e0145 STUDY OF MRI IN TRACKING MAGNETICALLY LABELLED MESENCHYMAL STEM CELLS

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Objective To investigate the potential ability of MRI in tracking magnetically labelled mesenchymal stem cells (MR-MSCs) in a swine myocardial infarction (MI) model.
Methods Adult Chinese mini pigs (n=6) were subjected to open-chest experimental MI. Their autogeneic bone marrow-derived mesenchymal stem cells (MSCs) was cultured and doubly labled with ferumoxides and DAPI. At the 14th day after MI, labelled MSCs were injected intramyocardially into peri-infarct zone and normal myocardium. At the 14th day after MSCs transplantation, the size and location of the myocardial infarction were assessed by using delayed-enhancement MRI (DE-MRI). The contrast and the volume of the MR-MSCs hypointense lesion from the FGRE images were acquired. At 24 and 3 weeks after injection, the contrast was determined using the difference in signal intensity between the hypointense and normal myocardium divided by signal intensity of the normal region. After humane euthanasia, the heart was excised and histology corresponding to MRI slices that demonstrated MR-MSCs lesions was performed.
Results At the 14th day after MSCs transplantation, DE-MRI showed the infarct in all animals and the mean infarction size was (33.60±9.80)% of the left ventricular area. At 24 h after injection, the contrast and the size of the lesions showed no statistical difference between in peri-infarct zone and in normal myocardium. At 3 weeks after injection, the contrast of the lesions in peri-infarct zone decreased rapidly than that in normal myocardium (26.88±7.27 vs 15.00±4.51, p=0.0003). Post mortem analysis showed that fluorescently labelled MSCs were demonstrated on histological sections. There were much more dense fluorescently labled MSCs per high power fields in injection sites of normal myocardium than in injection sites of peri-infarct zone (106±25/HPF vs 143±31/HPF, p=0.0293). At 3 weeks, there was less fibrosis in MSCs injection sites with more surviving myocardium. In MSCs injection sites of the peri-infarct zone, the capillary density was significantly more than that in control sites (13.40±4.00/HPF vs 9.40±3.10/HPF, p=0.0229).
Conclusions MRI of MSCs is feasible and represents a method for noninvasively tracking the quantity and location of intramyocardial delivery after MI. But to semi-quantitatively analyse the development of transplanted MSCs by MRI is not dependable.

e0146 ALTERED EXPRESSION OF ADAMTS-1 AND ITS INHIBITOR IN RATS WITH CHRONIC HEART FAILURE INDUCED BY ADRIAMYCIN

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Purpose The clinical progression of chronic heart failure (CHF) is largely determined by ventricular remodelling, which involves cellular and extracellular matrix disruption. A disintegrin and metalloproteinase with thrombospondin motifs-1 (ADAMTS-1) is known to regulate cell-cell and cell-matrix interactions, and may thereby influence cardiac structure. The present study was undertaken to investigate the expression of ADAMTS-1 and its endogenous inhibitor, tissue inhibitor of metalloproteinases-3 (TIMP-3), in rats with CHF.
Methods 60 healthy male Wistar rats were randomly divided into a control group (n=30) and a CHF group (n=30). Adriamycin was administered intraperitoneally (2.5 mg/kg each week) to rats in the CHF group for 6 weeks. Rats in the control group received saline in the same regimen with adriamycin treatment. Animals in both groups were observed for 4 weeks after the last injection for general appearance, behaviour, and mortality. Before and 10 weeks after initiating the study, body weight (BW), left ventricular weight (LVW), and LVW/BW were measured; left ventricular end diastolic diameter (LVEDD), left ventricular ejection fraction (LVEF), and fractional shortening (FS) were assessed; and left ventricular systolic pressure (LVSP), left ventricular end diastolic pressure (LVEDP), and maximum rates of rise and fall of left ventricular pressure ($\pm dp/dt_{max}$) were recorded. 10 weeks after the study started, pathohistological and ultrastructural changes in ventricular tissue were examined by light and electron microscopy. Collagen volume fraction (CVF) and apoptotic index were analysed by Masson staining and TUNEL assay, respectively. Levels of ADAMTS-1, Syndecan-4, and TIMP-3 were evaluated using immunohistochemistry and western blot, respectively.
Results After the adriamycin treatment, BW in the CHF group was slowly increased, while LVW was quickly increased, resulting in a higher LVW/BW than that in the control group ($p<0.01$). Compared with the control group, LVEF, FS, LVSP, and $\pm dP/dt_{max}$ were reduced in the CHF group ($p<0.05$), whereas LVEDD and LVEDP were augmented ($p<0.01$). There was a significant increase in myolysis, fibrosis, and apoptosis in the CHF group ($p<0.01$). The protein expression of ADAMTS-1 and Syndecan-4 was dramatically up-regulated in the CHF group ($p<0.01$), and that of TIMP-3 was down-regulated compared to those in the control group ($p<0.05$). In addition, there was a positive correlation between the protein expression of ADAMTS-1 and LVEDD in both groups ($r=0.804$, $p<0.01$).
Conclusion Along with decreased TIMP-3, ADAMTS-1 is over-expressed in the ventricle of CHF rats and is associated with ventricular remodelling via cleaving the ectodomain of Syndecan-4. Therefore, ADAMTS-1 may provide a new therapeutic target in the prevention and treatment of ventricular remodelling in CHF.

e0147 MECHANISM OF DIFFERENT ACTIVATORS OF PPARαREGULATING PLASMINOGEN ACTIVATOR INHIBITOR-1 EXPRESSION

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Objective To observe the effects of fenofibrate and linoleic acid which was the different activators of PPARα on the expression of PAI-1 and PPARα in HepG2 cells. To investigate the relationship and mechanisms between the promoter and expression of PAI-1 that how the fenofibrate and linoleic acid to act on PAI-1. And to observe if PPARα involved in this procession.
Methods HepG2 cells were exposed to fenofibrate and linoleic acid in varying concentrations, RT-PCR was used to determine the mRNA expression of PAI-1 and PPARα. Several luciferase reporter gene recombinant plasmid containing different length sequences of human PAI-1 gene promoter from −804 to +17bp were constructed and transiently transfected into HepG2 cells. At the same time, co-transfected with PPARα-pSG5 expression plasmid, then different stimulating factors were added to induce the transfected cells. Transcriptional activity of PAI-1 was demonstrated by the measure of luciferase activity.
Results 1. Fenofibrate could remarkably decreased PAI-1 mRNA expression in HepG2 cells ($p<0.05$ or $p<0.01$), but linoleic acid could significant increased PAI-1 mRNA level ($p<0.05$ or $p<0.01$), and they were all in a concentration-dependent manner. 2. Fenofibrate and linoleic acid could raise the mRNA level of PPARα ($p<0.05$ or