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EPO treatment after myocardial infarction in mice improves cardiac function by enhanced homing of bone marrow-derived cells


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Objective:

Bone marrow derived stem cells either transplanted or mobilised by cytokines improve cardiac function after myocardial infarction (MI). Besides of its classical function in erythropoiesis recent reports have shown additional effects of EPO like antiapoptotic effects and stem cell mobilisation. These effects are known to improve myocardial regeneration after MI. Therefore, we analysed in a murine model of surgically induced MI the influence of EPO treatment on survival, functional parameters as well as stem cell mobilisation and homing.

Methods: Human EPO (3000 IE/kg) was injected intraperitoneally immediately after ligation of the left anterior descendens (LAD) as well as on the two consecutive days (1000 IE/kg) ? a dose which did not significantly affect erythropoiesis. 6 and 30 days after the surgical procedure, pressure volume relationships were investigated in vivo. Cardiac tissues were further analysed by histology. To show the impact on stem cell mobilisation and homing as well as serum cytokine levels FACS and ELISA was performed.

Results:

EPO treated animals showed a significant improvement of survival post MI (62% vs. 36%). FACS data demonstrated mobilisation of CD31, c-kit and Sca-1 positive stem cells and homing of Sca-1 and CXCR4 positive stem cells was enhanced after EPO treatment. Serum levels of G-CSF were significantly increased after EPO administration, whereas SDF-1 levels were decreased and VEGF remained unchanged. Histology of EPO treated hearts showed less reduction of LV wall thickness and a smaller size of infarction at day 30 (22% vs. 42%). In addition, myocardial function of PTH treated mice was improved (EF: 23% vs. 15%) and elasticity demonstrated a less degree of infarct remodelling (Elasticity: 21.0 mmHg/µl vs. 8.1 mmHg/µl).

Conclusion:

We have shown that EPO application after MI ameliorates myocardial function. This may be explained - beside direct effects via the EPO receptor - by mobilisation and homing of bone marrow-derived stem cells and a change in the serum cytokine pattern, which may lead to improved neovascularization and cell survival.
Therefore, EPO treatment presents a promising non-invasive approach to ameliorate heart failure post MI.