

Stem Cell Therapy in Myocardial Infarction: Latest Trends

Ashfaq UI Hassan^{1*}, Ghulam Hassan², Zahida Rasool³ and Muneeb⁴

¹Anatomy Department, SKIMS Medical College Bemina, Srinagar, Kashmir, India

²Department of Anatomy, Al Qassim University, Saudi Arabia

³Islamic University of Science and Technology, Awantipora, Kashmir, India

⁴PHC Chanapora, Srinagar, Kashmir, India

Abstract

Heart Diseases are a major cause of morbidity and mortality world wide. Myocardial infarction is the leading cause of congestive heart failure and death in the industrialized world. Current therapy is limited in preventing the progression of ventricular remodeling and congestive heart failure. Recent interest has focused on stem cells, which are undifferentiated and pleuropotent cells that can proliferate, potentially self-renew, and differentiate into cardiomyocytes. The article tries to underline the beneficial effects of the stem cell therapy for use in patients where other modes of therapy are not advisable and the multi purpose effects of such as therapy.

Keywords: Pleuropotent cells; Stem cells; Implantation; Angiogenesis; Ventricular remodeling

Introduction

The sources of stem cells are varied such as pre-implantation embryos, children, adults, aborted fetuses, embryos, umbilical cord, menstrual blood, amniotic fluid and placenta.

Stem cells or mother or queen of all cells are pleuropotent and have the remarkable potential to develop into many different cell types in the body. Serving as a sort of repair system for the body, they can theoretically divide without limit to replenish other cells as long as the person or animal is alive. When a stem cell divides, each new cell has the potential to either remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell [1]. Stem cells differ from other kinds of cells in the body. All stem cells regardless of their source have three general properties:

They are unspecialized

one of the fundamental properties of a stem cell is that it does not have any tissue-specific structures that allow it to perform specialized functions.

They can give rise to specialized cell types

These unspecialized stem cells can give rise to specialized cells, including heart muscle cells, blood cells, or nerve cells.

They are capable of dividing and renewing themselves for long periods

Unlike muscle cells, blood cells, or nerve cells-which do not normally replicate themselves-stem cells may replicate many times. A starting population of stem cells that proliferates for many months in the laboratory can yield millions of cells.

Because heart muscle cells do not replace themselves naturally, those who now suffer from a heart attack, from congenital heart disease, or from congestive heart failure have few treatment options. And while heart transplants potentially could help more patients, the supply of organs is limited. It may become possible to generate healthy heart muscle cells in the laboratory and then transplant them into patients with chronic heart disease. These cells have shown remarkable ability to produce cardiomyocytes and vascular cells in vitro and in vivo.

Patients who feel they have exhausted treatment options such as Coronary Artery Bypass Surgery (CABG) or balloon angioplasties are candidates. For patients with other medical conditions that make these

conventional procedures too risky or otherwise not possible, adult stem cell therapy may be a viable alternative.

Discussion

The heart is the first organ to form as the embryo develops in the uterus, the heart also apparently lacks the ability to repair itself. However, the researchers hope that what they learn about mouse stem cell differentiation can be used as a blueprint for prompting human stem cells to differentiate in the laboratory into cells that could then be used therapeutically to repair damaged or diseased hearts.

Ideally stem cells must be able to:

- Divide to produce sufficient cells
- Differentiate into the cell types needed
- Survive after transplant
- Mesh into the surrounding tissues
- Function properly for long enough to extend the recipient's life or to improve it significantly
- Avoid harming the recipient [1].

Stem cell therapy

We use stem cells taken from your own blood so there is no danger of your body rejecting them. In the absence of new treatments unique capacity to develop into any kind of human tissue and they can divide indefinitely in laboratory cultures. Stem cells are found throughout the body

Cardiologists and heart surgeons are currently using stem cells to improve the quality of life of patients suffering from ischemic heart disease, (or coronary artery disease), cardiomyopathy, and congestive

*Corresponding author: Dr. Ashfaq UI Hassan, MBBS, MS Anatomy, A 50 Khan Colony Chanapora Srinagar, Kashmir, India, E-mail: ashhassan@rediffmail.com

Received November 26, 2012; Accepted December 24, 2012; Published December 26, 2012

Citation: Hassan AUI, Hassan G, Rasool Z, Muneeb (2012) Stem Cell Therapy in Myocardial Infarction: Latest Trends. J Cytol Histol 3: 162. doi:10.4172/2157-7099.1000162

Copyright: © 2012 Hassan AUI, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

heart failure by increasing the blood flow through the heart and thereby relieving debilitating symptoms such as chest pain, shortness of breath and loss of energy.

