

CXCR4-stem cell therapy in old myocardial infarction

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Abstract

For cell therapy on myocardial infarction, many kinds of cells have been studied. In our experience since 2001, the implant of mesenchyme stem cells CD34+ obtained from peripheral blood showed inconsistent improvement in the contractile function of infarcted myocardial tissue, but better survival in long term. For improved cell therapy, in 2014 we characterized the kind of cells that were mobilized to peripheral blood in patients with acute myocardial infarction, which were identified as a response of bone marrow to myocardial insult. In 2015, we began a clinical trial with CXCR4-stem cells and specific cells markers in patients with old myocardial infarction and reduced LVFE. Cells with specific markers were separated with immune-magnetic auto MACS Pro Separator machine and implanted on infarcted myocardial tissue guided by epicardial ultrasound.

Results: To the date we have evaluated 15 patients followed by 12 months, we observed a standardized respond in myocardial perfusion and LVEF at six months, as well as improvement in their functional class from NYHA III to I in all patients.

Conclusion: CXCR4-stem cells with specific cells markers improve the myocardial perfusion and contraction of left ventricle in patients with old myocardial infarction in a standardized way.

Myocardial infarction (MI) is the most common cause of heart failure and the most common cardiovascular disease worldwide. Obesity, low physical activity, and stresses, mostly known to be attributes of modern life styles, are the major contributors to cardiovascular diseases. From a pathological standpoint, necrosis in the heart tissue is the major sequel of an MI depending on whether transient or permanent ischemia occurs in this tissue. Notably, necrotic cell death of heart myocytes triggers an inflammatory response in the tissue due to release of pro-inflammatory cytokines and activation of the innate immune system.

C-X-C chemokine receptor type 4 (CXCR4) is the receptor of stromal cell-derived factor 1(SDF-1) and a critical factor for stem cell migration, implantation and survival. SDF-1 is one of the main chemokine's that is released in response to hypoxia and acts as a chemo-attracting factor to use of CXCR4-expressing cells to the site of ischemia. In fact, the SDF-1 chemokine and its receptor play an axial role in the development of normal cardiovascular system. They are key regulators of host defence pathways and migration of leukocytes. CXCR4 is expressed in many tissues including immune and central nervous systems, and on migrating leukocytes and hematopoietic progenitor cells in response to SDF 1. Some studies have shown that SDF1 and CXCR4 are noticeably up regulated in myositis shortly after MI and help optimize the situation for stem cell or heart tissue

transplantation by improving the viability of cardiac cells. So it is expected that MI can increase the expression of CXCR4 on the surface of peripheral blood leukocytes via increasing the secretion of SDF. Moreover it's expected at various time intervals after ischemia and reperfusion, expression of this receptor on the surface of white blood cells change and measuring the alterations in the expression of CXCR4 may be helpful in monitoring heart disease. The present study aims to provide new insight into the MI-associated gene alterations by exploring CXCR4 gene expression pattern following induced experimental MI in rats. We think that CXCR4 may be used as a monitoring marker for myocardial infarction.