Nabil Dib, MD, MSc: Generating The Future With Effective Stem Cell Therapy

Nabil Dib, MD, MSc, is director of cardiovascular research and clinical studies in cardiovascular cell therapy at Mercy Gilbert Medical Center in Gilbert, Arizona. Doing double duty as an associate professor of medicine and director of clinical CV cell therapy at the University of California, San Diego Medical Center, Dr. Dib also serves as president of the International Society for Cardiovascular Translational Research, and as co-editor and founder of its peer-reviewed journal.

Dr. Dib started his medical education at Damascus University before coming to the United States for internships at the Albert Einstein School of Medicine and Boston University School of Internal Medicine. Following a general cardiology residency at Tufts University School, he pursued a postgraduate degree earning a Master of Science in Epidemiology and Research from the University of Wisconsin. He was a fellow in Investigational Interventional Cardiology at the Harvard School of Public Health, Beth Israel-Deaconess Medical Center.

In 2003, Dr. Dib was honored as one of America's Top Doctors in interventional cardiology, receiving the Annual Medical Staff Scientific Award. In a wide-ranging conversation with CardioSource WorldNews, Dr. Dib talked about the evolution of stem cells for repair of damaged heart tissue without further trauma or adverse reaction.

CardioSource WorldNews:

Has the 2000 study for the myoblast treatment shown positive results with follow-up?

Dr. Dib:

This is one of the first experiments done with stem cells in the United States. We take the patients who are candidates for heart transplants with severe heart failure, implant using the 3D catheter, and then transplant the skeletal muscle cell into them. Every patient receives 300 million cells. Now, when the patient has the new heart donor, the original heart is examined under the microscope. We can, with very high accuracy, know that we are seeing healthy tissue from the cell that we transplanted.

CSWN:

The heart is actually regenerating with the transplanted stem cells?

Dr. Dib:

The heart in this case was regenerating; however, the cell and the tissue are not exactly like the heart. It lacks connection receptors to transmit the electrical activity. There is more formation of new blood vessels. The area that received the cells—the graft—has about a three-fold increase in the number of blood vessels in comparison to the area that did not receive the cell.

So what we conclude from this is that cell therapy can regenerate in new tissues. It might not be exactly perfect like the heart, but it will be close. They play an important role building a new blood vessel around them.

CSWN:

How is the safety for the transplanted stem cell patients?

Dr. Dib:

The safety is very good. Then we developed the catheter technology because everything we talked about back in 2000 was open chest.

In 2004, the FDA approved the 3D catheter-based technology to deliver the first stem cell to humans in the United States. The trial, called the "Translational Clinical Trial Utilizing Three-Dimensional Guided Catheter Based Delivery," was presented and published in *JACC*. The trial included 23 patients randomized to standard of care versus myoblast therapy, which means the cell was taken from the muscle. The classic standard of care takes a biopsy, expands it in the cell laboratory, and then transplants it into the heart. The catheter doing the 3D injection and optimization lets us inject anywhere between 30 and 600 million cells directly into the patient's heart tissue.

So the procedure is safe and had no safety issues. When we image and follow those patients, in 3 months, you see the area of heart damage has become viable.

Every single time you see the image or histology, it reveals that myocardial regeneration can occur. But the stem cell we used from muscle is the only cell that has shown evidence of myocardial regeneration. We show improvement with decreased size of the heart with the cell transplant versus a control where the heart remained enlarged.

The goal is that cellular processes or cells might decrease the inflammatory process, since inflammation occurs following a heart attack. So, hopefully, this technique also might reverse some of the tissue damage.

CSWN:

Then the approach is either using an autologous stem cell or allogeneic stem cell following a heart attack to regenerate damaged heart tissue?

Dr. Dib:

That is another bone marrow cell, but this is a meschymal stem cell. So as you can imagine, there is a variety of cell lines, and everyone has a different receptor. They are different in the way they function and the way they work. In the bone marrow there is mononuclear and that's autologous.