Orlic et al. [2] reported on an experimental application of hematopoietic stem cells for the regeneration of the tissues in the heart. In this study, a heart attack was induced in mice by tying off a major blood vessel, the left main coronary artery. Through the identification of unique cellular surface markers, the investigators then isolated a select group of adult primitive bone marrow cells with a high capacity to develop into cells of multiple types. When injected into the damaged wall of the ventricle, these cells led to the formation of new cardiomyocytes, vascular endothelium, and smooth muscle cells, thus generating de novo myocardium, including coronary arteries, arterioles, and capillaries. The newly formed myocardium occupied 68 percent of the damaged portion of the ventricle nine days after the bone marrow cells were transplanted, in effect replacing the dead myocardium with living, functioning tissue. The researchers found that mice that received the transplanted cells survived in greater numbers than mice with heart attacks that did not receive the mouse stem cell.

Myocardial regeneration with stem-cell transplantation is a possible treatment option to reverse the deleterious hemodynamic and neurohormonal effects that occur after myocardial infarction and can lead to congestive heart failure. Various preclinical animal studies show the potential to regenerate myocardium and improve perfusion to the infarct area to improve cardiac function but also suggest that stem cells may have proarrhythmic effects. Early phase I clinical studies indicate that stem-cell transplantation is feasible and may have beneficial effects on ventricular remodeling after myocardial infarction. Future randomized clinical trials will establish the magnitude of the benefit and the effects on arrhythmias after stem-cell therapy [3].

Implantation of bone-marrow stem cells in the heart might be a new method to restore tissue viability after myocardial infarction. Bone-marrow cells were injected into the infarct border zone in six patients who had had a myocardial infarction and undergone coronary artery bypass grafting. 3-9 months after surgery, all patients were alive and well, global left-ventricular function was enhanced in four patients, and infarct tissue perfusion had improved strikingly in five patients. It was believed that implantation of stem cells to the heart is safe and might induce angiogenesis, thus improving perfusion of the infarcted myocardium [4].

Intracoronary infusion of progenitor cells is safe and feasible in patients with healed myocardial infarction. Transplantation of BMC is associated with moderate but significant improvement in the left ventricular ejection fraction after 3 months [5].

Results of experimental studies have shown that intramyocardial implantation of bone marrow cells induce neovascularisation and improve heart function after myocardial infarction. Blood flow to the heart was improved in these patients, and the heart muscle doubled its ability to contract [6].

New arteries can be grown with the help of stem-cell therapy. The isolated cells showed expression of endothelial marker proteins including VE-cadherin, von Willebrandt factor, KDR and endothelial nitric oxide synthase. Most importantly, infusion of these ex vivo expanded EPCs augmented blood flow and heart function in animal models after hind limb ischemia or myocardial infarction [7-9]. Preclinical studies have also established that implantation of bone marrow-mononuclear cells into ischemic limbs increases collateral vessel formation.

Paracrine effects

Bone marrow-derived stem and progenitor cells home to sites of ischaemia. This may allow the local release of factors acting in a paracrine manner on the surrounding ischaemic tissue. Bone Marrow-Derived Mononuclear Cells (BMCs) release angiogenic growth factors such as Vascular Endothelial Growth Factor (VEGF), basic Fibroblast Growth Factor (bFGF) and angiopoietins, thereby enhancing the local angiogenic response [10]. Isolated human EPCs also express various growth factors which can enhance cardiac myocyte survival and improve angiogenesis. Compared to acute myocardial infarction patient treated by standard therapy alone, a group that received additional stem cell treatment reduced infarct volume as well as increases in infarction wall movement velocity, stroke volume index, left ventricular end-systolic volume and contractility, and myocardial perfusion of the infarct region.

Types of stem cells should be used for cardiac therapy.

Skeletal myoblasts: One of the first cell-based cardiac regeneration strategies was injection of autologous skeletal myoblasts into ischaemic myocardium. Myoblasts are resistant to ischemia can differentiate into myotubes in vivo and improve ventricular function in laboratory animal experiments. This proved to be a failure [11].

Bone marrow cells: Most clinical studies have used bone-marrow mononuclear cells and showed either no benefit or small (but possibly clinically important) improvements in cardiac function. The mechanisms of these functional improvements are unknown, but it is unlikely that the improvements result from differentiation of the injected cells into cardiomyocytes. Growth factor and cytokine release by injected cells is frequently suggested as a potential mechanism of action, and improved micro vascular function has been shown [11].

