

Bone marrow cell transplants to benefit those with heart disease

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Two studies published in the latest issue of *Cell Transplantation* (18:12) may lead to new treatments for the treatment of heart diseases. The first study, carried out by a team of Brazilian researchers, found that cell transplantation of bone marrow mononuclear cells (BMMCs) directly into the heart benefited patients suffering from refractory angina. A separate study carried out by researchers in the Peoples' Republic of China found that apelin, a newly described inotropic peptide, improves heart function following transplantation of BMMCs.

The results of these studies and others are available on-line free of charge at <http://www.ingentaconnect.com/content/cog/ct/> .

ReACT bone marrow cell transplants help refractory angina

A team of Brazilian researchers has evaluated the safety and efficacy of a surgical procedure involving multiple injections into the heart (intramyocardial) of a [bone marrow](#) mononuclear cells (BMMCs) formulation derived from the patient (autologous) called "Refractory Angina Cell Therapy (ReACT)". The researchers found that the procedure benefitted all eight of the refractory angina patients in the study, all of whom had previously received surgical revascularization.

"The large fraction of monocytes in the ReACT formula appears to be related to the new [blood vessel growth](#), or [angiogenesis](#), that restores

perfusion on the myocardial ischemic areas after the [cell transplantation](#) ," said corresponding author Dr. Nelson Americo Hossne, Jr. of the Paulista School of Medicine, Federal University of Sao Paulo. "For our patients, angina symptom relief began as early as three months post-procedure with continuing improvement through the twelfth month and sustained improvement past 18 months. Symptom relief improved in all patients, suggesting that the effect is sustained, not transitory."

According to Prof. Enio Buffolo, co-author from the same institution, up to 15 percent of patients with [coronary artery disease](#) present severe, disabling angina pectoris that cannot be controlled by combinations of current therapies, including drug therapy, coronary angioplasty, or coronary by-pass surgery.

"This results in a substantial decrease in the quality of life for the refractory angina patient," added Prof. Enio Buffolo.

Bone marrow is a natural source of a broad spectrum of cytokines involved in controlling angiogenic and inflammatory processes. Bone marrow white blood cells therefore play an important role in the angiogenic mechanism, contributing to the revascularization of the heart.

The researchers selected the intramyocardial route for injection based on prior experimental data showing higher myocardial stem cell uptake. Endpoints for patient improvement were based on the Canadian Cardiovascular Society Angina Classification (CCSAC) system. According to Dr. Hossne, the ReACT formulation, designed in compliance with Good Manufacturing Practices (GMP) standards criteria, was found to be safe and effective, supporting further study with a larger number of patients.

"Patient improvement by the subjective CCSAC measures was followed by a correlated reduction in the myocardium ischemic area," concluded

Dr. Hossne. "This strongly suggests neoangiogenesis as the main mechanism of action for these cells."

Apelin helps heart function after bone marrow transplant

Apelin, a newly described inotropic peptide (related to the force of heart muscle contraction) with important cardiovascular regulatory properties, contributes to functional improvement in patients with severe heart failure after they have undergone implantation with bone marrow mononuclear cells (BMMC). The study, carried out at the Navy General Hospital in Beijing, evaluated 40 patients with severe heart failure following myocardial infarction. Twenty patients were assigned to receive BMMC transplants and 20 received standard medication. Another 20 healthy patients were assigned as controls.

"Baseline levels of plasma apelin were significantly lower in all heart failure patients as compared to normal, healthy subjects," said corresponding author Dr. Lian Ru Gao. "However, in patients who underwent cell transplantation, apelin increased significantly from three to 21 days post-transplantation. This increase in apelin was also followed by significant improvement in cardiac function."

In patients who received standard treatment, there was no increase in apelin.

According to the researchers, apelin, known to be a potent inotropic agent, was recently recognized as an important regulator of myocardial cell specification and heart development. In addition, reports that apelin concentration decreased with [heart function](#) impairment led the researchers to hypothesize that bone marrow transplantation might play a role in improving heart function by releasing apelin.

"Our objective was to assess how apelin plasma levels changed post-transplantation as well as to determine the relationship between increased apelin levels and heart function," added Dr. Gao.

Apelin levels increased in all patients who received BMMCs, and cardiac function improved as reflected by the relief of dyspnea and other measures, and so the researchers concluded that apelin signaling may play an important role in the heart function improvement observed after BMMC transplantation.

"Increased apelin levels may act as a paracrine mediator produced from BMMCs and may play an important role in the treatment of heart failure through autocrine and paracrine mechanisms," Dr. Gao concluded.

"Both studies demonstrate a possible mechanistic approach in a clinical trial either via the role of monocytes or Apelin to improve cardiac function" said Dr. Amit Patel associate professor of surgery at the University of Utah School of Medicine and the cardiovascular, skin, other tissue section editor of *Cell Transplantation* . "These important findings further enhance the understanding of the use of bone marrow derived cell therapy for the treatment of cardiovascular disease."

Provided by Cell Transplantation Center of Excellence for Aging and Brain Repair

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