The myoblast is autologous, meaning "from the same." The bone marrow that is allogeneic is meschymal, or it can also be bone marrow that is meschymal autologous—it can do both. Autologous means taking the same sample and transferring it to the same patient. Allogeneic means you can take that sample—those kinds of cells expand to a large number of cells—and then you can use it for many patients.

You don't want to build a stem cell facility in

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every place you do cell transplantation. You just give them the cell; like a product or a drug.

CSWN:

So these processed cells can be produced and distributed like a prescription drug?

Dr. Dib:

Myoblasts are easier to keep viable. They are used to an environment with low oxygen, and then you can transplant them. However, because of the myoblasts, there was a controversy in the data about possible rhythm problem because they do not express their electrical receptors. Our experience has been that there are no rhythm problems.

No one was able to demonstrate that the bone marrow cells survive anywhere. When you ask about whether or not they regenerate, the answer is that we don't know because they do not survive in the heart. After 2 weeks you don't see anything. There is improvement in the heart, so you must make a leap of faith that the implanted cells are making this improvement, because the placebo does not show this kind of results. So the allogeneic cell, reclassified as unipotent (making one kind of tissue) or multi-potent (making a variety of tissue)—that was in meschymal cell. The unipotent meschymal makes only the one kind of muscle tissue.

CSWN:

Can you manage or engineer the multi-potent cell to grow the right type of cell?

Dr. Dib:

Yes. Those are a variety of meschymal stem cells. Every company tries to find one kind of cell that has the different inceptors. A company called Osiris sponsored the first phase 1 clinical trial involving IV infusion stem cell for heart attack within 7 days. The scientific rationale is that during a heart attack, the inflammation process can attract the systemic cells circulating to the inflammation. The body recognizes that.

CSWN:

How about infusion versus injection delivery of stem cells?

Dr. Dib:

The retention rate is lower. The percent of cells retained is >2%, less even than 1%. And the issue is IV infusion. But the clinical trials argue that you can increase the number of cells if they are safe to increase that retention rate. The advantage of it is that one can take one sample of bone marrow and they can grow thousands of cells and even millions of cells. Literally, one donor can treat up to 20,000 patients. So you can expand those meschymal stem cells, package them, ship them to a facility anywhere, and store them in liquid nitrogen. They can be used when needed. The thawing process from frozen to human injection is about 10 minutes maximum.

CSWN:

And you've created or engineered a matrix for liquid- or solid-form delivery?

Dr. Dib:

We're developing something called a matrix, because the heart has the blood vessel, the muscle, and the conduction system, and it has the matrix that's keeping everything in place. You can make a matrix "ice cube," if you will. You can freeze it and cut it. You can make it solid solution and then make it liquid solution. And you can ship it anywhere in the world. It is injected in the same catheter to the heart.

So between the future of matrix and catheter technology, they're meant to affect the ease of infusion and make the cell therapy applicable in many patients worldwide. Anybody can use the system and the catheters; there's no other system attached to it to buy.

CSWN:

What's next for you?

Dr. Dib:

Method of delivery—improving on method of delivery and making it easy for many cells to be used with simple intracoronary infusion. For HF, the 3D technology looks very good.

For the cellular therapy, I think ischemia-tolerant stem cells will be important because we currently cannot inject them in the area of scar. We'll inject them around the scar. We would like to treat the scar itself and the area around the scar.

Developing the matrix to increase the stem cell retention is another important key. So I would say method of delivering the matrix in a new engineered cell would be the ideal.

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With ischemia-tolerant cells and cardiac-like cells right now, the procedure is very invasive. Many sick patients cannot tolerate it, so you cannot apply the therapy. The next process to work on is to create the least invasive injection. Ease-of-use is better, because then you can apply it to many patients, and many more physicians can do the procedure if it's easy to use.