Embryonic Stem (ES) cells: are the prototypical stem cells. They unambiguously fulfill all requirements of stem cells: clonality, self renewal and multipotentiality. ES cells can differentiate into any cell present in the adult organism and have the potential to completely regenerate the myocardium. Two of the obstacles that stand in the way of the therapeutic use of ES cells are immunological rejection and the propensity of ES cells to form teratomas when injected in vivo [12].

Endogenous cardiac stem cells: can be isolated and expanded from human myocardial samples obtained using a minimally invasive biopsy procedure. Thus, from autologous CSCs, it might be possible to generate enough cells to transplant into patients with heart failure, a procedure that would have minimal risk of immune rejection or teratoma formation [13].

From the discussion we can infer that stem cell therapy has advantages in the facts that:

- Stem cell therapy can be used in patients where conventional procedures are too risky or cannot be used.
- There is problem like shortage of donors
- Stem cells can be easily harvested.
- Sources of obtaining stem cells are multiple

The beneficial effects of treatment are multiple:

- Improve Angiogenesis
- Improve collateral circulation
- Improve neovascularization

- Improve ventricular function
- Have positive effects on ventricular remodeling

Understanding cardiomyocytes development and turnover both in normal development and after injury will be essential for guiding the development of stem-cell-based therapies. Defining the factors present in the hostile microenvironment of injured myocardium that limit the survival and functional integration of transplanted cells is also crucial. As the barriers that prevent human cardiac regeneration are further defined, clinical trials should proceed with caution and with a paramount concern for patient safety [14].

References

1. (2005) The benefits of stem cell research 2005 - Science Solidarity.
2. Orlic D, Kajstura J, Chimenti S, Jakoniuk I, Anderson SM, et al. (2001) Bone marrow cells regenerate infarcted myocardium. *Nature* 410: 701-705.
3. Lee MS, Makkar RR, Lill M (2004) Stem-Cell Transplantation in Myocardial Infarction: A Status Report. *Annals of Internal Medicine* 140: 729-737.
4. Stamm C, Westphal B, Kleine HD, Petzsch M, Kittner C, et al. (2003) Autologous bone-marrow stem-cell transplantation for myocardial regeneration. *Lancet* 361: 45-46.
5. Assmus B, Honold J, Schächinger V, Britten MB, Fischer-Rasokat U, et al. (2006) Transcatheter Transplantation of Progenitor Cells after Myocardial Infarction. *N Engl J Med* 355: 1222-1232.
6. Tse HF, Kwong YL, Chan JK, Lo G, Ho CL, et al. (2003) Angiogenesis in ischaemic myocardium by intramyocardial autologous bone marrow mononuclear cell implantation. *Lancet* 361: 47-49.
7. Kalka C, Masuda H, Takahashi T, Kalka-Moll WM, Silver M, et al. (2000) Transplantation of ex vivo expanded endothelial progenitor cells for therapeutic neovascularization. *Proc Natl Acad Sci U S A* 97: 3422-3427.
8. Kawamoto A, Gwon HC, Iwaguro H, Yamaguchi JI, Uchida S, et al. (2001) Therapeutic potential of ex vivo expanded endothelial progenitor cells for myocardial ischemia. *Circulation* 103: 634-637.
9. Urbich C, Heeschen C, Aicher A, Dembach E, Zeiher AM, et al. (2003) Relevance of monocytic features for neovascularization capacity of circulating endothelial progenitor cells. *Circulation* 108: 2511-2516.
10. Kamihata H, Matsubara H, Nishiue T, Fujiyama S, Tsutsumi Y, et al. (2001) Implantation of bone marrow mononuclear cells into ischemic myocardium enhances collateral perfusion and regional function via side supply of angioblasts, angiogenic ligands, and cytokines. *Circulation* 104: 1046-1052.
11. Laflamme MA, Murry CE (2005) Regenerating the heart. *Nat Biotechnol* 23: 845-856.
12. Abdel-Latif A, Bolli R, Tleyjeh IM, Montori VM, Perin EC, et al. (2007) Adult bone marrow-derived cells for cardiac repair: a systematic review and meta-analysis. *Arch Intern Med* 167: 989-997.
13. Garry DJ, Olson EN (2006) A common progenitor at the heart of development. *Cell* 127: 1101-1104.
14. Bearzi C, Rota M, Hosoda T, Tillmanns J, Nascimbene A, et al. (2007) Human cardiac stem cells. *Proc Natl Acad Sci U S A* 104: 14068-14073.