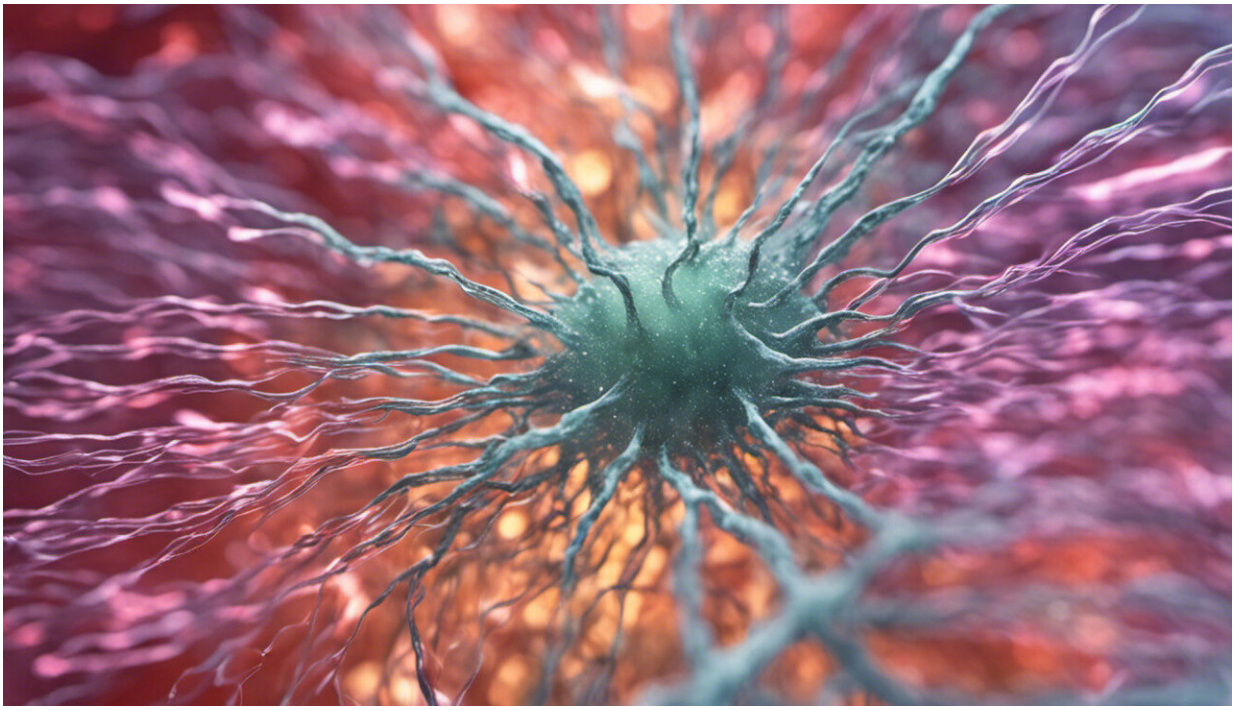
Does cell therapy treatment prolong the lives of heart attack patients?

February 28 2014, by Jalees Rehman



Credit: AI-generated image (disclaimer)

One of the world's largest clinical cell therapy trials has begun to enroll 3,000 heart attack patients, some of whom will have bone marrow cells extracted with a needle from their hip and fed into their heart using a catheter in their coronary arteries.

The BAMI trial has €5.9m in funding from the European Commission and will be conducted in ten European countries. Enlisted patients will be randomly assigned into two groups: one group will receive the standard care given to heart attack patients while the other will get an added infusion of bone marrow cells.

A number of studies, including one in the New England Journal of Medicine and another in the European Heart Journal, have suggested that bone marrow cells could be beneficial to patients with heart disease. However, because these studies were too small to work out whether cell infusions affected patients' survival, they instead focused on the extent of scar formation after a heart attack or the ability of the heart muscle to contract after cell infusion.

