Microbubbles improve myocardial remodelling after infarction

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German scientists from the Bonn University Hospital successfully tested a method in mice allowing the morphological and functional sequelae of a myocardial infarction to be reduced. Tiny gas bubbles are made to oscillate within the heart via focused ultrasound - this improves microcirculation and decreases the size of the scar tissue. The results show that the mice, following myocardial infarction, have improved cardiac output as a result of this method, as compared to untreated animals.

The study is now being presented in the professional journal *PLOS ONE*.

Every year in Germany, approximately 280,000 people suffer a myocardial infarction; more than 52,000 die as a result. Due to an occluded vessel, parts of the heart muscle no longer have sufficient circulation and the tissue dies off. These regions are not replaced by new heart muscle cells but instead by scar tissue – this generally causes the pump function of the heart to decrease following an infarction. Scientists from the Bonn University Hospital have now successfully tested a new method on mice with which scar tissue can be reduced and cardiac output increased.

Microbubbles are made to oscillate within the heart

"There are attempts to treat the scar tissue with gene therapy or stem cells - by contrast, we have chosen a physical approach to treatment,"

reports Adj. Professor Dr. med. Alexander Ghanem from the Department of Cardiology of the Bonn University Hospital. The researchers injected a total of 17 mice which had previously had a myocardial infarction with microscopically small, gas-filled bubbles in the bloodstream. Once the microbubbles reached the heart, they were made to vibrate there using focused ultrasound. "Through this mechanical stimulation, the circulation of the area of the infarction is improved - and the scar shrinks," says the cardiac specialist.

Treated animals demonstrate ameliorated post-infarction remodelling

The scientists compared the results of the mice treated with the microbubbles to those of a control group. Two weeks after the myocardial infarction, there was expected worsening of heart function in the control group due to the maturing of the scar tissue. In contrast, the mice treated with the microbubbles did not develop any cardiac insufficiency. Jonas Dörner, the first author of the study, summarizes the results: "The pumping function was significantly better in the treated animals as compared to the control group; there was also a significantly smaller amount of decayed heart muscle tissue." Along with the Department of Cardiology, the Departments of Cardiac Surgery and Anesthesiology and the Institute of Physiology took part in the investigations.

Ultrasound treatment stimulates growth hormones

The scientists sought the causes of the positive treatment success which is, however, unexplained to date. Following ultrasound treatment of the mice, it was demonstrated that the amount of the body's own growth hormones significantly increased in the heart. "This is evidently the reason why the scar formation decreased as a result of the oscillating

microbubbles," says Dr. Ghanem. The scientists now hope that humans will also be able to eventually be treated with the microbubble-ultrasound method, however further investigations are still needed. "Potentially, all patients who have had an acute myocardial infarction are eligible for this follow-up treatment," explains the cardiologist of the Bonn University Hospital. Interestingly, microbubbles are already used as a diagnostic contrast agent.

Patent for novel ultrasound method filed

The study, conducted with support from the BONFOR funding program of the Medical Faculty of Bonn University and the German Heart Foundation [Deutsche Herzstiftung e.V.], gave rise to a patent application. "Together with the company Philips Medical, we developed a novel ultrasonic probe which enables a standardized impulse discharge in the heart," reports the cardiologist. The special feature is that two ultrasound sources linked together are contained in one hybrid ultrasonic probe: one with low frequency for the focused stimulation of the microbubbles in the target organ and one with higher frequency for imaging. In this way, it can be very precisely determined where the scar tissue and the microbubbles are located. "This study demonstrates again that university research inspires technological developments in medicine," says Dr. Ghanem.

More information: Ultrasound-mediated stimulation of microbubbles after acute myocardial infarction and reperfusion ameliorates left-ventricular remodelling in mice via improvement of borderzone vascularisation, *PLOS ONE*, DOI: 10.1371/journal.pone.0056841

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