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EDITORIAL

# Granulocyte Colony Stimulating Factor, Peripheral Blood Stem Cells and Bone Marrow Stem Cells for Cardiac Repair After Myocardial Infarction

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Granulocyte colony stimulating factor (G-CSF), which can mobilize bone marrow stem cells into peripheral blood, has been reported to repair cardiac tissues and improve post-infarct left ventricular (LV) remodeling and function.[1–3] It has been reported that stromal derived factor-1 (SDF-1) and its receptor chemokine receptor 4 (CXCR4) play important roles in the homing of stem cells,[4] and G-CSF enhances the SDF-1-CXCR4 axis and results in the mobilization, migration and homing of progenitor cells or stem cells from bone marrow to the infarcted sites.[5,6] Various mechanisms for the beneficial effects of G-CSF in the infarcted heart have been proposed: regeneration of myocardium,[1,2] acceleration of the healing process,[2] protection from apoptosis,[3] reduction of myocardial fibrosis,[2,7] and a direct cardioprotective effect.[8] Because of these effects, the use of G-CSF to repair the injured myocardium in patients with myocardial infarction has generated keen interest. Some clinical trials have supported the idea that G-CSF could be effective in patients with acute myocardial infarction with late reperfusion,[9–11] while others have not been able to reproduce the beneficial effects observed in experimental models.[12,13] That is, the results of clinical trials have been controversial,[14] and, if any, the effect is modest. On the other hand, peripheral blood stem cells (PBSCs) or bone marrow stem cells have also been considered to repair cardiac tissues and improve post-infarct LV remodeling and function in animals.[15–17] In clinical trials, there are controversies as to the outcome of cell therapies.[18–20] However, meta-analysis of cell-based clinical trials has revealed that intracoronary transplantation of PBSCs or bone marrow-derived stem cells in several recent trials is associated with increases in the LV ejection fraction (LVEF) and a reduction of LV end-systolic volumes, although these effects are modest.[21]

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Therefore, the results of clinical trials of G-CSF, intracoronary bone marrow stem cells or PBSCs highlight the need for elucidating other methods to achieve better therapeutic outcomes. One such method may be a combination of G-CSF and intracoronary bone marrow stem cells or PBSCs and modifying the administration method. Steinwender et al demonstrated that the combination of G-CSF therapy and a single transcoronary transplantation of CD34+ cells resulted in a significant increase in global LVEF and regional systolic wall motion after 6 months, but implied there was a high risk of increasing the in-stent restenosis rate.[22]

In this issue of the Journal, Gu et al[23] demonstrate that repeated intracoronary infusion of PBSCs plus mobilization of G-CSF may be an effective strategy option for treating patients with refractory congestive heart failure after myocardial infarction. In patients with a recent large myocardial infarction and a lower LVEF, repeated intracoronary infusion of PBSCs plus one dose of G-CSF improved LVEF significantly higher than in the group with a single infusion of PBSC and a G-CSF dose or the group with neither PBSCs nor G-CSF dose. No side effects were observed during the study and they conclude that repeated administration of combined PBSC therapy and G-CSF therapy is safe. Although this is a pilot and small-scale clinical trial, it is the first report of the effect of combining repeated intracoronary infusions of PBSCs and G-CSF on cardiac function and myocardial perfusion in patients with congestive heart failure after myocardial infarction, which is a safe and less invasive method for cardiac repair. Larger scaled, randomized, placebo-controlled clinical trials will be needed to confirm the efficacy of treating patients with refractory congestive heart failure after a recent large myocardial infarction.

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