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Treatment for congestive heart failure with stem cells

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ABSTRACT

Heart failure is one of the leading death causes in world which records nearly 20% of deaths in India. Medical therapy, surgical procedures including heart transplantation and cardiac assist devices has only limited efficiency in such condition stem cell therapy represents as the new strategy for better therapeutic outcome. Generally stem cells are derived from few and they generated various organs and tissues. Few scientist has performed research on the stem cell therapy for congestive heart failure condition some of them has shown a good effect. Scientist has to keep effects regarding the development of the cell regeneration therapy with the use of stem cells. Currently in global clinical trails only few trails has been enrolled. At present BMMNC has shown a good effect in heart related treatment.

Keywords: HFrEF, HFpEF, Hypokinetic, Inotropic drugs.

INTRODUCTION

Congestive heart failure is chronic condition to heart where the heart loss its capability to pump the blood. It will happen when there is a defect in the heart which prevents the blood from getting out into the circulation or in case heart muscle is weaker than normal. Due to the failure of the heart capacity of pumping to the organs that leads negative impact on other organs for example when the less amount of blood is pumped into the kidneys by the heart that leads to filter less fluid out of the circulation through the urine. Extra fluid in the circulation raise in the liver, the lungs and some other places. Such kind of fluid accumulation is known as "congestion" this condition is called as "congestive heart failure".

Generally it is of two types those are systolic dysfunction and diastolic dysfunction in case of systolic dysfunction when the heart muscle doesn't contract properly with sufficient force that leads to less oxygen-rich blood will be pumped all over the body also known as Heart failure with reduced ejection fraction (HFrEF). In case of Diastolic dysfunction heart contracts normally, where as ventricles fail to relax properly, which leads to entry of less blood into the Heart during filling well known as Heart failure with preserved ejection fraction (HFpEF). [1]

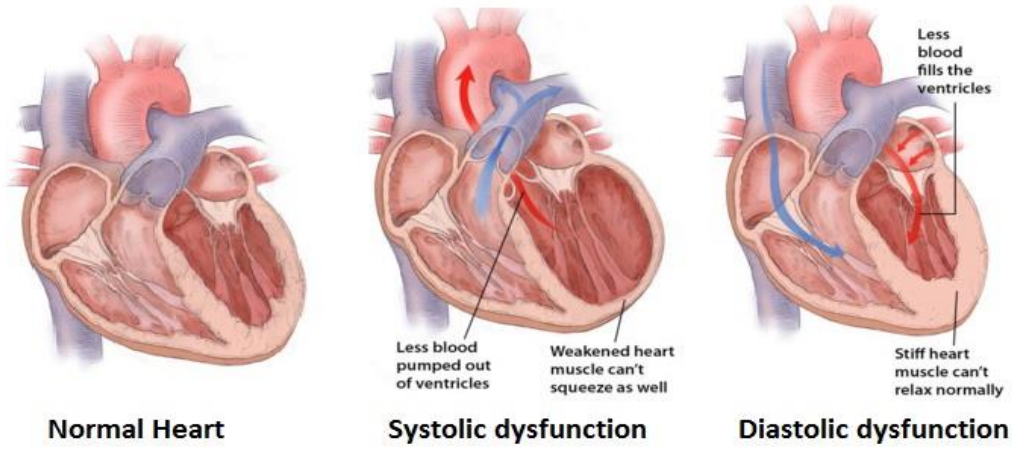

Fig: 1 Types of Congestive Heart Failure (systolic and diastolic dysfunction)

Patients complaints with the sign or symptoms like shortness of breath, persistent coughing or wheezing, building up high body fluids, tiredness, fatigue, lack of appetite, nausea, raised heart rate and some other complaints.

Heart attack can be diagnosed by blood test, EKG, echocardiography (Images produced by the echo can show how thick the heart muscle is and how well the heart pumps), exercises stress test (It says about the how an heart responses to normal stress), Radionuclide ventriculography (It says about the who well chambers of heart is working, which part of the heart has been damaged by the heart attack), cardiac catheterization (Shows block in heart), magnetic resonance imaging (Shows heart's structure and blood flow to major vessels from heart).

