ACC.15
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A961
JACC March 17, 2015
Volume 65, Issue 10S

Heart Failure and Cardiomyopathies

DOSE-DEPENDENT EFFECTS OF INTRACORONARY CARDIAC STEM CELLS IN RATS WITH ACUTE MYOCARDIAL INFARCTION

Poster Contributions
Poster Hall B1
Sunday, March 15, 2015, 3:45 p.m.-4:30 p.m.

Session Title: Fibrosis, Hypertrophy and Regeneration
Abstract Category: 15. Heart Failure and Cardiomyopathies: Therapy
Presentation Number: 1216-184

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Background: Intracoronary kit+ cardiac stem cells (CSCs) delivery preserves LV function and structure after myocardial infarction (MI). The CSC dose for optimal cardiac repair is unknown, thus CSC dose-response studies were performed.

Methods: PBS (vehicle) or syngeneic CSCs at 0.3, 0.75, 1.5, 3.0, and 6.0 x 106 (M) cells/ rat were given intracoronarily after 4 h of reperfusion following a 90 minute coronary occlusion. LV function, morphology, immunohistochemistry, and proliferation were assessed 35 days later.

Results: The 6.0 M group had significantly higher post-procedural mortality (Fig. A). Echocardiography showed ejection fraction (EF), infarct wall thickening fraction (IW ThF), and LV end-systolic volume (LVESV) were improved significantly in the 4 groups of rats that received CSCs at doses of 0.75 M CSCs and higher, but not in those that received PBS or 0.3 M CSCs (Fig. B). Similarly, hemodynamic studies revealed LV dP/dtmax, preload adjusted maximal power (PAMP), end-systolic elastance (Ees), and preload recruitable stroke work (PRSW) were significantly improved in the 4 higher dose groups, but not in the PBS or low dose group (Fig. C). CSC doses of 0.75 M or greater decreased infarct size, increased risk region viable myocardium, reduced collagen content and apotosis, and increased myocye proliferation.

Conclusion: Our data suggests CSCs dose-dependently improve LV function and structure where a minimum of 0.75 M CSCs is required to exert therapeutic effects. Very high doses could be harmful.