardial fibrosis in both ischemic and non-ischemic cardiomyopathies. We evaluated the effects of repeated peripheral vein injection of MSCs on collagen network remodeling and myocardial TGF-β1, AT1, CYP11B2 (aldosterone synthase) gene expressions in a rat model of doxorubicin (DOX)-induced dilated cardiomyopathy (DCM). Thirty-eight out of 53 SD rats survived at 10 weeks post-DOX injection (2.5 mg/kg/week for 6 weeks, i.p.) were divided into DCM blank (without treatment, $n = 12$), DCM placebo (intravenous tail injection of 0.5 mL serum-free culture medium every other day for ten times, $n = 13$), and DCM plus MSCs group (intravenous tail injection of 5×10^6 MSCs dissolved in 0.5 mL serum-free culture medium every other day for 10 times, $n = 13$). Ten untreated rats served as normal controls. At 20 weeks after DOX injection, echocardiography, myocardial collagen content, myocardial expressions of types I and III collagen, TGF-β1, AT1, and CYP11B2 were compared among groups. At 20 weeks post-DOX injection, 8 rats (67 %) survived in DCM blank group, 9 rats (69 %) survived in DCM placebo group while 13 rats (100 %) survived in DCM plus MSCs group. Left ventricular end-diastolic diameter was significantly higher and ejection fraction was significantly lower in DCM blank and DCM placebo groups compared to normal control rats, which were significantly improved in DCM plus MSCs group (all $p < 0.05$ vs. DCM blank and DCM placebo groups). Moreover, myocardial collagen volume fraction, types I and III collagen, myocardial mRNA expressions of TGF-β1, AT1, CYP11B2, and collagen I/III ratio were all significantly lower in DCM plus MSCs group compared to DCM blank and DCM placebo groups (all $p < 0.05$). Repeated intravenous MSCs transplantation could improve cardiac function by attenuating myocardial collagen network remodeling possibly through downregulating renin–angiotensin–aldosterone system in DOX-induced DCM rats.

Keywords Mesenchymal stem cells transplantation · Dilated cardiomyopathy · Collagen network remodeling · Doxorubicin

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Introduction

Doxorubicin (DOX) is commonly used to treat various types of human cancers [1]. Cardiotoxicity is its major

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