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Image-Guided Hydrogen Gas Delivery for Protection from Myocardial Ischemia-Reperfusion Injury via Microbubbles

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Abstract

Cardiomyocyte death induced by ischemia-reperfusion is a major cause of morbidity and mortality worldwide. Hydrogen (H_2), as an antioxidant, has been shown to have great potential in preventive and therapeutic applications against lethal injury that occurs from ischemia-reperfusion. However, H_2 is sparingly soluble in water, resulting in its poor bioavailability in blood and damaged tissues. Here, we have developed an ultrasound-visible H_2 delivery system by loading H_2 inside microbubbles (H_2-MBs) to prevent myocardial ischemia-reperfusion injury. Using this system, the concentration of H_2 in unit volume can be greatly improved under normal temperature and pressure conditions. H_2-MBs can be visually tracked with ultrasound imaging systems and can effectively release their therapeutic gas. In vivo systemic delivery of H_2-MBs in myocardial ischemic rats at the start of reperfusion resulted in a significant reduction of infarct size and pathological remodeling. Further analysis showed that this approach markedly inhibited cardiomyocyte apoptosis and reduced myocardial inflammation and oxidant damage in myocardial ischemia-reperfusion rats. These results indicate that H_2-MBs are a promising visual delivery system for H_2-based therapeutic applications.

Keywords: Hydrogen gas; drug delivery; microbubbles; myocardial ischemia−reperfusion injury; ultrasound imaging.

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