Cell Therapy of Chronic Heart Failure:  

Perspective of Clinical Approach

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Abstract

Treatment of chronic heart failure (CHF) remains an urgent medical and social problem. Serious prognosis of a pathological condition calls for the development and application of new methods of treatment, one of which is cell therapy. The use of this treatment in combination with the traditional therapy of CHF in patients with coronary heart disease (CHD) after myocardial improves myocardial contractility by reducing the areas of hibernation and myocardial ischemia, as well as an increase in the area of well-functioning myocardium. The purpose of the short comments is summarizing our experience regarding stem cell therapy in ischemic induced CHF. There are evidences regarding efficacy of autologous MSCs transplantation of bone marrow in patients with CHD. This procedure is safe and well-tolerated that leads to the improvement of general and local myocardial contractility, to the normalization of diastolic filling, as well as increases perfusion infarction.

Keywords: chronic heart failure, coronary heart disease, cell therapy

Although recent clinical trials using autologous bone marrow mononuclear cells (BM-MNC), healthy human cord blood mononuclear cells (CB-MNCs) or peripheral blood cells to treat myocardial infarction (MI) show controversial results, cell therapy remains to consider as a perspective treatment for ischemia-induced chronic heart failure (CHF) [1]. These discrepancies are likely caused by
factors such as aging, systemic inflammation, and cell processing procedures, all of which might impair the regenerative capability of the cells used [2]. In fact, autologous bone marrow cell transplantation could improve cardiac function after AMI, but the involving mechanisms have not been completely understood.

Preclinical studies have been elucidated that regenerative therapy using cellular technology opens up new possibilities in the fight against functional and structural cardiac changes after MI. It is indicated that administration of BM-MNC improved the therapeutic efficacy of contemporary treatment by improving the morphology of infarcted myocardium as well as decreasing inflammation in a host, but did not do so by inducing therapeutic angiogenesis [2, 3]. In clinical settings using CB-MNCs and BM-MNC to treat MI associates with significantly increases cell retention in the peri-infarct area, improves cardiac performance, and prevents cardiac remodeling. Moreover, using healthy cells to replace dysfunctional autologous cells may constitute a better strategy to achieve heart repair and regeneration [4-6]. Intravenous transplantation of BM-MNCs leads to the development of BM-MNC-derived myocyte-like cells and regulates the expression of repair-related cytokines that facilitate repair following myocardial infarction [7]. However, there is some technical limitation to implement of preclinical methods in the routine clinical practice. The modest of these limitations are instability of transplanted autologous bone marrow cells and unexpected long-term efficacy associated with co-morbidities and age-related diseases.

To establish autologous bone marrow cell transplantation strategy for MI and ischemia-induced CHF, an implantation of autologous cryopreserved mononuclear cells (MNCs) from bone marrow retrogradely into the myocardium via the coronary vein might be performed. Therefore, the optimal time point of administration of BM-MNC is still uncertain. Indeed, in patients with ST-segment elevation MI and LV systolic dysfunction after successful reperfusion, intracoronary infusion of BM-MNC at either 5 to 7 days or 3 to 4 weeks after acute myocardial infarction did not improve LV function at 4-month follow-up [8]. Contrary, in animal studies transplantation of BM-MNC into myocardium with ischemic reperfusion injury increases capillary density and decreases infarction area [9, 10]. It has significantly beneficial effect on cardiac systolic function rather than on diastolic function due to effectively improve of collateral perfusion and regional function in hibernating ischemic myocardium by its ability to mainly supply angiogenic factors and cytokines [11, 12].

Our experience has been shown the positive impact of autologous transplantation of bone marrow MSCs for ischemia-induced CHF in old MI patients who were not eligible as candidates for reperfusion procedure within acute MI [13, 14]. We have found that intravenously used the previously prepared cell transplant induces the migration of cells into the damaged areas of myocardium. Therefore, there is large body of evidence regarding directed transdifferentiation of mononuclear cells into cardiomyocytes that leads to the formation of new myocardial tissue in the scar area. Clinical results demonstrate the efficacy of the intravenous administration of autologous MSCs in the treatment of
chronic heart failure of ischemic etiology, resulting in a significant increase in left ventricular (LV) ejection fraction (EF), decrease of LV end-diastolic volume and improving the quality of life among patients. Interestingly, that the effect of a single intravenous administration of autologous bone marrow MSCs applied to increase the left ventricular pump function for 3 or 4 months. Perhaps the use of autologous bone marrow MSCs in the treatment at a stage prior to direct revascularization (CABG, PCI) in patients with low LVEF (< 30%) in order to achieve eligibility to further revascularization procedures, as well as after direct revascularization in low LVEF patients continuing to improve the quality of life. Taken together, these results exhibit a positive impact of cellular therapy on myocardial contractile function in patients with ischemia-induced CHF.

Finally, there are evidences regarding efficacy of autologous MSCs transplantation of bone marrow in patients with CHD. This procedure is safe and well-tolerated that leads to the improvement of general and local myocardial contractility, to the normalization of diastolic filling, as well as increases perfusion infarction. Experience in the use of autologous bone marrow MSCs in patients with heart failure of ischemic etiology showed that their use is relatively safe and able to varying degrees to improve perfusion and / or myocardial contractility. Further studies are required to identify the exact mechanisms underlying an effect of autologous bone marrow MSCs and to allow full exploitation of its therapeutic potential in different time of points after MI.

References


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