REGENERATIVE CHANGES OF THE PERI-INFARCT INJURY ALLOWS SUSTAINED RESTORATION OF THE INJURED MYOCARDIUM

Poster Contributions
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Background: The human amniotic mesenchymal stem cells (hAMSCs) exhibit immunomodulatory, partially pluripotent, and precardiac properties. They express the c-kit cardiac progenitor marker and are readily reprogrammed to iPSCs (MiPSCs). Dual contrast manganese-enhanced MRI and delayed-enhanced MRI (MEMRI-DEMRI) has been developed to compare the cardiac regenerative effects of hAMSCs, c-kit+ hAMSCs, and MiPSCs.

Methods: SCID mice underwent LAD ligation and received 250,000 cells or normal saline. The mice were divided into 4 arms: (1) normal saline (control group, n=5), (2) hAMSC (n=6), (3) c-kit+ hAMSC group (n=4), and (4) MiPSC group (n=6). Cardiac MRI measured the scar, viable myocardium, peri-infarct region, and LVEF at weeks 1, 2, and 4. Bioluminescence imaging was also performed with luciferase reporter gene transduced stem cells. PCR was performed at the end of the study to assess the expression of fibrotic genes.

Results: The hAMSC group demonstrated significantly improved LVEF compared to control (26.9±3.8%* vs. 17.9±0.6%, *p<0.01) at 1 week. However, the improved LVEF was not significant by 4 weeks. This correlated with decreasing bioluminescence signal. The c-kit+ hAMSC and MiPSC groups demonstrated significant LVEF improvement compared to control throughout the study (28.2±3.3%* and 29.5±1.4%* vs. 16.1±0.6%, respectively, *p<0.05). However, only the MiPSC group demonstrated a sustained increase of the viable myocardium by MEMRI at week 4 (89.1±0.7%* vs. 74.5±1.7%, *p<0.01). The MiPSC group also demonstrated a significant decrease in the peri-infarct injury zone from 18.6±1.7% to 10.5±2.0% at week 4 (p<0.05) by MEMRI-DEMRI. In contrast, the control group did not show any significant decrease in peri-infarct injury. PCR analysis of the MiPSC group demonstrated a significant decrease in fibrotic genes, collagen 3 and TNF alpha, compared to the control group.

Conclusions: The MiPSCs demonstrate a significant and persistent improvement in LVEF, myocardial viability, and peri-infarct injury after myocardial infarct. These changes suggest myocardial regeneration as the mechanism for the sustained benefit.