Abstract: P110

Effect of MMP-2 on compromised homing of intracoronary delivery of mesenchymal stem cell in a porcine reperfused myocardial infarction: comparison with intramyocardial cell delivery

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Background. Intracoronary injection of mesenchymal stem cells (MSC) results in a prompt decrease of absolute myocardial blood flow (AMF) with late and incomplete recovery of myocardial tissue perfusion, therefore it leads to less homing with consequent diminished regenerative effect of the ischemic injured heart tissue compared to intramyocardial (IM) cell implantation. We investigated the effect of AMF on the fate and homing of MSC after intracoronary or intramyocardial cell delivery in a closed-chest reperfused myocardial infarction (MI) in pigs.

Methods. One week after myocardial infarction, porcine GFP-Luc-MSCs were injected either intracoronary (group IC) or intramyocardially (group IM). AMF was measured before, immediately after, and 24h post cell delivery. In vitro bioluminescence signal was used to identify tissue samples containing GFP-Luc-MSCs. Myocardial tissue matrix metalloproteinase 2 (MMP2) (index of ischemic/oxidative stress) and CXCR4 receptor expression (index of homing signal) were measured in bioluminescence positive and negative myocardial areas one day post cell transfer. Biodistribution of the implanted cells was quantified by using Luciferase assay and confirmed by fluorescence immunochemistry. Global left ventricular ejection fraction (LVEF) was measured at baseline and one month post cell therapy using MRI.

Results. AMF decreased immediately after intracoronary cell delivery, while no change in tissue perfusion was found in the IM group. Intracoronary delivery led to a significant increase in myocardial MMP2 expression and decreased expression of CXCR4. Fluorescence immunochemistry indicated a higher expression level of a variety of homing (tenascin and cadherin) and angiogenic factor (FGF-2 and VEGF) in the IM group. LVEF increase was also significantly higher in IM group at the 1-month follow up.

Conclusions. Intracoronary stem cell delivery decreased AMF, increased myocardial expression of MMP2, and lead to reduced CXCR4 expression with enhanced biodistribution and diminished functional recovery post-infarction.