A SALINE-BASED THERAPEUTIC CONTAINING CHARGE-STABILIZED NANOSTRUCTURES PROTECTS AGAINST CARDIAC ISCHEMIA/REPERFUSION INJURY

Oral Contributions
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Background: Inflammation contributes to reperfusion injury after acute myocardial infarction (AMI). RNS60 is an isotonic saline solution containing charged-stabilized nanostructures introduced by Taylor-Couette Poiseuille flow in the presence of oxygen. RNS60 has shown anti-inflammatory and cytoprotective effects in models of neuroinflammation and pulmonary inflammation, and is currently under evaluation in a phase I clinical study for asthma.

Objective: To test the hypothesis that RNS60 reduces tissue damage after acute myocardial infarction, we conducted studies in a porcine model of myocardial ischemia/reperfusion.

Methods: Male pigs (25-35 kg) were subjected to myocardial ischemia for 60 or 90 minutes and treated with RNS60 or normal saline (NS) by single intracoronary injection (0.1 mL/kg) at reperfusion and by continuous intravenous infusion (1.0 mL/kg/hour) following reperfusion. Animals were sacrificed on day 2 or day 4, and the size of the infarct area was measured after staining with Evans Blue and triphenyltetrazolium chloride (TTC). Apoptosis in the peri-infarct region was measured by counting caspase 3-positive cells.

Results: Ischemia for 60 minutes followed by reperfusion for 4 days caused infarcts measuring 44% ± 6% of the area at risk (AAR) in NS-treated animals (n=14). RNS60 treatment reduced the infarct size by 32 % (n=13, P<0.001). In addition, the number of caspase 3-positive cells was significantly reduced in the RNS60 group compared to controls (17% reduction, P<0.05). Ischemia for 90 minutes caused infarcts measuring 61% ± 5% of the AAR in the NS group (n=8), and RNS60 still achieved a consistent, non-significant trend towards reduced infarct size (12% reduction, n=8, P=0.098). Furthermore, RNS60 treatment in this study resulted in a survival benefit. Only 1 out of 9 (11%) animals died in the RNS60 group compared to 6 out of 14 (46%) enrolled into the control group.

Conclusion: The ability of a saline-based therapeutic containing charge-stabilized nanostructures to reduce ischemia/reperfusion injury suggests novel possibilities to develop therapeutics that limit cardiac damage after coronary revascularization procedures.