Early heart attack therapy with bone marrow extract improves cardiac function

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A UCSF study for the treatment of heart failure after heart attack found that the extract derived from bone marrow cells is as effective as therapy using bone marrow stem cells for improving cardiac function, decreasing the formation of scar tissue and improving cardiac pumping capacity after heart attack.

Findings were published online and in the July 2009 issue of the *Journal of Molecular Therapy*. The cover of the journal features a microscope image of cells from the UCSF study.

The studies were done in mice using a novel stem cell delivery method developed by UCSF researchers to show that the extract from bone marrow cells is as beneficial to cardiac function as are intact, whole cells. Both the cell and cell extract therapies resulted in the presence of more blood vessels and less cardiac cell death, or apoptosis, than no therapy. The study also showed that heart function benefitted despite the finding that few of the injected cells remained in the heart at one month after therapy.

"Peer-reviewed medical literature is controversial as to whether bone marrow cells differentiate into cardiomyocytes, or cardiac muscle cells, but there is general agreement that stem cell therapy with these cells results in some level of functional improvement after a heart attack. The exact mechanism for this is not yet clear. Our results confirm that whole cells are not necessarily required in order to see the beneficial effects of bone marrow cell therapy," said Yerem Yeghiazarians, MD, study

author, cardiologist and director of UCSF's Translational Cardiac Stem Cell Development Program.

UCSF researchers are investigating these new therapies to improve cardiac function after heart attack in an effort to prevent heart failure. Heart failure occurs when cardiac muscle is damaged and scar tissue replaces beating cardiomyocytes. As scar replaces healthy tissue, it causes the heart to enlarge and lose its pumping capacity. When the pumping capacity decreases, the heart fills with fluid, which moves to the lungs and can lead to organ failure and death.

"Current therapies improve symptoms but do not replace scar tissue. Our hope is to use stem cells to decrease the scar, minimize the loss of cardiac muscle and maintain or even improve the cardiac function after a heart attack," Yeghiazarians said.

Using a novel, closed-chest, ultrasound-guided injection technique developed by Yeghiazarians and his colleagues, the team administered three different groups with bone marrow cells, bone marrow cell extract, or saline (for the control group). The injections were administered at day three after heart attack - a timeframe somewhat similar to human biology on days six-to-seven after heart attack.

The team found at day 28 that both the bone marrow cell group and the extract group had significantly smaller heart damage than the control group.

Left-ventricular ejection fraction (LVEF), or the measurement of blood pumped out of the ventricles per heart beat, fell uniformly in each group after heart attack from a level of about 57.2 percent to 38.4 percent. At day 28 (and after the therapies had been administered on day three), LVEF improved in both the bone marrow cell and extract groups to approximately 40.6 and 39.1 percent as compared to approximately 33.2

percent for the control group.

"We hope our findings can help in the development of new therapies for improving heart function after the deleterious effects of a heart attack," says Yeghiazarians.

The team is continuing to evaluate bone marrow cell and extract therapies in order to identify the proteins and factors within the extract and gain insight into the possible mechanisms of cardiac functional improvement.

"The best acute therapy for a heart attack remains early recognition and revascularization of the blocked artery to minimize the damage to the heart muscle," said Yeghiazarians. "Although the prognosis depends on multiple factors, what we know for sure is that the sooner a heart attack gets diagnosed and cardiologists open the blocked artery, the better the long-term outcome. There are a number of ongoing stem cell-based clinical trials, and depending on further research and the outcome of these studies, we might have new therapies for the treatment of patients who suffer from a heart attack in the not-too-distant future."

Source: University of California - San Francisco