Endovascular induction of a chronic heart failure model in swine: Feasibility study and evaluation using magnetic resonance imaging

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Purpose: The aim of this study was to develop an easy-to-induce, reproducible and low mortality clinically relevant closed chest model of chronic myocardial infarction in swine that could be useful in the preclinical evaluation of regenerative therapies.

Materials and Methods: 19 swine weighing 40.9±10.48kg were used for this study. Under general anesthesia, 3–4ml of ethanol were injected in the left anterior descending coronary artery through an inflated PTCA balloon. Animals were randomly divided into 3 groups (n=5) and euthanized at different times (Days 7, 30 and 90). MR was performed in all surviving animals immediately before and after induction, and on days 7, 30 and 90. Pathological examination of the explanted hearts at each timepoint was performed, including planimetry for infarct area calculation.

Results: Total mortality was 21% (4 pigs died during infarction). Postoperative MR revealed compromised contractility and significantly decreased Ejection Fraction (EF p=0.001) that decreased further over time (p<0.05). Left ventricular remodelling, with thinning of the infarcted area, was also seen. The EF and % of infarct at each follow-up are shown in the Table. A significant positive correlation was seen between MR- and planimetry-measured infarcts.

On day 7 pathology showed a well defined hemorrhagic area exhibiting coagulation necrosis; on day 30 a thinning of the LV wall was evident and pathology revealed increased collagen content, consistent with fibrous scar formation. Some preserved conduction system cells were evidenced at the subendocardial level. On day 90 the infarcted zones could be easily identified as very thin yellowish areas exhibiting a highly organized appearance with collagen fibers. Conduction cells were also preserved.

Conclusion: Intracoronary ethanol administration consistently results in a transmural infarct, with a mortality analogous to those obtained with other techniques. The sustained decrease in EF and myocardial thinning over time indicate that the model may be useful for testing therapeutic approaches to chronic heart failure.
Dodecafluoropentane emulsion decreases infarct volume in a rabbit ischemic stroke model

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Purpose: Dodecafluoropentane emulsion (DDFPe) has been demonstrated to absorb and transport very high levels of oxygen in vitro and in vivo (1). DDFPe has the potential to protect organs during diverse hypoxic crises including massive hemorrhage, heart attack, cardiac and vascular surgery, coronary and carotid interventions, and stroke. In stroke, tPA must be produced the largest ablation zone.

Materials and Methods: New Zealand White rabbits (n=28; 5.2±0.07 kg) received angiography. Three embolic spheres (diameter = 700–900 μm) were injected into the internal carotid artery occluding its branches. Those with only middle cerebral artery and anterior cerebral artery occlusions were accepted for testing. Rabbits were randomly assigned to groups: 1) control (n=7), 2) immediate DDFPe (n=8), 3) DDFPe at 30 minutes (n=6), 4) DDFPe at 60 minutes (n=7). Control rabbits were embolized without treatment. DDFPe dose was two 2% w/v DDFPe intravenous injections, 0.6 mL/kg, the first at the designated time and the second 90 minutes later. Following euthanasia at 4 hours infarct volume was determined using vital stains on brain sections.

Results: Percent infarct volume means decreased for all groups (2=0.66±0.74%, p=0.013; 3=0.58±0.85%, p=0.017; 4=1.03±0.79%, p=0.032) compared with controls (3.57±0.79%).

Conclusion: Intravenous DDFPe decreases infarct volumes and protects ischemic brain from hypoxia. This apparently is due to improved oxygen transport in spite of complete and permanent vessel occlusion. Clinical development may be much broader than these applications and is urgently needed.

Reference