G-CSF dependent stem cell mobilization does not influence the cardioprotective effects of PTH after myocardial infarction

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Abstract

Aims:

PTH administration after myocardial infarction (MI) is known to attenuate myocardial function, survival and cardiac remodeling. These effects mainly resulted from an increase of mobilization and homing of CD34+/CD45+ stem cells into the ischemic myocardium. PTH related stem cell mobilization was shown to be related to an endogenous G-CSF release. The aim of our study is to determine the role of G-CSF on the cardioprotective effects of PTH.

Methods:

G-CSF +/+ (C57BL/6) and G-CSF -/- mice were treated with PTH (80 µg/kg/d) for 6 days after inducing a MI by LAD ligation. The myocardial homing factor SDF-1 was analyzed on day 2 with ELISA. Stem cell populations in peripheral blood and heart were examined on day 6 by FACS. Cardiac function and immuhistochemistry were investigated on day 6 and day 30.

Results:

PTH treatment resulted in a significant increase of CD45+/CD34+ cells in peripheral blood in G-CSF +/+ , but not in G-CSF -/- mice. However, a significant increase of SDF-1 and enhanced migration of CD45+/CD34+ cells into the ischemic myocardium was revealed after PTH administration in both, G- G-CSF +/+ and G-CSF -/- mice. Enhanced stem cell homing was associated with an ameliorated cardiac function and post-MI survival after PTH treatment. Furthermore, infarct size, wall thickness and neovascularisation showed a significant improvement in both groups 30 days after MI.

Conclusion:

The cardioprotective effects of PTH could be shown to be independent from endogenous G-CSF release and therefore from stem cell mobilization. This puts more emphasis on the role of stem cell homing into the ischemic myocardium.