Generally the ejection fraction less than 20% is considered as serious condition, in normal humans ejection fraction would be between 50-75%. Fact for the failure of the heart ejection is one main chamber in heart that is left ventricle; it becomes enlarged and isn't beating effectively causing the EF percentage level to dangerously low levels. Ideally, EF percentages ought to be between 52% and 74%. Percentage of the EF says the quantity of blood sent out from the heart on every beat. The walls of the left ventricle are hypokinetic.

Hypokinetic condition says that they are not contracting correctly, they're considered "lazy". This is also why the EF% is low and the patients have Diastolic Dysfunction of the heart. [2]

Two Main goals for the drug therapy in CHF a) relief of congestive and restoration of cardiac performance this can be achieved by using of the inotropic drugs (changes the force of heart contraction. i.e., positive contraction and negative contraction), ACE inhibitors/ ARBs, vasodilators, β-blockers and b) Arrest or reversal of disease progression and prolongation of survival.

Stem cells are un-specialized cells that have 2 essential characteristics that differentiate them from other cells inside our bodies. Stem Cells are able to replenish their numbers naturally and indefinitely via cell division. If stem cells ever receive chemical indicators (ie dysfunctions, trauma, damage etc) they are able to migrate to the injured/dysfunctional area and transform themselves into the very specialized cells needed to perform a particular function. Functions or tissues or cells like nerve cells or even heart cells.

Main criteria required for the success of stem cell treatment are

1. Cell must possess the ability to self- renewal. Self-renewal is described as the capability of a cell to go through various cycles of normal cell division while being to maintain an undifferentiated state.
2. Cells should have the capability to differentiate into three germ layers of endoderm, mesoderm, or ectoderm.

Various kinds of the somatic cells are present in our body they have the capacity to perform single function to more specialized cells which are base for

the formation of the various kinds of the human tissues and organs. For example hematopoietic stem cell gives rise to blood cells like red blood cells, white cells and platelets. Mesenchymal stem cells forms cartilage, bone, tendon, ligaments, skin cells and some other cells. [3]

Few proposed mechanism for the action in orders to improve the heart function. Stem cells can generate vasculature through vasculogenesis or angiogenesis leads to activation of the endothelial progenitor cells and some other, but most of them remains as a controversial. Although stem cells can potentially repair the injured myocardium by increased angiogensisis by releasing the factors that has a capability to reduce cell death. And till now only paracrine activation has proven a good result when compare to remain mechanism

For the treatment with the stem cells they are mainly two kinds of cells those are autologous cells (cells from the subject own body) and allogeneic cells (donated stem cells from a person other recipient). [4] Types of stem cells that has a capability to regenerate the myocardial tissues Embryonic Stem (ES) Cells, Skeletal Myoblasts, Human Adult Bone-Marrow Derived Cells, Resident Cardiac Stem Cells, Endothelial Progenitor Cells and some other cells.

Embryonic Stem (ES) Cells

As it was known that embryonic cells are pluripotent it means which a cells having the capability to give rise to variety of cell types, more over this cells are used for the generation of the cardiac cells which got damaged not only cardiac cells but also few other cells. Under the consideration of the importance of the ES cells researches has been performed.

Experiments have been conducted on rats and human ES cells that have been shown some of the similarities. When the ES cells has been implanted into the rats which has the ischemically injured myocardium rats that differentiated into normal myocardial cells in the span of 4 months this reports has proven that ES cells can be helpful in the regenerative therapy in humans. However, several key hurdles must be overcome before human ES cells can be used for clinical applications.

Human Adult Bone-Marrow Derived Cells

In early 20th century few scientists has conducted a research by using the bone marrow derived cells from rat and infused to the damaged part of the heart after few days new cardiomyocytes has formed, vascular endothelium and smooth muscle cells. Few days after transplantation of stem cells, the newly-formed myocardium occupied nearly 70% of the damaged portion of the ventricle, and survival rates were greater in mice that received these cells than in those that did not. While several studies have questioned whether a cell actually differentiates into cardiomyocyte the evidence to support their ability to prevent remodelling has been demonstrated in many laboratories.

