ROUVASTATIN ENHANCES VIABILITY OF ADIPOSE- DERIVED MESENCHYMAL STEM CELLS TRANSPLANTED IN POST-INFARCTED MICE HEARTS

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Objectives

The aim of this study was to investigate whether rosuvastatin improved survival of adipose-derived mesenchymal stem cells (AD-MSCs) after transplantation into infarcted hearts.

Methods

AD-MSCs were isolated from transgenic mice, which were created on the FVB background to constitutively express firefly luciferase and enhanced green fluorescence protein (Fluc-eGFP). Myocardial infarction was created in inbred mice by coronary ligation, AD-MSCs were transplanted into the hearts of MI mice and Rosuvastatin or vehicle (saline) was administered by gavage. Transplanted ASCs were tracked by longitudinal in vivo bioluminescence imaging (BLI). Three-weeks after transplantation, cardiac function and structure were evaluated by serial echocardiography and histology. For mimic the ischaemic environment, AD-MSCs were subjected to hypoxia and serum deprivation (H/SD) injury in vitro. AD-MSCs survival and proliferation were assessed by BLI and MTT assays. Cells apoptosis was determined by TUNEL staining and caspase 3 activity assay. The expressions of Akt, phosphorylated Akt (pAkt), ERK1/2 and phosphorylated ERK1/2 (p ERK1/2) were detected by Western blot.

Results

In vivo, BLI indicated that rosuvastatin enhanced the survival of engrafted AD-MSCs at day 7 and 14 after cell transplantation. Furthermore, combined therapy of AD-MSCs and rosuvastatin preserved heart function, reduced fibrosis, decreased apoptotic cardiomyocytes. In vitro, the results showed that rosuvastatin (10^{-8} mmol/l) enhanced the viability of AD-MSCs and decreased their apoptotic rate. Western blot revealed that rosuvastatin supplementation increased Akt and ERK phosphorylation significantly and that this effect was abolished by addition of the PI3K inhibitor LY294002 and the MEK1/2 inhibitor U0126.

Conclusions

Combination therapy with rosuvastatin and AD-MSCs has a synergetic effect on improving myocardial function after infarction. The possible mechanism of rosuvastatin improve the survival of engrafted AD-MSCs in infarcted hearts may be associated with the PI3k/Akt and ERK1/2 signalling pathways.