Study reveals first six months best for stimulating heart growth

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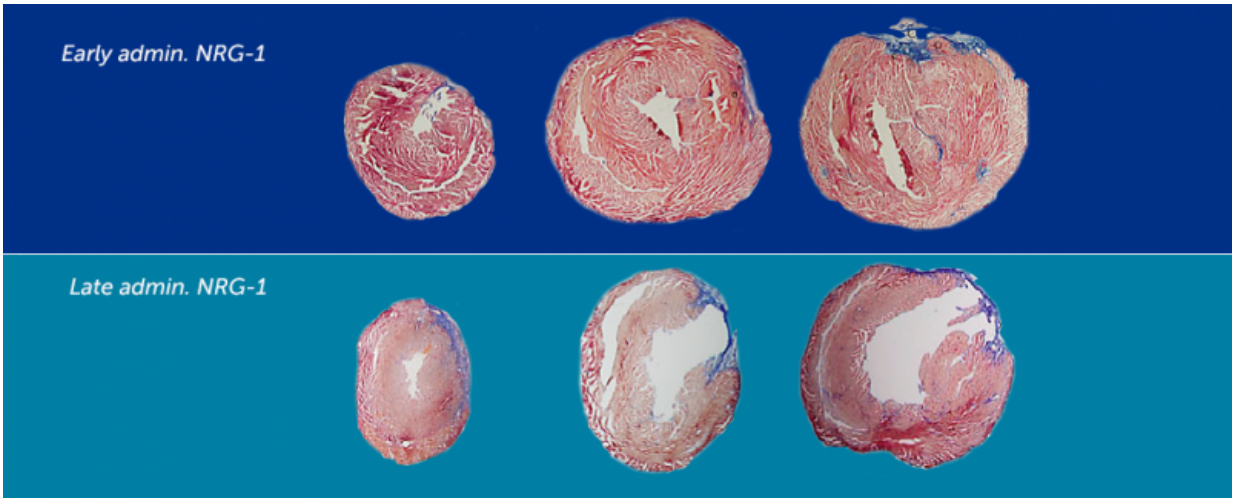

In these sample sections of mouse heart, the color blue signifies scar tissue. Damage from scarring was minimized by early administration of the drug neuregulin. Read more about this on our Boston Children's Science and Clinical Innovation Blog, Vector. Credit: Boston Children's Hospital

In a recent issue of *Science Translational Medicine*, Brian Polizzotti, PhD, Bernhard Kuhn, MD, Sangita Choudhury, PhD, and colleagues affiliated with the Boston Children's Hospital's Translational Research Center report that the optimal window of time to stimulate heart muscle cell regeneration (cardiomyocyte proliferation) in humans is the first six months of life.

"Our results suggest that early administration of neuregulin may provide a targeted and multipronged approach to prevent heart failure in infants with CHD. Beginning treatment as early as possible could save these hearts from long-term damage and symptoms of heart failure later in childhood," says Polizzotti.

The same group of Boston Children's Hospital researchers has proven that child hearts are more prone to cardiomyocyte proliferation than adult hearts are. They have also shown that the drug neruegulin stimulates cell cycling and improves overall heart function in adult mice with injured hearts. Neuregulin is currently under investigation as a drug treatment for heart failure in adults, but corresponding studies for pediatric applications had not been attempted before now. While heart attacks account for most instances of heart failure in adults, congenital heart disease (CHD) is the number one cause of heart failure in children. Based on their previous research, Polizzotti and Kuhn hypothesized that neuregulin would be just as effective against the unique forms of cardiac damage that cause heart failure in children.

Polizzotti and his team compared three groups of mice subject to the same kinds of cardiac damage present in many types of CHD (namely, increased scarring and a decreased ejection fraction, which is a measure of how much blood is pumped through the heart per contraction). One group of mice received their first neuregulin injections at birth, another received their first injections five days after birth, and a control group received daily injections of a neutral protein serum. The mice given neuregulin from birth were found to have a sustained increase in heart function, as observed by both echocardiogram and MRI.

The researchers also discovered that in the early administration group, stimulated proliferation of uninjured cardiomyocytes resulted in the formation of an additional 224,000 new heart cells. "We estimate that thirty-eight percent of the additional cardiomyocytes were present due to

cardioprotection, while sixty-two percent were the result of regeneration," says Polizzotti.

After the mouse trial, Polizzotti and colleagues tested their hypothesis on human heart cells. They focused specifically on one type of heart disease, Tetrology of Fallot (TOF), which typically requires surgery soon after birth. Heart muscle cells were collected at the time of surgery and then cultured for three days with either neuregulin or a harmless serum. The results mirrored those from the mouse study: neuregulin stimulated cardiomyocytes to regenerate in the diseased heart muscle of infants less than 6 months old. Polizzotti plans to take this research farther by testing neuregulin in hearts with other types of CHD. "It will be interesting to see if the results from animal studies translate to live pediatric patients with diseased heart muscle," says Polizzotti.

More information: Neuregulin stimulation of cardiomyocyte regeneration in mice and human myocardium reveals a therapeutic window Sci Transl Med 1 April 2015:
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