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Cell Therapy Improves Cardiac Function in Anthracycline-Induced Cardiomyopathy Preclinical Models: A Systematic Review and Meta-Analysis

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Abstract

Although anthracycline (ANT)-based treatment strongly contributes to cancer survivorship, the use of these agents is limited by the risk of cardiotoxicity. For those patients who evolve to heart failure, myocardial regenerative approaches are of particular interest, and a growing body of preclinical studies has been investigating the use of cell therapy for ANT-induced cardiomyopathy (AIC). However, since animal models and modalities of cell therapy are highly heterogeneous between studies, the efficacy of cell therapy for AIC is not clear. Thus, we conducted a systematic review and meta-analysis of experimental studies reporting the use of cell therapy with mesenchymal stromal cells (MSC) or bone marrow mononuclear cells (BMMNC) in animal models of AIC with regard to global cardiac function. The Medline, EMBASE, and Web of Science databases were searched from inception to November 2019. Two reviewers independently extracted data on study quality and the results of left ventricular ejection fraction (LVEF) and fractional shortening (FS) obtained by echocardiography. The quality of outcomes was assessed using the Cochrane, Collaborative Approach to Meta-Analysis and Review of Animal Data from Experimental Studies (CAMARADES), and SYRCLE bias risk tools. Pooled random-effects modeling was used to calculate pooled mean differences (MD) and 95% confidence intervals (CIs). Twenty-two studies comprising 381 small animals (rabbits and rodents) were included. A pooled meta-analysis of all treatments showed that cell therapy increased LVEF by 9.87% (95% CI 7.25–12.50, $P < 0.00001$) and FS by 7.80% (95% CI 5.68–9.92, $P < 0.00001$) in small animals with AIC. Cell therapy with MSC/BMMNC is effective to mitigate the deleterious effects of ANT on cardiac function in preclinical models. Nevertheless, due to the small number of studies and considerable heterogeneity, future translational studies must be designed to diminish between-study discrepancies and increase similarity to the clinical landscape.