One commonly used surrogate measure is the cardiac ejection fraction, which measures the fraction of blood squeezed out by the heart during a contraction. A healthy rate ranges from 55% to 65%. Bone marrow cell infusion has been associated with a modest but statistically significant improvement in heart function. In 2012, a comprehensive analysis of 50 major studies with a combined total of 2,625 heart disease patients showed that cardiac ejection fraction in patients receiving these infusions was 4% higher than in control patients.

While the results were encouraging, the study was a retrospective analysis with patients who had varying treatments and endpoints. There also remain questions over 400 patients included in the analysis from trials showing benefits of bone marrow cell infusions that were conducted by controversial German cardiologist Bodo Strauer, who some scientists have accused of errors in research.

The new large-scale BAMI trial will be able to provide a more definitive answer to the efficacy of bone marrow cell infusions and address the even more important question: does this experimental treatment prolong

the lives of heart attack patients?

A hard cell

Despite the impressive target of enrolling 3,000 patients, there is a problem with how the trial is being framed. The underlying premise of why bone marrow cells are thought to improve heart function is that the bone marrow contains stem cells which could potentially regenerate the heart. In media reports, the BAMI trial is portrayed as a study which will test whether stem cells can heal broken hearts, and a press release by Barts Health NHS Trust, which is leading on the trial, described the study as "the largest ever adult stem cell heart attack trial". But the scientific value of the BAMI trial for stem cell research is questionable.

In 2013, a Swiss study reported the results of treating heart attack patients with bone marrow cells. Not only did the study find no significant improvement of heart function with cell therapy, the researchers also reported that only 1% of the infused cells had clearly defined stem cell characteristics. The vast majority of the infused bone marrow cells were a broad mixture of various cell types, including immune cells such as lymphocytes and monocytes.

Scientific studies have even cast doubts about whether any of the scarce stem cells in bone marrow can convert into beating heart muscle cells. A study published in 2001 suggested bone marrow cells injected into mouse hearts could differentiate into heart muscle cells, but the finding could not be replicated in a subsequent study published in 2004.

If there are so few stem cells in the bone marrow and if the stem cells do not become cardiac cells, then how does one explain the improvements observed in the smaller studies? Researchers have proposed a variety of potential explanations, including the release of growth factors or proteins by bone marrow cells that are independent of their stem cell activity.

The disease machine

The success of modern medicine lies in its ability to isolate causal mechanisms of disease and design therapies which specifically target these mechanisms using rigorous scientific methods. Instead of using nebulous "fever tinctures" or willow bark, physicians now prescribe therapies with well-defined active ingredients such as paracetamol (acetaminophen) or aspirin.

Infusing heterogeneous bone marrow cell mixtures into the hearts of patients seems like a throwback to the era of mysterious herbal extracts containing a variety of active and inactive ingredients.

Even if the BAMI trial succeeds in demonstrating that infusion of bone marrow cell mixtures can prolong lives, then the scientific value of the results will still remain doubtful. We will not know whether the tiny fraction of stem cells contained in the bone marrow was responsible for the improvement or whether this effect was due to one of the many other cell types contained in the cell mixtures.

One could argue that it is irrelevant to know the mechanism of action as long as the infusions can prolong patient survival. But for any evidence-based therapy to succeed, it is essential for physicians to know how to dose or modify the therapy according to the needs of an individual patient. This won't be possible if we don't even understand how the treatment works.

We should also consider the impact of a negative result. If the BAMI trial fails to show improved survival, will the lack of efficacy be interpreted as a failure of stem cell therapy for heart disease? An alternate explanation would be that a negative result was due to infusing numerous cell types, most of which were not stem cells.

The ultimate test of a treatment's efficacy is how it fares in controlled, large-scale trials. And these trials need to be grounded in solid scientific data and provide answers that can be interpreted in the context of scientifically sound mechanisms. The BAMI trial might provide an answer to the question of whether or not bone marrow cell infusions are efficacious in heart disease, but it will not teach us much about stem cells.

This story is published courtesy of The Conversation *(under Creative Commons-Attribution/No derivatives).*

Provided by The Conversation