Curbside Consult

Stem Cells in Sports Medicine: Ready for Prime Time?

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The man sitting across from me said he was desperate. Osteoarthritis was causing excruciating pain in his knee. But he had found a solution: For $18,000, a doctor in Mexico would inject stem cells from a Russian embryo. What did I think?

"I don't know what to tell you," I said. "First, there has never been a controlled clinical study looking at embryonic stem cells that tells me it works for knee osteoarthritis. Second, I don't know anything about the safety."

Those concerns didn't stop this patient, and I am waiting to hear the results. But I'm not optimistic that these results will be any better than those of the man I met on an airplane flying to the Dominican Republic. When I caught up with him later, he had nothing to show for the $45,000 he spent on stem cells for his severed spinal cord.

That's the environment now in which orthopedic sports medicine specialists must operate. Right now, everyone loves the phrase "stem cells." It means hope for people who haven't found any relief for an ailment, whether it is arthritis, spinal cord injury, amyotrophic lateral sclerosis, or Crohn's disease. Unfortunately, unscrupulous physicians are taking advantage of the hype and cashing in on these patients' desperation.

Having participated in multiple trials of stem cells for orthopedic treatments, I share some of this hope. For a few limited indications, such as femoral head and femoral condyle osteonecrosis, stem cells may already be worth trying. I have helped develop a concentrated bone marrow aspirate (*Intraosseous BioPlasty*, Arthrex) for the related indication of knee osteonecrosis. And I am now involved in clinical trials of stem cell therapy for articular cartilage resurfacing and repair.

It is not hard to see why stem cells stimulate excitement. The progenitors of every cell in the body, they hold the potential to regenerate damaged tissues in a way that the body's own repair process cannot.

But overall, the treatments so far fall short of the hype. And they can sometimes overshadow other promising biologic treatments, such as platelet-rich plasma.[1]

The Devil Lies in the Details

Each category of stem cell, whether originating from adult tissue or embryonic or reprogrammed tissue, offers advantages and disadvantages. Moreover, stem cells must be combined with scaffolding and growth factors, and there are many choices of these as well.

The ideal combination may vary with every disease we wish to treat. With so many variables, the science remains in its infancy. As clinicians, we face a further barrier: Outside the protocol of a clinical trial, we can't culture, incubate, or expand our patients' cells. We are limited to harvesting, concentrating, and reimplanting a patient's cells in the quantity we harvested them.

I respect these restrictions. Stem cell therapy carries potential important risks of colonization of nontarget tissues, stimulation of cancer, and transmission of infections. And the potential is more than theoretical. Last year, a coroner in New South Wales, Australia, concluded that a patient's death was the result of a stem cell procedure.[2]

The example of knee cartilage provides an illustration of the potentials and the yawning gaps in the clinical science of stem cells. Because hyaline articular cartilage lacks vascularization, progenitor cells can get only limited access to chondral lesions.

That's why applying mesenchymal stem cells looks like a promising treatment. They can be extracted from a variety of sources, including bone marrow, adipose tissue, synovial membrane, umbilical cord blood, and peripheral blood.[3] They can differentiate into chondrocytes, osteoblasts and adipocytes. Their homing, trophic, and immunomodulatory behavior can influence cells in surrounding cartilage.

One recent study[4] showed mesenchymal stem cells to be equivalent to autologous chondrocyte implantation for repairing articular cartilage.

Scaffolds provide support for the growth of repair tissue. Gels, membranes, sponges, and foams have been tried, as have solid porous scaffolds such as ceramics.[5] In addition, growth factors including transforming growth factor beta, bone morphogenetic proteins, cartilage-derived morphogenetic protein 1, insulin-like growth factor I, platelet-derived growth factor, connective tissue growth factor, and myriad others also have been tried.[5]

Encouraging Clinical Trials

For the trials in which I am participating, we will apply stem cells congealed with calcium chloride thrombin. This aggregates platelets and gets them to adhere. We will cover this sticky paste with minced autologous cartilage or a hyaluronic acid scaffold. This creates a closure for the stem cells while they multiply and differentiate.

We're using this approach to resurface articular cartilage defects primarily caused by trauma. (We're not using it on osteoarthritis, which is a comprehensive degenerative process that is difficult to reverse.)

I have also used bone marrow aspirate concentration along with core decompression as a treatment for osteonecrosis of the knee. The published trials[6] have shown great results in patients with osteonecrosis of the femoral head. Our results in the knee look good so far; it appears to halt the progression of this devastating condition.

Also Promising: Platelet-Rich Plasma

In the meantime, I encourage my colleagues to consider platelet-rich plasma. While fewer researchers have focused on this treatment, as compared with stem cells, the few studies published have also shown promise.[1,7-9]

Platelets appear to summon stem cells—and not just any stem cells, but the appropriate ones for the injury being treated. They also provide growth factors to stimulate differentiation and multiplication. In the elbow, platelet-rich plasma has been shown to reduce pain.[10]

I am also participating in a study in which we inject platelets into grafted tendons in the knee and evaluate their maturation. In the first 30 patients, 90% of grafts have become mature within 3 months compared with 6-12 months for the controls.

The hopes of our patients play an important role in this work. If we didn't have hope, we wouldn't find the drive for innovation. But we also need the perspective to see the range of potential solutions for all of the problems we face in developing these biologic therapies.

As we go forward, I believe that painstaking research will eventually put powerful new treatments in the hands of orthopedic sports surgeons.

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