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Stem cell therapy in acute myocardial infarction: a review of clinical trials

Jon C. George

Deborah Heart and Lung Center, USA

The myocardium had been viewed as a terminally differentiated organ without potential for regeneration until recently. Although early reperfusion strategies for occluded arteries in acute myocardial infarction (AMI) have greatly improved morbidity and mortality in these patients, further advances in treatment are limited by the inability to repair concomitantly damaged cardiac tissue. This has led to increasing use of stem cell therapies with the assumption that replacement or repair of damaged vascular and cardiac tissue could lead to improvement in myocardial function after AMI.

Although multiple experimental animal models and clinical trials of cell based cardiac therapy have delivered promising results, the mechanisms of their effect are rather unclear. Stem cells (SC), depending on their lineage, possess the ability to differentiate into cells of various tissues. While the differentiation of SC into functional cardiomyocytes has been difficult to demonstrate and fraught with controversy, differentiation into functioning endothelium with improved blood flow has been better illustrated and accepted. Studies in animal models have demonstrated improvement in myocardial function after targeted repair of infarcted myocardium via implantation of endothelial progenitor cells by various delivery methods whether derived from peripheral blood (PB), bone marrow (BM), or umbilical cord blood (UCB). This has led to a variety of human clinical trials utilizing SC to determine safety, feasibility, and outcomes in the setting of AMI.

Clinical trials in humans have primarily utilized autologous BM derived SC due to feasibility without concerns of yield as with PB derived cells and rejection as with UCB derived cells. Clinical trials of SC therapy in AMI can be classified into three major approaches of delivery: direct *injection* using an intracoronary route (IC), indirect cytokine-induced *mobilization* using granulocyte-colony stimulating factor (G-CSF), or a *combination* approach using initial mobilization followed by direct injection. However, interpretation of these trials has been difficult due to multiple variables including differences in trial design, cell type, timing of cell delivery, and outcome measurements.

Biography

Dr. Jon C. George, MD completed his medical training at University of Cincinnati College of Medicine in Cincinnati, Ohio; residency and fellowship training at University Hospitals Case Medical Center in Cleveland, Ohio; and subspecialty fellowship training at Temple University Hospital in Philadelphia, Pennsylvania. He serves as the Director of Clinical Research at Deborah Heart and Lung Center in Browns Mills, New Jersey and Adjunct Research Instructor at Temple University School of Medicine in Philadelphia, Pennsylvania. He has published more than 50 papers in reputed journals, book chapters, and textbooks, and serves as a reviewer and editorial board member for multiple journals. In addition, he has received numerous honors and awards for his contributions to research and clinical cardiology.