Basic Science and Experimental Therapies

306 Interventional Cellular Cardiomyoplasty by Transendocardial Implantation of Mesenchymal Stem Cells

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Background: Mesenchymal stem cells (MSCs) administered by direct epicardial injection ameliorate ventricular dysfunction after myocardial infarction (MI) in small animal models. We investigated a catheter approach (BioCardia helical infusion system) for transendocardial injection of MSC in a swine model of myocardial infarction (MI). Delivery, engraftment, migration, and myocytic differentiation of the MSCs' phenotype were determined.

Methods: MI was produced by 1-hour occlusion of the left anterior descending artery in domestic swine, and the infarct territory was marked with surgical clips. Animals (n = 10) were treated 3 days after infarction by administration of 200 million allogeneic porcine MSCs or vehicle alone. The injection device was engaged into 10 to 12 endocardial sites in the infarct zone by fluoroscopic guidance of a deflectable guiding catheter and screw-in of a helical infusion needle followed by injection of 1-mL aliquots cell suspension over 30 seconds. Two additional animals were treated with Feridex-labeled mesenchymal stem cells for serial magnetic resonance imaging (MRI) study, allowing cell delivery and migration to be tracked within the infarct zone, which was delineated by gadopentetate MRI contrast enhancement.

Results: There were no deaths or cardiac perforations from transcatheter delivery of MSCs. Animals survived 1 to 2 months until they were killed. MSC engraftment in the infarct zone was observed in all animals receiving active therapy but none in controls. Transplanted MSCs expressed phospholamban, myosin heavy chain, and α-actinin, indicating myogenic differentiation. Labeled MSCs appeared as MRI hypointense blebs that had been successfully delivered into the infarct zone. Migration of cells was suggested by decreasing intensity and increasing volume of the injection site over 1 week.

Conclusion: Percutaneous implantation of MSC into damaged myocardium is feasible and can be achieved with high efficiency and safety. MRI may be particularly useful for tracking cellular myoplasty techniques. Transplanted cells engraft and differentiate, suggesting a role for this approach in the treatment of infarction and other cardiomyopathic processes.

Source: *Am J Cardiol 2002; 90(suppl 6A): 120H*