Cardioprotective Effects of Xenon-loaded Echogenic Liposomes in Acute Myocardial Infarction (AMI) Rat Models

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Abstract

Background: We have developed Xe-containing echogenic liposomes (Xe-ELIP). Using this delivery agent, we have demonstrated neuroprotective effects in myocardial infarctions remodeling in a rat AMI model.. The goal of this study was to evaluate the neuroprotective effects of Xe-ELIP on early treatment of ischemic heart injury caused by a lack of blood to the heart in association with muscle damage, or myocardial infarctions.

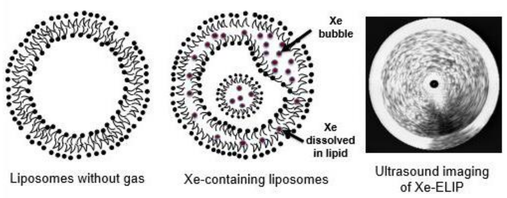
Methods: Echogenic air-encapsulated and Xenon-encapsulated liposomes are created. Echogenicity of the liposomes is measured and calculated through use of a catheter and computer programs. In-vivo experimentation on rat models is performed to deliver the liposomes, and infarction percentage is measured and compared through imaging and analyzing stained heart slices.

Results: The composition analysis and percentages of afflicted to healthy cardiovascular cells of specimens treated with Xe-ELIP most closely resembled the AMI sham (healthy specimen that did not experience myocardial infarction). Xe-ELIP administration prior to myocardial infarction reduced the myocardial infarct (MI) size as well as improved the cardiac function.

Conclusions: Xe-ELIP alleviates early myocardial infarction, reduces infarct size, and improves cardiac function. This novel delivery approach, using Xe-ELIP with ultrasound-controlled cerebral drug release, provides a relatively noninvasive strategy for therapeutic gas delivery.

Introduction

- Acute myocardial infarctions, commonly known as heart attacks, are the leading causes of heart-related deaths worldwide. These heart problems are caused by myocardial ischemia, which is a shortage of blood supply running through the heart.
- The reduced capacity of blood pumped from the left ventricle disrupts blood perfusion and degrades the overall wellness of the body.
- The noble gas Xenon has been shown to have beneficial effects on the heart in small doses, but it is expensive and must be directly delivered Xenon is also non-toxic and almost entirely free from harmful side effects.



- Echogenic liposomes reflect waves and return echoes from the air pockets within the liposome. They are used to deliver drug-encapsulated liposomes to various body. By replacing the air pockets with gaseous or liquid drugs, treatment can be delivered efficiently.

Hypothesis

When the pockets of air within echogenic liposomes are injected with the noble gas Xenon, these Xenon loaded echogenic liposomes (Xe-ELIP) will keep similar properties that will allow drug-encapsulated delivery to the heart. This will then prevent inadequate blood supply to the heart and restore heart homeostasis.

Methods and Procedures

- Make drug-loaded echogenic liposome
  - Produce the lipid film
  - Prepare liposome for lyophilization
  - Remove sample from lyophilizer and resuspend
- Collect echogenicity data of ELIP-Air and ELIP-Xenon
  - Prepare different dilutions of each liposome (50x, 100x, 200x, 400x, 800x)
  - Use a catheter computer to record 10 seconds of optimal positioning of the catheter when it produces a solid white circle on the perimeter
  - Repeat three times for each concentration for both ELIP-air and ELIP-Xe
- Capture echogenicity
  - Using the program Snappy, take screenshots of each concentration when the white circular perimeter is held most steady
- Analyze echogenicity
  - Using the program ImagePro-Plus, outline the areas of high echogenicity
  - Right-click and select the 'mean' for echogenicity value
  - Record echogenicity values in a spreadsheet and create a graph that compares the trend for both ELIP-air and ELIP-Xe
- In-Vivo experimentation and analysis
  - Xenon encapsulated liposomes are injected into unconscious and anesthetized rats through open-heart surgery
  - Hearts were removed for analysis
  - The hearts are cut into 2 mm slices and stained to emphasize the infarction areas in white
  - High quality images are taken for further analysis
- Comparison of infarction percentages
  - Using the program ImageJ, the volume of infarction is divided by the total volume of the heart to calculate the percentage of infarction
  - The infarction percentages of each group is collected

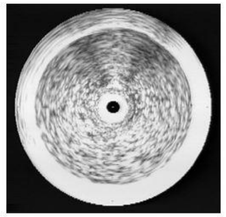


Figure 1. Peg-ELIP Air (200x).

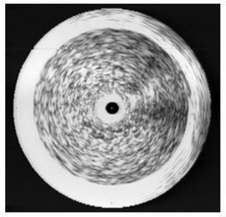
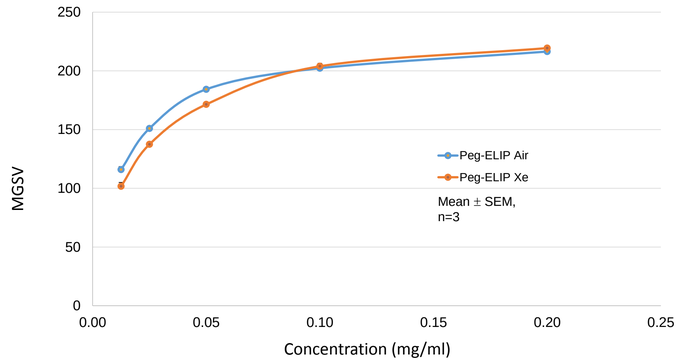


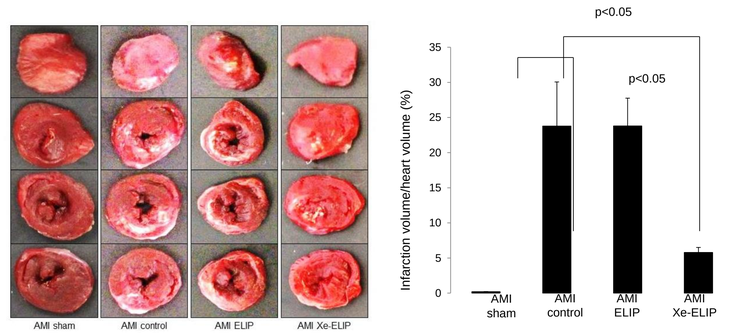
Figure 2. Peg-ELIP Xenon (200x).

Results

Echogenicity Analysis of Peg-ELIP Air *vs.* Peg-ELIP Xenon



Peg-ELIP Xenon Reduced Infarct Size in Rat AMI Model



Conclusions

The composition analysis and percentages of afflicted to healthy cardiovascular cells of specimens treated with Xe-ELIP most closely resembled the AMI sham (healthy specimen that did not experience myocardial infarction). Xe-ELIP administration prior to myocardial infarction reduced the myocardial infarct (MI) size as well as improved the cardiac function. The addition of Xenon played a role in decreasing the post-infarction cardiac contractility and prevented greater ventricular damage that may have resulted from MI. Our hypothesis is supported by our results as there is a significant correlation between the presence of Xenon and the therapeutic restoration of heart homeostasis following an acute myocardial infarction.

Contact

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