



2003

Abstract: 1176-175

Citation: Supplement to Journal of the American College of Cardiology, March 19, 2003, Vol. 41, Issue 6, Suppl. A

Catheter-Based Percutaneous Cellular Cardiomyoplasty Using Allogeneic Bone Marrow Derived Mesenchymal Stem Cells

Marcus E. St. John, Jinsheng Xie, Alan W. Heldman, Garrick C. Stewart, Stephen M. Cattaneo, David J. Caparrelli, William A. Baumgartner, Bradley J. Martin, Joshua M. Hare

Johns Hopkins Medical Institutions, Baltimore, MD, Osiris Therapeutics, Inc, Baltimore, MD

Background: Bone marrow derived mesenchymal stem cells (MSCs) administered by direct injection into a myocardial infarct (MI) improve ventricular remodeling and global function in both large and small animal models. In order to demonstrate therapeutic applicability without need for surgery, we tested the hypothesis that MSCs delivered percutaneously via catheter successfully engraft, migrate throughout a region of MI, and demonstrate evidence of myocyte differentiation in pigs. **Methods:** MI was produced by 1-hour occlusion of the left anterior descending artery in domestic swine (weight 30-45kg). Three days later either 200 million Dil and DAPI-labeled allogeneic porcine MSCs or vehicle alone (randomly assigned; total n=9) were injected into the LV (10-12 sites in the endocardium within the infarct zone) via a helical needle infusion catheter advanced through a deflectable guide catheter (BioCardia, Inc, CA). **Results:** Animals were euthanized between 2 to 8 weeks after injection. Pathology revealed transmural anteroseptal infarcts. MSC engraftment was observed in all treated animals, with transmural migration of implanted cells from endocardium to epicardium. MSCs were found associated with blood vessel walls and co-stained for factor VIII, consistent with neoangiogenesis. Transplanted MSCs expressed muscle specific proteins including phospholamban, myosin heavy chain and alpha-actinin, which were not present before implantation, suggesting myogenic differentiation. Implanted MSCs were not found in regions of myocardium remote from the injection site, or systemically. There was no evidence of immunorejection. No deaths, perforations or arrhythmias resulted from the catheterization or injections. **Conclusions:** MSCs can be successfully delivered via percutaneous catheter. Transplanted cells engraft, migrate transmurally, express myocyte phenotypic markers and may participate in neoangiogenesis. We conclude that catheter-based delivery of allogeneic MSCs is both safe and effective and will facilitate practical application of stem cell technology in the treatment of MI and potentially other cardiomyopathic processes.