Stem cell injections may offer hope to patients with no other options

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An injection of stem cells into the heart could offer hope to many of the 850,000 Americans whose chest pain doesn't subside even with medicine, angioplasty or surgery, according to a study in *Circulation Research: Journal of the American Heart Association*.

Patients who received the new treatment reported half as many chest pain episodes and improved exercise capability compared to those who received a placebo.

The study was the first randomized, controlled trial of stem-cell therapy to show significant improvements in both chest pain and exercise tolerance – the two debilitating features of "refractory" angina, or chest pain that persists in spite of medication, surgery or angioplasty.

Other studies have been negative and some have shown improvements in either chest pain or exercise time, but no previous study has shown improvements in both chest pain and exercise time, said Douglas W. Losordo, M.D., lead researcher and professor of medicine and director of the Feinberg Cardiovascular Research Institute at Northwestern University in Chicago.

"One exciting potential of this procedure is that it will offer these folks an opportunity to get part of their lives back," said Losordo, who is also director of the Program in Cardiovascular Regenerative Medicine at Northwestern Memorial Hospital.

Researchers used the patients' CD34+ stem cells, which circulate through the blood and are important in forming new blood vessels. The stem cell injection is meant to create new vessels in the diseased heart muscle, improving blood flow to the area and reducing episodes of chest pain.

In the study, 167 patients at 26 U.S. medical centers were randomized to one of three injection groups: low dose (100,000 CD34+ cells/kg body weight); high dose (500,000 CD34+ cells/kg body weight); or a placebo.

Normally, there are too few CD34+ cells to provide enough for therapy. So, researchers used a drug to increase the number of the cells in the body before collecting them.

Using a catheter threaded into the heart, the researchers injected CD34+ cells into muscle identified as receiving insufficient blood.

Among the study's findings:

- At six months, low-dose patients had 6.8 angina attacks per week – significantly fewer than 10.9 per week for those receiving placebo. High-dose patients had fewer episodes than the placebo group, but the difference was not statistically significant, so the results could be due to chance.

- At 12 months, the low-dose group had 6.3 episodes per week and the placebo patients had 11 episodes per week; high-dose patients had fewer angina episodes than the control group, but the difference remained insignificant. "It is not rare in clinical trials for high doses to be less effective than low doses," Losordo said.

- The improvement in exercise tolerance at six months in low-dose

patients was 139 seconds, which was significantly greater compared to the 69-second tolerance of the placebo patients.

- The high-dose group had a greater, but not significant, improvement than the placebo patients.

- At six and 12 months, both treated groups were using less nitroglycerine to treat angina than control patients, but the differences were not significant.

"The net difference in exercise tolerance is highly clinically significant, particularly in a patient population that is severely limited by symptoms," Losordo said.

"It translates as going from being able to watch television to being able to walk at a normal pace or going from being able to walk slowly to being able to ride a bike."

About a third of participants had minor elevations of troponin, an enzyme that signals a heart attack when accompanied by changes in an electrocardiogram (EKG), researchers said. However, patients felt no chest pain and experienced no EKG changes.

"Most troponin changes were inconsequential," Losordo said. "Nevertheless, we will continue to watch troponin levels, especially in phase III, where we will closely monitor cardiac enzymes."

Later this year, the researchers will begin a phase III trial of the therapy, the level usually required before the Food and Drug Administration considers approving a drug.

Provided by American Heart Association