Based on these results, researchers have found the potential of human adult bone marrow as a source of stem cells for cardiac repair. Generally adult stem cells contain cells like endothelial progenitor cells, hematopoietic stem cells, and Mesenchymal stem cells. From past few years, transplantation of bone marrow mononuclear cells (BMMNCs), which is a mixed populated cell that contains stem and progenitor cells. The results of BMMNC transplantation have promising. Few other studies performed they are Transplantation of Progenitor Cells and Regeneration Enhancement in Acute Myocardial Infarction (TOPCARE-AMI) and the Bone Marrow Transfer to Enhance ST-Elevation Infarct Regeneration (BOOST) trials. [5]

Mesenchymal (Bone Marrow Stromal) Cells

Mesenchymal stem cells are progenitor of non-hematopoietic tissues (*e.g.*, bone, muscle, tendons, fibroblasts, ligaments, and adipose tissue) which are obtained easily from autologous bone marrow. Which can also cultured easily under some special condition which is favour for them to grow and those cells can also resemble the cardiac myocytes. [6] This feature suggests their application to cardiac regeneration. MSCs converted into endothelial cells when cultured with cardiomyogenic (CMG) and vascular endothelial growth factor, when treated with the DNA-demethylating agent, 5-azacytidine. To be noted is that MSCs can differentiate into endothelial cells and cardiomyocytes where as in the lab condition transplantation of the cells into the heart following myocardial infarct (MI) or non-injury in mouse, pig, or rat models. [7]

Resident Cardiac Stem Cells

Recent studies have proven that heart do contains some cells that are with an ability to repair a minute

repair and turnover-mediated cell replacement. Cells have been isolated and characterized in rat, and human tissues. [8] Cells are taken in limited quantity from human endomyocardial biopsy specimens, which are healthy and can be injected into the site of infarction to propagate cardiomyocyte development and improvements in systolic function. Separation and expansion ex vivo over a period of weeks are required to get sufficient quantities of cells for experimental purposes.

Endothelial Progenitor Cells

The endothelium is a specialized layer that lays in the interior region of all blood vessels (including the heart). In case of ischemia endothelial progenitor cells (EPCs), which are bone marrow-derived stem cell that moves into the peripheral blood. When this EPCs are injected in the damaged region that leads to new vascularisation which prevents cardiomyocyte apoptosis and LV remodelling, thereby preserving ventricular function. Currently some clinical trials are going for the further investigation regarding the regeneration. [9]

Over the last few year the use of BMMNC as the injected cell has been increased which were produced through various techniques, given in various doses for the patients suffering with ischemic, chronic ischemia and non-ischemic heart failure. Even though there is some confusion regarding dose adjustment, time of administration and some other controversial questions has been raised during the trails. Due to the primary mechanism of action for cell therapy is thought to be paracrine effect by the release of cytokines, growth factors, chemokins and that inhibit fibrosis, enhance contractility, and activate endogenous regenerative mechanisms through endogenous circulating or site-specific stem cells. Currently Bone marrow-derived mononuclear cells on all-cause mortality in Acute Myocardial Infarction (BAMI: NCT01569178) study is largest stem cell trial using BMMNCs to date. This trial is recruiting 3,000 patients with AMI and LVEF <45% and is powered to detect a 25% decrease in 2-year all cause mortality after treatment. Results from this trial will help us determine whether further investment in BMMNCs is warranted.

CONCLUSION

In past few decades researches has achieved a mile stone in the field of the cell therapy, but in order to acquire pinnacle regarding the diseases treatment and effectiveness in it, lot of effects need to be kept by the scientists and physician for choosing stem cell therapy as an primary treatment. Further research should focus on the new methods to develop the knowledge regarding the stem cell science.

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