

PRECLINICAL STUDY IN A PORCINE MODEL OF ACUTE MYOCARDIAL INFARCTION

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Objectives Induced pluripotent stem (iPS) cells, a novel embryonic stem cell-like pluripotent stem cell, have potential to differentiate into different cardiovascular cells and repair the injured heart. The potential therapeutic benefits of iPS cells based treatment have been established in small-animal models of myocardial infarction, but the intramyocardial injection of iPS cells has not been assessed in large animals. So this study was to evaluate the feasibility and efficacy of intramyocardial injection of iPS cells for cellular therapy in a porcine model of acute myocardial infarction (AMI).

Methods Allogeneic undifferentiated iPS cells or phosphate buffered saline (PBS) were injected into the ischaemic myocardium induced by 90 min occlusion of left anterior descending (LAD) artery in a porcine model. The cardiac function, myocardial perfusion, cell differentiation, fibrosis and tumorigenesis were investigated.

Results One week after iPS or PBS delivery, global left ventricular ejection fraction (LVEF) decreased significantly in both iPS group and PBS group compared with Sham group ($p < 0.05$, respectively). Six weeks after iPS or PBS delivery, the LVEF of the iPS group improved significantly compared with the PBS group (56.68% vs 50.93%, $p = 0.04$) but still lower than Sham group. Likewise, the iPS transplantation improved regional perfusion compared with the PBS injection (19.67% vs 13.67%, $p = 0.02$). The infarct area was significantly smaller in the iPS group than PBS group (12.04% vs 15.98% $p = 0.01$). iPS cells engrafted into myocardium can differentiate into vessel cells and cardiomyocytes, which result in promotion of the neovascularisation in ischaemic zone and border zone. No tumours were detected in all pigs for any of the major organs (heart, lung, liver, spleen or kidney) after the morphologic and histopathology examination up to months after iPS transplantation.

Conclusions This study shows that direct intramyocardial injection of iPS cell can decrease infarct size, improve left ventricular function and perfusion for an immunosuppressed porcine AMI model. iPS cells may have the potential to be used in the treatments of ischaemic heart diseases.

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INTRAMYOCARDIAL INJECTION OF INDUCED PLURIPOTENT STEM CELLS IMPROVES LEFT VENTRICULAR FUNCTION AND PERFUSION: A