Proceedings of German Society for Stem Cell Research (PGSSCR)

Stem cell chemoattractant gene expression was upregulated by intramyocardial injection of Epoetin-α in a rat myocardial infarction model

Klopsch C\textsuperscript{1,*}, Furlani D\textsuperscript{1,*}, Gabel R\textsuperscript{1}, Wagner K\textsuperscript{2}, Wang W\textsuperscript{1}, Ong LL\textsuperscript{1}, Li W\textsuperscript{1}, Nizze H\textsuperscript{3}, Titze U\textsuperscript{3}, Ma N\textsuperscript{1}, Steinhoff G\textsuperscript{1}

\textsuperscript{1}Department of Cardiac Surgery, University of Rostock, Rostock, Germany
\textsuperscript{2}Department of Anaesthesia, Klinikum Sudstadt, Rostock, Germany
\textsuperscript{3}Department of Pathology, University of Rostock, Rostock, Germany
*Both authors contributed equally to this work.
nanma001@med.uni-rostock.de

Emerging evidence suggests that Erythropoietin (EPO) protects the myocardium from ischemic injury and promotes beneficial remodelling. However, the role of EPO and its receptor (EPO-R) in mediating cardiac regeneration remains unclear. We hypothesise that stem cell homing and proliferation modulated by EPO could contribute to its cardio-protective effects. After permanent left ventricular myocardial infarction (MI), Epoetin-α (3000 U/kg) was injected along the infarction border. At six weeks after MI, cardiac functionality was measured by pressure-volume loops in left and right ventricles. Infarction size, angiogenesis and pathologic effects were evaluated. Gene expressions of EPO-R, SDF-1, CXCR-4, c-kit, eNOS, TNF-α, IL-8, Integrin-β and CdK4 were analyzed by RT-PCR at different time points of the first week (24h, 48h, 96h and 7 days). Our findings indicated improved left ventricular function both at baseline levels and under Dobutamine stress (dp/dt maximum and minimum, tau, cardiac output, stroke work, ejection fraction n=11-14, p<0.05) and decreased right ventricular wall stress (maximum and endystolic pressure n=5-8, p<0.05). Infarction size was reduced from 27.8±3.4% to 20.1±2.8% (n=6-8, p<0.01). Capillary density was enhanced from 257.7±24.5 to 338.5±35.9 (vessels per square mm, n=6-8, p<0.05). Mortality was decreased from 29.0% to 22.2% (n=53-69). No thrombosis was observed in the intramural myocardium. EPO-R was down regulated in infarcted, peri-infarcted and non infarcted areas at all time points (n=7, p<0.05). Cardiac SDF-1?, CXCR-4 and eNOS expressions were increased at 24 hours. C-kit was up regulated significantly at 48 hours compared to 24 hours in the EPO treated hearts. In untreated hearts, c-kit expression remained constant. Proinflammatory cytokines (TNF-α, IL-8 and Integrin-β)? were down regulated. Cell cycle re-entry marker (CdK4) was increased at 24 hours in non infarcted zones. In conclusion, we demonstrate intramyocardium Epoetin-α injection induces an earlier up regulation of stem cell chemoattractants, reduces inflammation, enhances angiogenesis and restores heart function after MI.